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ABSTRACTS

Abstracts

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1. Hardware Developments

Analytical Characterization of the $In_{0.53}Ga_{0.47}As$ n^+nn^+ Infrared Detectors

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Abstract

One of the most critical parts in fiber communication system is the receiver of the optical signal. Optical receiver in a digital communication system contains the photodetectors, tranimpedance amplifier and post amplifier then followed by decision circuit. The photodetectors characterization based on electrical and optical parameters of the devices where the dimensions of the structure are comparable with the incident wavelength [1]. On the other hand, the appropriate choice of the photodetector is related to the responsivity value which is proportional to the efficiency absorption of the photons, the excess carrier generation, the free carrier concentration of the emitter layer and the optical incident power.

The photodetector performance depends on the development of the advanced devices: structures and materials. The homojunction nanostructures have been demonstrated as wavelength tunable infrared detectors in recent years. This concept was successfully tested on Si [2], Ge and InGaAs materials [1]. Moreover, the $In_{1-x}Ga_xAs$ has a high intrinsic carrier concentration with a high carrier mobility and saturated velocity. This material can detect and amplify radiation of wavelength within the range from 0.1 μm to 1.8 μm which is of recent interest in fiber-optic communication systems [1].

The random fluctuations in a detector's output limits its responsivity to a certain minimum detectable power. The power necessary to generate an output signal equal to the noise is known as the Noise Equivalent Power (NEP). The NEP is the optical power that generates sufficient photocurrent to equal the noise current. However, the current noise level, of the structures and the materials used for the detection, can determine the radiative noise arriving at the detector from the background environment [3]. In addition, the detectivity (D^*), gives a meaningful comparison between different detectors, is widely used for the infrared photodetector characterization.

This contribution presents an analytical model for the calculation of the responsivity and the detectivity of the $In_{0.53}Ga_{0.47}As$ n^+nn^+ diode by using the current spectral density (current noise) in a n^+nn^+ structure developed in Ref. [4]. The current noise is evaluated at room temperature and under a constant voltage applied between the diode terminals. The noise calculation considers the synchronous motion of the free carriers in each region of the structure, the so-called "returning" carriers and the plasma resonances at the n^+n homojunctions [5]. In addition, the model can calculate in a first step the responsivity of the n^+nn^+ structure to light by using the photocurrent evaluation.

The analytical approach takes into account the responsivity evaluation in the wavelength range of the $In_{0.53}Ga_{0.47}As$ absorption. Then in the second step, the detectivity is investigated at different doping concentrations and at different thickness of the emitter layer in one-dimensional inhomogeneous n^+nn^+ structure.

Ultra-high resolution concurrent fMRI/NIRS mapping using a specially designed probe

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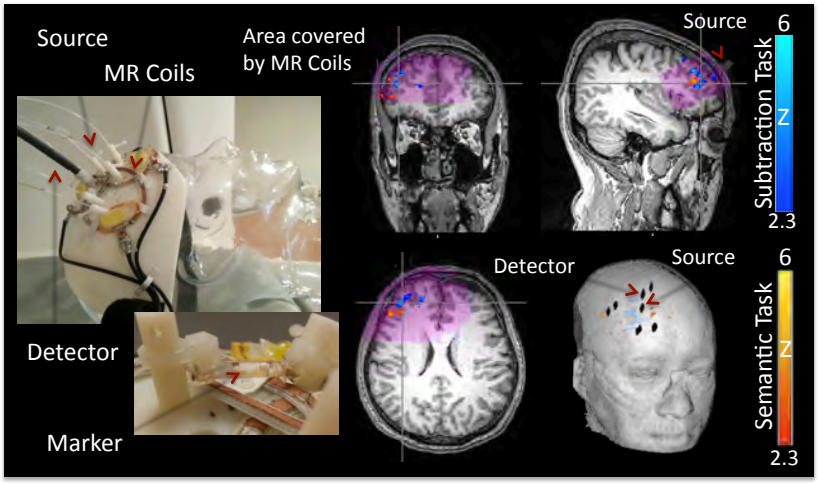
Introduction: Near-infrared spectroscopy (NIRS) has become increasingly popular to study brain functions as it is noninvasive, easy to use, highly adaptable, and low cost. However the spatial resolution is poor and putative neuronal signals are always contaminated by the blood signals from extra-cerebral layer [1,2]. To accurately localize the NIRS signal and understand the anatomical and physiological influences to the signal, we developed a special multimodal NIRS/fMRI probe. NIRS source-detector fibers were integrated into MR coils on a curved surface, enabling close contact between the probe and head (see Figure, left side). This coil can acquire high spatial resolution fMRI images (1.2x1.2x1.8mm) at ultrafast speed (2.5Hz), while simultaneously recording NIRS signals from the same area. We applied the probe in both resting state and mental task studies to dynamically map the NIRS signal with the fMRI with ultra high spatial and temporal resolution.

Methods: The 3D printed probe features 3 circular RF-coils, formed to the right frontal area of approximately 8x4.5cm with depth sensitivity of ~5cm. Integrated NIRS (6.25Hz) probes for deep (3-4cm source-detector distance) and shallow measurements (1cm source-detector distance) were integrated into the design. For comparison, peripheral measurements were also taken with NIRS. Measurements with the 3T (fMRI) and the ISS Imagent (NIRS) were acquired during resting state as well as 15 mins mental subtraction and rapid semantic task [2]. Two types of fMRI acquisition were performed; a high spatial resolution data on a broad field of view with 1.5s TR, and 5 consecutive stacked data sets (1.8mm x 5 for each stack) with a TR of 0.4s acquired using our previously described technique [3]. Outer volume suppression was used to limit the field of view. Data analysis was conducted in MATLAB (for NIRS) and FSL (for fMRI). FSL (FEAT) and in house Python software (RapidTiDe) [4] were used for localization of the focal activation detected by NIRS as well as fMRI.

Results: The high resolution multimodal acquisition allowed us to differentiate signals from the skin, skull, pial vessels and brain. The probe covered both task activation areas. Clear activation patterns below the probe for NIRS and fMRI are depicted (see Figure, right side). Short and long distance measurements of NIRS showed high involvement of the vasculature especially directly below the probes (not shown).



1.Gagnon et al. (2011), *Neuroimage*, *56*(3), 1362-1371. **2.**Kirilina et al. (2012), *Neuroimage 2012*, *61*(1), 70-81. **3.**Tong et al. (2012), *Neuroimage*, *61*(4), 1419-1427. **4.**Frederick et al. (2012) Neuroimage, 60(3), 1913-1923.

A Novel Optical Signaling Method for fNIRS Measurements

Abstract:

The mathematical development of a novel optical absorption spectrometry method enabling high SNR measurements is presented. The system may be understood as a multichannel, optical orthogonal signaling, lock-in amplifier.

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Background:

A tomographic optical absorbance spectrometer may be modeled as a multi-input multi-output communications system with the change in absorption along the optical paths comprising the information sources. Information theoretic considerations lead to the use of wide spectrum modulation techniques. These methods comprise high information content carrier modulations and correlation type receivers.

High information content wide-band carriers are commonly used in radio communications systems, most notably in CDMA (code division multiple access) and FHSS (frequency hopping spread spectrum) cell phone services, and in some metrology systems. An important characteristic of the method is processing gain, an increase in SNR due to the technique, and may be understood as the ability of the correlation receiver to separate the complex carrier from noise. This increase in SNR is an important enabler for small low-powered cell phones to achieve reliable and clear communications, and for metrology systems, enables high sensitivity measurements.

Previous spread spectrum communications and measurement systems have relied on radio, or other bi-phase energy forms as the carrier signal. Our novel technique extends spread spectrum methods to uni-polar sensing, of which optical absorption spectrometry and specifically fNIRS, forms a significant subset.

New algorithm for real-time scalp signal separation using multi-distance optodes

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Hemodynamic changes in the scalp sometimes affect near-infrared spectroscopy (NIRS) signals when light irradiates and is detected through the scalp. Therefore, several kinds of technique for compensating for scalp blood effects have been reported. Multi-distance independent component analysis (MD-ICA) using multi-distance optodes quantitatively separate scalp signals using the SD (source-detector) distance dependence on optical path length [1]. However, a real-time MD-ICA process has not been realized due to TDD (time-delayed decorrelation) ICA, which requires time-series data.

In this paper, the MD-ICA algorithm was modified for real-time processing as

$$\Delta A[d,t] = \varepsilon\Delta C_{\mathrm{deep}}[t]\cdot L_0\cdot(d-d_0) + \varepsilon\Delta C_{\mathrm{scalp}}[t]\cdot L_{\mathrm{scalp}},$$

where $\Delta A[d,t]$ is the absorbance change observed with SD distance d. ΔC_{deep} and $\Delta C_{\mathrm{scalp}}$ represent the hemoglobin concentration change in the deep region and scalp, respectively. L_0 is the slope of the partial path length in the deep region. The partial path length in the scalp L_{scalp} is approximately constant. Both the terms on the right side can be calculated from the simultaneous equations obtained with two SD distances when d_0 is given.

The new algorithm was validated by the experiments using a dynamic phantom that consisted of layers [Fig. 1]. Two layers were independently driven to simulate absorption changes in the brain and scalp [2]. The signal waves that were conventionally measured by using an SD pair with a 30 mm distance were distorted by mixing the deep and shallow signals. The deep (brain) signal wave and shallow (scalp) signal wave were separated by the new algorithm well, and they agreed with the appropriate true waves.

This kind of real-time separation will be useful for neuro-feedback systems, brain computer interfaces, etc.

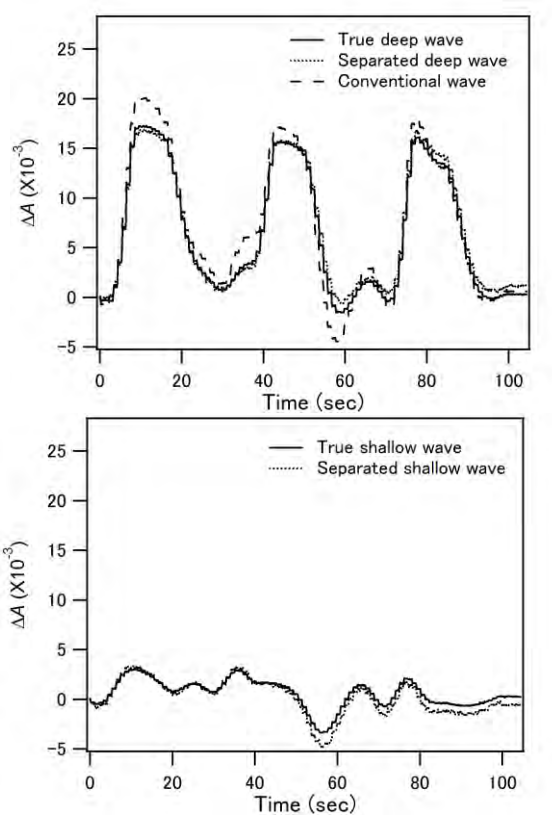

Fig. 1 Comparison between true, conventional waves and waves separated into deep (upper) and shallow (lower) signals by applying new algorithm.

References

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Time Resolved Whole-Head Diffuse Optical Tomography: How Fast Can We Go?

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The primary application of time-resolved optical tomographic imaging has been the production of three-dimensional, depth-resolved images of absolute values of optical absorption, optical scattering and therefore blood volume and saturation in the newborn infant brain[1,2] and the adult breast[3]. As time-resolved diffuse optical tomography (TR-DOT) requires the measurement of the flight time of photons across a volume of tissue, only a single source position can be illuminated at any one time. Furthermore, each illumination must last several seconds in order for enough photons to reach the detectors, which can be as much as 10 cm from the source when imaging the newborn infant brain. For these reasons, TR-DOT image acquisition is typically very slow. One full image sequence can take between 5 and 30 minutes[4].

By combining improvements in software design and source sequence optimization within UCL's second generation optical tomography system, MONSTIR II[5], we are able to demonstrate TR-DOT image acquisition times of less than 30 seconds for a volume comparable in size to the newborn infant head. Figure 1 shows a source illumination sequence where 12 source positions are illuminated within 30 seconds. Figure 2 shows the proposed fibre arrangement. By applying dynamic spatio-temporal filtering, TR-DOT images can be updated after each source illumination, i.e. every 2 seconds or faster. At this sample rate it will be possible to obtain 3D, depth-resolved images of transient events in the neonatal brain, including desaturation events and seizures. Furthermore, it will be possible to study low-frequency functionally induced changes in haemoglobin concentrations, such as those which form the basis of resting-state functional connectivity[6]. Development of these techniques may one day make it possible to image functional activations in deep regions of the brain using diffuse optical approaches, instead of being limited to the superficial cortex.

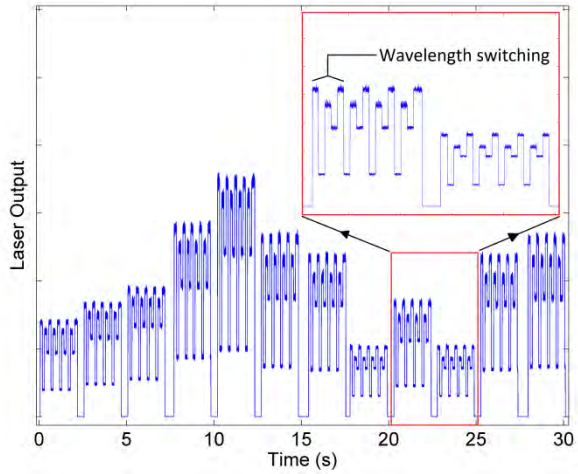

Figure 1. The intensity of output light for a given source sequence. Note the wavelength switching within each 2 second illumination period.

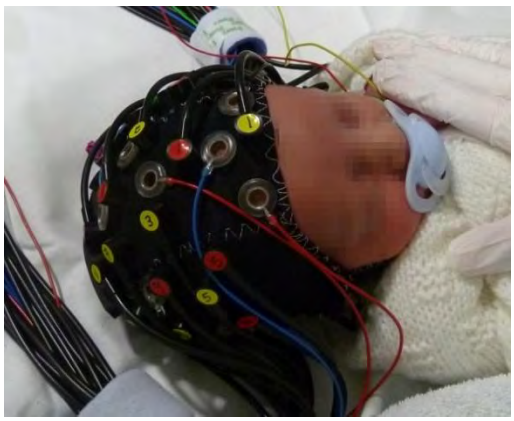

Figure 2. An infant in a soft DOT imaging cap. Prism-coupled fibres will be used to perform fast TR-DOT using this arrangement.

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Long term Ambulatory Monitoring of Cerebral Hemodynamics, Systemic Hemodynamics, ECG and Acceleration: Technology Development and Pilot Applications

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1. Introduction: Cerebral hemodynamics—including blood volume, perfusion and oxygenation levels—represent important measurements of brain function in many clinical and research applications. Traditional short term laboratory measurement of brain hemodynamics, such as fMRI, has several disadvantages, for example they do not provide long term assessment needed for sleep and circadian studies, their probability for catching transient symptoms (e.g epileptic seizure, sleep apnea and syncope) is low; lab measurements may introduce unwanted interruption or distortion of activity or the results, and they cannot be applied if the test must be performed outside the lab settings. While near-infrared spectroscopy (NIRS) and diffuse optical imaging (DOI) have been investigated for over three decades, only recently more advanced ambulatory near-infrared spectroscopy (aNIRS) devices have been developed, and human subject monitoring during activities outside the lab environment have become possible.

2. Method: Over the past 7 years, we have developed multiple generations of motion resistant ambulatory near infrared spectroscopy devices, the NINscan series. NINscan enables recording of brain function (via cerebral hemodynamics), systemic hemodynamics, ECG and actigraphy simultaneously and continuously for up to 24 hours at 250Hz sampling rate, during (and with minor restriction to) daily activities. We have performed NIN 4 ambulatory multi-modality monitoring under different experiment settings, including the first 24 hour multi-modal recording during daily activities.

3. Result: Our motion resistance tests demonstrated that NINscan 4's motion artifact at 1g head movement is smaller than physiological hemodynamic fluctuations during motionless sleep. In the comparison of hemodynamics of wakefulness and sleep in real life settings during a 24 hour period, we see a significant 21% reduction in HbT. During the 24 hour recording we have captured physiological changes prior, during and after of multiple unexpected transient events, including one sudden waken up in the night during sleep.

4. Conclusions and Discussions: The results from pilot applications demonstrate the first ambulatory 24-hour cerebral and systemic hemodynamics monitoring, and the unique advantages of ambulatory multimodality monitoring such as the capability to catch unpredictable transient events.

Further technology development and results from other experiments such as monitoring during parabolic flights will also be discussed.

5. References: 1. Zhang Q; Ivkovic V; Hu G; Strangman GE, Twenty-four-hour ambulatory recording of cerebral hemodynamics, systemic hemodynamics, electrocardiography, and actigraphy during people's daily activities, J. Biomedical Optics, 2014 (19), Issue: 4, Page: 047003; 2. Zhang Q, Yan X, Strangman GE, Development of motion resistant instrumentation for ambulatory Near-Infrared spectroscopy, J Biomedical Optics, 2011(16), Issue: 8, Page: 087008

Evaluation of Spatial Resolved Spectroscopy (SRS) for use in monitoring Traumatic Brain Injury (TBI) patients

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Spatial resolved spectroscopy (SRS), a technique developed in 1999 is aimed at obtaining a relative measure of deep tissue oxygenation by analyzing the gradient of the NIR signal over a series of multi-distance detectors [1]. In principle this technique provides a means of assessing cerebral oxygenation in TBI patients while minimizing the signal contributions from superficial layers (scalp and skull), which is currently a limiting factor in fNIRS systems [2]. This technique, as utilized in commercial systems by Hamamatsu is currently in widespread use, although the only validation study performed to date, has been on homogenous phantoms. The aim of this investigation is to assess the validity of SRS for TBI monitoring through finite element model (FEM) simulations of a realistic layered 3D head mesh.

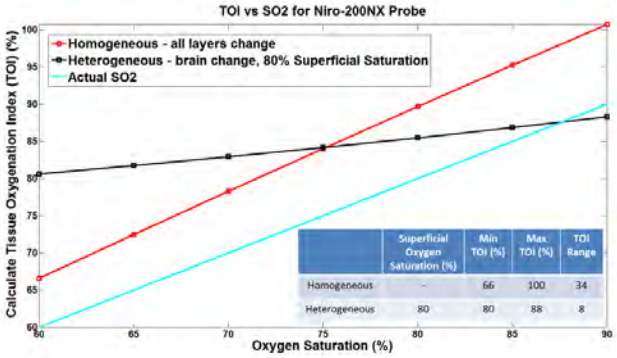

Figure 1 – Calculated TOI values from homogeneous and heterogeneous head meshes when brain saturation was varied from 60-90%.

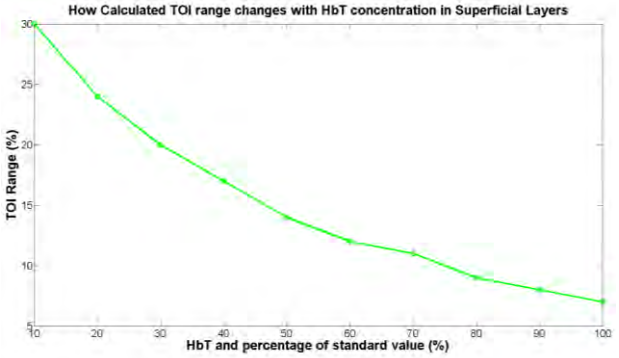

Figure 2 – Sensitivity of SRS to cerebral saturation when superficial HbT levels are varied.

Simulations based on a NIRO200 system were performed on the forehead of a realistic adult head model, for two specific cases: (1) where the head was assumed to be homogeneous and therefore for differing oxygen saturation levels the whole head was perturbed and (2) the head was assumed layered with only oxygen saturation in the brain being perturbed. Results show that SRS only works for a homogeneous model (***Fig. 1***); for example, when brain oxygenation saturation was change by 30% the derived Tissue Oxygenation Index (TOI) changed by 34%. With a heterogeneous model however the total derived TOI change for the same level of oxygen saturation change in the brain was only 8% showing that superficial layers were still obscuring deep tissue signals. In order to evaluate effect of signal attenuation due to the superficial layers, when the absorption in these layers was decreased by lowering HbT concentration (***Fig. 2***) the derived TOI range became increasingly more accurate. At 10% of standard HbT values, the TOI range matched the brain saturation change. So while SRS may sample the correct depth it is still limited by superficial layers. Therefore in order to improve the accuracy of deriving deep tissue parameters from NIR, **a novel hybrid fNIRS/DOT probe and reconstruction algorithm will be presented so that instead of bypassing or subtracting out superficial effects they can be instead recovered to give a true spatially resolved TOI map.**

Acknowledgements
This work has been funded by the Engineering and Physical Sciences Research Council (EPSRC). The FEM code is distributed as part of the NIRFAST modeling software at http://www.nirfast.org.

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Laser Speckle based tomographic imaging of deep tissue blood flow.

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Abstract: We present a novel tomographic imaging method to reconstruct three dimensional distribution of cerebral blood flow (CBF) at baseline (functional connectivity) and in response to functional stimuli in rodents. Three dimensional, optical imaging of CBF was previously demonstrated using diffuse correlation tomography [1, 2] but with a relatively slow system and poor resolution. Previously, a rapid diffuse optical tomography (DOT) using continuous wave source [3] was employed for volumetric functional neuroimaging of rodents. It was also shown that a DOT can achieve better spatial resolution by employing a high density source-detector distribution to measure the oxy-and de-oxy Hemoglobin concentrations [4,5]. Similar tomography of cerebral blood flow is currently lacking since the analogue, diffuse correlation tomography [2], is prohibitively expensive and complex to implement. On the other hand, laser speckle flowmetry [6] based on the analysis of the speckle contrast using uniform illumination of the tissue provides high density detection without any true depth resolution.

Here, we present a new speckle contrast based three dimensional tomographic approach that overcomes this limitation by merging the physical modeling of diffuse correlation tomography and the integral formulation used in laser speckle flowmetry. This new method, speckle contrast optical tomography (SCOT), [7] allows direct measurement of CBF using rapid scanning of a point source and a relatively standard 2D detector array such as a CCD or a CMOS camera with a high frame rate. The speckle contrast computed from measured dynamic speckles is related to CBF using the correlation diffusion equation [8]. We will present the physics of SCOT, an inversion algorithm for SCOT and experimentally demonstrate SCOT in phantoms and in preliminary *in vivo* studies. These results demonstrate the potential of SCOT for high density deep tissue perfusion imaging for functional neuroimaging in rodents.

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Towards fast optical signal detection through optical gating

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Abstract

There is evidence to suggest that diffuse optical methods can detect cell swelling that occurs in the 50–200 milliseconds following neuronal firing [1, 2]. This type of "fast" optical signal (FOS) appears to be significantly smaller than the hemodynamic signals (on the order of a .01% signal change) [3].There is controversy over the possibility of detecting fast optical signal in-vivo, but recently promising results have been achieved [4 - 6].We join these efforts to detect FOS using a novel detection system based on a second harmonic ultrafast fiber laser (Figure 1). This source produces a 100 MHz, 150 fs pulse train at 780 nm. Analysis will be carried out using second harmonic generation (SHG) frequency-resolved optical gating (FROG) [7]. This technique, widely used in nonlinear optical characterization, has a potential of detecting extremely small optical response. We hypothesize this shall overcome the disfavorable signal-to-noise ratio (SNR). In order to further enhance the detection capability we are setting a double wavelength closely spaced source based on the same laser system. Preliminary observations in leeches (*Haementeria officinalis*) suggest the feasibility of this method for in vivo FOS detection. We believe that when this technology improves will enable reliable in-vivo acquisition of FOS signal in humans.

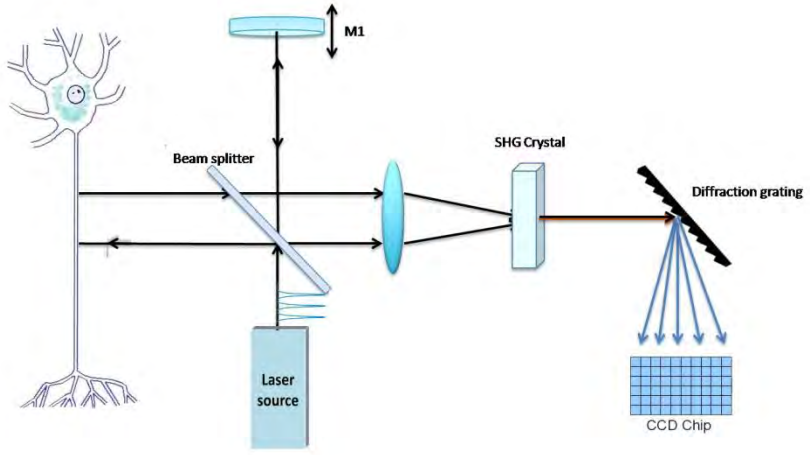

Figure 1. Basic SHG-FROG setup to be used to detect FOS.

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Investigation of time gated methods to control depth sensitivity in fNIRS time resolved data

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Aim: To use the experimental perturbation method to investigate quantitatively, the depth and layer sensitivity to time gated analysis of time resolved measurement.

Introduction: fNIRS relies on measuring optical signals of haemodynamic changes due to brain activity. However, absorption changes in NIRS signals are typically dominated by the superficial layers of the scalp [1] [2]. By utilising time resolved NIRS we can isolate the photons with shorter or longer path lengths in tissue and by using different analysis methods can change the depth sensitivity of the measurement to maximise information gained from deeper tissue. [3]

Methods: A 3-wavelength optical tissue monitor (TRS-20) from Hamamatsu Photonics K. K. was used to measure time resolved data during the experiment. The 2 channel, 3 wavelength (760, 800, 830nm) system irradiates picosecond pulses of NIR light onto tissue and measures the time of flight of the photons. The experimental setup used a 3-axis translation stage scanning system (Zaber LSR160A) to relocate a small local absorber in a diluted intralipid solution, Fig 1c. The solution enclosed in a clear glass tank contained 1% intralipid with an absorption coefficient (μ_a) of 0.029cm^{-1} and a reduced scattering coefficient (μ_s') of 10cm^{-1}. The absorber made from resin has μ_a = 0.14 cm^{-1} and μ_s'= 10 cm^{-1}. The source and detector separation was set at 3cm as is a typical spacing of fNIRS and default for the TRS-20. Each measurement had an integration time of 2 seconds. The absorber was raster scanned in two axis (x and y) in the tank, a reference measurement was performed after each scan along x by removing the absorber from the phantom, required in order to correct for sedimentation of the intralipid over time. At each absorber position a temporal point spread function (TPSF) was measured, Fig 1b. The depth sensitivity of the system was then measured using the percentage change in intensity for a specified region of the TPSF.

Results: By moving the region of interest of the TPSF from the early to late photons we see the depth sensitivity increase with mean penetration depths of 10.29mm, 13.20mm and 14.81 for time gates of 0-1.5ns, 1.5-3ns and 3-4.5ns respectively, fig 1a. As expected, the signal to noise ratio decreases with lower photon counts in which case longer integration time may have to be used.

Discussion: Time gating can control the depth penetration while also minimising the effect of superficial artefacts, such methods could be used by fNIRS when scalp changes are expected.

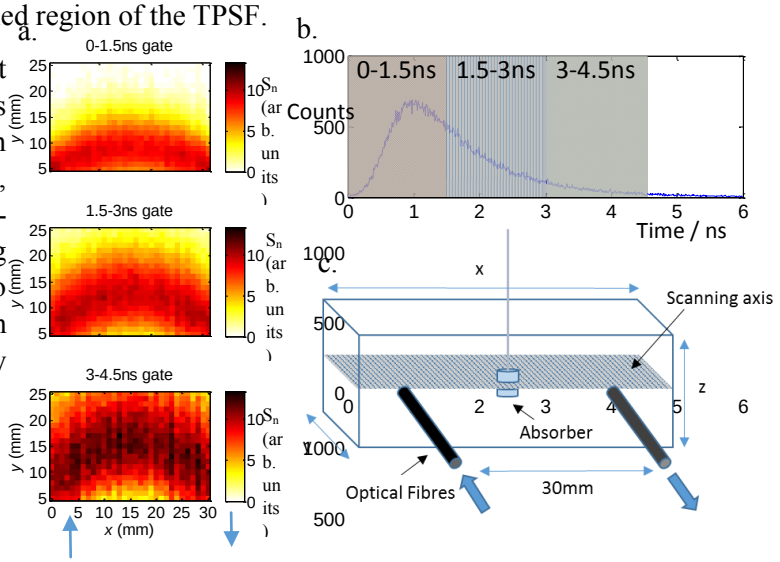

Figure 1a) Depth sensitivity (S_n) map of 800nm when using different time gates, b) Time gating shown on TPSF c) Phantom setup

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A multi-channel fNIRS brain imager based on Arduino microcontroller

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Nowadays, functional near infrared spectroscopy (fNIRS) is accepted as a powerful neuro-imaging tool by the neuroscientists. The main item that should be considered to spread out this rather new method is to provide the ability of prototyping fNIRS systems rapidly and simply in laboratory environments. Recently, Arduino boards were introduced as an open source electronic platforms for sensing and controlling a variety of sensors. We present, in current study, an inexpensive multi-channel fNIRS system with an Arduino DUE board as the heart of the system. In addition to portability and lower cost, the instrument is wireless, can be easily combined with other modalities such as EEG, and can be made resistive to motion artifact. Each module operates using two dual wavelength light emitting diodes (LEDs) at 730±15nm and 850±15nm and four optical detectors, which can be placed bilaterally on the subject's forehead. The emitted optical intensities were adjusted by controlling current through LEDs which can be between 10 to 50mA. Received light is converted into a voltage signal using an OPT101 photodiode with an integrated trans-impedance amplifier (TIA). The range of pre-amplified signal kept within ADC input swing by applying a variable offset and automatically adjusting the detector gain by a digital potentiometer. Schematic of the proposed system is illustrated in Figure.1 (A).

Performance evaluation of the prototype system was carried out by means of both in vitro and in vivo experiments. For in vivo experiments we aimed to monitor the changes of oxygenation in the lower arm and forehead tissue by changing the blood flow in and out from the tissue. The results showed the expected decrease in HbO_2 and increase in HbR during the occlusions. Moeover, several experiments for system calibration were carried out on tissue simulating phantoms consisting of gelatin, distilled water, titanium oxide (TiO_2) nano powder and Indian ink to represent scattering and absorbing coefficients of tissue respectively. The traces of light scattering in response to adding TiO_2 are illustrated in Figure.1 (E) .In conclusion, we have demonstrated the feasibility of constructing a wearable multi-channel fNIRS brain imager based on an Arduino microcontroller board.

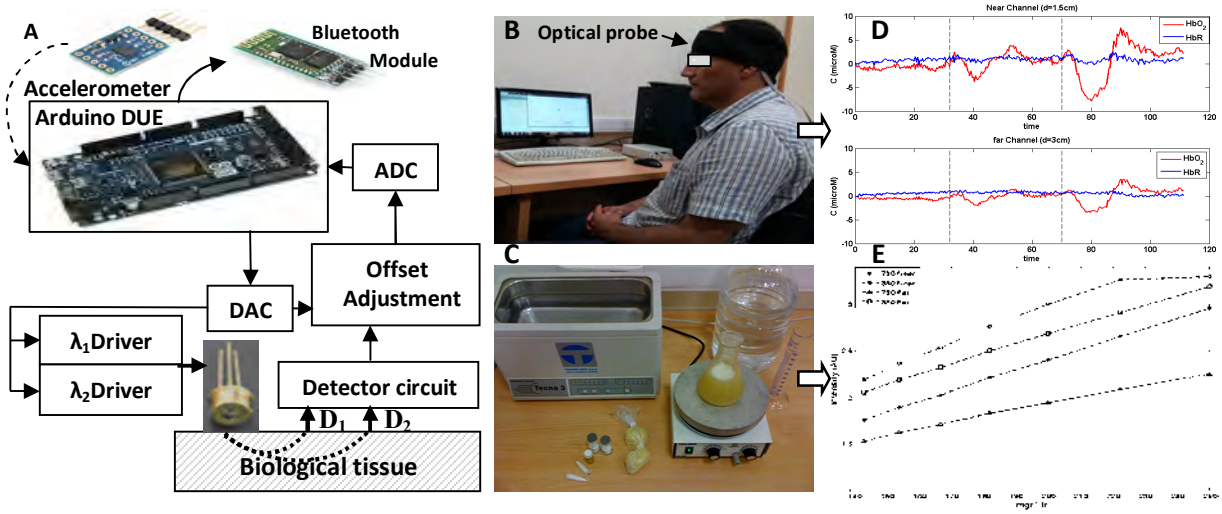

Figure1. A) Schematic of the proposed system B) in-vivo hypo-oxygenation test C) ex-vivo test on liquid-phantom D) trace of the changes in prefrontal tissue oxygenation E) recorded light intensities in response to increasing TiO_2.

Co-registering fNIRS and MRI in infants

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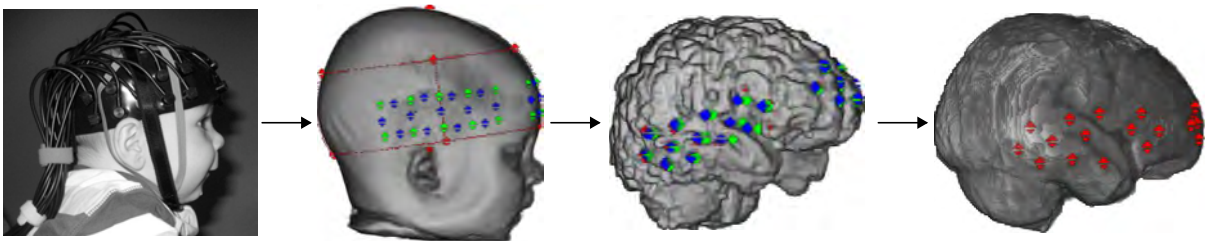
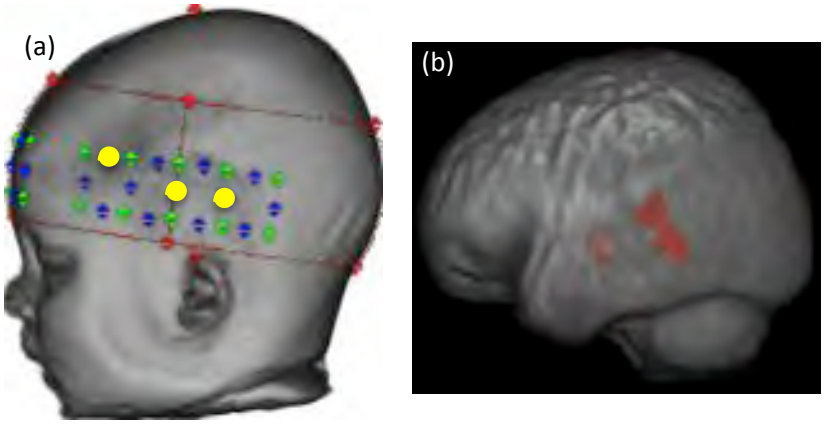
Functional Near Infrared Spectroscopy (fNIRS) is becoming a popular tool in developmental neuroscience for mapping functional localized brain responses. However as it cannot provide information about underlying anatomy, researchers have begun to conduct spatial registration of NIRS channels to cortical anatomy in adults. The current work investigated this in infants by co-registering fNIRS and MRI data from 55 individuals with available fNIRS data *and* structural MRI images.



Step-by-step guide to co-registration of scalp-surface NIRS channels & underlying anatomy.

Our findings suggest that NIRS channels can be reliably registered with regions in the frontal and temporal cortex of infants from 4 – 7 months of age. While some macro-anatomical regions are difficult to define consistently, others are more stable and fNIRS channels on age appropriate MRI template are often consistent with individual infant MRIs. We have generated a standardized scalp surface map of fNIRS channel locators to reliably locate cortical regions for fNIRS developmental researchers. This new map can be used to identify the inferior frontal gyrus (IFG), superior temporal sulcus (STS) region (which includes the superior and middle temporal gyri (MTG) nearest to the STS), MTG and temporal-parietal regions in 4-7 month old infants. Future work will model data for the whole head, taking into account properties of light transport in tissue, and expanding to different ages across infancy. As a first practical application, this work has enabled us to make direct comparisons within individuals between brain activation maps of fNIRS *and* fMRI data in a group of 18 infants (aged 154 ± 28 days) who underwent two separate studies involving a similar auditory protocol.



Activation maps for the auditory contrast from a single participant with fNIRS and fMRI data; (a) significantly activated fNIRS channels (yellow) superimposed on the 3D reconstruction of an average 4.5mth old infant head (showing optodes (green) & channels (blue)); (b) fMRI activation map normalised to the age-appropriate template.

A standardised protocol for normalisation of fNIRS data to a common template is a crucial step for comparing data across imaging modalities. Here, the activation maps from both studies show striking similarities, even though the data was collected by different techniques, at different sessions, and that during the fMRI session, the infant was asleep, whilst they were awake during the fNIRS. To our knowledge this is the first study to compare fNIRS and fMRI data within the same individual infants.

Continuous wave functional near infra-red spectroscopy combined with transcranial direct current stimulation for assessment of cerebral vascular status in patients with ischemic stroke

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Introduction: Near-infrared spectroscopy (NIRS) is a cerebral monitoring method that noninvasively and continuously measures cerebral hemoglobin oxygenation which is widely used for measurement of cerebral vascular status under various clinical condition. This paper describes the development of a 4-channel functional near infrared spectroscopy (fNIRS) based hardware that captures the hemodynamic changes in the frontal cortex of the brain, as a measure of cerebrovascular reserve (CVR), before and after anodal transcranial direct current stimulation. Impairments in CVR have been associated with increased risk of ischemic events and may stratify stroke risk in patients with high-grade internal carotid artery stenosis or occlusion. Transcranial direct current stimulation (tDCS) can up- and down-regulate cortical excitability depending on current direction and anodal stimulation can increase regional cerebral blood flow (rCBF) during stimulation. Thus combining NIRS with tDCS can be an easy and economical setup for use in clinical population at risk for ischemic stroke.

Methods: We recruited 14 patients with established and acute ischemic stroke (<1 month) localized to a single hemisphere (10 male and 4 females from age 42 to 73). NIRS electrodes which consisted of four detection channels were placed on the right and left forehead. Anodal tDCS with anode at Cz (international 10-20 system of scalp sites) and cathode over F3 (F4 when monitoring the right side) was conducted with current density 52.6μA/cm2. NIRS was performed for two minutes on the F3 site followed by anodal tDCS for three minutes. After Anodal tDCS the NIRS was performed again to measure the changes that happened as a result of anodal tDCS. The same process was repeated with the F4 site.

Results: The affected hemisphere with impaired circulation showed significantly less change in rCBF than the healthy side in response to anodal tDCS. There was significant change in HbO2 in the healthy side (3.43+/- 0.86) but not in side with stroke (0.26 +/- 0.28), $p<0.01$.

Conclusion: Combining NIRS with tDCS can thus be a good predictor of cerebral vascular status and be used for stratification and possible identification of acute stroke. Combining NIRS with tDCS thus appears to be a promising technology, but additional investigations are required to establish its clinical efficacy and justify its routine use in clinical poppulation.

DEVELOPMENT OF A HYPERSPECTRAL TIME RESOLVED DOT SYSTEM FOR THE EXPLORATION OF THE HUMAN BRAIN ACTIVITY

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Diffuse optical tomography (DOT) is a growing area of research in the field of biomedical optics and neurosciences [1]. Over the past 20 years, technical development allowed a more and more accurate detection of the brain activation, both spatially and in the calculation of the variations of chromophores's concentrations such as Hemoglobin, cytochrome c oxidase, etc… [2]. In particular, time resolved systems are able to distinguish between superficial layers (skin, skull) and deep layers (brain) allowing the differentiation between the systemic response and the response of the brain [3].

In order to increase the accuracy of the brain's activation detection, and to obtain its broadband optical characterization, we have developed a Hyperspectral Time Resolved DOT system. It is composed of a compact supercontinuum laser within the picosecond range for the source part and of an ICCD camera coupled with an imaging spectrometer for the detection part. This allows a simultaneous detection of the spatial (up to 70 reception points), time resolved (minimum gate width 200ps, minimum delay shift 10ps), and spectral informations (from 500 to 900 nm).

We have first performed simulations of the measurement of the hemodynamic response to a brain activation in the prefrontal cortex. To do so, we used the Buxton model of the hemodynamic response [4] to calculate the absorption change in the cortex due to the brain's response and then used the MMC code [5] for the optical simulation in a rest and active brain. It allowed us to determinate optimal parameters of our experimental system like the best time gate to set, and to estimate the reflectance spectrum of the hemodynamic response.

We then performed the measurement of a sequence of activation on a healthy subject involving the prefrontal cortex. The subject was asked to perform a simple calculation task. Through the information acquired by our system, we've been able to retrieve, to our knowledge, the first spectrum of the reflected light as a function of the arrival time of the photons. By fitting those spectra to a set of reference spectra of basic components of tissues (HB, HBO2, water, etc...), we could estimate more accurately the type of tissue probed as a function of the time delay and retrieve the optical spectrum of the brain's activation. We then computed the change in oxy- and deoxy-hemoglobin, retrieving the hemodynamic response of the brain activation.

Beside the hemodynamic response, optical signal have also been reported to bring information about neuronal activity itself with the Event Related Optical Signal [6], although this signal is still controverted [7]. We believe that the characterization of the spectral response of the hemodynamic response will be helpful to dissociate those two contributions in order to retrieve the hemodynamic response on the one hand and the EROS signal on the other hand.

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Application of time-resolved near infrared spectroscopy in assessment of response to head-of-bed positioning in healthy subjects

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The disorders of cerebral autoregulation appear often in patients with traumatic brain injuries, subarchanoid hemorrhages or stroke. Optical methods may allow for noninvasive assessment of autoregulation at bed-side [1-2]. The mechanism of cerebral autoregulation can be studied by a dynamic stimulation influencing the cerebral blood flow in patients with cerebral autoregulation disrders. The tilt test represents a stimulus of brain hemodynamic which has limited invasiveness and is available at every hospital bed.

Here we present results of monitoring of a tilt test in a group of healthy subjects with the high sampling rate time-resolved optical system for near infrared spectroscopy (trNIRS). The system is equipped with four picosecond laser diodes (at $\lambda 1$=687nm, $\lambda 2$=830nm). The laser pulses are emitted to the surface of both hemispheres of the head using two bifurcated fibers. Diffusely reflected light is delivered to the detectors by the 4 mm diameter fiber bundles. High speed hybrid photodetectors (HPM-100-50 Becker&Hickl, Germany) are applied together with electronics for time correlated single photon counting (SPC-130, Becker&Hickl, Germany) for acquisition of distributions of times of flight of photons.

The tilt test carried out on the healthy volunteers consisted of three stages: 60 seconds in supine positions (0 deg), 120 seconds of -30 deg positions with head positioned below the legs, 60 seconds in supine position (0 deg).

The recorded distributions of times of flight of photons were analyzed by calculation of their statistical moments: total number of photons (N_{tot}) and variance (V). It was shown that time-resolved near-infrared spectroscopy allows for separation of changes in hemodynamics in intracerebral tissue from changes related to extracerebral compartments (like a skin, bones of the skull) [3]. The lower order moments (N_{tot}) are more sensitive to changes in absorption in superficial layers and higher order moments (V) are sensitive to changes in deeper structures [4].

During the tilt tests we observed a significant drop in the total number of photons in reaction to change of head position to -30 deg while the change in variance is rather small. In healthy volunteers, in standard motor cortex functional stimulation the change in N_{tot} is in range o 1% and V in range of 0.1 % whereas during the tilt test the drop of N_{tot} reaches 35 % while the drop of variance is in the range of 5%. Comparison of these amplitudes suggests that the intracerebral reaction (revealed in change in V) to the tilt test stimulus is rather small in healthy subjects. We expect that this kind of test can be applied as a strong stimulus of cerebral perfusion and used for testing of the autoregulation mechanism in patients with cerebral circulation disorders.

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Development of compact continuous wave NIRS instrument based on small size spectrometers for assessment of brain hemodynamics

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Due to the relatively low cost and simple construction, continuous wave functional near infrared spectroscopy (CW NIRS) systems are widely used for brain tissue oximetry and functional brain imaging. The technical approach proposed in present contribution is based on wavelength-resolved measurements of diffuse reflectance at multiple wavelengths from near-infrared region and allows for monitoring of the brain oxygenation changes. The compact NIRS laboratory instrument is based on two small size (40 mm x 42 mm x 24 mm) spectrometers (STS-NIR, Ocean Optics) and is equipped with a supercontinuum high power light source (Fianium). The setup allows for carrying out spectroscopic measurements in the wavelength range between 650 to 850 nm on the surface of the human head. This spectral region was separated by edge pass filters. A two-meter long fiber (ø 1mm) terminated with the cap for beam expansion was used to transmit the light to the surface of the head. The remitted photons were transmitted to the spectrometer with the use of a same fiber ending with the collimator. The source and detector fibers were fixed on the surface of the head using a rubber-based optode holder at separation of 2.5 cm. A time-resolved multichannel spectral system based on time-correlated single photon counting electronics for broadband absorption and reflectance measurements was used for the reference measurements. Details of the time-resolved setup were described in detail elsewhere [1, 2].
In-vivo experiments were carried out on the head of adult healthy volunteers during controlled hypoxia sessions. A mask-system hypoxicator, which produce breathable hypoxic air with a known and adjustable O_2 concentration was applied. The volunteers were breathing with the air of reduced oxygen level until the level of arterial O_2 saturation (SpO_2) reached the threshold of 85%. The experiments were carried out after receiving of an agreement of the bioethical commission of the Warsaw University of Medicine and obtaining consent of the subject investigated. As expected, the number of detected photons decreases during the hypoxia session at shorter wavelength whereas at longer wavelength increase of number of photons can be noted. This pattern is directly connected with the deoxygenation of the tissue under investigation – increase of deoxyhemoglobin and decrease of oxyhemoglobin content.
The method of the multiple wavelength detection may allow for more precise estimation of hemodynamic parameters during controlled changes in the brain oxygenation. Analysis of the data acquired with the use of multi-wavelength setup based on solving the system of equations describing relation between the measured changes in attenuation of light and changes in oxy- and deoxyhemoglobin ΔHbO_2, ΔHb concentrations may allow to estimate changes in chromophore concentrations at different depths in the tissue.
The constructed setup is simple and compact and allows for acquisition of broad band spectral data. It can be easily applied in human studies in clinical environment. The detection part of the system is light and portable, whereas the source part can be optimized in the future. Further investigations will be focused on utilization of the compact broad-band spectral CW NIRS setup in measurements of the brain oxygenation changes caused by controlled hypoxic challenge.
The study was financed partly by Polish National Center for Research and Development within the project DOBR/0052/R/ID1/2012/03.

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Imaging Brain Function in Children with Autism Spectrum Disorder with Diffuse Optical Tomography

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Autism Spectrum Disorder (ASD) is a serious psychiatric disorder of childhood that is defined by deficits in social functioning, communication, and restricted interests/repetitive behaviors. Recent fMRI studies[1] have uncovered promising signatures for altered brain function in patients with ASD that may inform diagnosis and track responses to interventions. The wearability of DOT will allow a fuller assessment of brain function in severely affected children with ASD, exceedingly challenging to study with MRI methods. We present here a feasibility study imaging with our high density DOT system[2] (**Fig. 1a-c**) school-aged typically developing children (TDC) and sex/age/IQ-matched children with autism (ASD+) (**Fig. 1d**). Both groups of children are able to tolerate imaging for over 30 minutes, and exhibit good raw data quality (**Fig. 1e,f**), and maps of functional brain activity in response to simple language tasks like hearing words and verb generation (**Fig. 1g,h**). Group-matched brain responses of biological motion perception and resting state networks will also be presented.

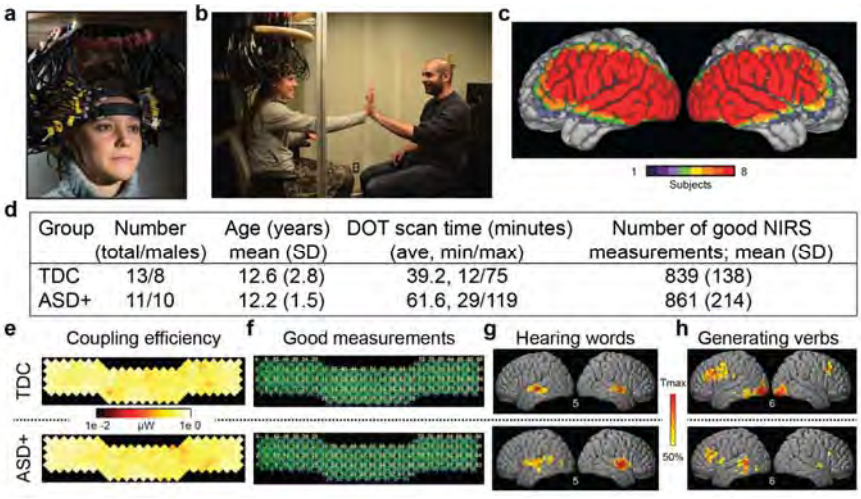

Figure 1: HD-DOT system and data on school-aged typically developing children (TDC) and children with autism spectrum disorder (ASD+). (a) Cap fit on model subject, **(b)** HD-DOT set-up facilitates within-room social interactions. **(c)** The FOV for each subject overlaid on the cortical surface view of the MNI atlas. **(d)** Recruitment demographics, contiguous time in the DOT system, and data quality comparison demonstrating TDC and ASD+ are well matched. (e-f) Raw data quality metrics showing **(e)** strong and consistent coupling efficiency and **(f)** even distribution of measurements (green lines) around cap for both groups. **(g-h)** Functional brain activations reflecting language processing averaged within the respective groups. While hearing words shows excellent agreement, there is an interesting difference between ASD and TDC for the generating verbs task. TDC exhibit a stronger visual response, possibly due to more consistent fixation. ASD exhibit a stronger response over Werneckie's area.

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Title
NIRS Probe Construction Accuracy and Inter-subject Variability

Abstract
Studies that use near-infrared spectroscopy to reconstruct brain activation can benefit from the use of an atlas volume for approximating the forward matrix using statistical methods (i.e. photon migration Monte Carlo). However, to accurately represent the source and detector locations in the simulation, the probe geometry must be mapped to the volume surface using 3D digitization or through the use of a probe design tool such as AtlasViewer. To determine the level of uncertainty when using either of these techniques, we have prepared two analysis tools to plot and quantify probe construction accuracy and inter-subject variability. Through the probe construction analysis tool we have observed variation from the original design with a mean of 6.68 millimeters and a standard deviation of 3.70 millimeters. Using the inter-subject probe variability tool we have measured the optode placement variation between subjects to have an average standard deviation of 4.72 millimeters. These results suggest that designing a probe using AtlasViewer is sufficiently accurate to not require mapping individual subject probe positioning using a 3D digitizer. The error and variation when creating and using probes with this system is sufficiently low relative to the approximately ten-millimeter resolution of the imaging technique being used.

Evolution of temporal synchrony between functional brain networks during state transitions

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Recent findings from resting-state functional magnetic resonance imaging (fMRI) studies have shown spatiotemporal correlations in spontaneous activity between functionally-related brain networks (Biswal et al. 1995). Recent human studies have investigated the functional significance of intrinsic brain activity to explain altered states of consciousness. Loss of consciousness during anesthetic sedation has been associated with reductions in network functional connectivity (FC, Boveroux et al., 2010). Extensive reduction of neural activity by anesthetics is evidenced by burst-suppression in the electroencephalogram (EEG) that have neurophysiologic models (Ching et al., 2012) and may increase mortality risk for critically ill patients (Watson et al., 2008). The corresponding features of FC network topology remain unclear. Several distinct spontaneous coherent networks persist in deeply anesthetized primates (1.25% isoflurane) (Vincent et al. 2007) but investigation in small rodents have been sparse (Liu et al. 2011). We asked whether coherent networks persist during electrocortical silence and may represent a fundamental and intrinsic property of functional brain organization. In order to understand the underlying mechanisms of spontaneous hemodynamic fluctuations in the brain under deep anesthesia, we imagine spontaneous activity in the mouse brain using functional connectivity optical intrinsic signal imaging (fcOIS, White et al., 2011) as mice transitioned from an awake state to increasing levels of isoflurane anesthesia (in %: 0, 0.5, 1, 2, 3). We quantified the extent of motor movement, spectral content in concurrently-recorded EEG activity, and the presence/absence of electrical burst-suppression. As mice transition from an awake-behaving state to a state of deep-anesthesia (2-3% isoflurane) we observe a progressive, regional reduction in the magnitude and coherence of spontaneous activity over the cortex (**Fig. 1**). While deep anesthesia (2-3%) was found to ablate functional connectivity globally over the brain (**Fig. 1C**), activity in some networks (e.g., somatosensory) persisted longer than others with increasing anesthetic dose (**Fig.1B**). Results from our study shed light on the functional significance of intrinsic brain activity as measured by hemodynamic fluctuations, and the role of functional connectivity as a correlate of consciousness in the mouse.

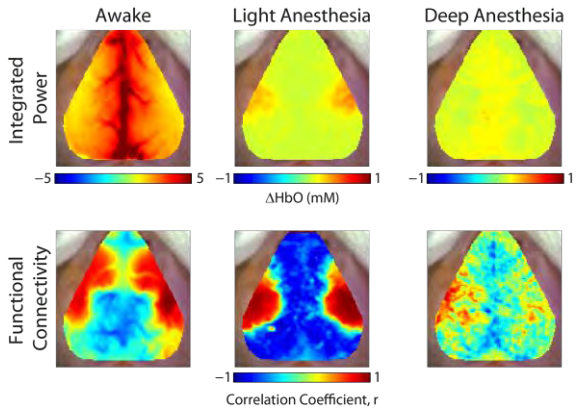

Figure 1. Evolution of spontaneous activity during state transitions. (**Left**) Spontaneous activity in the awake mouse brain exibits high, brain-wide variance over the entire cerebral cortex and high intra- and inter-hemispheric functional connectivity between somatomotor regions. (**Middle**) As the mouse transitions to light anesthesia (1-1.5%) network activity dramatically reduces in magnitude, with residual activity and functional connectivity existing only somatosensory cortex. (**Right**) Deep anesthesia (2-3% isoflurane) ablates all brain activty and temporal synchrony between brain networks.

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Development of NIRS system for translational studies of subcortical regions using implanted optical fibers

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Introduction: Current NIRS methods have extremely poor spatial localization, and are limited to the outermost regions of the cortex, since the measurements are performed from the surface of the head, or in some cases, of the cortex. This has reduced the utility of NIRS in substance abuse studies in animal models, as most of the regions of interest are subcortical. One way to remove this limitation and study subcortical locations is by performing measurements directly at the site of interest using implanted optical fibers to measure the optical properties of hemoglobin using backscattered light (fiber localized NIRS, or flNIRS) directly in the area of interest. We are developing such a system to study brain responses to drug cues in awake, behaving rats both during fMRI scans and while freely moving in their environment.

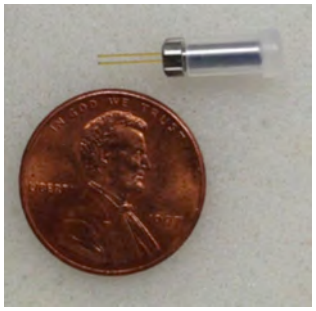

Figure 1 – 6.8mm implantable cannula

Methods:
For the implantable NIRS probe, we used a two-fiber cannula from Doric Lenses (Quebec, Canada), which allows precise, permanent stereotactic implantation of two fibers with a well controlled spacing and depth. The cannula connects to a two fiber cable with a ferrule, and we are able to reliably deliver and receive significant amounts of light to the target region. The data acquisition system is based on a single board pulse oximeter development board, the MOD-PULSE from Olimex (Olimex, Inc., Bulgaria) with modified firmware. A Honeywell SD3443 phototransistor is used as a detector, and high power LedEngin LZ4-4X LEDs at 660 and 850nm are driven with a scalable, high power driver board that can drive LEDs with a peak current of between 30 and 1500 milliamperes at full resolution. The MOD-PULSE hardware design (which is open source), the LED driver, and the sources and detectors, can all be combined onto a single board for the backpack system. The MOD-PULSE board transmits the NIRS data to a a platform independent GUI program for realtime display of acquired data, and data logging written in Python. The design of the system (both hardware and software) allows easy synchronization of multiple channels of data (which will be used in the proposed experiments) and synchronization to external events, such as stimulus presentation.

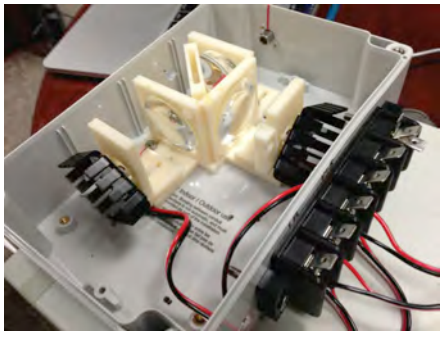

Figure 2 – Optical combiner system. The white 3D printed assembly pictured combines the output of two LEDs (in brackets at lower left and on the right) and focuses the combined beam to couple it to and optical fiber port (upper right). The system is designed to be modular; holders are individually printed to fit each LED and can be focused independently. This allows us to rapidly check LEDs at different wavelengths and power outputs.

Summary:
We have almost completed the design and test of the prototype in vivo acquisition system. Once the optical design is complete, we can move to animal measurements during stimulus presentation in the fMRI environment, while developing the deployable backpack system in parallel.

A Silicon Integrated Sensor Interface for Portable FDNIRS

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A silicon integrated sensor circuit (Fig. 1) has been designed for low cost and portable frequency domain near-infrared spectroscopy (fdNIRS). By integrating the amplification and signal processing electronics onto a standard silicon integrated circuit, the number of sensors and sensing locations can be scaled easily. Incident photons from NIR laser diodes, amplitude modulated at a 80-100MHz frequency, get multiply scattered and absorbed in the tissue. Avalanche photodiodes (APD) are used to collect the scattered light at known distances away from the source. The trends in the change of the amplitude and phase of the detected signal over the distance are used to quantify the optical coefficients of the tissue that are used to determine the absolute concentrations of hemoglobin (HbO_2) and deoxy-hemoglobin (Hb).

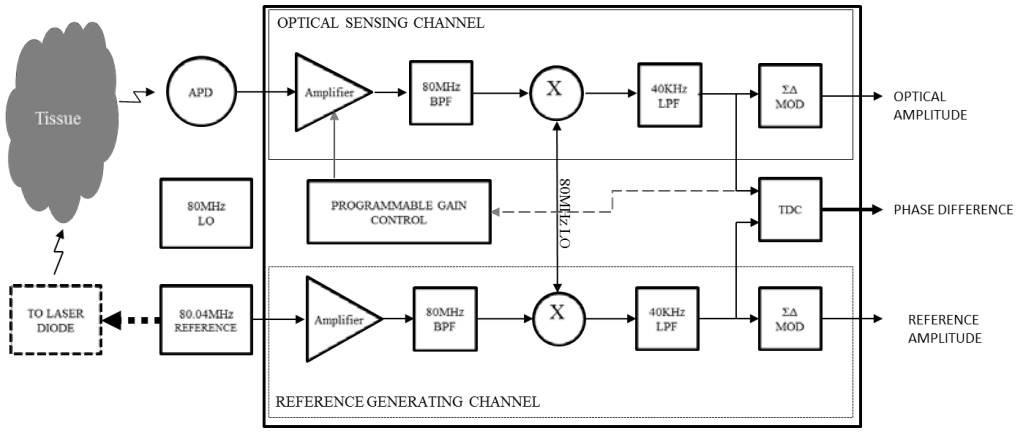

Fig.1 Architecture of the silicon integrated fdNIRS chip

An APD with a large active area and gain are critical for this detection to produce the maximum amount of current from the incident photons. Larger detectors present a larger parasitic capacitance to the circuit front-end resulting in a higher noise floor for the wideband amplifier. A first prototype [1] that used a 1.77mm^2, 3.6pF APD with a CMOS front-end amplifier showed a limited dynamic range of ~26dB due to the high noise floor and low voltage power supply. To mitigate these issues, a second prototype has been designed with Silicon Germanium (SiGe) heterojunction bipolar transistors for the front-end amplifier that have a better high frequency response. The amplifier with a 3-level programmable gain can be interfaced with an APD that has a higher active area of 7mm^2 and a parasitic capacitance of 8pF. The high frequency voltage signal generated by the amplifier is down-converted to a 40kHz signal using a mixer for further on-chip processing of the relative amplitude and phase difference between the optical channel and a reference channel using a ΣΔ modulator and a time-to-digital converter (TDC). The SiGe based amplifier has a simulated noise floor of 1.5pA/√Hz at 80MHz which is lower than ~10pA/√Hz of the CMOS design.

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2. Multimodal Monitoring

Validation of the hypercapnic calibrated fMRI method using DOT-fMRI fusion imaging.

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The blood-oxygenation-level dependent (BOLD) contrast in functional magnetic resonance imaging (fMRI) is a neuroimaging technique allowing for indirect mapping of neuronal activity in the brain. In order to extract physiological information such as the cerebral metabolic rate of oxygen ($CMRO_2$), the technique is traditionally calibrated using CO_2 mixed gas inhalation to account for the baseline differences. Some critical assumption (constant $CMRO_2$ assumption) related to this calibration technique has been the subject of intense debate. Here, we combined an optical imaging modality (Diffuse Optical Tomography (DOT)) and fMRI techniques (BOLD and ASL) to cross-validate the conventional calibration of BOLD.

Methods: Eight healthy male subjects (26±5 years old) with no history of neurological, cardiopulmonary, or psychiatric illness participated in the study. The study was approved by the Partners Healthcare Human Subjects Committee and all subjects gave written consent form. The study comprised two imaging sessions conducted over a period of one hour: 1) four 6-min simultaneous acquisitions of: a) blood oxygen level dependent functional magnetic resonance imaging (BOLD-fMRI), b) arterial spin labeled (ASL)-fMRI and c) diffuse optical tomography (DOT) during a finger tapping task, 2) two 10-min acquisitions of BOLD- and ASL-fMRI during hypercapnic challenge. Each finger tapping scan included ~20 finger tapping trials of 10 sec duration with a pseudo-random inter-trial interval of 5-10 sec. Each hypercapnic challenge scan comprised alternating conditions of eucapnia (3 min) and hypercapnia (2 min). During the hypercapnic condition, the inhalation gas was manually titrated to achieve an average increase in end-tidal CO_2 of 8 mmHg above each subject's baseline (habitual) end-tidal CO_2.

Results: All subjects showed significant BOLD, CBF and optical response to the finger tapping paradigm over the motor-sensory cortex (t statistics, $p<0.05$). BOLD typically increased up to 2% while CBF increased up to 50% during hypecapnia. M values obtained from the fusion model varied from 0.03 to 0.11. A subject-by-subject comparison of the M values was obtained with each method. A correlation of $R = 0.87$ ($p < 0.01$) was obtained between the M values computed from the two methods. The evoked changes in $CMRO_2$ recovered with each method were also compared. A high correlation ($R = 0.98$, $p<0.01$) was obtained between the two methods.

Conclusion: The constant inter-subject variability across modalities observed in the present study serves as robust and convincing evidence to support the hypercapnic fMRI technique in calibration of the BOLD signal.

Investigation of prefrontal NIRS signals during a working memory task by simultaneous NIRS-fMRI measurements

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Although near-infrared spectroscopy (NIRS) is commonly used for studying human brain function, a potential problem is that superficial hemodynamic changes such as skin blood flow can affect the NIRS hemoglobin (Hb) signals. As an initial step toward validating the use of NIRS to measure prefrontal activity, the present study investigated the functional signals during a working memory (WM) task by comparing the NIRS-Hb signals with blood-oxygen-level-dependent (BOLD) signals simultaneously acquired by functional magnetic resonance imaging (fMRI). Sensorimotor activity during a finger tapping (TAP) task was measured as a reference. Activated NIRS channels in the PFC and sensorimotor cortex were selected for the WM and TAP tasks, respectively, and a spatial sphere for analysis (SFA) was defined in the fMRI data for each NIRS channel on the basis of a simulation with a photon-path-distribution function. In the SFA of the activation channels, about half the gray matter voxels (45–66%) showed a significant correlation with the NIRS-Hb signals. In comparison, only 3–6% of the soft tissue voxels showed a significant correlation on average. The layer BOLD signals from the gray matter voxels (L-BOLD (GM) signals) were averaged in the SFA by using a weight given by the photon-path-distribution function; the L-BOLD (GM) signal was significantly correlated with the NIRS-Hb signal during both tasks. The same analysis using a laser-Doppler flowmeter (LDF) signal, which reflects superficial tissue blood flow, showed a significant correlation with the oxy-Hb signal for the WM task, suggesting that skin blood flow in the forehead also affects the prefrontal oxy-Hb signals to some extent. However, the correlation of the LDF signals was significantly weaker than that of the L-BOLD (GM) signals. While care must be taken when comparing the NIRS-Hb signal with LDF or extracranial BOLD signals, these results suggest that the NIRS-Hb signal mainly reflects hemodynamic changes in the gray matter for both WM and TAP tasks. Moreover, the signal amplitudes of the NIRS-Hb response to the WM task were significantly correlated with those of the L-BOLD (GM) response across participants (oxy-Hb: $r = 0.65$, deoxy-Hb: $r = -0.76$), indicating that participants with a stronger NIRS-Hb response also showed a stronger L-BOLD (GM) response. These results thus provide supportive evidence that NIRS can be used to measure hemodynamic signals originating from PFC activation.

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Autonomic correlates of prefrontal cortex activity during cognitive task

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Over the past decades, it has been demonstrated that the autonomic nervous system (ANS) is not just a "non-cognitive" system thus likely to be involved in any cognitive and emotional processes[1]. The ANS takes part in the homeostasis maintenance and regulates body functioning (i.e., heart, gastro-intestines, glandular secretion, blood pressure, and so on) through its efferent fibers. In particular, the autonomic nerves, especially the sympathetic ones, reach vessel walls providing a certain degree of contraction-relaxation resulting in blood flow regulation. As the autonomic control of cerebral blood flow is related to the subject's cognitive load, task-related vascular tone regulations can impact on the estimation of cortical activity by means of functional Near Infrared Spectroscopy (fNIRS)[2]. In fact, systemic cardiovascular changes can produce false positives in activation maps as fNIRS relies on neurovascular coupling.

In this study we combined fNIRS and functional Infrared (fIR) imaging measurements to evaluate the autonomic and the neural processes underlying cognitive functioning. Simultaneous fNIRS-fIR measurements were taken during a mathematical task on nine healthy subjects (mean age: 25.2 ± 5.0 years; 4M/5F). fIR was used to measure and to image the cutaneous temperature changes related to sympathetic regulation of facial skin blood flow[3]. We focused on the nose tip temperature changes as this region reflects the sympathetic alpha-adrenergic vasomotor activity. A temperature rise reflects the systemic increment of blood perfusion. Concentration changes of oxygenated (oxyHB) and deoxygenated (deoxyHB) hemoglobin were recorded over the prefrontal cortex (PFC) using a frequency-domain near-infrared spectroscopy instrument (Imagent, ISS Inc., Champaign, IL). Cortical signals were collected using a multi-distance setup with 4 cm, 3 cm and 2 cm source-detector separations.

Task-evoked responses were observed both for hemoglobin and thermal data. We found significant increases of oxyHB and decreases of deoxyHB in all the channels. Grand averaged responses across trials and across subjects of fNIRS and fIR signals showed a very similar task-related dynamic. A Wavelet Coherence analysis between the two kind of signals revealed a strong common power content in the Very Low Frequency Oscillations (VLFOs) range (~0.02 Hz)[4]. This band corresponds to the metabolic endothelium-related regulation processes, which in turn overlaps with task frequencies. Time lags analysis showed a high inter-subject variability.

Our results demonstrated that task-related vascular tone changes occur both superficially and more deeply in the brain and it needs to be considered when correcting for systemic interferences. We suggest to use a subject-based fNIRS signal denoising as the cognitive and/or the emotional state of the subject modulates the interference timing. The cognitive-emotional link and the role that one system exerts on the other could be effectively studied by simultaneously combining thermal IR and fNIRS imaging, while preserving the ecological context of the subject's natural actions.

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Probing the neural basis of visual working memory: A validation study using fMRI and fNIRS

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Visual working memory (VWM) plays a key role in visual cognition, comparing percepts and identifying changes in the world as they occur. Previously, functional magnetic imaging (fMRI) has identified activation in frontal, parietal and temporal areas involved in VWM. Here, we conducted a cross-modal neuroimaging study to determine whether functional near-infrared spectroscopy (fNIRS) is an effective tool to measure changes in activation during VWM tasks. Moreover, we examine the utility of a processing pipeline developed to move from channel-based fNIRS-analysis to a voxel-wise image-space analysis, synonymous with methodology used in fMRI studies. We used fNIRS in conjunction with fMRI during an event-related color change detection task with set sizes (SS) 2, 4 and 6. Half of the trials were change trials. Thirteen subjects participated. Positions of sources and detectors were digitized and transformed to a common adult atlas. Monte Carlo simulations generated probability distributions of photon migration for all channels. These were then transformed to MNI space and combined to create subject-specific masks as well as a union mask across participants. fMRI and fNIRS signals were corrected for motion (targeted principal components analysis for fNIRS), corrected for outliers, and de-convolved with the same gamma function to create maps of beta coefficients. The betamaps were multiplied by the union mask to identify common voxels across fNIRS and fMRI images. Voxel-wise correlations were computed between fMRI and fNIRS betamaps and analyzed. We estimated contrasts by subtracting the betamaps for SS2 from SS6 for correct (Hits and Correct Rejections) and incorrect (False Alarms and Misses) trials, each for HbO, HbR and BOLD activation. T-tests comparing the contrast maps to baseline were conducted. Common areas of activation across fNIRS and BOLD activation maps were estimated. Overall, oxy-haemoglobin (HbO) activation in the fronto-parietal areas was more correlated with BOLD activation for Hits and Correct Rejections than for Misses and False Alarm trials ($r^2 = 0.4$, $p<0.05$). Activation at SS6 was greater than SS2 for correct trials across the prefrontal cortex (i.e. superior, middle and inferior frontal gyri) which was consistent with literature suggesting that PFC is involved in maintaining and manipulating task-based information in working memory. Activation observed at the angular gyrus and occipital cortex for incorrect trials may reflect erroneous encoding of stimulus features on error trials. Robust voxel-based correlations between fNIRS and fMRI signals validate our processing pipeline. Further, we have demonstrated that fNIRS is an effective tool to measure functional activation in the VWM network. This is significant because fNIRS is cheap, portable, and can be used with infants and aging and clinical populations.

Improving motor performance by personalizing non-invasive cortical stimulation with perturbation transcranial direct current stimulation (ptDCS)

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Transcranial direct current stimulation (tDCS) can be combined with rehabilitation to facilitate plasticity that leads to improved motor performance after brain injury. TDCS is a non-invasive cortical stimulation technique that modulates cortical activation by delivering weak current through a pair of anodal-cathodal (excitation-suppression) electrodes, placed on the scalp over the targeted cortical centers. Current tDCS interventions entail the uniform application of a chosen electrode montage to a subject population without personalizing electrode placement for optimal motor gains. The resulting study outcomes remain variable and there is no current consensus as to what electrode pair montage could yield optimal outcomes.

We propose a novel perturbation tDCS (ptDCS) paradigm for determining a personalized electrode montage which yields maximal motor task performance improvements during stimulation. We show that by applying a current of 0.5 mA for 40 s, measurable tDCS effects on cortical activity, muscle activity, and performance return to baseline in just 3 minutes. The short lifetime of perturbative stimulation effects enables for a large number of different pair-wise electrode montages to be applied over the sensorimotor cortex without any carryover effects. The ptDCS method was applied to ten healthy adults and five hemiparetic stroke patients as they performed an isometric wrist flexion task with their non-dominant arm. Simultaneous recordings of muscle activity by electromyography (EMG) and cortical activity by functional near-infrared spectroscopy (fNIRS) during ptDCS helped interpret how cortical activity perturbations by any given electrode montage relate to changes in muscle activity and task performance. In this study the product of reaction time (RT) and Error metrics was used to measure performance.

Unexpected and surprising results were found for the tDCS electrode montage maximizing performance in all healthy adults, as this optimal montage did not match any of the ones being explored in current literature. Furthermore, in the five hemiparetic stroke patients measured with ptDCS the optimal electrode montage was found to be different in each patient.

The findings from this novel ptDCS method present a shift in current practices as they indicate that not all patients benefit from the same stimulation montage. The above findings are very exciting due to the potential generalized application of the ptDCS method to many other types of brain injury and to the possible performance enhancement of healthy adults. Nevertheless, clinical studies employing ptDCS-guided tDCS treatment, combined with physical therapy or other interventions where appropriate, would need to be performed in the future to confirm the potential of this method.

Towards Affective Hybrid Brain-Computer Interfaces based on fNIRS, EEG and Peripheral Physiological Signals.

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Introduction. Today, there is a growing need to create affective, sensitive, and interactive human-machine interfaces (HMI) in order to reduce the gap between man and machine. Within this light, affective brain-computer interfaces (BCIs), also known as passive BCIs, have emerged. Affective BCIs monitor the user's affective and mental states and adapt themselves in order to improve the user experience. As an example, a brain speller may adjust its scan speed based on the user's stress level. A robotic interface, in turn, may respond to the user in a different tone based on his/her emotional state. Detecting user emotions, however, is not a trivial task. Typically, a single modality is used, such as electroencephalography (EEG) or peripheral physiological signals, such as the galvanic skin response. Recently, near-infrared spectroscopy (NIRS) has also emerged as a useful tool to characterize mental states, particularly cognitive load (*Strait et al*.). In the present work, we propose a multimodal approach to emotion characterization based on a combination of NIRS, EEG, and peripheral physiological signals.

Method. To validate the proposed affective BCI, the publicly available 'eNTERFACE 06' database was used (*Savran et al*.). The database is comprised of NIRS, EEG, galvanic skin response (GSR), respiration, and plethysmograph (PPT) signals collected from subjects as they watched 150 images from the International Affective Picture System (IAPS) belonging to 3 different classes (positive, negative and calm). Subjects then rated their perceived levels of valence and arousal using a 5-point scale. To develop the affective BCI, three steps were involved: feature extraction, feature selection, and classifier design. For feature extraction, 3925 features were extracted. Of these, 3800 were extracted from the EEG signals, including spectrum, coherence, amplitude modulation, phase, and synchronization based. From the peripheral physiological signals, in turn, 100 features were extracted including temporal, power spectral, and statistical parameters. Lastly, from the NIRS signals, oxygenated (HbO2) and deoxygenated (HHb) haemoglobin concentrations were computed via the Beer-Lambert law. From these concentrations, 25 parameters were extracted, including HbO2 and HHb peaks, area under the curves, latency, and slopes.

Secondly, in order to reduce the number of EEG and physiological features to a workable number, the minimum redundancy maximum relevance feature selection (mRMR) algorithm was used separately to select the top 25 features from each modality. Lastly, for classification two binary classifiers were tested: support vector machine (SVM) and relevance vector machine (RVM). Both classifiers map features to a higher dimensional space using kernels and find the optimal hyperplanes that separate high/low arousal and high/low valence ratings. The RVM adds an additional Bayesian step that allows for class memberships to be computed, thus resulting in "soft" decisions (as opposed to SVM hard decisions).

To test the effects of the different modalities, seven different classification schemes were tested: (1) top-25 EEG features alone, (2) top-25 physiological features alone, (3) 25 NIRS features alone, (4) top-25 NIRS-EEG, (5) top-25 EEG-peripheral, (6) top-25 NIRS-peripheral, and (7) top-25 NIRS-EEG-peripheral. An eighth setup was also tested within the RVM classifier and consisted of decision level classifier fusion, where the class membership values produced by each classifier (EEG, NIRS, and peripheral) served as the weights in a weighted decision.

Conclusion. We show the proposed affective BCI achieving reliable results with the NIRS modality contributing important information for emotion characterization. The results are based on a small dataset, but show the importance of cerebral hemodynamics information, obtained via pre-frontal NIRS, for affective BCIs.

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The significance of systemic changes (blood pressure and P_aCO_2) in functional studies using NIRS – An investigation using a mathematical model of brain physiology

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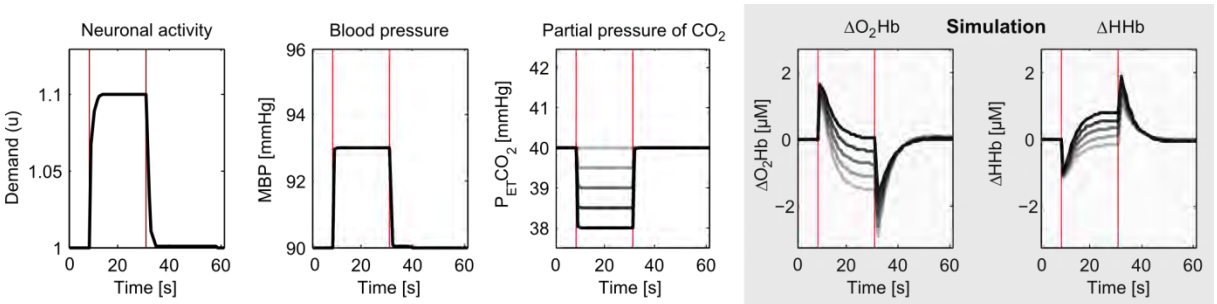
Introduction: Signals measured with fNIRS consist of a combination of three major components that can be distinguished according to three aspects: (i) the signal source location (intracerebral vs. extracerebral), (ii) the stimulus/task relation (evoked vs. non-evoked), and (iii) the physiological cause (neuronal vs. systemic). The recorded fNIRS signals (when assuming to steam completely from intracerebral tissue) originate from mainly three processes [1]: (i) evoked neurovascular coupling by a stimulus/task, (ii) non-evoked (i.e., spontaneous) neurovascular coupling, and (iii) processes that are not induced by neurovascular coupling, i.e., evoked and non-evoked systemic physiological processes. **Aim:** We assessed the impact of evoked systemic physiological processes on recorded fNIRS signals from the intracerebral compartment with the use of a computational model of brain physiology [2]. It is recognized that systemic physiological changes, such as changes in blood pressure (BP) [3] and partial pressure of CO_2 ($PaCO_2$) [4], can accompany functional tasks and influence the fNIRS signals. These changes can interfere with the measurement of the local neurovascular coupling and can cause false positives and negatives. **Material and methods:** In order to investigate the impact of BP and $PaCO_2$ on fNIRS signals systematically we simulated cerebral hemodynamics and oxygenation (HD/OX) changes during task-evoked neuronal activity in conjunction with simultaneous changes in BP and $PaCO_2$. To this end, an advanced mathematical model of brain circulation and metabolism (BrainSignals) was employed [2]. The model has been validated in previous studies [5]. **Results:** Our analysis revealed that (i) even small changes in BP (e.g ~1%) and $PaCO_2$ (e.g. ~4%) have a significant effect on cerebral HD/OX; (ii) changes in $PaCO_2$ lead to changes in fNIRS signals that have a shape similar to a typical hemodynamic response function (HRF, i.e. HD/OX changes caused by local neurovascular coupling); (iii) changes in BP cause fast transients in fNIRS signals due to the slowly working cerebral autoregulation; (iv) both BP and $PaCO_2$ changes can mask the neuronally-driven HRF or can cause changes in fNIRS signals that resemble the HRF. **Discussion and conclusion:** We showed by physiological modelling that changes in BP and $PaCO_2$ can have a strong impact on cerebral HD/OX measured with fNIRS. Simulations with the BrainSignals model help to understand the complex interaction between local cerebral and systemic changes in HD/OX. For a proper interpretation of fNIRS signals, changes in BP and $PaCO_2$ should be considered.



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The effect of colored light on human cerebral hemodynamics and oxygenation, end-tidal CO_2 and skin conductance – A multimodal fNIRS study

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Introduction: The effect of exposure to colored light on human physiology (e.g. behaviour, cognition and endocrine functions) is receiving more and more attention in the field of neuroscience, chronobiology, and integrative human physiology. In two previous studies of our group [1,2] we showed that exposure to red or blue color differently affected cerebral hemodynamics and oxygenation (HD/OX) as measured by functional near-infrared (fNIRS). **Objective:** The aim of the present study was to assess how four different light exposures (red, green, blue, yellow) elicit changes in (i) HD/OX, as well as (ii) arterial partial pressure of CO_2 (measured as end-tidal CO_2, $P_{ET}CO_2$), and skin conductance (quantified as the skin conductance level, SCL). HD/OX were measured over the left and right prefrontal cortex (PFC) as well as the left and right part of the visual cortex. **Material and methods:** 17 subjects participated in this study. The experimental protocol consisted of a pre-stimulus (8 min), stimulus (light exposure, 10 min) and post-stimulus (15 min) interval. For the data analysis, only physiological signals with a sufficient signal-to-noise ratio were employed. **Results:** The analysis revealed the following significant ($p < 0.05$) effects: (i) all four colors caused an increase in tissue oxygenation (StO_2), oxyhemoglobin (O_2Hb) and total hemoglobin (tHb) as well as a decrease in deoxyhemoglobin (HHb) in the PFC; (ii) StO_2 decreased in the visual cortex; (iii) SCL increased during red and green; (iv) $P_{ET}CO_2$ decreased during yellow; (v) after the light exposures (i.e. in the recovery phase) StO_2 increased in the PFC, StO_2 decreased in the visual cortex, and SCL increased continuously; (vi) the strongest change in StO_2 was observed for blue in the PFC and for green in the visual cortex. (vii) SCL increased the strongest for red, $P_{ET}CO_2$ decreased the strongest for yellow. (viii) the differences in these parameters between the different colors were often significant. **Discussion:** These changes proof that (i) different light colors elicit different (neuro-) physiological effects; (ii) the PFC and visual cortex react differently to the long-term light exposure; and (iii) the measured systemic signals (SCL, $P_{ET}CO_2$) assist to interpret the fNIRS changes. The SCL changes are in agreement with previous studies. **Conclusion:** We measured changes in HD/OX, $P_{ET}CO_2$ and SCL that were specific to different light exposures. The presented methodology (fNIRS combined with capnography and skin conductance measurement) is a promising approach to assess neuronal as well as systemic physiological task-evoked changes.

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Correspondence of EEG and NIRS sensitivity to the cerebral cortex using a high-density layout

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This study investigates the correspondence of the cortical sensitivity of electroencephalography (EEG) and near-infrared spectroscopy (NIRS). Sensitivity maps for source localization analysis can be computed from the EEG and NIRS forward models. These sensitivity maps are often computed when analyzing the signals of the EEG and NIRS independently. The inverse of the forward model can be used to compute tomographic maps of the cortical activity. Computing joint forward models for EEG and NIRS allows for the reconstruction of multimodal recordings. Joint reconstructions of the cortical activity often rely on statistical priors that apply the appropriate weighting between NIRS and EEG data. Interpretation of EEG data can be improved upon, and the number of electrodes needed for measurement can be reduced, by using NIRS hemodynamic responses as statistical priors.

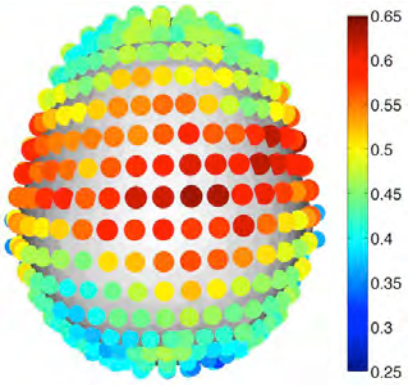

Figure 1. Correlation between NIRS channel group sensitivity and EEG channel sensitivity for each corresponding EEG electrode.

The forward and inverse models for EEG and NIRS were computed and their correspondence was calculated to help with analysis and interpretation of multimodal studies. EEG forward model sensitivity to the cerebral cortex was calculated for 329 EEG electrodes following the 10-5 EEG positioning system using a segmented structural MRI scan of a human subject. NIRS forward model sensitivity was calculated for the same subject using 156 NIRS source-detector pairs selected from 32 source and 32 detector optodes positioned on the scalp using a subset of the 10-5 EEG positioning system calculated with an algorithm for automatic computation of the 10-5 scalp coordinates [1]. Groups of NIRS source-detector pairs with maximum correlations to EEG electrode sensitivities were generated. Sensitivity correlations between co-localized NIRS source-detector pair groups generated and EEG channels yielded $R_{channel}$ = 0.46 ± 0.08 (Figure 1). The mean correlation between the point spread functions (PSF) for EEG and NIRS was R_{PSF} = 0.17 ± 0.10 (Figure 2). These sensitivity correlations between EEG and NIRS should be taken into account when designing multimodal studies of neurovascular coupling and when using NIRS as a statistical prior for EEG source localization.

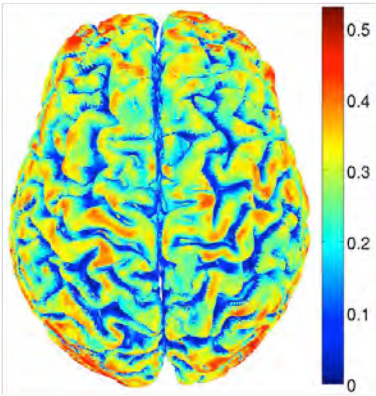

Figure 2. Correlation between NIRS and EEG point spread functions

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Title: Cortical temporal response to surface lightness change

Authors (presenter in bold): **Jan Mehnert**[1,2,3,4], Hongfan Shen[2], Seong-Whan Lee[2], Huseyin Boyaci[5], Klaus-Robert Müller[1,2], Daniel Kersten[6,2]

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Preference: oral presentation

Topic area: Multimodal monitoring, Neurocognition (adults)

Abstract:

Under most natural viewing conditions, the *lightness*, or perceived degree of grayness of a surface, is more closely related to the surface's reflectance than to its retinal image intensity. The neural basis of the transformation from intensity to lightness is not well-understood. Computational studies have shown that the estimation of reflectance at a given image location is a complex problem that requires taking into account the larger scene context.

Figure 1: The set of stimuli used in this experiment

This raises the question of how context influences locally perceived lightness in the human visual system. One approach to this question is to measure responses to stimuli in which the visual system constructs lightness based on context rather than local intensity, such as with the classic Craik-O'Brien-Cornsweet illusion (COC; [Cornsweet 1970], Figure 1). Previous fMRI measurements of responses to the COC illusion have shown that retinotopic areas as early as V1, as well as V2 and V3, respond to changes in perceived lightness even in the absence of local intensity change, suggesting mediation through inter- or intra-area cortical connections [Boyaci 2007, 2010].

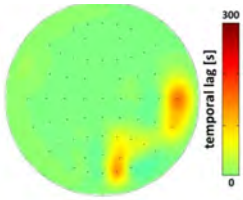

Figure 2: Significant temporal lags between real and illusion in EEG.

However, we do not know how such cortical activity changes in time. We made simultaneous recordings of neuronal (using electroencephalography) and hemodynamic (measured by near-infrared spectroscopy) responses, which we then track back to their cortical origins. We found that the response to a lightness change requires around 150-200 ms more processing time than to physical intensity changes, consistent with activation through inter- and intra-area connections of the visual cortex and higher visual areas (V2, V3, see Figure 2) in the dorsal and parietal pathways are necessary to perceive the COC-illusion (Figure 3).

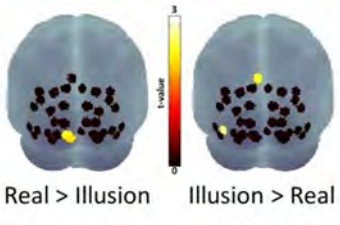

Figure 3: NIRS results comparing real and illusion.

This study highlights the fruitful combination of EEG and NIRS to study fast temporal aspects and high spatial resolution at the same time.

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Robust pre-clinical software system for real time monitoring of NIRS and EEG

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Introduction:

Monitoring cerebral activity is widely used in both research and clinical settings. It is a valuable source of information for the investigation of developmental cognitive neuroscience and an important tool in detecting various pathological disorders, ranging from stroke and rehabilitation units to psychology and neuroscience. It is also a promising tool for epilepsy monitoring. Due to the unpredictable nature of epileptic seizures, we need to monitor patients' cerebral activity continuously and over long periods of time, with minimum discomfort for the patients.

Methods:

This paper presents the real-time monitoring software system for a high channel count wearable NIRS-EEG monitoring device. The device has 128 NIRS channels and 32 EEG channels that image the entire adult cortex. The system is capable of recording and real-time display of information for an uninterrupted period of up to 24 hours. The system also allows changes in monitoring parameters in real-time to improve the acquisition quality. In addition, the automatic calibration setting greatly simplifies the process of optode verification and significantly reduces the installation time prior to a test session.The data is processed and displayed as it is received over the Bluetooth connection, as well as being saved for further analysis. A 2D image reconstruction of the hemodynamic variations helps in better visualization of the activity during a task.

Results:

The performance of the real-time aspect of the system was assessed by measuring the time required for the display of the results based on user input. The processing algorithm and robustness of the system was validated based on data acquired in a finger-tapping protocol on 3 patients. The results were compared to those of the nirs10 toolbox (available upon request) [1] developed in-house which is based on SPM8 [2] and NIRS-SPM [3]. The results indicated good correlation, based on the Pearson's correlation coefficient r. The correlation coefficient varied from 0.69 – 0.91 for HbO values and between 0.855 – 0.976 for HbR values. Further 2D image reconstruction of the values indicated a task-related ΔHbO_2 increase during the finger-tapping tapping phase, and ΔHbR decrease during the rest periods.

Conclusion:

The presented real-time software is capable of continuous recording and display of hemodynamic variations. Real-time parameter adjustment and an automatic calibration feature allow for easy and simple customization of the test parameters without interruption. The hemodynamic variations are validated and the activated regions can be verified on a 2D image.

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A New Framework for fNIRS-EEG Fusion in Network Space

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Abstract: fNIRS and EEG measurements are able to reveal the brain activity of multiple functional networks distributed in the cerebral cortex. Identifying network distributions from the complementary neuroelectric and hemodynamic signals are essential to explain the complex interactions among different brain areas. In this study, multimodal functional network connectivity (mFNC) analysis is developed for the fusion of fNIRS and EEG in network space. First, functional networks (FNs) are generated using independent component analysis (ICA) and Granger causality analysis for both fNIRS and EEG. Then fNIRS FNs are employed to help construct EEG FNs in the spatial domain using network based EEG source imaging. Simulation results show that mFNC has the potential to reveal the underlying neural networks of each modality separately and in their combination.

Keywords: fNIRS, EEG, Fusion, Multimodal Imaging, Brain Network.

EEG-NIRS based assessment of neurovascular effects under transcranial direct current stimulation - a stroke case study

Anirban Dutta, Shubhajit Roy Chowdhury, Abhijit Das

Abstract—The paper presents electroencephalography (EEG) - near-infrared spectroscopy (NIRS) based assessment of neurovascular coupling (NVC) during anodal transcranial direct current stimulation (tDCS). Here, anodal tDCS modulated cortical neural activity leading to hemodynamic response which can be used to identify impaired neurovascular coupling functionality leading to impairments of cerebral blood flow that may cause impairments in the cerebral functions. During cortical neural activity, the electric currents from all excitable membranes of brain tissue superimpose at a given location in the extracellular medium and generate a potential, which is referred to as the EEG when recorded from the scalp. Here, neural activity has been shown to be closely related, spatially and temporally, to cerebral blood flow (CBF) that supplies glucose via neurovascular coupling. The hemodynamic response to neural activity can be captured by NIRS, where it provides continuous monitoring of cerebral oxygenation and blood volume. Our prior work showed that tDCS can perturb local neuronal activity which can be used for assessing regional neurovascular coupling (NVC) functionality. It is postulated that tDCS leads to rapid dynamic variations of the brain cell microenvironment that perturbs the hemodynamic and electromagnetic responses. Based on these preliminary studies, we recently proposed EEG-NIRS based screening and monitoring of neurovascular coupling functionality under perturbation with tDCS [1].

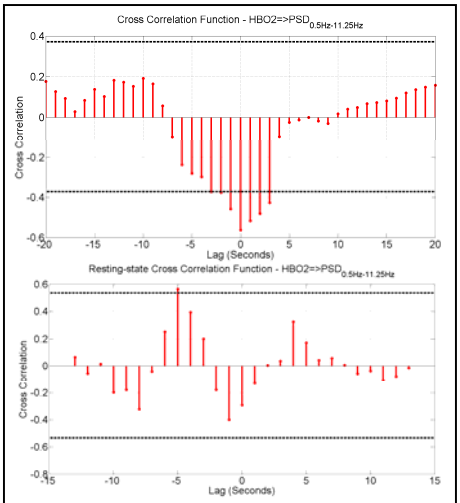

Figure 1: Top row: Cross-correlation function (CCF) between mean (cortical) tissue oxy-(*HbO*2) haemoglobin concentration time-series and averaged PSD time-course from EEG spectrogram. Bottom row: CCF between mean *HbO*2 time-series and averaged PSD time-course from EEG spectrogram of the resting-state (i.e., no task/no tDCS). Dashed lines show 95 percent confidence interval.

Anodal tDCS-induced alterations of the underlying neuronal current generators in the cortical region located under the electrode and in-between the light sources and detectors were captured with EEG while the hemodynamic response was estimated with NIRS. The case study showed detectable changes in the degree of NVC to a 0.526A/m^2 square-pulse (0-30sec) of anodal tDCS [1] where these alterations in the vascular system may result in secondary changes in the cortical excitability. The objective of this case study was to evaluate an empirical method to assess NVC (see Figure 1) using cross-correlation function (CCF) between mean (cortical) tissue oxy-(*HbO*2) haemoglobin concentration time-series and averaged PSD time-course from the EEG spectrogram. The CCF based assessment of the patient-specific status of NVC are currently being studied in a larger cohort with small vessel diseases.

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A multimodal approach to calibrating age-related neurophysiology in a fNIRS study of the semantic words processing

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Functional near-infrared spectroscopy (fNIRS) has found its application into the neuroscience, yet interpretation of data remains a challenge. As a hemodynamic based technique, fNIRS signals are the result of a complex interaction between cerebral blood flow (CBF), blood volume and oxygenation. Moreover, the baseline values of these quantities change with aging in a heterogeneous fashion. In aging studies, the measured hemodynamic response does not merely reflect neuronal activities but also age-related modifications of the above mentioned neurovascular coupling. The importance of meeting this challenge has led us to calibrate fNIRS data by integrating modalities measuring complementary neurophysiological characteristics of individuals. Despite some cognitive decline, older adults show a good preservation of semantic knowledge. Thus, exploring the neural substrates underpinning word processing seems essential to understand how the brain confronts neurobiological declines.

In this study we used a TechEn CW6 system to measure relative changes in oxy- and deoxyhemoglobin concentrations ([HbO_2] and [HbR] respectively). A multi-distance 58-channel helmet containing 10 sources and 28 detectors was made to cover language-related brain regions. One short channel (1.4 cm) on the forehead was included to be used later as a regressor. Two groups of 23 old and young French-speaking individuals were screened for their overall health and cognitive performance. They underwent a lexico-semantic decision task in an event-related paradigm with randomly intermix trials (4s<SOA<11s). A home-made time-resolved spectroscopy (TRS) system was used to measure absolute hemoglobin concentrations of each participant at rest. We acquired anatomical magnetic resonance images for co-registration of the optical channels using the Brainsight stereotactic system (Rogue Research Inc.). An Arterial-Spin Labeling (ASL) sequence was acquired to quantify the individual's baseline CBF at rest.

Both groups performed equally accurately with shorter response times for young adults, except for one lexical condition (p = .017). Group mean comparisons on TRS measures revealed decreased [HbO_2] and oxygen saturation ($SatO_2$) in old adults (p=.0007 and p=.01 respectively). Analysis of ASL revealed a different group average of CBF over the gray matter (p = .02). We applied a factorial ANOVA on fNIRS data over all channels set contrasts from a GLM fit to the HRF with time and dispersion derivatives. We observed an age-related difference at bilateral dorsolateral prefrontal cortex (DLPFC), inferior frontal (IF) and right posterior middle temporal (MT) gyri in Δ[HbR], and right posterior MT and DLPFC in Δ[HbO_2]. From individual activation maps to group analysis, the extent of significant activities was reduced. This observation was interpreted by the lack of precision in co-registration due to the inconsistency in helmet positioning and different form and size of participants' head. To evaluate the impact of this confound, we applied a channel-wise ROI based approach with subjective screening. Including measures of baseline [HbO_2] and [HbR] as regressors to the GLM, we observed a modified frontal age-different pattern of activity by diminished right DLPFC and accentuated IF engagement.

The present study supports the reliability of fNIRS application in word processing whilst exerting caution in the interpretation of data. We showed that when controlling for baseline physiology, the degree and extension of neural activity could vary in some language-related brain regions in old adults. In studies aiming at exploring the age-related functional reorganization, it is thus essential to take into account individual physiological characteristics. In order to compensate for the spatial resolution, ROI approach reinforces the observation of small activation maps for group comparison. The observation of inverted hemodynamic responses amongst young adults demands further attention to the age group analysis.

Comparison of functional near-infrared spectroscopy and electrodermal activity in assessing risk attitude

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Abstract

Excessive or reduced risk-taking behavior can constitute a major problem in people with psychiatric disorders. Individual risk attitude therefore represents an important factor impacting patient's symptom burden or approach to social or individual decision-making.

We aimed to quantify individual risk attitude using a methodological combination of functional near-infrared spectroscopy (fNIRS) and electrodermal activity (EDA). fNIRS measures cortical hemodynamic responses associated with neural activity and has so far not frequently been applied in decision-making research. EDA represents a core measure of peripheral affective processes and is a well-established method in decision-making research.

Twenty healthy subjects were investigated during performance of a financial risky decision-making task in which they were asked to make decisions between either a high or low risk option or a safe (risk-free) option. Results revealed that fNIRS signals over lateral prefrontal cortex correlated negatively with individual risk attitude, i.e., fNIRS signals were enhanced in response to high compared to low risk in risk-seeking individuals, but reduced in risk-averse individuals. This is in-line with individual-specific risk processing reflecting the subjective value of risk. By contrast, EDA showed enhanced responses to high compared to low risk independent of individual risk attitude, in-line with the notion of objective risk processing. Thus, the dissociation observed between fNIRS and EDA suggests that this methodological combination could provide a measure of both the subjective value of risk (fNIRS) and the objective amount of risk (EDA) people are presented with.

From a clinical point of view, these findings suggest fNIRS as a useful method for studying risk behavior that may in the long-term, represent a faster, more cost-effective and less physically demanding method, which could be taken beyond controlled laboratory settings into clinical practice, especially in conditions unsuitable for routine fMRI such as in psychiatric populations.

Keywords: Decision-making; risk attitude; lateral prefrontal cortex; coherence analysis.

Dynamic functional connectivity during resting-state assessed by functional near-infrared spectroscopy and capnometry

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Abstract

Traditional studies investigating resting-state are based on the assumption that functional connectivity (FC) in neural networks is static over time. However, recent studies begun to capitalize on the phenomenon that FC changes over time, thereby focusing on the temporal features of dynamic FC (DFC).

We present data of a pilot study investigating DFC based on cortical hemodynamics during resting-state as assessed by functional near-infrared spectroscopy (fNIRS). Respiration related changes in partial end-tidal carbon dioxide ($PetCO_2$) were assessed using capnometry. Ten healthy subjects were recorded during four experimental condition: resting-state (RS) (20 min), eyes opening (EO) (5 min), hyperventilation (HV) (5 min) and breath holding (BH) (5 min). Data analysis included the calculation of block averages as well as functional connectivity measures, i.e., wavelet transform coherence, and causal connectivity measures, i.e., Granger causality.

Preliminary results reveal 1) the presence of time-varying characteristics of DFC in prefrontal hemodynamic during resting-state that are pronounced in the very low frequency range, and 2) the presence of respiration related variations in terms of a directional coupling between $PetCO_2$ and hemodynamic responses. Together these data may give additional insight into the intrinsic fluctuations in cortical hemodynamics during resting-state and its relationship to $PetCO_2$ reactivity. In the long term, these investigations aim to establish fNIRS as a useful method for routine assessment of DFC during resting-state, such as to monitor disease related alterations in neurological or psychiatric populations.

Keywords: dynamic functional connectivity; resting-state; partial end-tidal carbon dioxide; coherence analysis; Granger causality.

Functional Imaging of Preterms Neuronal and Hemodynamic Syllabic Responses by Using high density EEG and NIRS

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Many studies have investigated the development of language and the various neural networks involved in either language production or the information integration process that are prerequisites for developing language abilities. The electrical and hemodynamic coregitration open a new field of interest for the understanding of neurophysiological phenomena such as those which underlie language processing. This task can only be successfully addressed by applying various assessment techniques integrated into a multimodal approach. Methods such as EEG–NIRS coregistration, combining high temporal and spatial resolution, may offer unique opportunities for studying functional activity in linguistic experiments. We report on the use of functional optical imaging approaches and EEG to evaluate the cerebral responses to language stimuli in preemies. In this age range the brain is still under development, and at the earliest age at which cortical responses to external stimuli can be recorded in humans (28-32 weeks gestational age) many neurons are still migrating and thalamo-cortical afferents establish transient connections with the sub-cortical plate. Measurements were performed in healthy preterm neonates using NIRS and EEG. We observed that the immature brain can already discriminate a change of phoneme and of voice (male/female). The perisylvian networks are similar to those involved later in development. Thus, particular cortical regions, critical for language acquisition and processing, support language-specific representations in very early infancy. In addition, we observed that regular auditory stimulation elicited stable and successive topographies implying a temporally ordered succession of coherent neural sources. ERPs adapted to repetition of the same syllable and reacted to a change of consonant (ba vs ga).

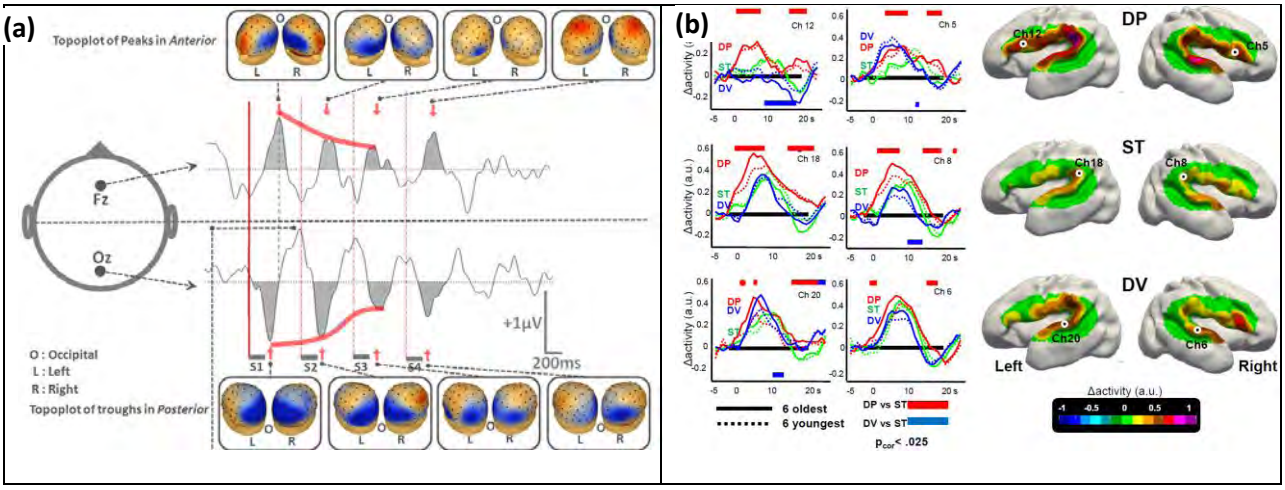

Fig.1: (a) Grand average topoplots, the evoked response to each syllable (S1,S2,S3,S4) induced a positive peak of response around 340 ms (mean peak latencies to S1,S2,S3,S4; 344, 336, 310, 343 ms, respectively) in frontal areas and negative trough in parieto-occipital in premature infants. (b) Discriminative responses to auditory stimuli in premature infants. On the right, surface-based topographic color map of the HbO response at the peak of the hemodynamic response for the three conditions and on the left, HbO time-courses for the youngest and oldest subsets of 6 infants, recorded over left Broca's area (ch 12), left planum temporale (ch 18), left superior temporal gyrus (ch 20) and their counterlateral right channels (ch 5, ch 8 and ch 6, respectively). The colored rectangles indicate the time-windows during which the deviant conditions differ significantly from the standard condition using cluster-based statistics over the whole group. The direction of the effect is given by the location of the bar under or above the x-line.

Neurovascular coupling in preterm neonates with Intra-Ventricular Hemorrhage: Combined high density EEG-NIRS study

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Can we detect auditory neurovascular impairment during the early phase of infancy? Continuous measurements during sleep were performed in healthy (n=12) and Intra Ventricular Hemorrhage (IVH grade III & IV, n=7) preterm neonates (28-32 weeks GA) using functional Near-Infrared Spectroscopy (fNIRS) in conjunction with EEG. We have shown that the preterm brain is able to discriminate a change of phonemes (ba vs ga) and a change of voices (male vs female) (Mahmoudzadeh, 2013). The dynamic of the responses reveals a structured network evolving differently in time and space (temporal/frontal lobes areas, left/right hemispheres). The study described here aims also to investigate the impact of the IVH on auditory hemodynamic responses. While EEG disclosed active language neural network, fNIRS revealed much weaker auditory hemodynamic responses, showing neurovascular coupling impairment. The present data confirm the existence of neurovascular coupling in healthy premature brain. It also shows that IVH premature neonates have lack of local mechanisms that allocate blood oxygen and to the active neurons. These results demonstrate that particular regions of the cortex, critical for language acquisition and processing, contain innate language specific representations in early infancy. In addition, the approaches we developed provide early diagnosis of auditory neurovascular coupling impairment in IVH preterms which is known to induce learning disabilities.

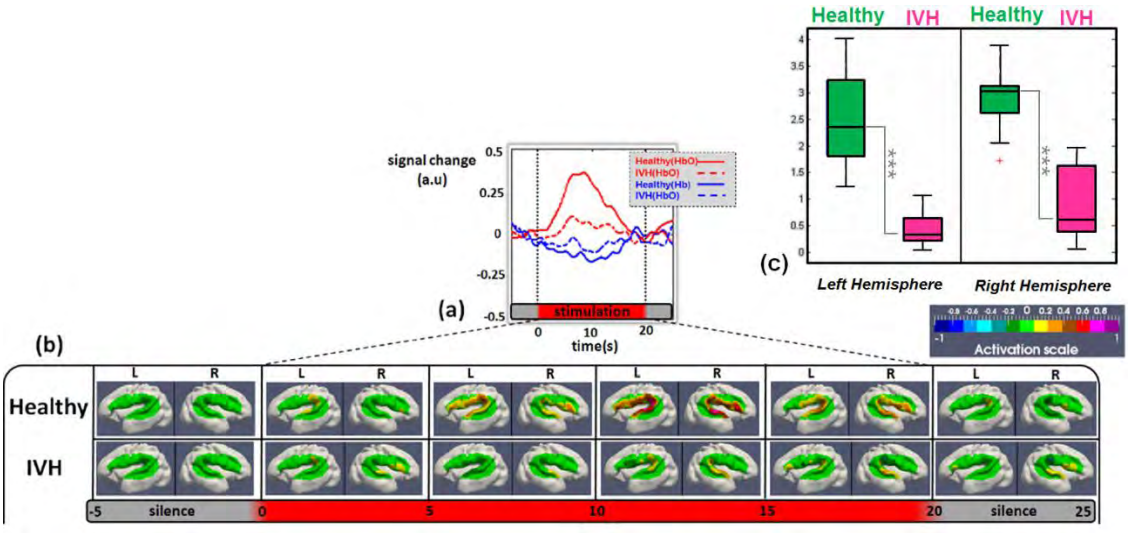

Figure (1): *(a) Shows an example of grand-average NIRS channel HBO (red lines), Hb (blue lines) for healthy newborns (solid lines) and IVH (dashed lines) for auditory stimulation. The thick horizontal red bar indicates the period of stimulation (20 seconds). This response is more pronounced for healthy newborns, with a significant increase in the HBO signal. (b) Mapping of activations HBO signal in time. (c) comparison between healthy subjects and IVH, mean changes (AUC) of oxy-hemoglobin induced by auditory stimulation. For each hemisphere, activations in IVH group were significantly lower than those on healthy subjects.*

Neurovascular coupling and Hemodynamic responses of the somatosensory and auditory rat cortex

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The nature of the coupling between the hemodynamic signal and electrical activity of the brain is still under debate. However, optical imaging does not measure neural activity per se; rather, it measures the changes in concentration of blood oxygen in the tissue which is associated with changes in brain neural activity. This complementary method with higher temporal resolution (rather than fMRI) has been used to investigate the hemodynamic basis of neuronal activity in human and animals in more detail. In our study, spectroscopic optical measurements of hemoglobin oxygenation were performed simultaneously with electrophysiological recordings (ECoG) [n=14 rats]. We used electrical forepaw and auditory stimuli which are two robust paradigms for studying neurovascular coupling. For probing the somatosensory and auditory cortex, a special electroptode® was designed to hold the emitter/detector fibers and electrodes to fit to the small skull of the rat. The hemodynamic responses are characterized by an *initial dip* followed by an increase in total hemoglobin (tHb), an increase in oxyhemoglobin (HbO) concentration with a peak latency of 5 to 6.5 sec after stimulus onset. A decrease in deoxyhemoglobin (Hb) occurred simultaneously. Our electro-optico-cortical imaging setup presently used is efficient to obtain specific responses according to the stimulus modality used in term of the location of the area being activated. In addition the results show that somesthetic vs auditory, give different electrical and hemodynamic responses in terms of pattern but also in terms of location. The respective localization fits well with auditory and somesthetic areas in rats.

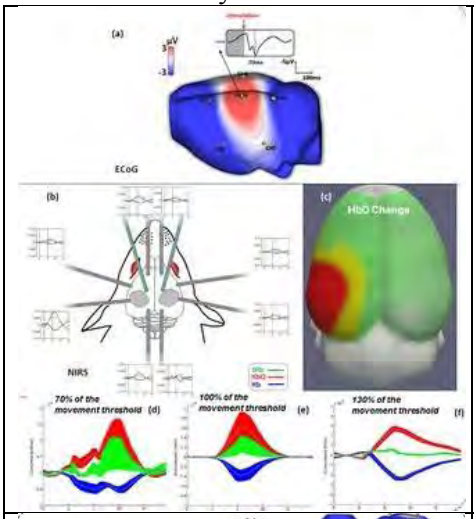

Figure 1: Rat Somatosensory response (a) ECoG signal of the response peak 70ms after onset of the electrical stimulation of right forepaw in one sample rat and topographical mapping on a rat headmodel (extracted from rat MRI) b) Grand average over 10 rats, cortical hemodynamic response time series for 5 s stimulation. Topography map of HbO activation Mean cortical hemodynamics in response to sensory stimuli as measured by optical imaging spectroscopy. Changes in Total Hemoglobin(tHb,green), oxyhemoglobin(HbO,red) and deoxyhemoglobin(Hb,blue) following application of electrical forepaw stimuli of 5 s, 3Hz and 70%, (e)100%, (f)130% of the movement threshold, (Note that tHb was calculat ed as the sum of Hb and HbO).

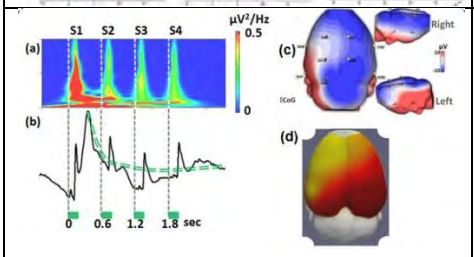

Figure 2: Rat Auditory response, Habituation in amplitude and power spectrum of one ECoG channel .(a) power spectrum of AEP. (b) AEP trace in response to each trial (Green bars). (c) ECoG topography map of the S1 response peak (360ms) after onset of auditory stimulation in one sample rat (d) Topography map of HbO activation.

Fast Optical Signal Changes in Penicillin-Induced Generalized Spikes in Animal Model

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Because Electrocorticogram (ECoG) evaluate electrical changes and fast optical signal (Fast NIRS) evaluate changes in membrane configuration due to neuronal activation, we investigated the simultaneous changes in electrical and membrane configuration occurring during hypersynchronisation and neuronal activation that characterize epileptic interictal spikes, using a combined simultaneous ECoG/Fast NIRS approach in a model of epileptic rat.

18 male/female rats were prepared under urethane anesthesia. Three craniotomy holes were drilled on each side 0.25 mm apart from the midline. The penicillin was injected in the right ECoG position.

The ECoG signals were recorded with 1024 Hz sampling rate and Optical signals used two wavelengths (690 and 830nm)with a frequency-domain spectrophotometer (Imagent®,ISSInc).

Optical signal was filtered (3-30Hz) and normalized. ICA was used to reduce heart beat artifact. A maximum likelihood clustering method clusters components in frequency domain into two clusters (with/without artifact). Then the component with artifact was removed and a new signal was reconstructed with the remaining components. Epileptic spikes are detected after pre-processing of the ECoG data with a 3 to 15Hz band-pass filter. The epochs (-1280 / +1280ms) around the peak of the spikes were selected from NIRS data. Finally, the epochs surrounding the spikes were averaged.

The fast optical signal showed a triphasic response, nearly in mirror to that of the epileptic spike. A first relatively small increase in intensity of optical signal occurred together with a positive component in ECoG signal, preceding the synchronization of neurons characterized by a large negative component in ECoG simultaneously to a large decrease in intensity of optical signal. This is followed by the last decrease in fast optical signal which occur simultaneously to a positive peak in ECoG. It should be noted that for both ECoG and Fast NIRS the first and the third component are very symmetric.

This constitute the first study which, using simultaneous recording of ECoG and Fast NIRS, allows to detect the changes in scattering properties of the cerebral cortex occurring simultaneously to the neuronal hypersynchronisation of epileptic spikes. This suggests modification in neuronal and/or glial membrane configurations that occur around cortical activation. Also Fast NIRS can show some neural activity before spike (300 ms before spike) that ECoG is blind to detect it.

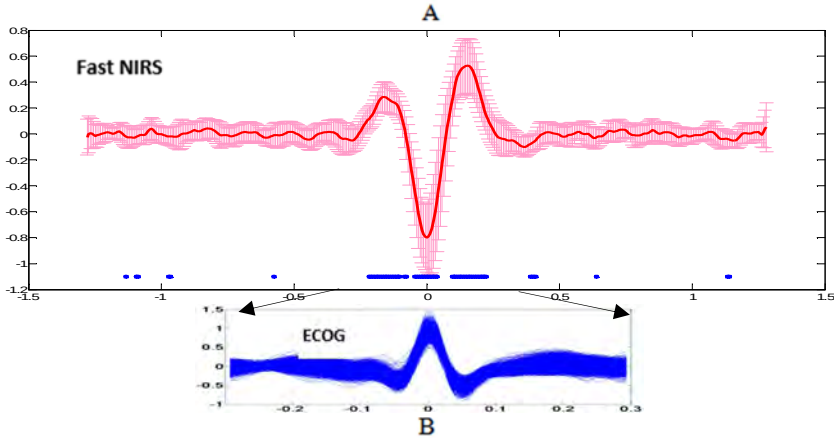

Fig.1. (A) Grand average spike-related optical signal response (n=14). Bold line shows grand average. Errors bars show standard Errors deviation for the corresponding signals at each time point. (B) Super imposed spikes in ECoG. The horizontal axes shows time in second,"0" second shows the time of max-peak in ECoG spike and the vertical axes shows intensity changes(Au) in (A) and amplitude of the signal(µV) in (B). Blue Triangles in (A) designate time bins with significant difference of responses from baseline (t-test, $p<0.04$).

Hemodynamic changes preceding interictal spike development in GABA disinhibition model of epilepsy in adult rat: electrocorticography and near-infrared spectroscopy study.

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Last decades neurovascular coupling have been largely studied by brain imaging techniques but still has many unclear spots, particularly, the fact that hemodynamic changes precede the electrical one needs to be investigated and is actually highly debated because of its unclassical view on the relationship between neurons and supporting vascular system. The goal of this study was to study the hemodynamic pattern during acutely evoked interictal spike activity in rat's cortex. Experiments were performed on 23 adult Sprague-Dawley rats anesthetized by intraperitoneal injection of urethane. Epileptiform focus was created by local injection of penicillin G (14 rats) or bicuculline methiodide (9 rats) in left somatosensory cortex. We analyzed the oxyhemoglobin (HbO), deoxyhemoglobin (HbR) and total hemoglobin (HbT) levels around the isolated well-shaped spikes. The main results are that the hemodynamic changes starts about 2 s before the spikes and get to baseline about 5-10 s after the spike appearance. The shape of hemodynamic changes was similar in all rats. Pre-spike decrease in HbO/HbT and increase in HbR reflect an increased local activity – neuronal and/or non-neuronal – even before the time when synchronization of neurons becomes enough strong to be detected by ECoG. In post-spike period the hemodynamic changes correspond to classical view of neurovascular coupling (increase in HbO/HbT to get more oxygen and glucose to the region) with recovery to baseline. Bicuculline and penicillin are GABAa receptor inhibitors – competitive and non-competitive, respectively. On the GABAa receptor site they interact by different mechanisms but resolve the same task – inhibition of the chloride flow in chloride channel of the GABAa receptor. We suggest that in GABA disinhibition model of acute epileptiform activity the hemodynamic changes play a crucial role in local neuronal and/or non-neuronal activity which underlie and support the neuronal synchronization and spike development with later energy supply of activated foci.

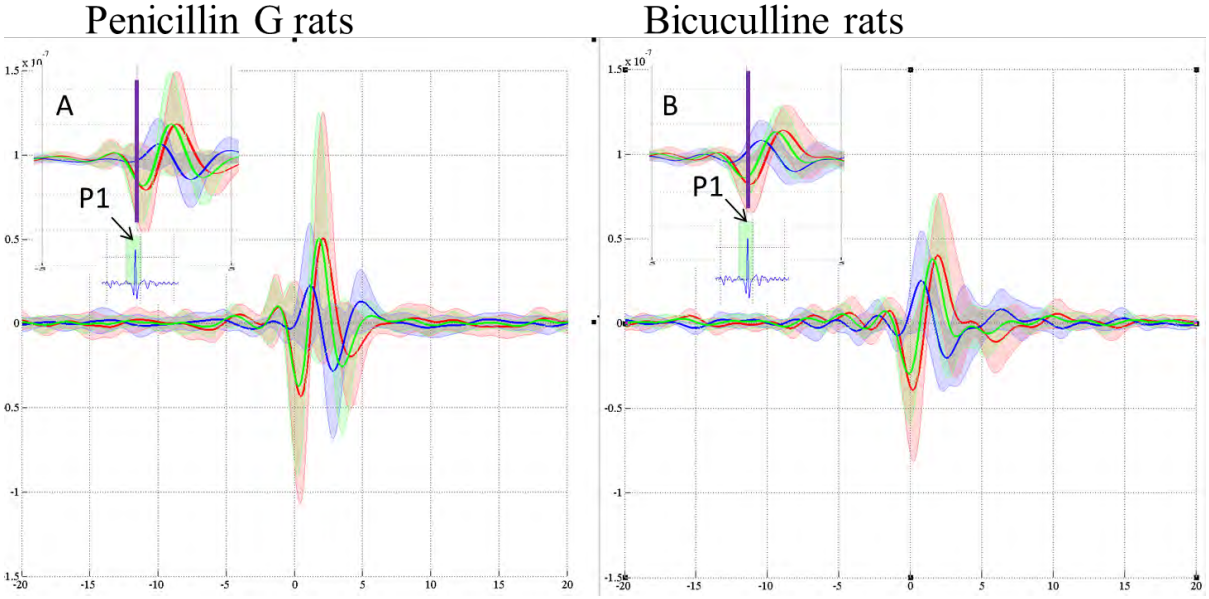

Figure 1 : Grand average with standard deviation: HbO – red, HbR – bleu, HbT – green; Y-axis – molar concentration, X-axis – time in seconds; P1 – peak of spike (zero on X-axis). Windows A and B: examples of synchronization of ECoG to NIRS data (time -5 s to 5 s to P1); Distance between two vertical dotted lines on ECoG image (below in windows A and B) is 1 s.

Simultaneous fNIRS-EEG recordings during infantile spasms :

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To investigate cortical hemodynamic changes occurring around infantile spasms, Functional Near InfraRed Spectroscopy (fNIRS) was performed with simultaneous video/electroencephalography (EEG) and EMG (bilateral deltoid muscles) monitoring.
A multichannel patch with 4 coupled emitters and 1 detector fiber was designed and positioned, over the frontal area in patients with heterogeneous etiological and electro-clinical spasms. The onset of deltoid EMG contractions was considered as the beginning of the spasm.
In all the patients, fNIRS data demonstrated Cerebral Blood Volume (CBV) changes (simultaneous changes in HbO and HbR) in the frontal area, beginning before the spasms as defined by the onset of EMG contractions. This occurred whatever the etiology of the spasm and thus suggested that these hemodynamic changes were diffuse. They were inconsistently followed by a typical neurovascular coupling (opposite changes in HbO and HbR). Such frontal results suggested a rather diffuse cortical activation.
The initial CBV changes, before the spasms and before any EEG modifications occurring even in patients with diffuse anoxo-ischemic lesions is in agreement with the involvement of subcortical, notably brainstem, structures in the elaboration of each spasm sustained by a motor program. The following neurovascular coupling which was inconstant is in agreement with a secondary diffuse cortical activation.
Taken together our results suggest a fine interplay between the vascular and the neuronal system with a complex vascular sequence involving changes in CBV together with neurovascular coupling.
EEG-fNIRS data highlighted this complex interaction between sub-cortical and cortical structures with a prominent role for subcortical structures.
The mechanisms that trigger the cluster of spasm will be discussed.

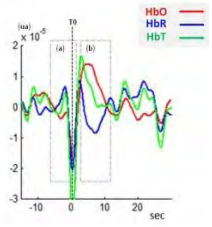

Figure 1: Spasms hemodynamic response characterized by
(a) : First: a decrease in cerebral blood volume (CBV) which beginning before the spasm
(b) : Second : a typical neurovascular coupling following the CBV changes

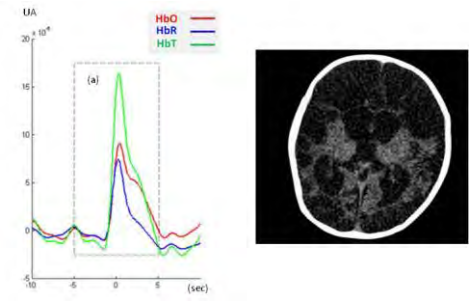

Figure 2: Spasms hemodynamic response in a patient with diffuse anoxo-ischemic lesions (cf cerebral CTscan on the right)
Hemodynamic response was characterized by a change in CBV only, without any neurovascular coupling. Note that the CBV changes started before the spasm

Hemodynamic Response Patterns During Sleep
- a concurrent time-domain fNIRS/EEG study in adults -

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Human sleep is associated with profound changes in consciousness and information processing (1). Different sleep stages are shaped by cyclic inhibition of thalamo-cortical neurons resulting in distinct sleep oscillations (2). So far, little is known about the hemodynamic response associated with functional stimulation during sleep. In this study, we investigated the nocturnal sleep during an entire night (~11pm to 8 am) and the influence of visual stimulation during different stages of sleep by combined time-domain functional near-infrared spectroscopy (td-fNIRS) and electroencephalography (EEG) in 7 healthy adult subjects.

Binocular goggles equipped with two light-emitting diodes allowed long-term 8 Hz flicker light stimulation with closed eyes. Flicker light trains and subsequent off-periods continuously altered (30 s stimulation followed by 30 s rest interval) throughout the night sleep. Before subjects were explicitly allowed to sleep, they perceived 10 repetitions of flicker light trains (awake pre sleep session). EEG was recorded from 13 standard positions according to the 10–20 system (Fp1/2, F3/4, Fz, C3/4, Cz, P3/4, Pz, O1/2).

The hemodynamic signals were measured by a time-domain NIRS system (3) with four detection channels. The optodes (one source and four detectors) were attached to the right occipital region around electrode position O2. The time courses of (cerebral) changes in oxy- and deoxyhaemoglobin concentrations (HbO, HbR) were derived from changes in variance of the measured time-of-flight distributions that is known to be preferentially sensitive to deep absorption changes.

From the off-period EEG recordings slow wave sleep (SWS) stages: S1, S2, S3/4, and rapid eye movement (REM) sleep were visually scored by an independent, experienced neurologist according to the criteria of (4). Time courses of HbO and HbR of the same sleep state were averaged and mean baseline activity (-4 s to -2 s) was subtracted to obtain stimulation-related concentration changes. For further analysis, the NIRS channel with the largest response was selected for each subject. Mean values in the interval from 10 s to 40 s after stimulus onsets were tested for deviations from zero using non-parametric permutation tests (5). The following results are related to the mean over all 7 subjects.

Flicker light stimulation during wakefulness induced the typical stimulus related hemodynamic response in the visual cortex, characterized by a significant increase in HbO and a significant decrease in HbR compared to baseline. The response during S1 sleep was similar. However, the magnitude of the hemodynamic response gradually decreased with the depth of the SWS stages and showed a reversed response pattern, possibly indicating a ‘deactivation’ for sleep stages 2 and 3/4. During REM sleep, the hemodynamic response essentially vanished.

To the best of our knowledge, this is the first concurrent fNIRS-EEG study exploring the stimulus-related hemodynamic response during different stages of sleep. These results suggest that primary cortical areas are deactivated during deep sleep. A more detailed investigation of the relationship between electrophysiological and hemodynamic changes will follow.

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Investigation of the neurovascular coupling from simultaneous fNIRS-EEG system using the triplet holder

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Introduction. Individual imaging techniques provide only limited information about neurovascular coupling due to the complexity of the relationship between neural activity and localized vascular response. In order to make further progress, multimodality approaches are needed, which combine the advantages of individual techniques (e.g. high temporal resolution of EEG) and mitigate their limitations (e.g. volume conduction). We have studied the feasibility of using an fNIRS-EEG system to investigate neurovascular coupling by placing probes on the scalp which are integrated into a set of triplet holders. We analyzed the synchronized signals over the whole head in order to elicit relationships between the electrical and hemodynamic activity in cortex during task-dependent and resting states.

Methods. EEG data were acquired from three healthy young adults, using a sampling rate of 250Hz with a wireless data acquisition system (Bio-Signal Group Inc., Brooklyn, New York). Simultaneous fNIRS measurements were acquired with the NIRScout extended system (NIRx Medical Technologies, New York) with a sampling rate of 7.81Hz. At 16 clinically relevant standard 10-20 locations, an EEG electrode was placed between a NIRS source detector pair separated by 3cm. All probes were held together by a new version of our thin plastic triplet holder. Each experiment lasted 15 minutes while the subject was under an eyes-closed resting state or performing Verbal Fluency task. Optical signals were converted to oxy- and deoxy-hemoglobin concentrations (HbO and HbR) using the modified Beer-Lambert law. We performed principal components (PC) analysis on the signals to generate activity maps, and selected a subset of channels that were dominant in the most active PC. The time lagged correlations between EEG band power and the concentrations of HbO and HbR were computed.

Results. In the EEG gamma band as well as Hb concentrations, the PC with highest variance was dominated by the temporal and frontal regions represented by the sites T3, T4, F7, F8. Fig. 1 shows the time lagged correlation between the EEG and the concentrations of HbO (red) and HbR (blue) averaged over these sites. We found that EEG power in the gamma frequency range correlated strongly with hemodynamics following the activation pattern in the figure. The correlation was smaller in the beta band and insignificant in the other bands. Similar results were obtained from the task performance experiments.

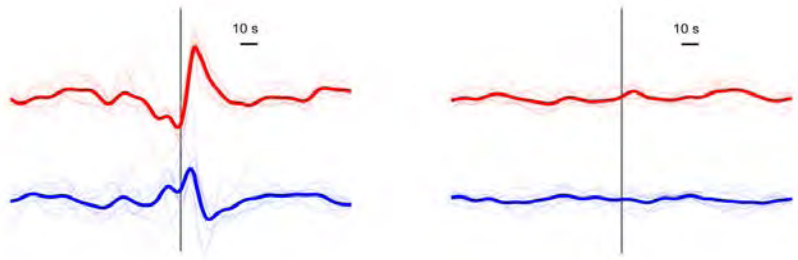

Fig. 1. Lagged correlation of oxy- (red) and deoxy-hemoglobin (blue) concentrations with EEG band power at the sites T3, T4, F7, F8 in the resting-state experiments. The vertical lines shows the location of zero time lag. EEG power in the 30-70Hz (gamma, left) and 8-12Hz (alpha, right) band are shown. The thin curves indicate individual channels and experiments, while the thick curves are averages over the corresponding thin curves.

Conclusion. Simultaneous whole head fNIRS-EEG recordings provide a promising technique for studying neurovascular coupling and its relationship with pathological brain physiology.

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Diffuse optical tomography using optimal optode montage dedicated to study epileptic discharges.

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Rationale: Functional near-infrared spectroscopy (fNIRS), acquired simultaneously with electroencephalography (EEG), allows the investigation of hemodynamic brain responses to epileptic activity [1]. Because the presumed epileptogenic focus is patient-specific, an appropriate Source/Detector (SD) montage has to be reconfigured for each patient. Using a linear integer programming model, we presented a method for computing an optimal SD montage with a limited number of sources and detectors on an EEG/fNIRS cap that maximizes the spatial sensitivity on one or several specific brain regions [2]. We observed that optimal montages yielded improved spatial density of fNIRS measurements over the targeted regions together with an increase in signal-to-noise ratio of the measured signals. Contrary to topographic imaging which suffer from poor quantitative accuracy due to unknown partial volume effects, Diffuse Optical Tomography (DOT) can provide accurate estimates of the internal distribution of absorption changes (Δμa). However, as an ill-posed inverse problem, DOT requires overlapping sets of measurements taken near the activated cortical region and prior spatial information. Therefore, we hypothesize that the optimal montages are well adapted for DOT and allow solving the ill-posed inverse problem more accurately.

Methods: We simulated realistic $\Delta\mu a^{830nm}$ signals (30s duration) in 20 spherical Volumes Of Interest (VOI) at different locations in the gray matter of an anatomical head model. We also simulated realistic physiological noise (cardiac, respiration and Mayer waves) in the superficial layers of the head model at different amplitudes in order to generate realistic optical density changes on the scalp at different signal to noise ratios. The forward model was calculated using Monte Carlo simulations [3]. For each VOI, two EEG/fNIRS arrangements were evaluated. For both arrangements, 8 light sources and 16 detectors were distributed on a subset of the international 10/05 EEG positioning system. The first arrangement was an optimal montage [2], the second was a regular montage with sources and detectors positioned in alternating coronal rows above the VOI. The tomographic inverse problem was formulated using a depth weighted restricted maximum likelihood model [4] using the Euclidean distance of each voxel to the skin. The reconstruction was constrained in the gray matter. $\Delta\mu a^{830nm}$ tomographic maps were thresholded at 25% of the amplitude of the simulated activity. We evaluated the tomographic reconstructions for the two arrangements using metrics to quantify the spatial accuracy and extent of the reconstructed activity. The quantitative accuracy of the reconstructions and the presence of physiological noise in the reconstructed responses were also evaluated.

Results: 1) Independently of the simulated signal to noise ratio, we found that the proportion of reconstructed voxels in each VOI (spatial sensitivity) was larger for the optimal arrangements. In addition, the deviance index, which measures the dispersion of the reconstructed activity outside the VOI, was smaller for the optimal montages. 2) Quantitatively, the difference between the mean amplitude of the reconstructed $\Delta\mu a^{830nm}$ signal (averaged over all voxels in each VOI) and the mean amplitude of the simulated $\Delta\mu a^{830nm}$ signal (0.06 mm^{-1}) was smaller for the optimal montages. 3) After performing the regression of the simulated $\Delta\mu a^{830nm}$ signal from the noisy reconstructed signal in each VOI, we evaluated the power ratio between the noise free estimated signal and the power of residuals representing mainly the contamination from physiological interferences. This ratio was larger for the optimal montages meaning that they were less sensitive to physiological noise.

Conclusions: We found that the tomographic maps of optimal SD montages had better spatial properties than regular arrangements. With optimal montages, most of the activity was captured in the original VOIs and the remaining activity was reconstructed in their vicinities. In addition, we observed that optimal montages yielded better quantitative accuracy and were less sensitive to the physiological noise coming from superficial layers of the head. We intend to validate these affirmations on finger tapping experimental data.

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How does fNIRS compare with fMRI to study cognitive tasks?

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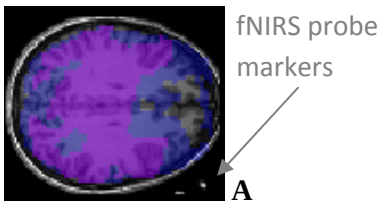
Introduction Functional MRI (fMRI) has been recently used in various neuroscience studies in aging populations. fNIRS could provide a portable, low-cost alternative to fMRI, in particular for elderly people, with easier access to the scalp due to finer hair. However, obtaining statistically interpretable results with fNIRS, comparable to those in fMRI, is still a field of research. This study aimed to compare the hemodynamic response to a cognitive task between age and fitness groups using fNIRS and fMRI.

Methods Forty-two healthy adult right-handed volunteers participated in this study, divided in two age groups: 19 young adults (10 females, 18-30 years-old, mean age 24.4 ± 2.5) and 23 older adults (16 females, 62-72 years-old, mean age 67.6 ± 2.9). They (except 2 subjects) were classified into high-fit (N = 8 young, 10 old) and low-fit (N = 9 young, 13 old) groups based on their VO_2max.
A continuous wave NIRS system (CW6, TechEn Inc., Milford, MA, USA) with two wavelengths (690 and 830 nm) was used. The probe was positioned over the left prefrontal cortex, with two rows of 4 detector fibers bordering one row of 4 source fibers, with a source-detector distance of 2.5 cm.
The subjects responded to a 2-color modified Stroop task with conditions Congruent, Incongruent and Switching. The event-related design for each of 3 sessions comprised 15 trials of each condition separated by 5-23 s.
fNIRS data was analyzed in Matlab (The MathWorks, Natick, MA), using the nirs10 toolbox, based on SPM (Wellcome Trust Centre for Neuroimaging,) and NIRS_SPM (Bio Imaging Signal Processing, KAIST, Korea) with additional modules for ANOVAs.
During with the fNIRS acquisition, the subjects were inside an fMRI scanner (Siemens Trio 3T) and BOLD contrast (TE/TR/α = 30/1010/60) was measured during one session. The position of the fNIRS probe was indicated in fMRI scans by vitamin markers. SPM8 was used for preprocessing and statistical analysis of the fMRI data using standard preprocessing.
For both modalities, statistical comparison of the age and fitness groups was done using a 2-way ANOVA with factors Age (Fitness) and Condition of the Stroop task. F-statistic maps were thresholded at a significance threshold of 0.05, corrected for multiple comparisons (family-wise error). The uncorrected maps were also examined.

Results fMRI revealed regions where the BOLD contrast was higher in older and in lower-fit subjects, in regions overlapping with the fNIRS probe, as shown in Fig. 1A (main effect of age, purple: p>0.05 FWE, indigo: p>0.05 uncorrected). fNIRS contrasts HbO and HbR also revealed age and fitness differences, however these were not statistically significant when using a corrected threshold. Fig. 1B shows the uncorrected F-map for main effect of age for HbO. The regression of fMRI time courses in fNIRS data or vice-versa also yielded mitigated results.



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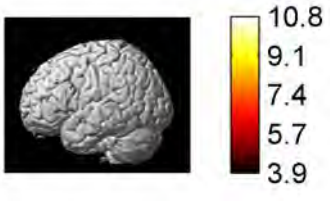

B

Conclusion Our results suggest that fNIRS is less sensitive (but could be more spatially specific) than BOLD-fMRI for studying cognitive tasks. Advanced preprocessing techniques might be necessary to improve the power of fNIRS.

Diffuse Optical Spectroscopy Measurement Of Cerebral Hemodynamics And Oxygen Metabolism During Anesthesia-Induced Burst Suppression In Rats

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Burst suppression is a state operationally defined by a spontaneous, global EEG activity consisting of quasi-periodic intervals of activity and quiescence. This state can arise naturally in pathological conditions such as hypothermia and coma or can be induced by deep levels of general anesthesia. The potential harms or benefits from entering or remaining in a state of burst suppression are not understood and the basic mechanisms which initiate and sustain burst suppression have not been established. While EEG patterns of burst suppression are well known, the underlying cerebral metabolism during burst suppression has been less investigated but has been implicated in the mechanism driving neuronal activity.

Using near infrared spectroscopy (NIRS) and optical diffusion correlation spectroscopy (DCS), we are able to measure, in a non-invasive manner suitable for both humans and animals, changes in cortical oxy- and deoxy- hemoglobin (HbO and HbR, respectively) and cerebral blood flow (CBF) synchronously with EEG activity as bursting occurs. Burst-related hemodynamic changes were measured in rats as a range of isoflurane concentrations were used to modulate cortical electrical activity from continuous activity under low anesthesia to fully isoelectric EEG under deep anesthesia, with various levels of burst suppression occurring in between. The measured changes in hemoglobin concentrations were used to estimate the oxygen extraction fraction (OEF), which, together with the CBF measurement, was used to calculate cerebral metabolic rate of oxygen ($CMRO_2$).

At moderate isoflurane concentrations (~2%) a clear burst suppression pattern is observed in the EEG activity and the cerebral hemodynamics (Fig. 1, top). In contrast, at low anesthetic concentrations (~1%), both EEG and hemodynamics show high activity, while at high concentrations (~3%) EEG activity is isoelectric and there is little variation in hemoglobin concentration or cerebral blood flow. These patterns of activity are reversible with isoflurane dose.

The quasi-periodic burst activity generally occurs more rapidly than hemodynamic recovery, leading to overlapping hemodynamic responses. In the case of the overlapping responses, we recover burst-associated hemodynamic and oxygen metabolism response functions by deconvolution (Fig. 1, bottom) and found them to be similar to the response observed in isolated bursts.

Burst suppression hemodynamic responses appear similar to evoked responses. Oxygen metabolism during bursts has similar magnitude to the metabolism during functional stimulation and flow-metabolism coupling is also similar. Importantly for the mechanism, we do not observe changes in oxygen metabolism before bursts nor find the cerebral oxygen supply to be limiting, despite the synchronized global activity across the brain during bursts.

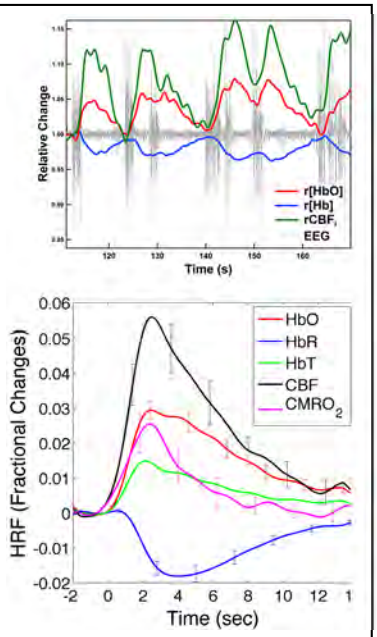

Figure 1. EEG, hemodynamics and cerebral oxygen metabolism during burst suppression.

Optical spectroscopy is sensitive to anesthetic-induced changes in cerebral metabolism. The fully non-invasive nature of these techniques allows their use for both basic studies of pathophysiological mechanisms in animal models and clinical monitoring applications in human patients.

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In-vivo measurement of cerebral metabolic rate of oxygen consumption in mouse brain using multimodal MR and near-infrared spectroscopic imaging

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Purpose: To utilize multimodal near infrared spectroscopy (NIRS), arterial spin-labelling MRI (ASL-MRI) and photon transport modelling to measure the cerebral metabolic rate of oxygen consumption ($CMRO_2$) in mouse brain for the first time, enabling the future study of $CMRO_2$ in animal models of neurodegenerative disorders, including the EAE mouse model of multiple sclerosis.

Methods: C57BL/6 mice (n=4) were spontaneously ventilated with 3% isofluorane, 30% O_2, and 67% N_2. Breathing, heart rate and temperature were all monitored and kept as constant as possible. CMRO2 is calculated using the Fick principle, given by $CMRO_2 = 1.36(\mathrm{ml}\cdot\mathrm{g}^{-1})\times CBF\times(S_a - S_v)\times[tHb]$. Cerebral blood flow ($CBF$) is obtained with ASL-MRI; S_a is arterial blood saturation and is obtained through pulse oximetry (MouseOx Plus, Starr Life Sciences); S_v is venous blood saturation and is calculated from NIRS data; and $[tHb]$ is total hemoglobin concentration, also obtained with NIRS. Arterial spin labelling data was collected with a 9.4T Bruker animal MRI system using the Bruker Avance II console, an CASL HASTE sequence and a spin-tagging plane through the carotid artery, matrix dimensions of 128 x 128 pixels, FOV=3cm, TE=2.66ms, TR=3000ms. The arithmetic difference between two 'tagged' and two 'control' images were used for the perfusion-weighted images. NIRS data was obtained by transmitting broadband light through fibre optics onto the dorsal skull and collecting via another fiber placed 6mm laterally into a spectrometer (Shamrock i303, Andor Technology Inc.), where it was digitized with a CCD camera (iDus, Andor Tech.). Data was processed using an in-house MATLAB (Mathworks Inc.) software package based on a second-differential spectrum least-squares fitting algorithm[1], giving [Hb] and [tHb]. To determine regions of the brain that were contributing to the NIRS signal, transport of NIR light in skin, skull and brain tissue was modelled using a finite element mesh derived from an MR image of a mouse in the NIRFAST software package[2] and ROIs were placed in the centre of the light path. The MR image was obtained with a helium-cooled low-noise surface coil (CryoCoil, Bruker Biospin GmbH) using a FLASH sequence at 512x512 pixels, TR=1500ms, TE=6.5ms, FOV=19.2mm x 19.2mm for a resolution of 37.5 x 37.5 x 250 µm.

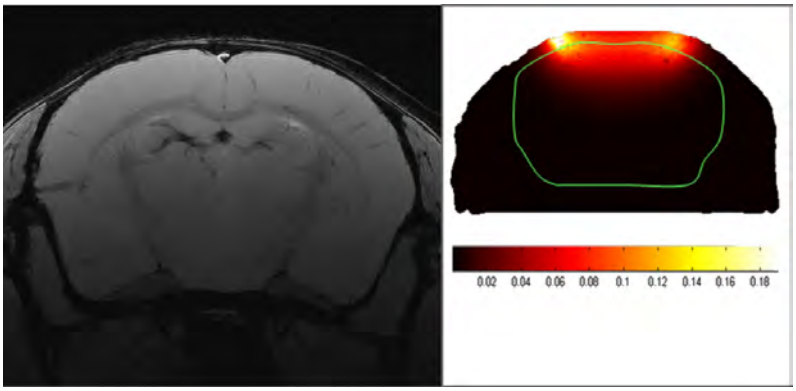

Figure 1: Photon transport modelling through mouse head. (**Left**): Axial MR image used for finite element mesh creation. (**Right**): results of photon transport simulation with optodes spaced 6mm apart. The green outline indicates boundaries of brain tissue. Whiter colours indicate a greater contribution to the signal from that region. The classic "banana" shape of the photon path is clearly visible.

Results: The results of NIR photon transport modelling are shown in Fig. 1. These data were used to guide ROI selection in ASL perfusion-weighted images, shown in Fig. 2. $CMRO_2$ for the group (n=4) was calculated to be 2.03 ± 0.48 mL O_2/100g/min using data shown in Table 1. These results agree with previously known lab data for rats.

	CBF (mL/g/s)	S_a	S_c	$CMRO_2$ (mL/100g/min)
M1	0.040766272	0.992	0.802581	1.730523
M2	0.054511943	0.992	0.786363	2.512154
M3	0.035614037	0.992	0.816707	1.39907
M4	0.046938927	0.972	0.738095	2.460508

Table 1: Experimentally determined values of cerebral blood flow (CBF), arterial saturation (S_a), capillary saturation (S_c) and calculated $CMRO_2$ values for each mouse.

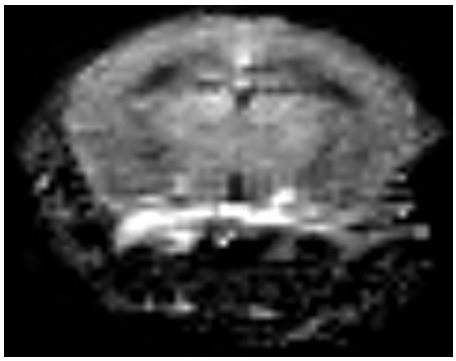

Figure 2: Perfusion weighted axial MR image of mouse brain. Pixel intensity, calculated as the difference in magnitude between two "tagged" images and two "control" images is proportional to cerebral blood flow in the region. The circled region indicates the ROI that was used in calculating cerebral blood flow.

Conclusion: By combining NIRS and ASL-MRI we have shown it is possible to obtain in vivo measurements of $CMRO_2$ in mice. Due to the high utility of mice as a model organism, this technique will be useful in investigating neurodegenerative disorders and other diseases that might affect brain metabolism.

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3. Data Analysis

Targeted Principle Component Analysis: A new motion artifact correction approach for Near-Infrared Spectroscopy

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As Near-Infrared Spectroscopy (NIRS) broadens its application area to different age and disease groups, motion artifacts in the NIRS signal due to subject movement is becoming an important challenge. Motion artifacts generally produce signal fluctuations that are larger than physiological NIRS signals, thus it is crucial to correct for them before obtaining an estimate of stimulus evoked hemodynamic responses. There are various methods for correction such as principle component analysis (PCA), wavelet-based filtering and spline interpolation.

Methods: We introduce a new approach to motion artifact correction, targeted principle component analysis (tPCA), which incorporates a PCA filter only on the segments of data identified as motion artifacts. We compared the new approach with the most effective motion artifact correction algorithms on a set of data acquired simultaneously with a collodion-fixed probe (low motion artifact content) and a standard Velcro probe (high motion artifact content).

Five healthy adult subjects were recruited for this study (1 female, 4 male; 23-52 years old). The study included collection of NIRS data from collodion-fixed optical fibers (left motor region) and Velcro-based probe (right motor region) during the performance of several commonly-encountered motion artifacts i.e. reading aloud, nodding their head up and down, nodding sideways, twisting upper body right, twisting upper body left, shaking head rapidly from side to side and raising their eyebrows (randomized inter-trial interval between 5 and 10 seconds. Data were obtained using a TechEn CW6 system (Medford, MA, USA). Each probe contained 2 sources and 4 detectors. The study was approved by Massachusetts General Hospital and each subject gave written consent.

Results: Our results show that tPCA gives statistically better results in recovering HRF as compared to wavelet-based filtering and spline interpolation for the Velcro probe. It results in a significant reduction in mean-squared error and significant enhancement in Pearson's correlation coefficient to the true HRF. The collodion-fixed fiber probe with no motion correction performed better than the Velcro probe corrected for motion artifacts in terms of mean-squared error and Pearson's correlation coefficient.

Conclusion: If the experimental study permits, the use of a collodion-fixed fiber probe may be desirable. If the use of a collodion-fixed probe is not feasible, then we suggest the use of tPCA in the processing of motion artifact contaminated data.

Dynamic Causal Modelling for Near-Infrared Spectroscopy

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Introduction: There is great interest in using near-infrared spectroscopy (NIRS) to study brain connectivity changes. However, current approaches usually analyze NIRS data in sensor rather source space and use linear measures of dependence such as correlation. Therefore, there have been limited studies focusing on the inference of directed connectivity. In this work, to address these shortcomings, we apply dynamic causal modelling (DCM)[1] to NIRS, which allows for making inferences about the changes in directed connectivity among underlying neural populations.

Methods: DCM for NIRS is a framework for fitting differential equation models of neural activity to NIRS data using Bayesian inference. Specifically, the generative model for NIRS data comprises three components: (i) neurodynamics[1] describing neural activity in terms of inter-regional interactions and its experimentally induced modulation, (ii) hemodynamics linking the neural activity with the changes in total hemoglobin, and deoxy-hemoglobin, and (iii) optics relating the hemodynamic sources to optical density changes. Here, the hemodynamic equation uses the Balloon model and its extension[2], and the optics equation models the sensitivity of optical measurements to the absorption coefficient changes. This sensitivity matrix can be estimated by simulating photon migration through the brain based on the Monte Carlo method[3]. After a generative model for NIRS is specified, the neural and hemodynamic parameters of DCM are estimated using the Variational Laplace method[4]. To validate the proposed method, we use experimental data recorded during motor execution and motor imagery using a 16 channel NIRS system (NIRScout, NIRx). Regions of interest (ROIs) include supplementary motor area (SMA) and primary motor cortex (M1).

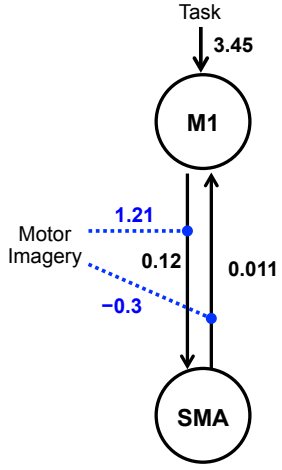

Fig. 1. Estimated effective connectivity (changes in blue)

Results: Prior to DCM analysis, brain regions whose dynamics are driven by experimental conditions were identified using the statistical parametric mapping (SPM) analysis[5]. We found that SMA was significantly activated during both motor execution and imagery, whereas M1 was only activated during motor execution. The most significantly activated voxels within SMA and M1 were then selected as the source positions for DCM analysis: SMA, [−51, −4, 55]; M1, [−44, −16, 65]. To explain the reduced M1 activity during motor imagery in terms of interactions between SMA and M1, we tested a DCM as shown in Fig. 1. Results indicate that while task input increases regional activity in M1, motor imagery negatively modulates the connection from SMA to M1. Moreover, Fig. 2 shows that during motor imagery, estimated neural response in M1 is significantly reduced, while neural activity in SMA is highly increased compared with activity during motor execution. These results are consistent with findings of previous fMRI studies[6].

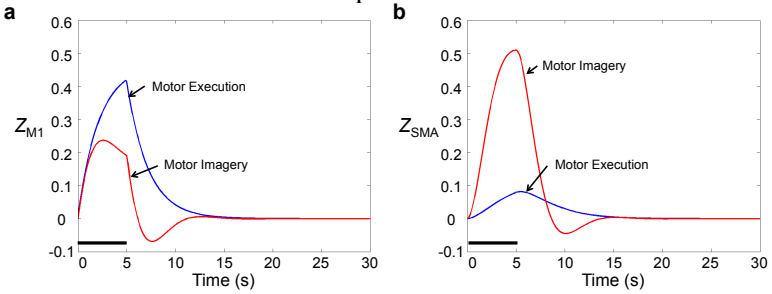

Fig. 2. Estimated neural responses in (a) M1 and (b) SMA. The solid black line indicates the motor task period.

Conclusion: We presented DCM for NIRS data. Using experimental data, we showed that the proposed method allows for making inference about directed connectivity in the brain mediated by neural dynamics.

References: [1] Friston et al., NeuroImage 19: 1273−1302, 2003. [2] Buxton et al., NeuroImage 23: 220−233, 2004. [3] Fang, Biomed. Opt. Express 1: 165−175, 2010. [4] Penny, NeuroImage 59: 319−330, 2012. [5] Ye, NeuroImage 44: 428−447, 2009. [6] Kasess, Neuroimage 40: 828−837, 2008.

Title: Supplementary use of fNIRS data in psycholinguistic research: A Japanese-English bilingual case study

Presenters: **TAURA, Hideyuki** (Ritsumeikan University, JAPAN) and TAURA, Amanda (Setsunan University, JAPAN)

E-mail: pdf02662@gmail.com

[abstract]

An early Japanese-English balanced bilingual born and brought up in the USA for 15 years was tracked, to examine what changes her two languages underwent during the 3 years after her return to Japan. Linguistic and fNIRS data were collected four times – firstly upon her return to Japan and then one, two, and three years later. Her English production data, elicited in both spontaneous spoken and written formats were analyzed in terms of accuracy, fluency, and complexity. A verbal fluency task (VFT) was employed in both languages to tap into her brain activation in Broca's area using fNIRS data.

The linguistic analysis showed both improvement/maintenance and a slight deterioration (attrition) in English, depending on the aspects examined: Table 1 summarizes the improvement of her English writing skills while Table 2 demonstrates her fluency deterioration.

Table 1. Writing skills

Data collection	writing basic rules	grammar vocab	story construction	overall Quotient
2010 (16;06)	13	15	15	128
2011 (17;06)	13	16	14	128
2012 (18;05)	14	18	14	134
2013 (19;04)	15	18	15	139

Table 2. Fluency

data collection	total time (ms)	total #words	time needed to produce a word
2010	123.388	445	277.3
2011	102.747	426	241.2
2012	91.321	369	247.5
2013	228.574	552	414.1

A strikingly different picture to this linguistic analysis, however, was manifested in the fNIRS data analysis (Table 3), which clearly reflected her language use at each data collection time – for instance, there was a higher level of oxy-Hb flow for English rather than Japanese tasks, when she was at the stage of intense Japanese study to catch up to her peers.

Table 3. ANOVA results

task	*F value*			fNIRS order in Broca's area	fNIRS order in right hemisphere
		Broca	Right		
Jletter	F(2,435)=	16.189	65.024	2010=2012<2011	2010<2012=2011
Eletter	F(2,435)=	47.836	81.257	2010<2012=2011	2010<2012=2011
Jcategory	F(2,435)=	17.213	20.607	2012<2011<2010	2012<2010=2011
Ecategory	F(2,435)=	73.471	9.068	2012<2011<2010	2011=2010=2012

(p<.01)

Thus, the linguistic data analysis and fNIRS data analysis seem to complement each other by detecting different aspects of language processing.

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Thus, the linguistic data analysis and fNIRS data analysis seem to complement each other by detecting different aspects of language processing.

Functional connectivity analysis in patients with dysfunction of the corpus callosum: A preliminary study

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Highly correlated neural activities in spatially distinct brain regions in the temporal domain during the resting condition are called 'resting-state functional connectivity'. It has been demonstrated that this connectivity markedly changes during infancy and childhood. Moreover, various recent findings suggest that clinical conditions such as Alzheimer's disease and attention deficit hyperactivity disorder can alter the functional network. In the present study, we applied analysis to patients in the intensive care unit with various brain injuries, such as dysfunction of the corpus callosum due to stroke or severe head injuries, to evaluate the clinical condition and prognosis regarding the brain function.

In our preliminary study, we measured two patients showing severe deficit of the corpus callosum and four patients without a deficit. In addition to the patients, we collected data from eight healthy adult volunteers as controls. We placed 3 x 5 probe sets on the bilateral parietal regions and measured spontaneous hemodynamic responses.

In order to evaluate connectivity in the patients, we analyzed the differences between the patient and control groups on a channel pair basis in five frequency ranges (0.009 – 0.02 Hz, 0.02 – 0.04 Hz, 0.04 – 0.06 Hz, 0.06 – 0.08 Hz, and 0.08 – 0.10 Hz). As in a previous study (Homae et al., 2011), we calculated the correlation coefficient (r) between the homologous channels and converted the r-values into z-scores. Multiple comparisons among the pairs of channels were considered by adopting a measurement-channel false discovery rate correction at $p < 0.05$. As a result, the inter-hemispheric connectivity was significantly different across groups in the 0.02 – 0.04-Hz (1 channel), 0.04 – 0.06-Hz (11 channels), 0.06 – 0.08-Hz (12 channels), and 0.08 - 0.10-Hz (4 channels) range.

The results indicate that analysis of 'functional connectivity' based on NIRS data may facilitate evaluation of the brain state of patients and patient's prognosis which cannot be measured with MRI.

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Title : SPM toolbox to analyse and visualise fNIRS data (NIRSHSJ)

Authors :

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Data inspection and artifact detection are crucial steps for analyzing and understanding neuroimaging data. We developed the NIRSHSJ SPM toolbox to provide a visual interface allowing the inspection of functional Near-Infrared Spectroscopy (fNIRS) data during each stage of analysis. First, automatic artifact detection is implemented on normalised raw data to identify excessive and abrupt changes in intensity, generally related to movement artifact. This detection is performed based on a roll average technique to identify 'bad intervals' independently for each channel. Then temporal correlation between channels for previously identified bad interval periods is processed in order to detect lower amplitude signal that are correlated with the artifact. After automatic artifact detection, the user may visually review and adjust the selection of bad intervals, if required. In addition, offset correction, interpolation of bad segments; linear drift subtraction, principal component analysis subtraction, filtering, averaging, region of interest selection and export are implemented to offer a great flexibility to the analysis process. This toolbox is compatible with HoMer (MA, USA) and the LIOM Lab package (nirs10), both using MatLab (Matworks, USA). Optode localisations are recorded using Polaris Brainsight (Rogue Research Inc, Montréal, Canada) and registered on individual or template MRI based on the fiducially landmark of the participant. Skin or cortical topographic reconstruction can also be used for group or multimodal analyses. In conclusion, we have created a flexible, semi-automatic tool that can be easily adapted for other types of analysis, such as functional connectivity studies.

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Type: Poster presentation

Topic areas your abstract covers: Data analysis

Semi-virtual registration and virtual channel synthetization in fNIRS imaging

Felipe Orihuela-Espina[1,2], Daniel R. Leff[1], Javier Herrera-Vega[2], Kunal Shetty[1], David R. C. James[1], Ara W. Darzi[1], Guang-Zhong Yang[1]
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Abstract
Background. Registration maps intended channel location on the scalp surface to their likely projection on the cortical surface. Registration realises reproducible measurements, facilitates comparison of data and allows interpretation in terms of cortical active foci. It may be achieved by co-registration to structural magnetic resonance [1, 2], projection to a brain atlas [4], or virtually using a synthetic head [5] among others with varying degree of acceptance among the fNIRS community.
Aim. Extending our prior method for computing distances from real to standard locations [3], we present a registration approach that permits inferring channel behaviours at standard locations for which probabilistic anatomical cranio-cerebral correlation has been established [2]
Methods. Following channel 3D position digitization, discrepancy between the intended cranial marker and the real recorded location is quantified by computing the geodesic distance along a hemi-spheric mesh representing a standard positioning system and deformed according to the real location of reference locations [3]. A spherical variogram is then fitted using least squares to establish the degree of spatial dependence among the recorded locations. Finally, haemodynamic behaviour at any standard location (or any arbitrary location over the scalp) i.e. virtual channel, is then synthesized by interpolating the haemodynamic response at spatially correlated observed channels using 3D kriging.
Results. An illustrative example of the algorithm is illustrated in Fig 1.
Conclusions. The presented extension to derive haemodynamic behaviour at virtual channels completes a semi-virtual registration approach affording inference of haemodynamic behaviour at well established standard locations. This solution may (i) reduce data harvesting demands, (ii) permit off-line correction of mispositioned channels and (iii) enable integration of datasets recorded during originally distinct experiments promoting data reuse and complex hypothesis evaluation.

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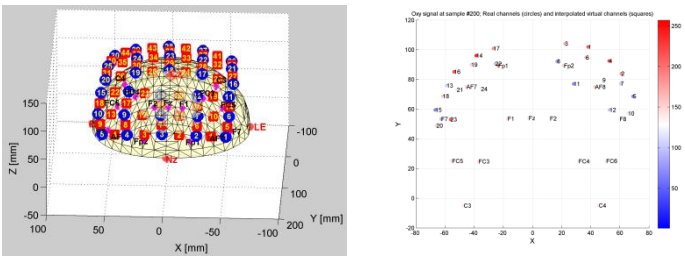

Figure 1. Left: The hemi-spheric grid after deformation. Optodes (blue circles), channels (red squares) references (red circles) and some standard scalp locations (magenta diamonds) are shown. Right: Top axial view of measured haemodynamics (acquired using Hitachi ETG-4000) and exemplary virtual channels at selected standard locations.

Blush or brain: A novel approach to decouple systemic surface blood flow from cortical neural activities in the fNIRS signal

Xiaoqing Gao[1]; Xiao Pan Ding[1&2]; Pu Zheng[1]; Guowei Chen[2];Genyue Fu[2]; Kang Lee[1]

(1. University of Toronto, Canada; 2, Zhejiang Normal University, P.R. China)

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Functional Near-Infrared Spectroscopy (fNIRS) is a non-invasive technique for measuring cerebral hemodynamics with wide applications. However, a major challenge of fNIRS is that its signal is vulnerable to contamination by the systemic fluctuations of hemodynamics in the superficial layers of the head. Several methods have been proposed to separate the cerebral and extracranial signals in fNIRS. Some of these methods provide additional measurements of superficial hemodynamics and use them to eliminate the extracranial contribution in the fNIRS signal. For example, short separation recordings are used to measure superficial NIRS signal from scalp and Skull. The superficial signals are then regressed out from the fNIRS signal. However, these methods require great effort to set up extra NIRS detectors or make additional physiological recordings to obtain the systemic signals. Here we introduce a novel approach to separate neural signals from systemic surface hemodynamic fluctuations in the fNIR signal. Using our novel signal processing techniques, we are able to obtain directly and noninvasively systemic hemodynamics from the face while fNIRS signals are being recorded. To verify this new approach, we asked participants to perform the classic go-no-go task while the fNIRS and surface blood flow signals were simultaneously recorded. An ETG-4000 (Hitachi Medical Co., Japan) was used to acquire and record fNIRS data in the frontal regions. We bandpass-filtered the fNIRS time series data and facial blood flow data to a frequency range of 0.02 to 0.5 Hz. We performed time-lagged correlational analyses between the fNIRS and surface blood flow signals in a 20s time window. We calculated Pearson correlations between the variation of oxygenated hemoglobin [oxy-Hb] and deoxygenated hemoglobin [dyoxy-Hb] and the variation of surface blood flow, where 99% confidence interval of the correlation was estimated with a permutation test. We found that the variations of the two types of signals are not significantly correlated without time lag. However, the correlations increased significantly when the two sets of signals were off-set by 8 seconds. After removing the systemic blood flow signals, we successfully found significant frontal activations between the go and no-go conditions. We also explored the change of contrast to noise ratios before and after removing systemic surface blood flow signal. Thus, our novel approach to measure facial surface blood flow provides a convenient and noninvasive way to reduce systemic contamination in the fNIRS signal.

Effective functional connectivity of own- and other-race face processing in children: A Granger causality analysis

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Previous studies showed that children and adults showed a robust neural other race effect that the brain responds to own- and other-race faces differentially (NORE: Ding et al., 2014; Liu et al., 2014). To further examine the functional interaction of different brain areas involved in NORE, the present study used Granger causality analysis (GCA) to examine how differently children's cortical networks are organized to process own-race faces compared to other-race faces. An old-new paradigm was used to assess children's recognition of own- and other-race faces, and ETG-4000 (Hitachi Medical Co., Japan) was used to acquire and record fNIRS data. The time course of [oxy-Hb] changes of each channel was first low-pass filtered (HRF) and high-pass filtered (Wavelet-MDL) to respectively remove low-frequency noise and high-frequency noise, such as the drift and the noise induced by breathing and motion. Then, the filtered time courses were baseline-corrected. After preprocessing for each participant and under each task condition, the causal relationship map was obtained by calculating the weights of causal relations between the time courses of [oxy-Hb] of each pair of channels using GCA. Finally, at group level, a paired t-test was performed between the causal relationship maps of the own-race and other-race condition across all participants to reveal the difference in effective connectivity patterns between these two tasks with the statistical threshold of $p< 0.01$.The results showed that the recognition of own-race faces recruited more occipital-frontal causal couplings than that of other-race faces, whereas the recognition of other-race faces recruited more intra-occipital causal couplings than that of own-race faces. Our findings suggests that, for 7- to 13- year-old children, the recognition of own-race faces may rely on both visual encoding at the visual cortex and memory retrieval at the frontal gyrus (Haxby et al., 2000), whereas the recognition of other-race faces may mostly rely on face visual encoding in the visual cortex. This study also illustrates the potential of using GCA to reveal causal functional connectivities in fNIRS data.

Functional Connectivity of the PFC via Wavelet Partial Correlation Analysis

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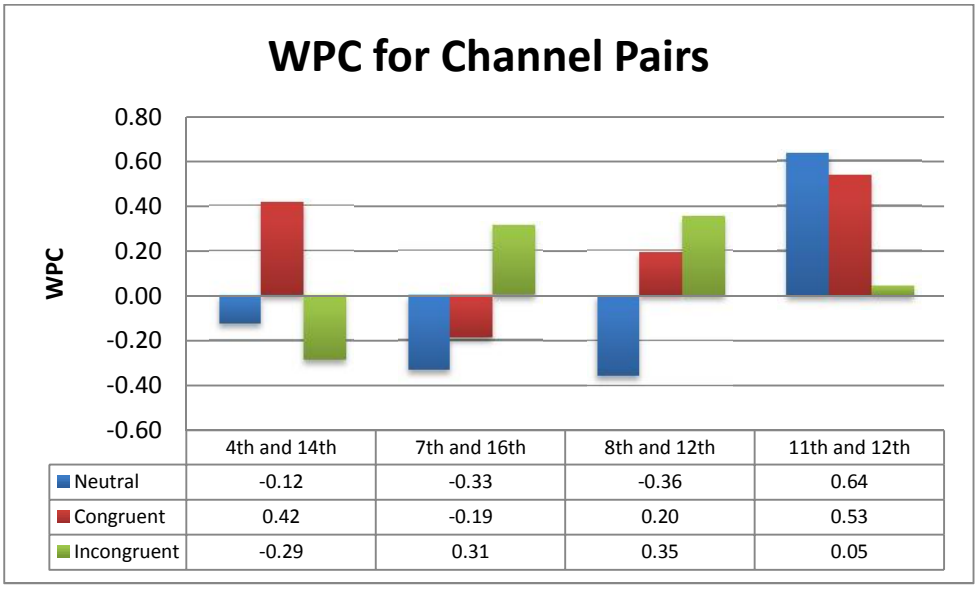
In this study, we aimed to investigate the functional connectivity in the prefrontal cortex (PFC) by applying partial correlation to wavelet coefficients (WPC) derived from fNIRS data. 10 subjects were asked to complete the computerized version of the color-word matching Stroop task that has three stimulus conditions, namely the neutral (N), congruent (C) and incongruent (I).

We used a continuous wave 16 channels near-infrared spectroscopy device to record concentration changes of the oxy-hemoglobin and ($\Delta[HbO_2]$) deoxy-hemoglobin ($\Delta[Hb]$).

First, we applied the discrete wavelet transform (DWT) to decompose each fNIRS signal into 8 levels.. We then investigated the functional connectivity via partial correlations between wavelet coefficients for each stimulus type, and called it the wavelet partial correlation (WPC). WPC values were computed for each stimulus condition for each of the 4, 5, 6, 7 and 8 levels which correspond to 0.003-0.11 Hz frequency range. The only significant result on WPC values was obtained for analysis of level 4, representing 0.055-0.11 Hz frequency range.

We report the major WPC change in pairs of channels that reside on two hemispheres: 4^{th} and 14^{th} with $F(2,27) = 3.37$, $p = 0.0493$, 7^{th} and 16^{th} with $F(2,27) = 3.95$, $p = 0.0311$, 8^{th} and 12^{th} with $F(2,27) = 4.77$, $p = 0.0167$, and 11^{th} and 12^{th} with $F(2,27) = 3.67$, $p = 0.039$.

Although very small in value, significant WPC changes observed in bilateral dorsolateral PFC regions is a marker of Stroop effect. Interestingly, significant connectivity change was observed only between the interhemispheric pairs. The WPC method is preferable to standard cross correlation due to its inherent elimination of the most common and underlying activity in all the channels and highlighting only the actual correlation between the two channels.



	4th and 14th	7th and 16th	8th and 12th	11th and 12th
Neutral	-0.12	-0.33	-0.36	0.64
Congruent	0.42	-0.19	0.20	0.53
Incongruent	-0.29	0.31	0.35	0.05

Benchmarking Algorithms for Image Reconstruction of Cerebral Diffuse Optical Tomography

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Diffuse optical tomography (DOT) extends fNIRS by applying overlapping 'high density' measurements, thus providing a three-dimensional imaging with improved spatial resolution. Reconstructing brain activation images with DOT requires solving an underdetermined inverse problem with far more unknowns in the volume than in surface measurements.
This simulation study mimics a cerebral DOT experiment. It provides a very realistic framework using an atlas-based five-layered head model in combination with real-world noise data, which are added to the simulated signals to take into account fiber distance-dependent noise levels. This study was performed on a semi-infinite medium with a highly attenuated light sensitivity in deeper layers.
We start out by demonstrating how the quality of cerebral DOT reconstructions alters with the choice of the regularization parameter for different methods. To select the regularization parameter independently, we propose a cross-validation procedure which achieves a reconstruction quality close to the optimum.
Furthermore, we compare the outcome of seven different image reconstruction methods for cerebral functional DOT. The methods selected include reconstruction procedures that are already widely used for cerebral DOT (minimum L2-norm estimate [l2MNE] and truncated singular value decomposition [tSVD]), recently proposed sparse reconstruction algorithms (minimum L1 and a smooth minimum L0-norm estimate [L1MNE, L0MNE, respectively]) and a depth- and noise weighted minimum norm [wMNE]. Furthermore, we expand the range of algorithms for DOT by adapting two EEG-source localization algorithms (Sparse Basis Field Expansions [S-FLEX] and linearly constrained minimum variance [LCMV] beamforming). Independent of the applied noise level, we find that the LCMV beamformer is best for single spot activations with perfect location and focality of the result, whereas the minimum L1 norm estimate succeeds with multiple targets.

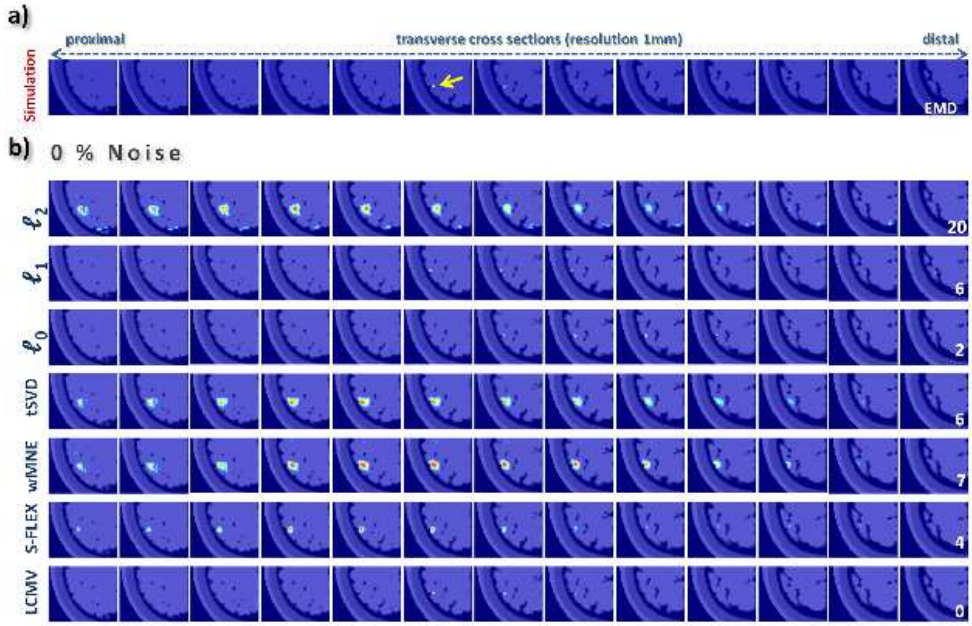

Fig. 1 Example for the comparison of the outcome of seven reconstruction methods with one simulated target and no noise. (a) Simulated activation (b) Reconstruction result (normalized t-values) for seven methods.

Evaluating motion processing algorithms for use with fNIRS data from young children

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Establishing an optimal method of motion artifacts removal for functional near-infrared spectroscopy (fNIRS) data is a topic of current discussion. To date, analyses have approached this issue by comparing the efficacy of multiple motion artifact correction techniques in the context of either simulated data or functional data from adult subjects. These studies have succeeded in identifying motion artifact correction procedures that function optimally when motion artifacts are relatively low-frequency and low-amplitude. However, it remains unclear if these insights hold for data recorded from challenging populations, such as young children. Here, higher-amplitude motion artifacts are common, causing many experimental trials to be rejected by most well-established motion artifact correction procedures. Thus, there is a particularly strong need to effectively identify and remove motion artifacts when analyzing data from these populations to retain an adequate number of trials for analysis.

The goal of the current study was to identify a motion artifact correction procedure and associated parameters that are best suited to processing fNIRS data from children with high-amplitude motion artifacts. The data sample was from a study of 11 3-year-olds and 14 4-year-olds who performed a visual working memory task while functional fNIRS data was recorded from frontal, parietal, and temporal areas. We analyzed these data with 7 motion artifact correction techniques, including principle component analysis (PCA), spline interpolation, wavelet filtering, correlation-based filter improvement (CBSI), and an in-house artifact correction procedure. We applied each processing approach with two different sets of motion artifact rejection parameters, one more stringent and one less stringent. We compared these methods quantitatively by measuring statistics regarding the amount of data rejected due to noise, as well as metrics related to the hemodynamic response.

As expected, fewer trials were rejected with the less stringent motion artifact rejection parameters. Importantly, this tended to have little effect on data quality. Across the 7 processing methods, targeted PCA (tPCA) preformed best, resulting in the smallest number of trials rejected while also producing the best quality hemodynamic data. The current data add to the literature by providing recommendations for effective motion processing approaches and optimized parameter values when analyzing fNIRS data from challenging populations.

Intrinsic connectivity network strength modulated by working memory load: An fNIRS Study

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Background: In light of findings showing similar resting-state and task-evoked functional network architecture in fMRI, we examined whether intrinsic connectivity networks (ICNs) identified with fNIRS (functional Near-Infrared Spectroscopy) during the resting-state were sensitive to cognitive load demands. We identified ICNs in the resting state and used regression to examine working memory (WM) load-dependent activation and functional connectivity (FC) of individual networks.

Methods: Sixteen subjects (6 male) were subjected to a 10-minute resting scan followed by a 6.5-minute letter n-back task with loads of 1-, 2-, and 3-back. Optical data were recorded on a two-wavelength (690 and 830 nm) continuous-wave CW5 imaging system (TechEn, Inc., Milford, MA). The 40 optical channels covered: ventrolateral prefrontal cortex (vlPFC), dorsolateral prefrontal cortex (dlPFC), frontopolar cortex (FP), and parietal cortex (Par). Raw signals were converted to oxygenated hemoglobin concentration. Resting-state signals were then filtered to .009-.09 Hz, downsampled to 2 Hz, and trimmed to the middle 6 minutes. Each channel was then normalized such that its root-mean-square (i.e., quadratic mean) was equal to 1. Data from each subject was concatenated to produce a group timecourse for each channel. Independent component analysis (ICA) was performed using FastICA. The positive and negative portions of each component were separated, doubling the number of components (Figure 1). The task signals were filtered to .009 - 2 Hz and downsampled to 10 Hz. The unmixing matrix from the resting-state ICA was used to project the task data into network space for each subject. The task-related components were then analyzed for WM load-dependent activation using NIRS-SPM. To assess FC, the outer product of the network channel weights was taken to produce a connection weight matrix for each network. These matrices were used to compute mean within-network correlation for each n-back load. The correlation values were then regressed against load for each network.

Results: ICA yielded 6 networks: 1) parietal, 2) frontopolar, 3) anterior PFC, 4) vlPFC and frontal pole, 5) lateral PFC, 6) dlPFC, parietal, and frontal pole. Network activation increased with increasing n-back load for IC #5 ($t=2.18$, $p<.05$). FC increased with increasing n-back load for ICs #1 ($t=3.51$, $p<.005$) and #6 ($t=3.08$, $p<.005$).

Conclusions: These results show that ICNs identified from resting-state fNIRS signals exhibit cognitive-load sensitive activation and FC. Thus, cognitive load effects can be expressed as a modulation of engagement of specific ICNs. Network-level analyses may facilitate probing cognitive phenomena using fNIRS.

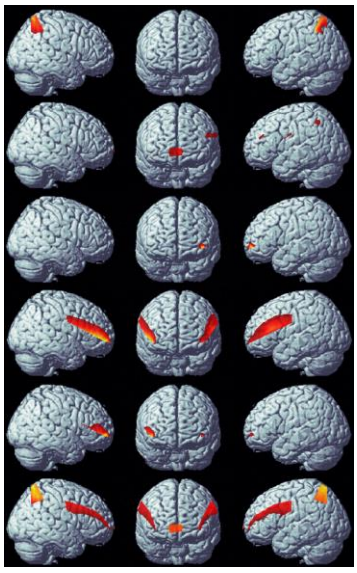

Figure 1. Intrinsic connectivity networks delineated using ICA

An fNIRS investigation of associative recognition in the prefrontal cortex with a rapid event-related design

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Background: Functional near-infrared spectroscopy (fNIRS) measures hemodynamic changes at the cortical level during brain stimulation. The use of fNIRS is growing in popularity for studying cognitive neuroscience in which fast event-related designs are already widely used with functional magnetic resonance imaging (fMRI). However, the applicability of fast event-related designs with fNIRS has been examined with only a couple of papers [1,2], particularly with complex cognition. Thus, the present study employed fNIRS with a rapid-presentation event-related design for investigating prefrontal cortical activity during complex associative recognition.

New Method: Participants studied a list of word pairs and were later given an associative recognition test (Fig. 1). Throughout the experiment, each event was presented rapidly (~4s) without inter-trial interval. Data were sorted based on accuracy of associative memory judgments and analyzed using the general linear model (GLM) with a rapid event-related design.

Results: During retrieval, significant increases in oxygenated hemoglobin concentrations were observed in dorsolateral and ventrolateral prefrontal regions for successful associative recognition (Fig. 2). When comparing retrieval to encoding, significant increases in oxygenated hemoglobin concentrations were also observed in dorsolateral prefrontal cortex (Fig. 3).

Comparison with Existing Method: The current fNIRS results corroborate previous fMRI findings that have demonstrated the involvement of dorsolateral and ventrolateral prefrontal cortex in associative recognition. Therefore, the present study validates the versatile use of fNIRS with a rapid-presentation event-related design in the investigation of neural mechanisms of associative memory.

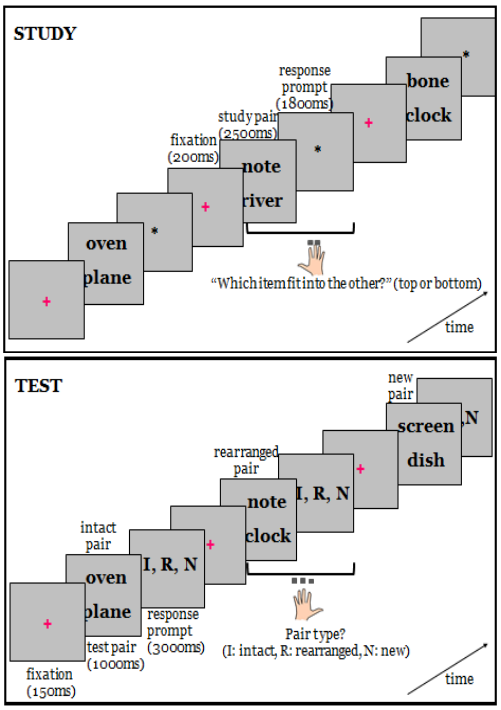

Fig. 1 Schematic of experimental design

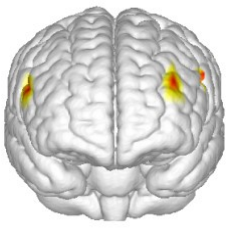

Fig. 2 *Associative recognition Associative Hit > Associative*

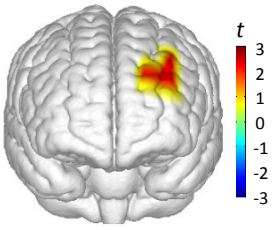

Fig. 3 *Associative Memory Retrieval > Encoding*

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Presentation preferred: oral;
Topic area: Data analysis and Neurocognition.

Probe Pressure Modulation Algorithm Reduces Extra-cerebral Contamination in Optical Measurements of Cerebral Blood Flow

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Diffuse correlation spectroscopy (DCS) is a novel optical method with strong potential for continuous, noninvasive bedside monitoring of cerebral blood flow (F_c); such instrumentation would improve individual patient management of stroke as well as other brain diseases. DCS measurements on the head are sensitive to both cerebral blood flow and extra-cerebral blood flow. Consequentially, DCS measurements obtained from the widely used homogeneous tissue models (e.g., semi-infinite) are subject-specific weighted averages of the cerebral and extra-cerebral blood flows. Extra-cerebral blood flow is typically not negligible and is sensitive to environmental factors such as probe pressure, which makes cerebral monitoring with DCS prone to extra-cerebral contamination.

Here we report on a novel scheme that employs DCS measurements of the brain tissues at two probe pressures and two source-detector separations to reduce extra-cerebral contamination. In essence, our algorithm determines the subject-specific fractional contributions of extra-cerebral and cerebral tissues to the DCS signal by using pressure to induce variations in extra-cerebral flow while cerebral flow is constant. The head is modeled as a two-layer medium, and the source-detector separations are chosen such that detected light at the long separation (e.g., $\rho_l = 3$ cm) travels through both layers, but detected light at the short separation (e.g., $\rho_s = 1$ cm) is predominantly confined to the extra-cerebral layer (Fig. 1).

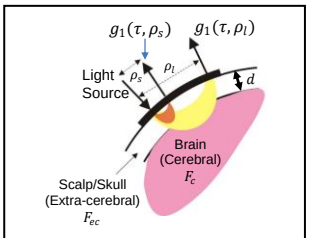

Fig. 1: Two-layer Geometry

To relate temporal changes in extra-cerebral flow (ΔF_{ec}) and cerebral flow (ΔF_c) to the temporal changes in the measured DCS signal ($g_1(\tau,\rho)$), we extend the well-known Modified Beer Lambert Law to the DCS measurement:

$$\Delta OD_{DCS}(\tau,\rho) \equiv -\log\left(\frac{g_1(\tau,\rho)}{g_{1,0}(\tau,\rho)}\right) \approx -\frac{\partial}{\partial F_{ec}}\left[\log g_{1,0}(\tau,\rho)\right]\Delta F_{ec} - \frac{\partial}{\partial F_c}\left[\log g_{1,0}(\tau,\rho)\right]\Delta F_c = D_{ec}(\tau,\rho)\Delta F_{ec} + D_c(\tau,\rho)\Delta F_c \quad (1)$$

Since the short separation signal is independent of cerebral flow, $D_c(\tau,\rho_s) = 0$, which in turn means

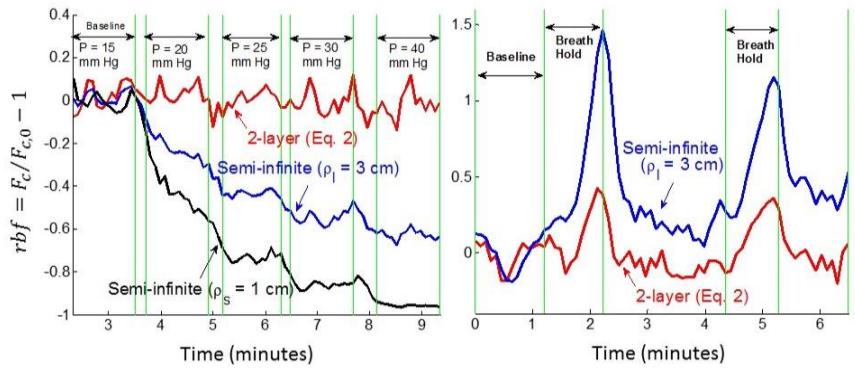

Figure 2. DCS cerebral flow monitoring in a healthy adult volunteer during different probe pressures (left) and breath holding (right). Flow was calculated from the DCS signal using the two-layer DCS Modified Beer-Lambert (Eq. 2) and homogeneous semi-infinite tissue models.

that $\Delta F_{ec} = \Delta OD_{DCS}(\tau,\rho_s)\,/D_{ec}(\tau,\rho_s)$ (see Eq. 1). Further, the change in the long separation signal from pressure variation is given by $\Delta OD_{DCS}^{\Delta P}(\tau,\rho_l) = D_{ec}(\tau,\rho_l)\Delta F_{ec}^{\Delta P}$, because $\Delta F_c^{\Delta P} = 0$. We use Equation 1 to form a system of four equations (two separations, two probe pressures), which can then be solved for the cerebral flow change:

$$\Delta F_c \approx \frac{1}{D_c(\tau,\rho_l)}\left(\Delta \mathrm{OD}_{\mathrm{DCS}}(\tau,\rho_l) - \frac{\Delta \mathrm{OD}_{\mathrm{DCS}}^{\Delta P}(\tau,\rho_l)}{\Delta \mathrm{OD}_{\mathrm{DCS}}^{\Delta P}(\tau,\rho_s)}\Delta \mathrm{OD}_{\mathrm{DCS}}(\tau,\rho_s)\right) \quad (2)$$

Equation 2 has been successfully applied in a healthy adult volunteer to reduce the sensitivity of the measured cerebral flow to probe pressure and to scalp effects during breath holding (Fig. 2).

A comparison of procedures for co-registering scalp-recording locations to anatomical MRI images

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Functional brain imaging involves ascribing activity to particular anatomical structures. However, several brain-imaging techniques lack anatomical information, and therefore depend on structural data obtained through Magnetic Resonance Imaging (MRI) or Computed Axial Tomography (CAT). These techniques, including Electroencephalography and Event-Related brain Potentials (EEG and ERPs), Magnetoencephalography (MEG), Near Infrared Spectroscopy ((NIRS; Villringer & Chance 1997; Boas et al., 2014), Fast Optical and Event-Related Optical Signals (FOS and EROS; Gratton & Fabiani, 2010) typically rely on sensors placed on the scalp. For these techniques, an accurate anatomical localization of the sensors on the head surface ("co-registration") is required. A widely used method for co-registering scalp sensors to an anatomical frame of reference is to estimate the positions of anatomical landmarks (Jasper, 1958). These anatomical landmarks, or "fiducial", alignment has been shown to be a simple and fast method for sensors to scalp co-registration. However, due to the low number of clearly identifiable anatomical locations, it is highly sensitive to human errors. Surface-fitting procedures are alternative or supplemental methods to fiducial-based approaches (Whalen et al., 2008). They consist in the fitting of a discrete sampling of two surfaces, one described by scalp digitized points (sensors plus additional samples) and one by points extracted from a scalp representation derived from a structural image (typically MRI). Because of the non-linearity of the fitting problem no simple analytical solution can be obtained. Typically, the problem is addressed by using iterative procedures that tries to minimize an objective function. A common problem of iterative procedures is the possibility of local minima in the error function that do not guarantee finding the "correct" solution of the problem (global minimum). For a given objective function this problem is typically attenuated if the initial guess (i.e., the guess used at the first iteration) is relatively close to the correct solution. However this is not always possible. Another method to address the local minima problem is to change the error metric to be minimized. Euclidean distance error metric has been used for sensor to scalp co-registration purposes. Euclidean distance minimization using the Levenberq and Marquart iterative algorithm (LMA) has been previously shown to be very accurate (errors <4 mm) when an initial guess based on precise fiducial alignment is used (Whalen et al., 2008). However the accuracy of LMA decreases in the presence of fiducial placement errors. In fact the nearly spherical shape of the head can easily cause erroneous solutions of the iterative algorithm when the euclidean distance metric error is used. We compared the fiducial+LMA method to another procedure, the Iterative Closest Point to Plane (ICP2P) method both on synthetized and real data. In the ICP2P the error metric is changed so that it relies both on euclidean distances of the two surfaces and normals (i.e., estimated curvatures) of the destination surface. ICP2P lets flat regions slide along each other whereas it emphasizes regions with high curvature (Rusinkiewicz & Levoy, 2001). We found that this different error metric helps to overcome problems of local minima making ICP2P highly stable to initial guess errors. This characteristic of the ICP2P permits co-registration without manual fiducial identification making the algorithm suitable for an automatic co-registration procedure However, ICP2P is more sensitive to correlated noise in the sampling procedures used to describe the scalp and it typically requires a higher sampling of the head surface when applied to real data. Hence, the best algorithm for co-registration depends on the type of data available to describe the scalp. We found that, under controlled conditions, surface fitting co-registration procedures can reduce the error to 3 mm on average.

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Monitoring attentional state with fNIRS

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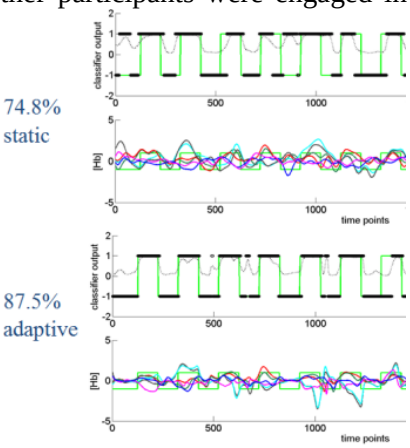
The ability to distinguish between different levels of task engagement in safety-critical situations is important for detecting and preventing decrements in task performance. We therefore investigated whether changes in the concentration of hemoglobin ([Hb]) - a marker of brain activity - detected with Functional Near Infrared Spectroscopy (fNIRS) can distinguish between high and low levels of task engagement during the performance of a visual selective attention task. We recorded such changes from a key region (the dorsolateral prefrontal cortex) of the "task-positive" network (TPN), which is associated with relatively high levels of task engagement, and from a key region (the medial frontal gyrus) of the "task-negative" network (TNN), which is associated with relatively low levels of task engagement (e.g., resting and not performing a task) (Fox et al., 2005). We previously showed that negatively correlated activity between these two regions can be detected with fNIRS at the group level (Harrivel et al., 2013). Here, we show such activity can be used to distinguish between high and low levels of task engagement at the single-subject level. Specifically, using time traces of activity in these regions as inputs to a multivariate pattern classifier, we predicted above chance levels whether participants were engaged in performing the task (a "work" state) or not engaged (a "rest" state).

Classifier input features were selected from an array of probe channels at each of the two probe locations using a "training" data set, which was distinct from a "testing" data set. We determined the accuracy of state prediction using [Hb] signals after they were filtered to remove noise. More specifically, standard linear regression was implemented for both static and dynamic filtering to remove concurrently measured physiological noise. The resulting classifier outputs (work at +1, rest at -1, both in black), the known task state (green), and six time-trace input features (other colors) are shown for one subject, separately for each type of filtering (see figure).



Our dynamic filter extended existing implementations of an adaptive general linear model (Abdelnour and Huppert, 2009; Gagnon et al., 2011) to use both real physiological nuisance traces and real hemodynamic responses evoked by a cognitive task. Considering unequal sampling of arterial and venous vascular compartments across optodes, we used both oxy- and deoxygenated [Hb] changes measured with shorter-separation optodes as superficial nuisance regressors to clean both the oxy- and deoxygenated traces of interest.

Dynamic filtering produced the best accuracy (84% ± 6%). Minimally-processed measurements were best when no knowledge of the task being performed was used (70% ± 11%), representing a real world characterization. Across-network correlation measures at the single subject level were not useful for prediction purposes. Simultaneously-recorded functional magnetic resonance imaging (fMRI) data verified our assumptions about the sources of brain activity and validated our fNIRS classification results. These findings suggest that fNIRS could prove quite useful for monitoring cognitive state in real-world settings. Additionally, more complex models of variable network activity may improve future results.

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Near-Infrared Spectroscopy of Image Clarity Perception in the Human Brain

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Perceived image clarity depends, not solely on optics, but on the brain's ability to process visual stimulation and adapt to environmental change. Neural adaptation plays a role in the perception of image clarity, as blur judgments depend on the state of adaptation. Adaptation refers to the manner in which the visual system adjusts its operations (or recalibrates) in response to environmental change and is observed by measuring human responses to a test image after prolonged exposure to an adapting image. After adapting to a blurred image, subsequent images would appear sharper, and vice-versa.

The purpose of the present work is to quantify perceived image clarity (blur) physiologically with measures of the brain's hemodynamic response function using near infrared spectroscopy (NIRS).

We performed NIRS on the brain of many subjects while they observed different images categories (natural, animals, etc.). The image clarity was changed from sharp to blur and their appearance, on a calibrated screen, was randomized. The working wavelengths were 705 nm and 830 nm. The spectroscopy was done in cortical areas such as the occipital and frontal lobes. The study obtained ethics approval from the CERES (Comite d'ethique de la recherche en sante) of Universite de Montreal where all the testing took place. Informed written consent was obtained from all participants of the study.

We used an Entropy function to analyze the NIRS data and found that the best image clarity for a subject is the one with the highest Entropy value. This result would help the current technique for prescribing lenses.

Correlation Analysis between fNIRS, EEG and EMG during Treadmill Walking Task

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Background: To evaluate walking ability of stroke patients before and after rehabilitation, functional assessment tools *e.g.*, lower extremity Fugl-Meyer motor function scale (FMA), modified Ashworth scale (MAS), or Holden walking function rating scale (FAC), have been widely adopted. Although they have performed to judge the effect of functional motor recovery of lower limb, they cannot verify the change of cortical activity and reorganization of motor network occurring with motor function recovery. Therefore the aim of the study is to investigate the correlation between cortical activation measured with fNIRS and EEG and muscular activation measured with EMG during treadmill walking task.

Methods: A healthy subject (aged < 30y) performed treadmill walking motor task in a block design (3 repetitions with 30-s task and 20-s rest). The experimental setup consisted of EEG (28 channels, Biosemi Active Two System, USA), fNIRS (45 channels, foire-3000, Shimadzu, Japan), and EMG (4 channels, Delsys Trigno Wireless, USA) systems. fNIRS and EEG probes were placed corresponding to the motion related cortices region of the subject's scalp using a modified version of the 10-20 electrode-placement system and EMG probes were attached to the rectus femoris (RF) and semitendinosus (ST) of the subject's both thighs. To determine the relationship between fNIRS, EEG and EMG series over the 4 blocks during treadmill walking, their individual features were selected. EMG features were extracted from RMS (root mean square of series) value divided by RVC (reference voluntary contraction). EEG features were calculated by the ratio of ERD (event related desynchronization) and ERS (event related synchronization). fNIRS features were chosen by measuring of HbO (oxygenated haemoglobin). After enveloping all features of fNIRS, EEG, and EMG, their relationship using Pearson's correlation were calculated.

Results and Discussion: fNIRS ($r=0.668$, C_1) and EEG ($r=0.898$, C_1) at the contralateral motor cortex region were significantly correlated with EMG at the right ST. A significant correlation ($r=0.766$) between fNIRS (C_1) and EEG (C_1) was also shown at the contralateral motor cortex corresponding to right ST. This indicates that NIRS is comparable to EEG to determine correlation between cortical and muscular activation during motor tasks. In conclusion, our initial findings show strong spatiotemporal correlations between fNIRS, EEG and EMG data collected simultaneously during treadmill walking task. Future effort should implement these approaches to investigate the neural plasticity effect of recovery after rehabilitation training.

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Adaptability of MR head image using new pulse sequences for fast segmentation algorithms to construct subject-specific head models

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Realistic human head models to analyze light propagation in the human head have been used to predict spatial sensitivity profiles in order to reconstruct brain function images measured by fNIRS. The anatomical structure of subject-specific head models is usually derived from T1-weighted (T1W) or T2-weighted (T2W) individual MR images. Although the accurate segmentation of the superficial tissues, such as the scalp, skull and cerebrospinal fluid (CSF) is important for the subject-specific head models, contrast among superficial tissues in the T1W and T2W images is sometimes not sufficient for the automated segmentation of the superficial tissues. This causes time-consuming manual correction during the segmentation process. It is important for the construction of subject-specific head models to reduce the manual correction process. In a previous study [1], we revealed that fat saturated proton density weighted (FSPDW) and fast imaging employing steady-state acquisition (FIESTA) are adequate pulse sequences to segment the superficial tissues. In this study, the superficial tissues were segmented from the MR head images acquired by the FSPDW and FIESTA using publicly available software for the automated segmentation to demonstrate the adaptability of these MR head images to the segmentation software.

MR head images of healthy volunteers with informed consent were acquired with the T1W, T2W, FSPDW and FIESTA pulse sequences by a 3.0-T MR system. In both the T1W and FSPDW images, the skull produces a dark signal. A brain extraction tool (BET) [2, 3] was used to segment the scalp and skull regions in the T1W and FSPDW images. The CSF produces a bright signal whereas the brain and skull produce dark signals in both the T2W and FIESTA. FMRIB's automated segmentation tool (FAST) [4] was used for the segmentation of the CSF region in the T2W and FIESTA. The results of the automated segmentation were compared to the results of the manually generated ground truth data.

The general tendency of the scalp and skull regions segmented from the FSPDW images is almost the same as that segmented from the T1W images, however, the significant error in segmentation is observed around the bone marrow in the skull region in the results segmented from the T1W because the bone marrow produces a bright signal in the T1W images. This type of error is not observed in the segmentation results from the FSPDW images because the bone marrow in the skull produces a dark signal as does the skull region. The CSF region segmented from the FIESTA images is almost the same as that from the T2W. The acquisition time of the FIESTA is much shorter than that of the T2W. Noise is mainly observed around the CSF-brain boundary in both results. This noise might be caused by the blood vessels on the brain surface and can be easily reduced by a post processing using a morphological operation and label processing.

These results show that the FSPDW images are appropriate to segment the scalp and skull regions using the BET, and the FIESTA images are suitable to segment the CSF region using the FAST. They are suitable for the publicly available software for the automated segmentation of the MR head images and are expected to reduce the time-consuming manual correction process compared to the segmentations from the T1W and T2W images.

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Analysis of time-resolved spatial sensitivity of NIRS using null source-detector separation

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Recently, a time-resolved near-infrared spectroscopy system using fast-gated single-photon avalanche diode detectors has been developed [1]. This system can selectively detect the late arrival photons, which potentially propagate into the deeper part of the tissue, at the same position as the light source by the time gate method whereas the detector should be placed about 30 mm from the source in the conventional NIRS system. The small source-detector separation reduces broadening of the spatial sensitivity, and NIRS using null source-detector separation is expected to improve the spatial resolution of the diffuse light imaging. In this study, light propagation in the head models is simulated in order to investigate the influence of the optical heterogeneity of the head on the time-resolved spatial sensitivity of NIRS using the null source-detector separation.

Light propagation in three types of head models was predicted by a Monte Carlo simulation. A five-layered head model consists of the scalp, skull, cerebrospinal fluid (CSF), gray matter and white matter. In a four-layered model, the CSF is replaced by the skull. The depth of the gray matter surface from the scalp surface in the four-layered model is the same as in the five-layered model. The optical properties of each type of tissue were chosen from the literature. Optical heterogeneity of the head is ignored in the homogeneous model. A collimated beam was perpendicularly incident on the scalp surface and the light scattered out from the model within a 0.5 mm radius around the incident point was detected in order to calculate the temporal variation of the photon density, time-resolved intensity of the detected light and partial optical path length in each tissue as a function of the detected time. The temporal variation in the spatial sensitivity profile for the detected light was calculated from the photon density.

The light detected later than 1 ns penetrates into the gray matter both in the four- and five-layered head models. The intensity of the light detected at 1 ns is about 10^{-6} to the peak value. The partial optical path length in the gray matter increases with an increase in the detected time, and the partial optical path length in the gray matter in the five-layered head model is slightly longer than that in the four-layered head model. The partial optical path length in the gray matter is about 10% of the total optical path length for the light detected at 1.5 ns in the five-layered model. The light detected later than 2 ns penetrates into the white matter, however, the intensity of light detected at 2 ns is about 10^{-9} to the peak value and it is probably lower than the detection limit in the practical measurements.

Fig. 1 shows the spatial sensitivity profiles of the light detected at 1.2 ns. The light penetration into the deeper region in the four- and five-layered head models tends to be reduced by the tissue heterogeneity compared to that in the homogeneous model. The spatial sensitivity in the gray matter in the five-layered model is laterally broadened because of the influence of the CSF.

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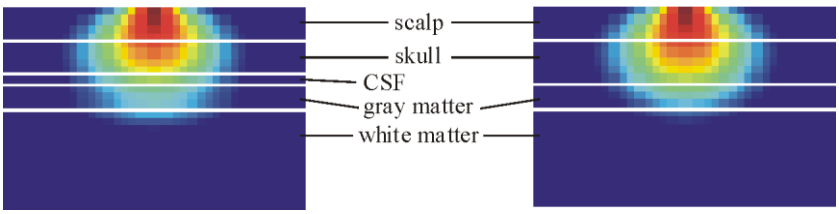

(a) five-layered model (b) four-layered model

Fig. 1 Spatial sensitivity profile of light detected at 1.2 ns in five- and four-layered head model.

Evaluation of relationship between density of measurement points and point spread function of diffuse optical imaging

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One of the serious problem with near-infrared topography is the limitation of the spatial resolution caused by the sparse probe arrangement and broadened spatial sensitivity profile for each probe pair. By using overlapping measurements and a forward model that describes the light propagation in the underlying tissue, high-density probe arrangement diffuse optical tomography can generate three-dimensional images of the changes in the hemoglobin. In this study, light propagation in a head model was predicted in order to analyze the relationship between the probe density and point spread function of the diffuse optical imaging.

In the lattice arrangements, the source and detector probes are alternatively attached at 30 mm interval lattice points and the source-detector pairs of which their distance is 30 mm are selectively used for the measurements. In the high density lattice arrangement, the source-detector pairs are added to form overlapped lattices. The distance between the neighboring measurement points in the single, double, quadruple, octuple and 16-hold probe arrangements is 21, 15, 10.6, 7.5, and 5.3 mm, respectively. The number of measurement points in the 30 mm × 30 mm region of interest (ROI) for these probe arrangement is 4, 9, 13, 25, and 41. The multi-distance arrangement is shown in Fig. 1. The first nearest neighbors for the measurements is defined as the source-detector pairs of which the distance is 30 mm. The second and third nearest neighbors of which the distances are 36 and 41 mm were also used to increase the density of the measurement points, however, the measurement points for the second and third nearest neighbors are the same as those for the first nearest neighbors. The image quality was evaluated by the point spread function. The change in intensity caused by the absorption perturbation in a 1-mm cube in the gray matter detected by each source-detector pair was predicted by a Monte Carlo simulation and the image, which represented the point spread function, was reconstructed from the change in intensity and spatial sensitivity profile of the source-detector pairs. The position of the absorption perturbation is changed in the ROI. Fig. 2 shows the relationship between number of the measurement points in the ROI and FWHM of the point spread function. In the case of the lattice arrangements, the average FWHM decreases with a decrease in the distance between the neighboring measurement points when the distance is longer than 10 mm. When the distance between the neighboring measurement points is less than 10 mm, the point spread function was slowly improved with a decrease in the distance. In the case of the multi-distance probe arrangement, the density of the 30-mm distance probe pairs is slightly higher than that of the quadruple probe arrangement, and the FWHM of the image reconstructed from the change in intensity detected by the 30-mm distance probe pairs alone was slightly smaller than that for the quadruple probe arrangement. The image reconstructed from the change in intensity detected by the first and second nearest neighboring measurement points was improved compared to that reconstructed from only the first nearest neighboring measurement points. In the case of using the first to third nearest neighbors, the number of measurements points in the ROI was 80, however, the average of the FWHM was almost the same as that reconstructed from the first and second neighbors.

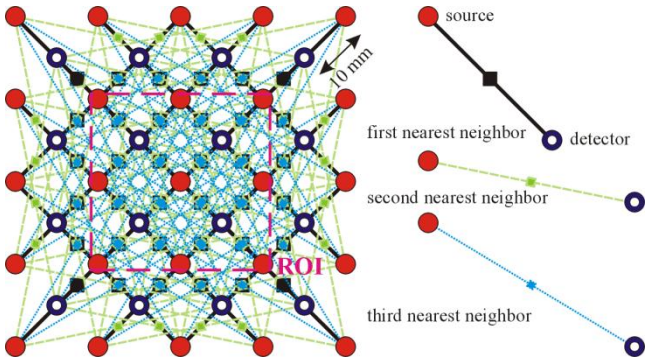

Fig. 1 multi-distance arrangement.

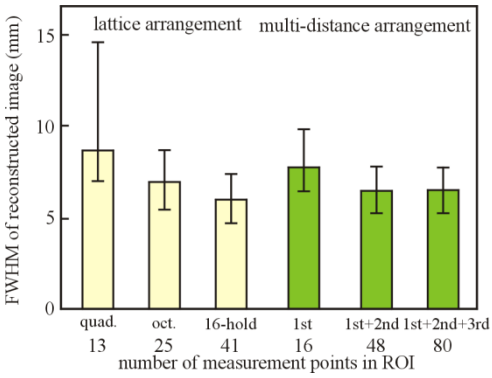

Fig. 2 FWHM of reconstructed images.

Evaluation of semi-subject-specific head model for fNIRS based on MR images of Japanese human head

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A high-density probe arrangement and image reconstruction based on the light propagation in a subject-specific head model can significantly improve the image quality of functional near-infrared spectroscopy. A semi-subject specific head model, which was generated from the standard head model based on the ICBM 152 nonlinear atlas and a set of external fiducials based on the 10-20 international standard, was proposed for patients who cannot have their head images acquired by MRI [1]. Since the structure of the inner tissues in the semi-subject specific model was determined by the set of external fiducials, the boundaries of the inner tissue structure of the semi-subject-specific head model were different from those of the subject-specific head model. In this study, an average head model was constructed from the MR head images of Japanese people. The semi-specific head models were generated from the average head model and a set of external fiducials on the subject-specific head models. The boundaries of the inner tissue of the semi-subject specific head models were compared to the corresponding subject-specific head models in order to evaluate the semi-subject-specific head model based on the average head model.

The MR head images of 46 healthy Japanese volunteers (26 males, 20 females; aged 37 ± 12) with informed consent were obtained in order to construct the subject-specific head models. The images were segmented into four types of tissues, the scalp, skull, cerebrospinal fluid and brain. The 46 head models were normalized by SPM [2] to generate an average head model. In the subject-specific head model and average head model, a set of external fiducials were determined based on the 10-10 international standard. A set of external fiducials on the average head model was registered to that on a subject-specific head model for each volunteer using an affine transformation to generate a semi-subject head model. The ratio of the thickness of the superficial tissues to the size of the head in the semi-subject head models was the same as that in the average head model.

Fig. 1(a) shows the scalp and brain surfaces of a subject-specific head model, and Fig. 1(b1) and 1(b2) show those of the semi-specific head models generated from the average head model based on the MR head images of Japanese volunteers and the ICBM 152 nonlinear atlas from the Montreal Neurological Institute [3], respectively. The cephalic index, which shows the ratio of the maximum width of the head to its maximum length, of the average head model generated from Japanese volunteers is smaller than that from the ICBM 152 nonlinear atlas. The difference in the boundary of the inner tissue structure between the semi-subject specific head models and the corresponding subject-specific model varies between individuals. The averaged error in both the semi-subject-specific head models is almost the same in the whole area of the head except for the CSF thickness around the longitudinal fissure and the skull thickness around the frontal sinus.

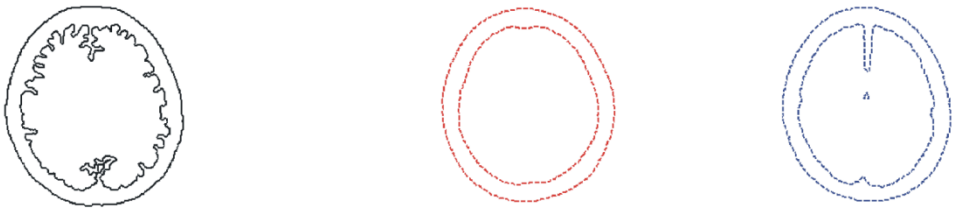

Fig. 1 The boundaries of the scalp and brain surfaces in the subject-specific and semi-subject-specific models.

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Analytical Characterization of the $In_{0.53}Ga_{0.47}As$ n^+nn^+ Infrared photodetectors

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Abstract

One of the most critical parts in fiber communication system is the receiver of the optical signal. Optical receiver in a digital communication system contains the photodetectors, tranimpedance amplifier and post amplifier then followed by decision circuit. The photodetectors characterization based on electrical and optical parameters of the devices where the dimensions of the structure are comparable with the incident wavelength [1]. On the other hand, the appropriate choice of the photodetector is related to the responsivity value which is proportional to the efficiency absorption of the photons, the excess carrier generation, the free carrier concentration of the emitter layer and the optical incident power.

The homojunction nanostructures have been demonstrated as wavelength tunable infrared detectors in recent years. This concept was successfully tested on Si [2], Ge and InGaAs materials [1]. Moreover, the $In_{1-x}Ga_xAs$ has a high intrinsic carrier concentration with a high carrier mobility and saturated velocity. This material can detect and amplify radiation of wavelength within the range from 0.1 μm to 2 μm which is of recent interest in fiber-optic communication systems [1].

The power necessary to generate an output signal equal to the noise is known as the Noise Equivalent Power (NEP). The NEP is the optical power that generates sufficient photocurrent to equal the noise current. However, the current noise level, of the structures and the materials used for the detection, can determine the radiative noise arriving at the detector from the background environment [3].

This contribution presents an analytical model for the calculation of the responsivity and the detectivity of the $In_{0.53}Ga_{0.47}As$ n^+nn^+ diode by using the current spectral density (current noise) in a n^+nn^+ structure developed in Ref. [4]. The current noise is evaluated at room temperature and under a constant voltage applied between the diode terminals. The noise calculation considers the synchronous motion of the free carriers in each region of the structure, the so-called "returning" carriers and the plasma resonances at the n^+n homojunctions [5].

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Total Variation Based Reconstruction for Diffuse Optical Tomography

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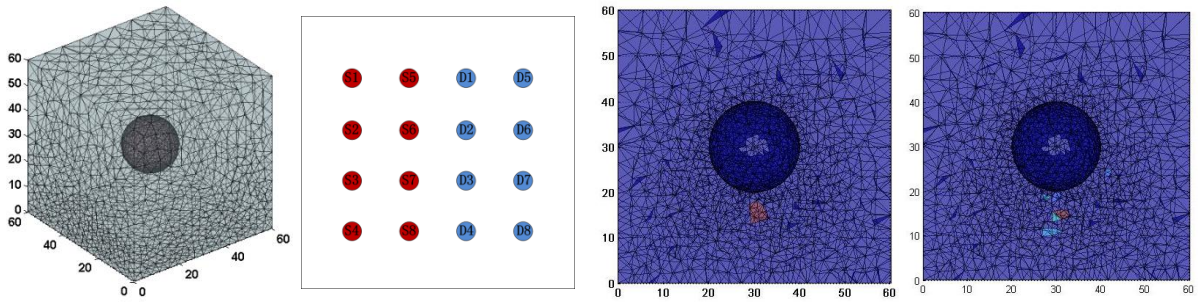
Diffuse optical tomography (DOT) has been developed to map two-thirds of brain functions with over hundreds of channels with desirable spatial and temporal resolution [1]. The imaging modality has been employed to a variety of applications to perform efficient imaging of hemodynamic response of a subject's brain [2]. System progress and application extension required DOT provide image or distribution of hemodynamic response within a region of a brain. However, the reconstruction is challenging in fact, because the number of channels measuring data in DOT system is dramatically fewer than the number of positions in a brain, wherein hemodynamic response need to solve.

The reconstruction problem has been cast into an inverse problem, since the diffusion process from activated region to data measured on a subject's scalp was modeled as a forward problem. Given a measurement sensitivity matrix, *A*, data measured, *b*, could be expressed as, $Ax = b$. Here *x* is the response we expect to know from data, *b*. Tikhonov regularization has been often utilized in DOT to achieve a solution. However, brain response to a task could not be confined to a smooth response. Therefore, a smooth minimum to cost function could lose specificity of a functional response. To overcome the shortcoming, we would propose to utilize total variation regularization to solve the reconstruction problem. By the regularization, the problem is to reach the minimum, $\min_x \|x\|_1$ s.t. $Ax = b$ and $x \geq 0$. Here $\|\square\|_1$ is the l_1 norm.

We did a simulation experiment to demonstrate the performance of this reconstruction method. In the experiment, we supposed a box object, 60mm*60mm, containing a sphere in the center with a radius of 5mm with different optical properties. Then the estimation of photon flux from positions of sources and detectors of DOT would be used to get the measurement sensitivity matrix, *A*. Given a cubic activation at [30, 30, 15] mm. We calculated the measurement, *y*.



(a) (b) (c) (d)

Fig. 1. Phantom (a), optode arrangement (b), original activation (c) and reconstructed activation (d).

Fig. 1 shows original activation and reconstructed activation. In subfigure (c), original activation presents a cubic activated region at [30, 30, 15] mm. Subfigure (d) shows reconstructed activation. The activation also locates at [30, 30, 15] mm and with a shape similar to cube. The simulated experiment demonstrates that the reconstruction method with total variation regularization is sufficient to obtain a solution with sparsity.

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A new linear regression method for fNIRS data mapping

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Introduction. We propose a new algorithm, based on a linear regression model, to statistically discriminate the hemodynamic activations in fNIRS data sets. The method is tested on simulated data and then validated on in-vivo measurements. In particular, we focus on time domain (TD) fNIRS in order to better discriminate between cortical activation and superficial physiological changes [Torricelli et al., 2014]. However, the proposed method is also applicable to CW or FD fNIRS datasets.

Simulated data. A simulated dataset is created to mimic multichannel TD fNIRS measurement on healthy adult during a motor task (10 trials; 10s baseline, 20s right handgrip, 10s recovery; 400s overall length). The head is modeled as a bilayered medium with 1cm thick the upper layer (scalp, skull and cerebrospinal fluid). Reference values for O_2Hb and HHb in the superficial (lower) layer are 12 μM (30 μM) and 7 μM (20 μM), respectively. The O_2Hb and HHb concentrations in the upper layer are kept constant at the reference value, while in the lower layer we computed the hemodynamic response function (HRF) [Scarpa et al., 2013]. The optode locations for 30 independent channels around C3 and C4 are shown in Figure 1. A not uniform activation was simulated: 100% HRF in channel 17; 50% HRF in channels 18, 21 and 29; 25% HRF in channels 16 and 28.

Regression model. A pre-processing algorithm (sample mean subtraction and smoothing spline interpolation) was initially applied to the fNIRS data set. For each channel, rather than using all the 400s for a single linear regression model, we divide the data in 10 sub-intervals of 40s length, applying to each one a linear regression model. We obtain the regressors through a convolution between a step-function and the HRF. For each channel we use the following linear regression models:

$y^i = X\beta^i + \varepsilon^i$, where *i*, is the channel number and

$$y^i = \begin{bmatrix} y_1^i \\ \dots \\ y_{40}^i \end{bmatrix}, X = \begin{bmatrix} 1 & rest_1 & task_1 \\ \dots & \dots & \dots \\ 1 & rest_{40} & task_{40} \end{bmatrix}, \beta^i = \begin{bmatrix} \beta_0^i \\ \beta_{rest}^i \\ \beta_{task}^i \end{bmatrix}, \epsilon^i = \begin{bmatrix} y\epsilon_1^i \\ \dots \\ y\epsilon_{40}^i \end{bmatrix}.$$

Then, for each channel and sub-interval, we calculate the Ordinary Least Squares estimators for β_i. In this way we obtain fitted values $\hat{y}^i$ more similar to y_i than the ones found through a single linear regression model. We test the Gaussianity of the $\hat{\beta}^i$ coefficients and the Gaussianity of the linear combination $\hat{\beta}_{task}^i - \hat{\beta}_{rest}^i$. For each channel a hypothesis test on the expected value of these linear combinations was conducted. We expect the rejection (acceptance) of the null hypothesis for the activated (non-activated) channels. An example of statistical activation map is shown in Figure 1 for both the head layers. It's clear how with this new method is possible to well discriminate the cortical activations in the deeper brain region.

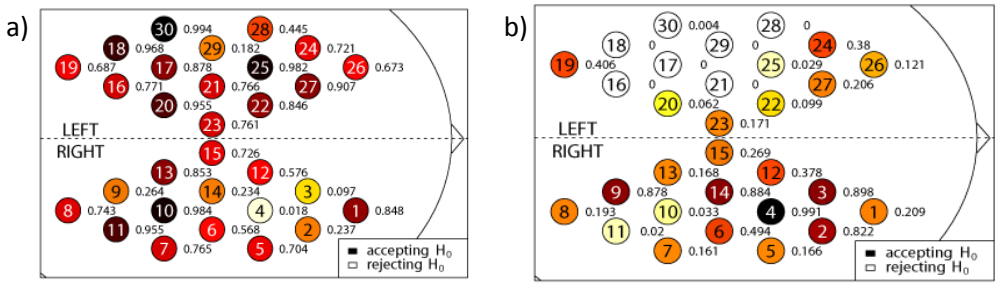

Figure 1. Statistical activation map for upper layer (a) and deeper layer (b). The numbers inside the circles are the channel numbers while the numbers outside the circles are the p-values.

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Non-linear Kalman filtering-based approach for physiological noise reduction in HRF estimation using SS-channel signals

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fNIRS signals are contaminated by extra-cerebral physiological noise, which makes the estimation of the hemodynamic response function (HRF) difficult. Information brought by short-separation (SS) channels (i.e. source-detector distance < 1 cm), which probe head superficial layers but not the cortex, has been proven to be useful to deal with physiological noise affecting long-separation (LS) channels [1]. Many methods have been proposed to deal with this issue [2, 3]. However, none of them has become a standard procedure and reducing physiological noise in fNIRS studies is still an open issue.
Here we propose a three-stage method to estimate HRF by exploiting the availability of SS-channel data. First, physiological noise is modeled as a sum of sinusoidal waves with parameters fitted against SS-channel data by employing a non-linear version of the Kalman filter (KF). Two different implementations are assessed, the Unscented Kalman Filter (UKF) and the Extended Kalman Filter (EKF). In the second stage, the so-modeled noise is subtracted from LS-channel signals. Finally, the HRF is modeled as a specified set of normalized Gaussian functions [3] whose parameters are fitted against the corrected data through a linear KF.

To assess the proposed method, simulated data were created by adding to resting state data, acquired from 7 healthy participants, 36 different synthetic HRFs. Mean HRFs were recovered for each participant and channel, and the percentage estimation errors were computed. Results were compared with those obtained by Conventional Averaging (CA), KF without SS signal regression (equivalent to the 3rd stage of our method), the non-parametric method proposed in [1] and the linear KF proposed in [3]. Results suggest that the proposed approach, in both its EKF and UKF implementation, performs better than the other available methods (Fig. 1). In particular, the error is reduced by ~75% compared to CA and by ~36% compared to KF without SS signal regression, further strengthening the advantage of recording SS-channels in fNIRS acquisitions. Furthermore, the -20% of error with respect to [1] suggests that model-based approaches can provide better results than non-parametric ones. Finally, the new approach performs better than the LKF method proposed by [3], reducing the error by ~15%. This last result might indicate that non-linear approaches are required to correctly model physiological noise contaminating fNIRS signals. Notably, the participants were acquired whilst performing a right-hand finger-tapping task. Preliminary results on these data showed the ability of the proposed method to recover HRFs in accordance to literature (i.e. higher in the contralateral hemisphere), while HRFs estimated without the regression of SS signals were most of the time non-physiologically shaped.

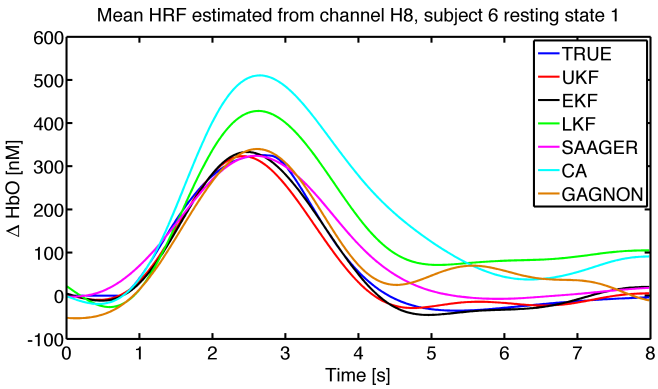

Fig.1: examples of estimated mean HRFs

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Thermal Impact of Functional Near Infrared Optical Brain Imaging

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The propagation of laser light energy in tissues is an important issue in optical imaging, especially with the use of lasers as light sources in certain application like Diffuse correlation spectroscopy (DCS) [Durduran et al., 2011]. DCS uses the temporal fluctuations of near-infrared (NIR) light to measure cerebral blood flow (CBF) non-invasively [Roche et al., 2011]. Often a slight difference in delivered energy (raise the temperature) separates a harmfulness/uselessness of an optical imaging approach, which has to be investigated to ensure consideration of safety standards for its application (e.g. preterm infants, children, adults). As a temperature increases greater than 1°C can have long-term effects on the brain tissue according to IEEE standard [LaManna, 1989]. To evaluate the temperature increase in the different head tissues due to NIR light, a 3D-CAD model composed of six layers (skin, fat, bone, dura, CSF and brain) is used by numerical simulation using finite element analysis (FEA). Tissue parameters (dielectric, thermal conductivity, density, heat capacity at constant pressure, metabolic rate, blood perfusion, relative permittivity, electrical conductivity, absorption coefficient and diffusion coefficient) were used to simulate the optical propagation of the line of a laser through human head tissues. The laser light is defined by a point source and model an optical fiber positioned orthogonally at the surface of the head. The laser source sends out a Gaussian pulse and the diffusion equation of fluence rate is represented by the Helmholtz equation. A 3D bio-heat equation thermal diffusion model computed the temperature distribution within the tissue at different times during laser irradiation. Temperature field calculations show a higher subsurface temperature for a highly scattering medium during laser irradiation. Neglecting the anisotropic properties of tissue as well as the optical discontinuity would result in maximum temperature increase about 0.0196°C for the power consumption of DCS about 28 mW. The thermal impact of a laser light source do not show high thermal elevation in tissue more than standard 1°C which also depends on the time duration of laser irradiation as exponential function asymptotic to ΔT=0.02°C. The thermal elevation rate decrease after 1200s due to blood perfusion which plays a significant role in thermal regulation of a living body (the brain blood circulation remove heat away from the laser point source). These results for opto-thermal temperature distribution could be used for choosing appropriate number of laser sources to design optical imaging cap specifically for human head.

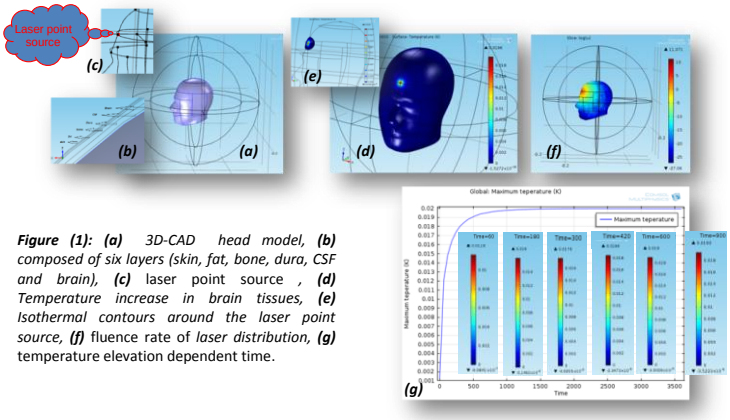

Figure (1): (a) *3D-CAD head model,* ***(b)*** *composed of six layers (skin, fat, bone, dura, CSF and brain),* ***(c)*** laser point source *,* ***(d)*** *Temperature increase in brain tissues,* ***(e)*** *Isothermal contours around the laser point source,* ***(f)*** fluence rate of *laser distribution,* ***(g)*** temperature elevation dependent time.

FC-NIRS: A Functional Connectivity Analysis Tool for near-infrared spectroscopy data

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Abstract: As an emerging optical brain connectivity tool, functional near infrared spectroscopy (fNIRS) has displayed the valued potential in the identification of resting-state functional connectivity (FC) [1]. However, corresponding software packages for functional connectivity analysis are still lacking. In order to facilitate the fNIRS-based human functional connectome studies, we developed a MATLAB software package for the fNIRS-based connectivity analysis, called FC-NIRS (functional connectivity analysis for near-infrared spectroscopy). The package's functions include preprocessing, quality control, FC calculation and network analysis. The preprocessing supports signal conversion of optical denstidy to hemoglobin concentration information, correction of motion-induced artifacts, and improvement of low signal-to-noise ratio signal. Some codes were modified based on Homer2 [2]. In order to control the quality of fNIRS data for connectivity analysis, we recheck the data good or not from meaures of motion artifacts and signal to noise ratio. Then, We offer seed-based and whole-brain FC analysis in our FC calculation section. In the Network analysis module, we provide comprehensive analysis on the topology of brain network in parallel way by calling our in-house software package GRETNA[3]. In addition, FC-NIRS has a friendly graphical user interface(GUI), allowing the researches to do data analysis in an easy, flexible and quick way.

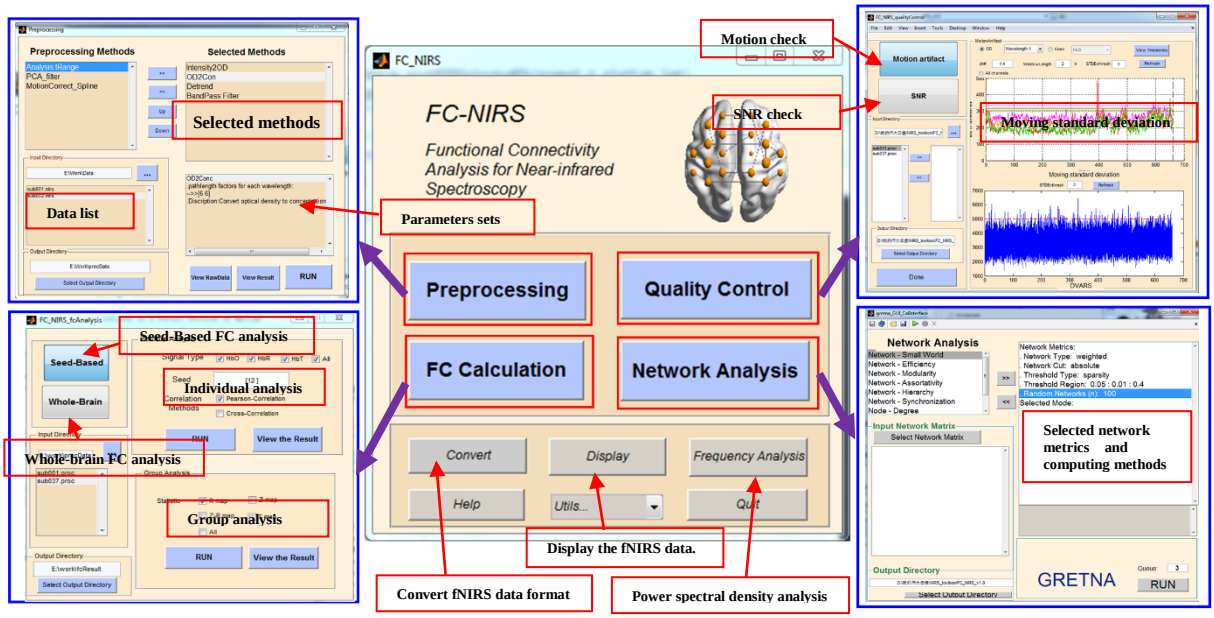

Figure. The software package's main window and four sub-windows.

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Separation of superficial and cerebral hemodynamics based on time-domain fNIRS and two-layer analysis

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In fNIRS measurements cerebral hemodynamic signals are often superimposed by superficial hemodynamics which can be both spontaneous or task evoked [1]. We developed a new method to separate superficial and cerebral signals employing time-domain fNIRS measurements at a single source-detector separation and a two-layered model of the head [2]. The sensitivity factors used in the reconstruction were calculated from individual optical properties. The method was validated on a two-layer liquid phantom and applied to *in vivo* data.

All phantom and in-vivo measurements were carried out with a time-domain brain imager described previously [3]. The liquid phantom consisted of two layers (1 cm and 6 cm thick), filled with solutions of Intralipid and ink. The amount of absorber was increased stepwise for each layer separately. Various *in vivo* experiments on adult subjects were analyzed, in particular with cognitive stimulation (continuous performance task) [1] and motor stimulation (ball squeeze exercise).

The layered reconstruction was based on statistical moments (integral, mean time of flight m_1 and variance V) of the measured time-of-flight distributions of photons [4]. Given the sensitivity factors for the two layers skin and brain for these moments, the concentration changes of oxy- and deoxy-hemoglobin (HbO, HbR) for these two layers were calculated. It was assumed that there are no relevant hemodynamic changes in an intermediate (skull) layer. For each subject, effective homogeneous baseline optical properties were derived from m_1 and V according to [4] and used to obtain subject-specific sensitivity factors. This was facilitated by a look-up table (LUT) for sensitivity factors for a set of values of the (homogeneous) optical properties and layers of 2 mm thickness, based on a forward model for time-resolved light propagation in a layered turbid cylinder [5]. For the phantom experiment the thickness of the layers was known. For the *in vivo* studies the thickness parameters were taken from anatomical MRI, if available, otherwise typical values were assumed.

Absorption changes in the two-layer phantom were retrieved with an accuracy of better than ±20% of the true value. For *in-vivo* data the application of the method resulted in a robust separation of superficial and cerebral hemodynamics producing physiologically reasonable time courses for the scalp and brain compartments. Limitations of the approach include the simplifying assumptions regarding geometry and optical properties. However, at present there is no reliable method available to determine subject-specific optical properties for several compartments of the head. Thus our approach is a reasonable compromise. Having in mind the substantial inter-subject variability of tissue optical properties, the method is superior to the use of fixed literature values. The novel method improves the quantification of cerebral hemoglobin concentration changes by separating interfering superficial contamination from cerebral signals, taking into account subject-specific parameters. The new approach enhances the inter-subject comparability in fNIRS studies, decreases inter-subject variability and thus enables improved fNIRS results on the group level.

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Optimization of the general linear model for fNIRS with an adaptive hemodynamic response function

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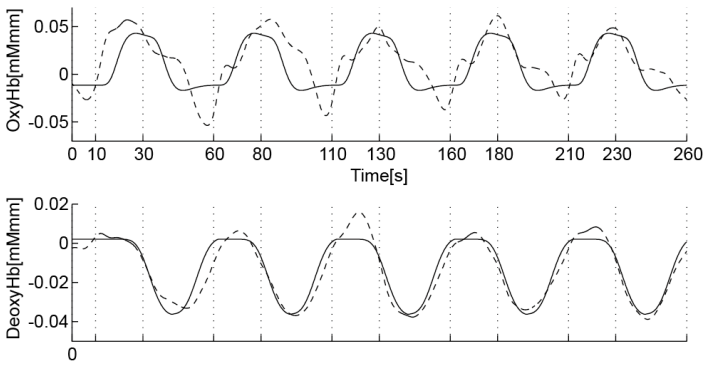
fNIRS allows the acquisition of a wider variety of parameters than does fMRI. While fMRI measures blood oxygen level dependent (BOLD) signals mostly reflecting deoxygenated hemoglobin (deoxy-Hb) concentration changes, fNIRS can utilize both oxygenated (oxy-) and deoxy-Hb signals. In addition, fNIRS enjoys higher temporal resolution than fMRI: While the typical sampling rate of fMRI is on the order of seconds, that of fNIRS is on the order of 100 ms for typical measurements or of 10 ms for highly-tuned settings. An increasing number of functional near-infrared spectroscopy (fNIRS) studies utilize a general linear model (GLM) approach, which serves as a standard statistical method for fMRI data analysis. In actual data analysis, it is the general practice to use default settings for temporal parameters such as peak delays of the gamma functions as provided by data analysis tools such as SPM (statistical parametric mapping). These parameters were first proposed by Boynton, et al. (1996, JNS 16:4207) so as to empirically describe the observed BOLD signal in response to the preceding neural activity. Although these temporal parameters stand as the fundamental basis of GLM, little consideration has been given to the validity of their selection. Thus, we devised a novel GLM-based method utilizing an adaptive hemodynamic response function (HRF). We sought the optimum temporal parameters to best explain the observed time-series data during verbal fluency and naming tasks. The peak delay of the HRF was systematically changed to achieve the best-fit model for the observed oxy-Hb and deoxy-Hb time-series data. The optimized peak delay showed different values for each Hb signal and task. When the optimized peak delays were adopted, deoxy-Hb data yielded comparable activations with similar statistical power and spatial patterns to oxy-Hb data. The adaptive HRF method could suitably explain the behaviors of both Hb parameters during tasks with different cognitive loads during a time course, and thus would serve as an objective method to fully utilize temporal structures of all fNIRS data.



The observed timeline data for fNIRS and optimized HRF for the verbal fluency task. The dashed lines indicate the observed timelines. The solid lines indicate the HRFs, which were calculated using the optimal temporal delays for each condition.

Linear and nonlinear hemodynamic models for the study of cerebral microcirculation with coherent hemodynamics spectroscopy (CHS)

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We have derived a general solution for the nonlinear relationship between changes in cerebral blood flow (input) and the spatially averaged changes in brain capillary hemoglobin saturation (output). This input-output "system" is strictly nonlinear but it can be approximated by a linear system when the changes in blood flow are relatively small. This assumption was used in a previous work where a new hemodynamic model and a novel method for retrieving physiological information from optical measurements with near infrared spectroscopy (NIRS), namely, Coherent Hemodynamic Spectroscopy (CHS), were proposed [1]. CHS is based on inducing periodic hemodynamic oscillations in the brain or in other organs (either by paced breathing, cyclic thigh cuff occlusion, tilting bed etc.) and by measuring the relationships between the oscillations of oxy- (**O**), deoxy- (**D**) and total hemoglobin (**T**) concentrations in the target organ. The bold-face characters indicate that the oscillations in the measured parameters are associated with phasors, which are two-dimensional vectors whose phase and amplitude describe sinusoidal oscillations at a given frequency. The hemodynamic model [1] links the changes in blood flow, blood volume and cerebral metabolic rate of oxygen (inputs) with the phasors **O**, **D**, and **T**. Following our initial work [1], we have implemented an inversion procedure that uses four quantities [|**D**|/|**O**|, |**O**|/|**T**|, Arg(**D**) –Arg(**O**), Arg(**O**)-Arg(**T**)] measured at different oscillation frequencies in order to retrieve a number of baseline physiological parameters related to the microcirculation, such as the capillary ($t^{(c)}$) and venous ($t^{(v)}$) blood transit times [2]. In this study we were motivated to understand to what extent a linear time invariant model (as assumed in [1] and [2]) could be used when the changes of blood flow are larger than 10% (as it is reported in the literature during brain activation). For this purpose we are proposing an original exact solution for the relationship between blood flow changes and hemoglobin saturation changes that can be used potentially for any arbitrary temporal trend of the blood flow. In particular for CHS, where the changes in blood flow are assumed sinusoidal, we were able to derive a semi-analytical relationship, based on the numerical solution of a transcendental equation. For typical values of the baseline physiological parameters ([1] Table 2), the discrepancies between the four spectral quantities calculated by the linear and nonlinear models are less than 5% for **D**|/|**O**| and |**O**|/|**T**| and less than about 0.5° for Arg(**D**) –Arg(**O**) and Arg(**O**)-Arg(**T**), when the changes in blood flow are in the range 15%-33%. For smaller changes in blood flow the discrepancy between the two models are negligible. These preliminary results confirm that a linear time invariant model can be used for describing the change of oxygen saturation in the capillary system when the change in blood flow is up to about 10%. We will report more detailed quantitative results about the limitations of a linear model based on results obtained with our inversion procedure [2].

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Identification of biomarkers suitable for predicting cognitive decline in patients undergoing cardiac surgery

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Introduction: Postoperative cognitive decline (POCD) is a complication that remains significantly high in patients undergoing cardiac surgery[1,2]. At time of discharge, 50-80% of patients exhibit POCD, persisting in 20-50% of patients 6 weeks after surgery[3]. Currently available cerebral oximeters that use near-infrared spectroscopy (NIRS) for patient monitoring are based on small-area, low-density arrays and utilize declines in cerebral hemoglobin saturation (Hbsat) to predict POCD, but these devices have demonstrated poor sensitivity[4]. We hypothesize that large, high-density arrays (HDA) of NIRS probes, used in combination with biomarkers based on cerebral autoregulation[5], will provide better predictions of POCD.

Methods: 17 patients undergoing elective cardiac surgery were recruited. Each patient performed a series of neurocognitive tests before surgery and at time of discharge. Patients with >20% decrease in performance in at least 2 of the tests were considered to have acquired POCD as a result of the surgery. Intra-operatively, patients were monitored with a HDA consisting to 48 optical sources and 32 detectors, arranged into 104 overlapping source-detector pairs (channels), with an inter-optode distance of 4 cm. Several biomarkers derived from the NIRS data were tested using rank-sum tests to differentiate the deficit and no-deficit groups. The biomarkers that provided the best discrimination were used as input for binary logistic regression (BLR) analyses, with age and duration of surgery as covariates.

Results: 6 out of the 17 patients were unable to complete the neurocognitive testing. Of the 11 remaining patients, 5 met the criteria for POCD. Rank-sum tests showed that patients with POCD were significantly older than those without ($p < 0.02$), while duration of surgery was not significantly different. Several biomarkers, based on changes in Hbsat, total hemoglobin (Hbtot), or a marker for cerebral autoregulation (Hbsat correlated with mean arterial pressure (MAP)), were tested. The number of autoregulatory failures (defined as Hbsat/MAP correlation > 0.4) was significantly larger in patients with POCD ($p < 0.009$). In the BLR analyses, the autoregulation marker was selected as the single most strongly predictive variable, over age and duration of surgery.

Conclusion: A biomarker that is a surrogate for cerebral autoregulation accurately predicted postoperative cognitive decline in a small patient population. Larger studies using this marker are warranted.

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Fractal structure of cerebral hemodynamics reflects structure of auditory input and motor output variability

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Introduction: The variability present in even the simplest of human movements is not random, but deterministic, with a characteristic fractal structure[1]. In the cases of the much-studied basic actions of rhythmic tapping and human gait, it has been found that this fractal structure can be driven by synchronizing movements with a fractal-structured auditory stimulus[2,3]. Similar fractal structure has been detected in fMRI BOLD[4] and fNIRS[5] signals in resting states and during simple movements, but the relationship between sensory input, motor output variability, and more slowly-changing cerebral hemodynamics has yet to be investigated. This study demonstrates that this relationship is detectable using fNIRS during a simple tapping task. **Methods:** Participants (N = 14) first performed 5 continuous repetitions of 30 seconds of right-hand tapping followed by 30 seconds of rest. Mean levels of oxygenated (HbO) and deoxygenated (Hb) hemoglobin during the tapping periods were compared to those of the previous rest periods, over regions of interest (ROIs) located over the left and right primary motor cortex. The experimenter then conducted a series of fifteen-minute auditory stimulus trials. The auditory stimuli (white-, pink-, and brown-noise structured versions of "Für Elise") were presented in random order, and participants were instructed to tap in synchrony to the notes. HbO and Hb were measured for all trials, and finger taps were recorded using a pressure sensor. The mean, standard deviation, and detrended fluctuation analysis scaling exponent (DFA α) of stimulus inter-beat interval (IBI) and inter-tap interval (ITI) were calculated for each stimulus. Mean, standard deviation, and DFA α of HbO and Hb were compared over stimulus and ROI. **Results:** Comparison of the tapping and rest conditions shows a significant increase in HbO with a corresponding decrease in Hb during tapping, in ROI 1, located over the left side of the primary motor cortex[6]. No such differences were found in ROI 2, on the right side. Mean and standard deviation of ITI of the various stimuli were not significantly different, but DFA α of ITI showed a significant main effect of stimulus, with significant differences between the white- and brown-noise conditions. Mean and standard deviation of HbO and Hb were not significantly different across stimulus or ROI, but DFA α of HbO in ROI 1 (left side) shows a significant main effect of stimulus. **Discussion:** As expected, right-hand tapping was detectable in the cerebral hemodynamics localized over the left primary motor cortex, and as shown in previous work, the fractal structure of the auditory stimulus drives the structure of motor output. In addition, the link between the fractal structure of auditory input and motor output variability was captured by the hemodynamics of the system. This finding suggests that despite the differing timescales of the various subsystems, important information about the dynamics of the system as a whole is carried through the temporal structure of variability.

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nirsLAB: A Problem Solving Environment for fNIRS Neuroimaging Data Analysis

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Access to well-configured computing environments is a necessary factor for accelerating the development of applications derived from data-intensive sensing platforms. In the field of neuroimaging, publicly available resources that support processing of EEG [1], MEG [2] and fMRI [3] measures, among other types of data-intensive platforms, already are well developed. In recent years commercial devices supporting high-density NIRS data have become available, but development of well-configured computing environments that support data processing by non-domain experts has been lagging. Several publicly available platforms have been developed, including Homer 2 [4], NIRS-SPM [5], NAP [6], NILAB and NAVI [7], but each has strengths and weaknesses. Motivating the configuration of resources available in the nirsLAB platform described here was consideration of the need for: 1) improved resources to facilitate editing of data and event-timing information; 2) the capacity to process data collected at a larger number of measurement wavelengths, and to restrict processing to specified subsets of the available wavelengths; 3) improved visualization tools; 4) access to additional utilities that support application development.

Key functionalities of nirsLAB include sensor registration for arbitrary arrays; data- and event-editing tools; artifact correction tools; parameter estimation from up to 8 wavelengths of input (instantaneous, or canonical event-related responses); display resources, including block-averaging and movies, onto planar, scalp and cortical surfaces; anatomical structure identification; Level-1 and Level-2 GLM-based statistical parametric mapping; data-export utilities; recording of data-processing history; and inter-subject comparisons for hyperscanning studies. Also available are utilities for reformatting data, in support of inter-platform compatibility, and for performing batch processing of multiple data sets. User-specified parameter values can be assigned either through keyboard entry or graphically. Access to other utilities for use of machine learning algorithms [8] and 3D image recovery are under development.

As examples of nirsLAB applications, results of analyses performed on data from a hyperscanning experiment, four-wavelength measurements, and an optical-source comparison experiment are presented in this report.

[1] http://sccn.ucsd.edu/eeglab/
[2] http://www.sourcesignal.com/
[3] http://www.fil.ion.ucl.ac.uk/spm/
[4] http://www.nmr.mgh.harvard.edu/PMI/resources/homer2/home.htm
[5] http://bisp.kaist.ac.kr/NIRS-SPM.html
[6] http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0024322
[7] http://www.nitrc.org/projects/fnirs_downstate
[8] http://bbci.de/toolbox/

Transient Artifact Reduction Algorithm (TARA) using Sparse Optimization and Filtering

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In this work, we address the problem of attenuating artifacts arising in biomedical time series, such as those acquired using near infrared spectroscopic (NIRS) imaging devices. Our approach is to formulate an optimization problem, which in turn is based on a signal model that is intended to capture the primary characteristics of the artifacts. We presume only that the artifacts are transient in nature. Specifically, we model the measured time series, $y(t)$, as

$$y(t) = f(t) + x_1(t) + x_2(t) + w(t)$$

where $f(t)$ is a low-pass signal, $x_i(t)$ are two distinct types of artifact signals, and $w(t)$ is a white Gaussian noise process. The 'Type 1' artifact signal, $x_1(t)$, is intended to model 'spikes' and sharp, brief waves, while the 'Type 2' artifact signal, $x_2(t)$, is intended to model additive step discontinuities. Both types of artifacts are observed in NIRS time series.

For the purpose of flexibility and generality, we avoid defining the artifact signals in terms of precise rules or templates. Instead, we define them in terms of sparsity.

1. The 'Type 1' artifact signal x1(t) is defined as being sparse and having a sparse derivative. That is, it usually adheres to a baseline value of zero, as does its derivative. We use sparsity to encode the transient (brief) nature of the artifacts. Modeling the derivative of x1(t) as sparse helps to distinguish it from noise.
2. The 'Type 2' artifact signal is defined as having a sparse derivative. That is, its derivative is mostly zero; hence, x2(t) is an approximately piecewise constant signal. This type of artifact signal is composed of step discontinuities (or approximate step discontinuities), and it does not adhere to a baseline value of zero.

The suppression of Type 1 and Type 2 artifacts individually was addressed in our previous work.[1] However, we had assumed that the measured time series is affected by the presence of either Type 1 or Type 2 artifacts, but not both. Complex artifacts often comprise both types. To handle both types simultaneously, in this work we develop a new algorithm, denoted 'Transient Artifact Reduction Algorithm' (TARA). TARA performs joint optimization to explicitly estimate both types of artifacts. After the artifacts are estimated, they are subtracted from the raw data to obtain a corrected time series.

The TARA approach is non-parametric in the sense that the transients are not modeled through the use of any specified parametric shape. The method is flexible and general enough to encompass a variety of low-frequency background and artifact behaviors, through the tuning of the three parameters and the selection of the low-pass filter.

TARA was devised to have high computational efficiency and low memory requirements by constraining all matrices to be banded, which allows us to leverage fast solvers for banded systems. Moreover, the new algorithm does not require the user to specify auxiliary parameters, such as step sizes, etc. In order to attain computational efficiency and avoid algorithm parameters beyond those appearing in the cost function, the algorithm requires several techniques beyond those used in the previous work.

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Biomarkers for Breast Cancer Detection in the Resting-State Dynamics of the Hemoglobin Signal

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Introduction: Increased tissue stiffness, presence of structural malformations, and altered perfusion of the vascular bed are known phenotypic markers for the presence of breast cancer [1,2]. Awareness of these phenomena has motivated our development of instrumentation platforms that can explore the naturally occurring dynamics of the hemoglobin signal. The dimensionality of the information space that could be explored has prompted us to consider simplified data-collection conditions. An example is a simple resting-state measure, wherein time-series optical measures are obtained from both breasts simultaneously under defined conditions of optode contact [3]. As evidenced by the reported results, promising findings have been obtained based on examination of the resting-state responses.

Methods: Data were obtained during an fNIRS-based breast imaging study conducted primarily to evaluate the potential of applied-pressure and respiratory-gas maneuvers to enhance discovery and characterization of breast tumors. These maneuvers were preceded by a five-minute resting baseline scan. For analysis, a high-pass filter (frequencies > 0.01 Hz) was applied, followed by use of the Normalized Difference Method to reconstruct images of oxygenated and deoxygenated hemoglobin, tissue oxygen saturation, and blood volume [4]. The 4D image time series were reduced to scalar metrics by computing: first, the temporal standard deviation (TSD) in each image voxel (4D→3D) or the spatial mean (SM) or standard deviation (SSD) for each image time frame (4D→1D); second, the spatial mean and standard deviation of TSD, temporal mean of SSD, and temporal standard deviation of SM and SSD.

Results: In most unilateral breast cancer cases the TSD metric in is larger in the tumor-bearing breast, and the region of elevated TSD extends well beyond the known structural borders of the tumor. Corresponding results for cases of benign breast lesions, or no known breast pathology, do not show a comparable asymmetry. In group-level comparisons, all scalar metrics have larger values in the tumor-bearing breast, and show little inter-breast disparity in non-cancer subjects. Using the left-to-right-breast ratio of metric values for bilateral comparisons, there are highly significant group-mean differences between the non-cancer and breast-cancer groups. ROC analysis [5] yields area-under-curve values in the range of 74-86%, sensitivities in the range of 70-84%, and specificities in the range of 76-92%.

Discussion: While the elevated TSD metric extends into regions far from the structural borders of the tumor, imaging results derived from fNIRS data collected during response to either applied-pressure [3] or respiratory-gas [6] maneuvers have shown that tumor locations and sizes can be accurately extracted from the latter. This suggests that resting-baseline recordings are sensitive to dynamic vascular phenomena that do in fact extend over a large percentage of the breast volume. A potentially significant corollary is that it may be possible to conduct breast-cancer screening by means of a simplified bilateral measurement involving a small number of probes distributed over the surface of both breasts.

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Phenotype-Motivated Strategies for Optical Detection of Breast Cancer

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Introduction: Blood delivery to tissue, and bulk fluid redistribution among tissue compartments, frequently are impacted by disease or trauma: for example, derangements in hemodynamic states, accompanied by increased tissue stiffness and local edema, in many breast cancer cases [1]. Accordingly, we have hypothesized that dynamic responses markedly different between diseased and healthy tissues can be induced via applied-pressure or respiratory-gas maneuvers [2,3], and that diagnostic image contrast can be thereby enhanced. Here we present results from pilot studies conducted to evaluate the hypothesis, using an instrumentation platform that facilitates the application of the considered maneuvers, while recording time-series optical measures are obtained from both breasts simultaneously [4].

Methods: Research participants were seated and the sensing heads, which contain the articulating elements used to execute the pressure maneuvers and monitor the resulting skin displacements, were adjusted to make good contact with both breasts. Following a five-minute baseline scan, the skin-optode contact pressure was alternately rapidly (~2 s) increased to a level of either 4.4 N or 7.1 N and lowered to its initial value, and data were continuously collected during the alternating periods (60-120 s duration) of stress relaxation and stress recovery. The preceding sequence was performed twice in succession, with the subject breathing room air in one cycle and a 98% O_2, 2% CO_2 in the other. The Normalized Difference Method was used to reconstruct images of oxygenated and deoxygenated hemoglobin (HbO, HbD), tissue oxygen saturation (HbSat), and blood volume (HbT) [5].

Results: Imaging results obtained from 61 subjects (17 breast cancer, 21 benign pathology, 23 healthy control) are consistent with the hypothesis that the articulation maneuvers enhance the contrast between tumor and healthy tissue. Image contrast is improved by transforming pairs of co-varying image-values to measures of the statistical extremeness for each image voxel [6], and the preceding effect is maximized by referencing the image-pixel data of one breast to the distribution of image values for the other breast. At the group level, paired differences between the numbers of image pixels identified as abnormal is greater for subjects with breast cancer than for either of the other sub-groups, for both types of maneuver. Depending on the Hb signal components and maneuver(s) considered, diagnostic accuracies for breast cancer of ranging from 85% to 97% were obtained (ROC analysis [7]).

Discussion: The controlled manipulations studied had the effect of enhancing detectability of cancer, by exploiting known tumor phenotypes. The impact of the maneuvers on reconstructed images is maximized when the image-voxel data of one breast are referenced to the distribution of image values for the contralateral breast, demonstrating the utility of the simultaneous dual-breast measurement approach.

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Studying the systemic low frequency oscillations using peripheral NIRS recordings

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Introduction: It has been demonstrated that part of the low frequency oscillations (LFOs: 0.01-0.15Hz) observed by functional NIRS (fNIRS) and fMRI have been associated with cerebral blood flow[1, 2]. They have been demonstrated to travel through the brain following the cerebral vasculature using concurrent fNIRS/fMRI [3]. Moreover the same LFOs have been observed in the periphery by NIRS with certain time delays[4]. The origins and functions of these systemic LFOs (sLFOs) are still not clear[5, 6]. We do not even know if there is a single physiological process associated with these sLFOs, or several. To further understand these pure sLFOs, we recorded the LFO signals by NIRS at different peripheral sites (i.e fingertip and toes) to avoid any neuronal contamination and study the correlations between them to explore if they are associated with the same physiological process or different ones.

Method and analyses: In this study, 10 healthy subjects were recruited. Three NIRS probes, designed specifically for fingertip and toe measurements, were placed over the subject's left middle finger and the two big toes. The NIRS data was acquired by the ISS Imagent (ISS, Champaign, IL) at 12.5 Hz for 6-10 mins while the subject was lying quietly looking at a fixation point. For each subject, the total hemoglobin concentration changes (Δ[tHb]) were calculated for three peripheral sites and then selected by a moving window bandpass filter (from 0.01Hz to 0.15Hz with 0.05Hz window size). Time delays between Δ[tHb] measured at: 1) fingertip and left toe; 2) fingertip and right toe; 3) left toe and right toe were calculated (using cross correlation) for each frequency range. Lastly, the time delays were compared to assess if the sLFOs are moving with the same speed (indicating the same origin) or the speed is frequency dependent (indicating different origins).

Result: The time delays between the sLFOs measured at different peripheral sites (i.e. fingertip and toes) are frequency dependent. Greater delays were observed for lower frequencies (<0.05Hz), while the delays are stable for the frequency band above 0.05Hz.

Conclusions: The result indicates that the sLFOs might not be originated from one physiological process. They might have multiple origins and nevertheless travel with the global blood flow circulation to different sites. These features can be measured by NIRS and used in the future as biomarkers to monitor different physiological processes.

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Examining the Effectiveness of Sliding-window Motion Artifact Rejection (SMAR) Algorithm in Detecting Head Motion Artifacts

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Functional near-infrared spectroscopy (fNIRS) is becoming increasingly popular among researchers as a tool for examining neural activation. This technology provides a non-invasive, highly portable, and cost effective option for monitoring the hemodynamic oxygenation of the cortical surface. As a result, it serves as a viable neuroimaging tool that can be used in diverse environments, especially in naturalistic field settings. Although fNIRS is more resistant to motion artifacts compared to imaging modalities such as functional magnetic resonance imaging, motion artifacts still provide a significant source of noise that may contaminate findings. As a means of addressing this issue, a simple and iterative method, named Sliding-window Motion Artifact Rejection (SMAR), was recently introduced for detecting and rejecting motion artifacts from raw fNIRS light intensities[1]. It was demonstrated that SMAR provides an effective automated approach for detecting signal segments that are contaminated with motion artifacts, and even allows this process to be used during real-time applications. The present study sought to examine the effectiveness of SMAR in detecting and rejecting motion artifacts in a multi-channel fNIRS system with a higher frequency of measurement, as compared to the initial SMAR study. More specifically, we evaluated the effectiveness of SMAR in detecting head motion artifacts observed in the raw data acquired by a Hitachi ETG-4000 ® system. Findings demonstrated that, as hypothesized, SMAR was efficient at detecting and rejecting noise associated with motion in the raw fNIRS data. This study adds further credence to the validity and effectiveness of SMAR as an essential tool for addressing motion artifacts in fNIRS studies.

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Evaluation of Functional Near Infrared Spectroscopy (fNIRS) for Assessment of the Visual and Motor Cortices in Adults

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Introduction: Functional near-infrared spectroscopy (fNIRS) is a relatively young technique in the field of medical imaging. As such, it has yet to be widely implemented for clinical use, despite its promising advantages. However, unlike fMRI–its much bulkier and costly counterpart–fNIRS has yet to be proven as a standalone imaging tool within a clinical setting, particularly that of ophthalmology or physical therapy.

Methods: Ten healthy young adults (23.8 ± 4.8 years) participated in the study. Activation of the visual cortex was achieved utilizing various reversing checkerboard stimuli across three data collection sessions for each participant. Further, activation of the motor cortex was achieved using simple grasping and finger tapping tasks. Data was processed with MATLAB scripts and statistical analysis was performed using JMP.

Results: Quantitatively, statistically significant differences in the level of activation were elicited by some stimuli, but not others. No differences were discovered between the levels of activation for the two motor tasks. However, as expected, differences were observed between the hair types of participants for both visual and motor activation. Additionally, one of the three data collection sessions for each participant tended to give statistically different results than the other two. Qualitatively, the number of stimulus events and data channels which showed activation were inconsistent.

Conclusions: It has been shown, both previously (by others) and within this study, that fNIRS is indeed feasible for investigating the visual and motor cortices. However, a reliable level of robustness and sensitivity is required for clinical implementation. This research shows that fNIRS can in fact achieve an appropriate level of sensitivity for visual studies, but it still lacks an appropriate level of robustness in terms of repeatability and corporal differences for assessment of visual or motor dysfunction.

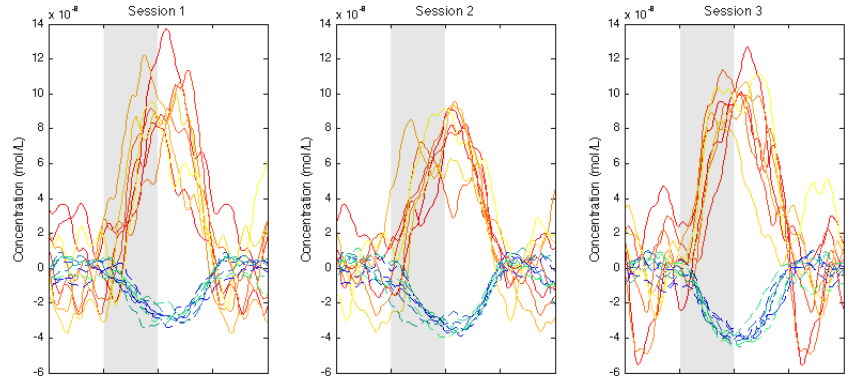

Fig 1: Responses for three trials of the finger opposition task–one from each data collection session–for Subject 1. All eight stimulus events from each trial are overlaid on a single graph for a representative channel. HbO curves range from red (first event) to yellow (eighth event) and Hb curves range from blue to green. The shaded region indicates the duration of the stimulus.

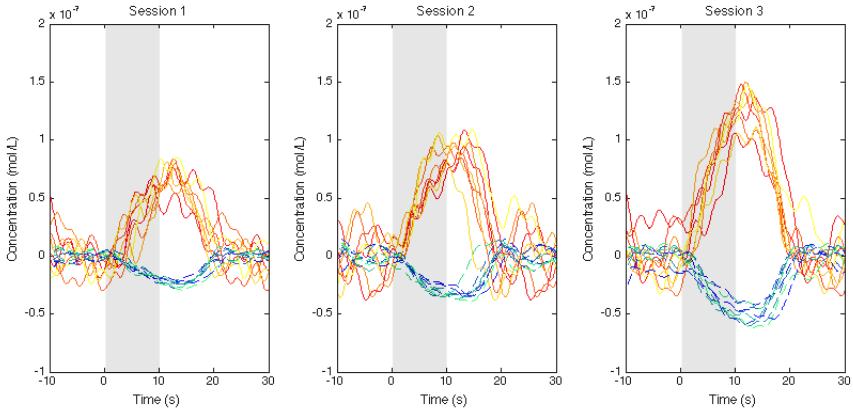

Fig. 2: Responses for three trials using the extra-small checker size–one trial from each data collection session–for Subject 2. All eight stimulus events from each trial are overlaid on a single graph for a representative channel. HbO curves range from red (first event) to yellow (eighth event) and Hb curves range from blue to green. The shaded region indicates the duration of the stimulus and the third session was found to produce significantly different ($p < 0.05$) results than the other two for both HbO and Hb.

Removal of Motion Artifacts from Recorded NIRS Data During Walking

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Introduction

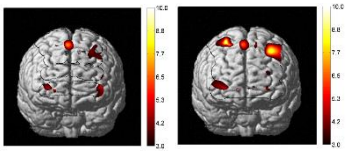
The goal of this study was to investigate methods for movement artefacts reduction in near-infrared spectroscopy (NIRS) data in realistic moving conditions. Clinical data acquired with a portable NIRS system with 16 sources and 16 detectors were used. Subjects were asked to walk and perform a cognitive task during NIRS recordings. The helmet was designed to keep optodes fixed on the subject's head and minimize motion artifacts (MA), however, some MA remained. While previous MA removal algorithms (MARAs) have already featured independent components analysis (ICA) and accelerometers [1] [2], none have been applied on walking subjects, or tested on a large sample. The current study was designed to examine an ICA and accelerometer-based MARA during walking for 25 elderly subjects.

Methods

The testing consisted of three distinct tasks: cognitive, motor, and dual. The cognitive (cog) task was a 2-back working memory test in which the participant had to repeat the number he heard 2 numbers back. The motor task (walk) was free walking on a gym track at a self-selected pace. Cog and walk were also performed concurrently (dual). Ten runs were recorded, with each run lasting 30 seconds, in the following order: Cog–cog-walk–dual–dual–dual–dual–walk–cog–cog. One triaxial accelerometer was placed on the helmet and another on the right ankle. For MA removal, the FastICA algorithm was applied 20 times. Each component was correlated with the accelerometer signals, producing a matrix Corr of coefficients. Components that were most correlated with the accelerometer were removed (Corr (component) > mean (Corr) + 2xdeviation), and the data were reconstructed. The mean square error (Err) between the original data and the reconstructed one was calculated for each decomposition, separately during moving intervals and during rest. To choose the decomposition for optimal MA removal, the criterion used was to maximize Err during moving intervals (Err_max) and minimize Err during rest (Err_min). The quotient $Q = \frac{Err\_max}{(Err\_\min)\hat{}\propto}$ was calculated and α was chosen so that the value of Q is at the corner of the L-curve. Then, Q was calculated for each decomposition, and the one that maximized Q was selected. The NIRS10 toolbox was used to generate maps of the data before and after the application of MARA.

Results

Using MARA had a significant impact on the statistical results: on average a much larger area of the brain was significantly activated, e.g. supplementary motor cortex (Fig. 1) with MA removal than without. For all subjects, the exponent α was found to lie in a narrow range between 0.16 and 0.20. This was indicative that Err_max had a far greater influence on selecting the decomposition than Err_min. The stability of α was surprising given that artifacts in NIRS recordings seemed to feature much heterogeneity.



(a) **(b)**

Fig. 1 HbT, Anova, main effect: (a) without MARA, (b) with MARA

Conclusion

Analyses concatenated all runs from a single subject and the effect of analyzing each run separately will be the subject of future studies. In summary, using MARA appears to remove a significant amount of walk-related movement from NIRS data.

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Comparison of motion artifact correction algorithms for resting state NIRS

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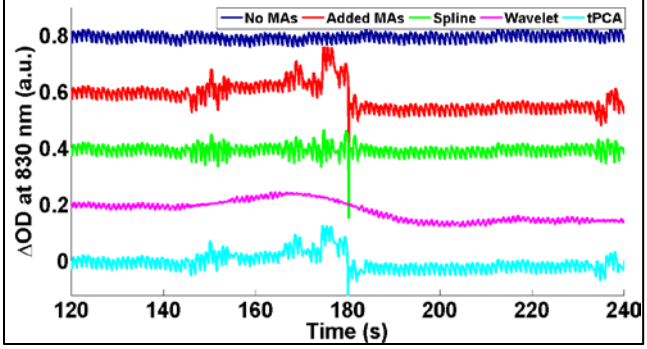
Introduction. Adaptable to challenging populations such as neurocritical care patients, infants, and children, functional near-infrared spectroscopy (fNIRS) is prone to contamination by motion artifacts (MAs). Recently, multiple approaches have been proposed to identify and correct these MAs [1–5]. The performance of some algorithms have been compared based on their ability to accurately measure the cerebral hemodynamic response to functional activation [3–5]. In parallel, a growing body of fNIRS work relies on analysis of physiological oscillations [6], e.g. functional connectivity [7] and cerebral autoregulation studies [8,9]. Here, we investigate the effect of MAs and their correction on such resting-state data, by studying their impact on cross-correlation between symmetrical channels.

Methods. On 28 healthy subjects, we recorded 10 min resting-state datasets symmetrically on the forehead, with minimal motion contamination (MA < 5% of total time, Fig.1 dark blue line). We added MA segments obtained from similar recordings on 28 stroke patients, paired one-to-one to the healthy subjects (Fig. 1, red line). We then applied three MA correction algorithms: spline interpolation [1], wavelet filtering [2], and targeted principal component analysis (tPCA) [5] (Fig.1, green, magenta and cyan lines respectively). All datasets were compared in terms of inter-hemispheric cross-correlation (IHCC) in 4 frequency bands: cardiac (around 1 Hz), respiration (0.25 Hz), low frequencies (LF, 0.1 Hz), and very low frequencies (VLF, 0.04 Hz).

Fig.1- Example ΔOD signal before and after MA addition and correction.



Results. The addition of MAs decreased the average IHCC in all frequency bands and increased variability between subjects. Wavelet filtering failed at recovering the true IHCC, because of its inability to correct for data offsets. Spline and tPCA showed the best correction, with an advantage to spline in the low and very low frequency bands most commonly employed for oscillation studies. Identification of MAs is critical to interpreting quantitatively cross-correlation data, and spline interpolation appears to perform best at retrieving the true IHCC.

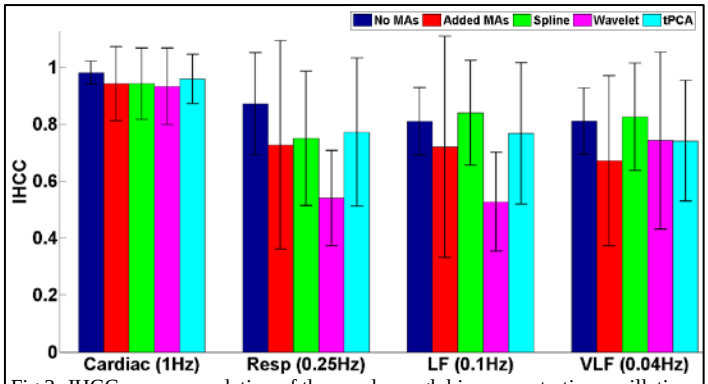


Fig.2- IHCC: cross-correlation of the oxy-hemoglobin concentration oscillations between symmetrical forehead channels, averaged across all subjects.

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Optimizing factors to achieve high quality infant fNIRS time-course data

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Abstract

fNIRS studies of infants are approaching 100 publications, growing exponentially since the first publication by Meek [1] in 1998, and of these only about 30 test alert upright infants within the age range of 6 to 9 months, a juncture at which infant subjects are becoming considerably less compliant. Research to date has tended to publish group averaged rather than individual infant data due to research goals that make broad claims about infant cognition. Acquisition of individual infant time-courses hold interest, however, both for cognitive science and particularly for clinical applications. The limiting factors in acquiring single-infant data are rarely discussed in detail. In this study, we aimed to identify and optimize the factors that affect the quality of NIRS data from individual 6 to 9 month old infants exposed to a visual stimulation paradigm.

The number of fNIRS publications that investigates the cognitive development of pre-verbal infants is relatively low [2-4] compared to adult studies because of the very nature of studying infants. That is, infants will move around and are not necessarily motivated to comply with a given experimental set-up. Most NIRS studies on upright and alert 6 to 9 month old infants report having to reject approximately 50% of measurement trials due to motion artifacts and subject non-compliance. We describe several modifications that address motion/compliance issues and thereby improve NIRS measurements from upright and alert infants. First, the NIRS headpiece is reconfigured with fewer optical fibers to reduce inertia, increase comfort, and improve conformity to the head; at the same time, however, fiber density over the sampled region remains dense to avoid missing the activation. Second, the visual-stimulation protocol is altered significantly to keep the attention of the infants focused on the screen throughout the measurement sequence. Lastly, optical signal strength is screened at the outset of each trial, enabling a quick determination of whether the probe position needs adjustment. With these revisions to the experimental process, we have significantly reduced the typical motion artifacts seen during trials of alert, upright infants, and we obtain visual activation signals from a large majority of infants.

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Understanding Signal-to-Noise ratio for image reconstruction in optical topography

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Abstract

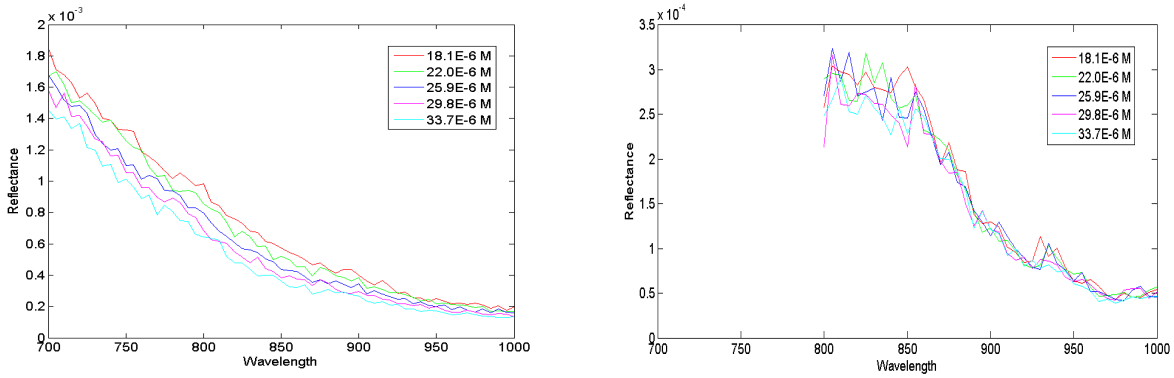
Motivation. Reconstruction of the brain haemodynamics is only possible if the measured reflectance at head tissue surface varies monotonically in the parameter space permitting bijective relations between variations in histophysiological parameters and reflectance observed at head surface. Reconstruction benefits from a high signal-to-noise ratio (SNR), with the key effect of interest being the variations in the haemoglobin concentration irrigating the grey matter.

Aim. Characterize the diffuse reflectance as a function of the changes in oxyhaemoglobin (HbO_2) and deoxyhaemoglobin (HHb) concentrations in the gray matter and evaluate the SNR for the haemoglobin variations in a plausible physiological range.

Methods. A four layered forward Monte-Carlo model of the radiation transport approximating Mie scattering within the adult human head is simulated in *mcml* [1]. To simulate the brain haemodynamics, the absorption coefficient of the gray matter has been altered with absorptions due to a linear combination of HbO_2 and HHb concentrations. The absolute haemoglobin concentrations have been coarsely discretized in five levels covering the plausible physiological range of concentrations at the visual cortex [3]. We have simulated the diffuse reflectance of the adult head model in the wavelengths range from 700nm to 1000nm. The presented reflectance results from integrating backscattered light between 2.5cm and 3.5 cm from the light source where light coming from the cortex is expected to be maximal.

Results. As expected, monotonic decrease in the diffuse reflectance was observed while simulating irradiation at specific wavelengths over the gray matter layer alone. Also as expected, the SNR of the remitted spectra diminishes as other layers of the model are included as depicted in figure 1, but importantly the monotonic behaviour soon seems to be lost.

Conclusions. A number of factors affect reconstruction that ought to be circumvented. The reported deviation of monotonic behaviour complicates reconstruction posing questions regarding how accurate *in-vivo* functional optical neuroimaging can be.



(a) (b)

Figure 1. Simulated remitted spectrums as function of HbO_2 concentrations: (a) considering gray matter layer alone and (b) considering gray matter and skull layers.

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Recording auditory cortex responses using NIRS.

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Near infrared spectroscopy is a non-invasive neuroimaging method with several advantages relative to other hemodynamic-based techniques, such as PET and fMRI. The technique is easy to use on any population, can be used repeatedly and allows us to measure both oxygenated and deoxygenated haemoglobin. This experiment was designed to examine the possibility to employ near infrared spectroscopy to measure responses within the auditory cortex to complex sounds. Stimulations used were 20-seconds blocks of short piano, violin and speech stimuli, previously employed in behavioural and fMRI studies. Recordings were performed with a Brainsight NIRS 32-channel system set to a sampling rate of 20 Hz. Signals were analysed using both deconvolution and averaging techniques. We were successful in recording auditory cortex responses to these stimuli, with both analysis approaches producing similar results and similar source-localizations, which were in superior temporal regions. The results extend previous fMRI results by showing robust responses in oxygenated haemoglobin concentrations.

Optimization of the NIRS technique as a way to measure latency differences in the onset of the haemodynamic response: A comparison of single-subject and jackknife approaches

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Near infrared spectroscopy is a neuroimaging technique that produces measurements of changes in the concentration of oxygenated and deoxygenated haemoglobin concentrations, typically with a higher sampling rate than with other imaging methods based on the haemodynamic response. This project examined the potential of NIRS methods to estimate variations in the latency of haemodynamic responses to experimental events. We used Monte-Carlo simulations using subsamples of real NIRS measures (sampled at 20 Hz using a Brainsight NIRS system) to estimate the statistical power of different approaches (such as fixed threshold, percent of peak, fractional-area latency, for both individual-subject estimates and estimates from jackknife averages) to detect a known simulated latency shift. The simulations used measures of haemodynamic responses in the temporal lobe from a group of young adult participants who listened to auditory stimuli. We estimated the relative sensitivity of different latency measures and approaches to the measurement of latency effects of different magnitudes using realistic noise and signal-to-noise characteristics. The results allowed us to estimate the shortest latency shift that could be estimated with a given statistical power for each combination of measurement and statistical approach.

Analysis of breath hold and hypercapnia *in vivo* DCS data using a layered slab Monte Carlo model

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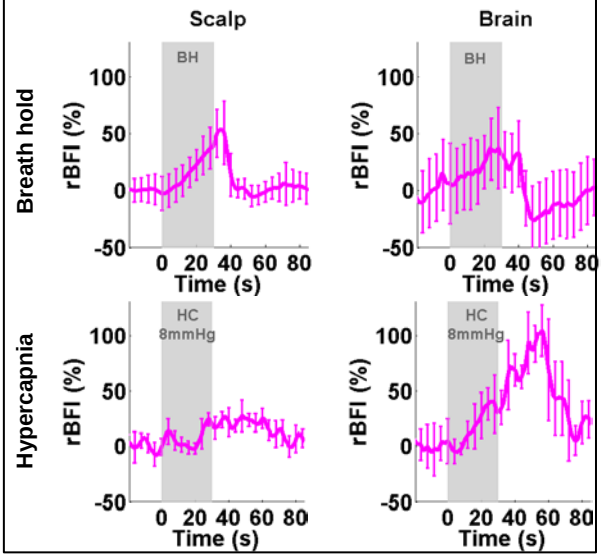
Diffuse Correlation Spectroscopy (DCS) measurements of cerebral blood flow are traditionally analyzed using a semi-infinite homogeneous model [1]. More accurate models have been proposed recently to take into account the heterogeneity of the head, and in particular to distinguish contributions from the scalp and from the brain. For instance two- and three-layer slab analytical models [2,3], and Monte Carlo simulations on a layered slab or head model [4] have been developed, as well as a novel empirical approach that combines probe pressure modulation with an extension of the modified Beer-Lambert law to DCS data [5,6]. Here we use Monte Carlo simulations on a two-layer slab model to fit *in vivo* multi-distance DCS data during breathing tasks.

DCS data were obtained on 4 adult subjects, during hypercapnia (end-tidal CO_2 increased 8mmHg above baseline for 30s) and voluntary 30s breath hold sequences. The probe located on the forehead consisted of one source (785 nm) and 2 detector positions at 8 mm (1 single-mode fiber) and 30 mm (7 SM fibers). Data were analyzed using Monte Carlo simulations on a two-layer slab with a fixed 8 mm thick first layer. We assumed constant and homogeneous background optical properties $\mu_a = 0.15\ cm^{-1}$ and $\mu'_s = 12\ cm^{-1}$, and fitted the autocorrelation curves, at both separations simultaneously and each time point, for BFI in the scalp and in the brain.

Figure 1 shows an example of the retrieved relative BFI (rBFI) in the scalp and brain in response to breath hold and hypercapnia, for Subject 1. We observed a cerebral flow increase in response to both respiration tasks. However, breath hold also induced a strong systemic contribution, with an approximate 50% scalp flow increase, similar to previous results by Mesquita *et al* [5]. Conversely, the hypercapnia task induced a smaller scalp contribution (20% flow increase). The cerebral response was observed in all subjects, while the extra-cerebral contribution varied from subject to subject. We will discuss how this variability may arise from differences in individual head structures, and strategies to optimize the model parameters in the Monte Carlo simulations.

Fig.1 – Recovered scalp and brain blood flow index (BFI) changes in response to breath hold (top) and hypercapnia (bottom) tasks.



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Preference: Poster presentation Topic: 3. Data Analysis

Title: Modeling specific hemodynamic response function in fNIRS

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Introduction: Current methods to analyze functional near-infrared spectroscopy (fNIRS) data often apply the general linear model (GLM), which relies on an assumed shape of the hemodynamic response function (HRF). However, as the HRF can vary across subjects and regions, the assumption of a standard HRF in these classical approaches may not be appropriate. This leads to the modeling of a specific HRF in the analysis of event-related fNIRS data.

Methods: In this work, we proposed a deconvolution algorithm to extract a specific HRF for fNIRS. Validations on the adequacy of the algorithm were first performed with noisy simulated data, and then on fNIRS data obtained from 18 healthy subjects using right hand finger tapping included in [1]. In the simulations, the area under the curve (AUC) of the deconvolved HRF was calculated, and was compared directly with the AUC of the true HRF. For each subject performing block-design finger tapping task, the specific HRF to one stimulus block was reconstructed by averaging the deconvolved response functions of all activated channels, and was used in a GLM analysis to produce contrast topographical t-statistic maps for hemoglobin concentration changes. Comparison between maps generated with the specific HRF (thereinafter, spHRF) and with the SPM8 canonical HRF (thereinafter, cnHRF) was then made.

Results: In the simulations of highly noisy data (with both auto-correlated noise and Gaussian white noise, SNR = 2dB), the deconvolution algorithm was able to extract the simulated HRF, providing an AUC ratio of 0.99 ± 0.14 of the reconstructed HRF over the true HRF. From the analysis of finger tapping data, we observed that, (1) in 17 out of 18 subjects, the t-statistic maps generated with deconvolved spHRF presented higher t-scores for the activation clusters, and showed areas of activation that could not be detected on the contrast maps obtained with the cnHRF in the meantime, see e.g. Fig.1 where t-maps of subject 1 are depicted. (2) The parameters of the deconvolved spHRF of each subject, including the time-to-peak delay and peak amplitude ratio, can be slightly different from those of the cnHRF.

Conclusion: The improvement in activation detection using deconvolved spHRF with finger tapping data is encouraging. Future work will be to employ the method on epileptic data to investigate whether it can be a robust choice in the reconstruction of a specific HRF for epilepsy.

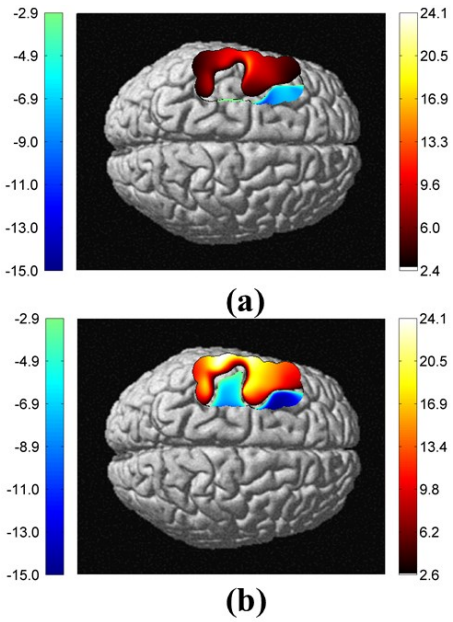

Fig.1, Subject 1: T-statistic maps of HbO obtained with GLM analysis using (a) SPM8 canonical HRF, and (b) specific HRF, dorsal view, $p < 0.05$, Euler characteristic-corrected [2]. Maximum t-value (canonical/specific): 15.0/24.2, number of pixels being activated (canonical/specific): 114847/117787.

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Effective superficial layer thickness recovery using simultaneous multi-distance fitting of diffuse correlation spectroscopy data using a realistic Monte Carlo forward model

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The emerging technique of Diffuse Correlation Spectroscopy (DCS [1]) offers an alternative way to directly estimate cerebral blood flow (CBF), and the combination of DCS and near-infrared spectroscopy (NIRS) measurements can offer robust quantification of the cerebral metabolic rate of oxygen ($CMRO_2$). However, both techniques employ diffusely reflected light that has traveled mostly through extracerebral tissues. This contribution must be accounted for if accurate monitoring of cerebral physiology is desired.

Attempts to increase cerebral sensitivity of the DCS measurements have been reported, either by limiting the data analysis to the shorter correlation times that are more sensitive to deeper propagating photons [2] or using two or multi-layer theoretical models based on the correlation diffusion equation [3,4]. More recently, our group has demonstrated the use of Monte Carlo (MC) based multi-layer, multi-distance fitting [5], which offers increased accuracy for complex tissue structures such as the adult brain.

A key element in multi-layer modeling is determining the layer thickness. In this paper we present a method to estimate the effective extracerebral layer thickness based on the intrinsic information contained in the DCS signal, in conjunction with a MC based forward model. For this we use a version of the tMCimg Monte Carlo software package [6] modified to store momentum transfer at each scattering event. We test our method both with simulations and on data acquired from adult human subjects. The simulated data was computed using a head geometry derived from the segmented MRI scan of an adult subject. We considered two layers: the scalp and skull, and the combined CSF, gray matter and white matter region and we defined 1 virtual source and 4 virtual detectors in the frontal area. The MC based DCS model used a variable thickness 2-layer model derived from the actual head geometry by sequentially eroding 22 1-mm thick tissue layers (Fig. 1, colorbar indicates layer index). Photon history from the superficial and deep layer groups, respectively, was concatenated to achieve an effective 2-layer representation. The subject data was acquired at two distances, 8 and 30 mm in the left frontal area.

Fig. 2a shows the fitting residual variation vs the thickness of the superficial layer has a clear minimum at the effective thickness used in the forward MC simulation for various assumed layer dynamic properties. Fig. 2b displays a similar result for actual subject data, with the effective superficial thickness being estimated to be 14-15 mm at various points during a 5 minute recording. This method can thus be used to approximate scalp/skull thickness in the absence of other structural information.

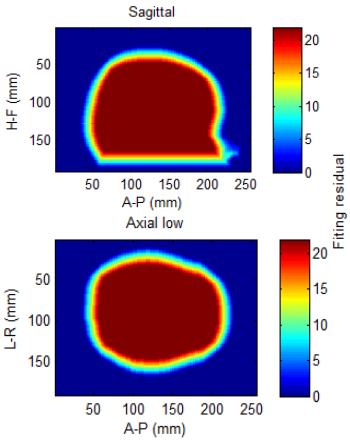

Fig. 1. Multi-layer inverse MC definition

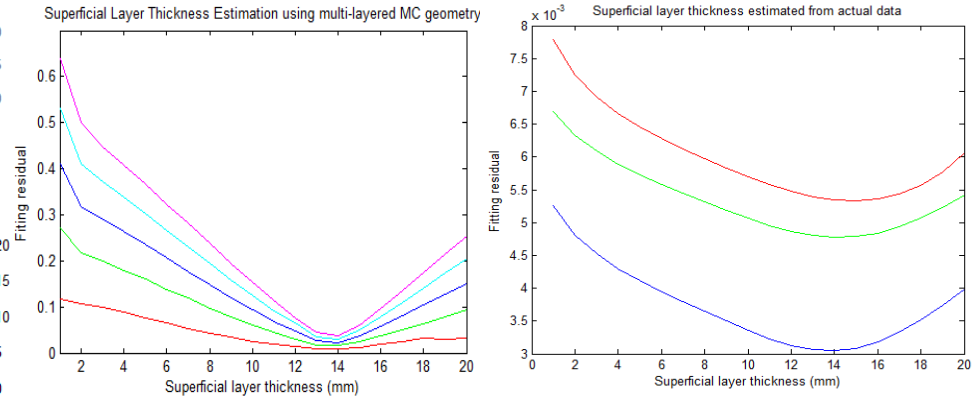

Fig. 2 Fitting residual vs assumed thickness for (a) simulated data at multiple Db values and (b) for actual subject data at multiple time points during a recording

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Quantification of head motion during infant near-infrared spectroscopy sessions for motion correction strategy selection

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Abstract: Near-infrared spectroscopy (NIRS) is a useful tool for measuring brain activity in infants. One common application of infant NIRS is the study of neurodevelopment, employing either longitudinal or cross-sectional study designs to quantify changes in brain activity patterns over the first year of life. However, using NIRS signals from different ages of infants raises questions about how to compare inferred brain activity, given the anatomical, physiological and cognitive changes that occur during development. In this study, we quantify head probe motion in a cross-sectional study of 5, 7, and 12 month-old infants as they are undergoing a NIRS session. Three-dimensional acceleration was recorded from an accelerometer attached to the frontal region of a 46-channel head probe that covered the frontal, temporal, and parietal cortices. The experimental stimuli presented were female faces with happy, angry or fearful expressions. We show that on average, the mean probe velocity during a trial increased over the course of the session. Additionally, we show that mean probe velocity during a trial is inversely correlated with number of principal components needed to describe 95% of the variance in the raw NIRS signal for that trial in 5-month-old infants (r=-.28, $p<0.001$) and 7-month-old infants (r=-.26, $p<0.01$). These results indicate that principle component filtering, a common strategy for motion correction in infant data, should perhaps be applied on a per-trial basis with parameters linked to the amount of recorded motion. Future work will include simulation studies to test this hypothesis.

4. Neurodevelopment

Neural Responses to Affective Touch in Infants at Elevated Risk for ASD

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Background:
Affective touch is a slow, gentle touch that is often observed during interactions between close social partners. This type of touch is an important means of social communication between parents and infants and facilitates social interactions throughout the lifespan. Neuroimaging studies have revealed that affective touch selectively activates areas of the brain also involved in social perception of visual stimuli (e.g., posterior superior temporal sulcus, medial prefrontal cortex) and that the level of activation in these areas negatively correlates with autistic traits in typical adults. Additionally, individuals with autism spectrum disorder (ASD) and infants at risk for ASD show diminished responses in these brain regions during visual social perception tasks. It is not clear whether similar deficits are apparent in the neural responses to tactile social perception tasks in infants who are at elevated risk for ASD.
Objective:
To investigate neural responses to affective versus non-affective touch using functional near infrared spectroscopy (fNIRS) in infants at high- and low-risk for ASD.
Methods:
Participants were 16 infants at high-risk (*n*=6) or low-risk (*n*=10) for ASD. High-risk children had at least one older sibling with ASD, while low-risk children had no known family history of the disorder. Infants visited the laboratory with their parent at approximately 3 months of age. Prior to the experimental procedures, infants were outfitted with the fNIRS optode headgear and were seated on their parent's lap across from a screen. The tactile social perception task consisted of 8 periods each of slower and faster-paced brushing to the skin of the infant's leg, which alternated with periods of no tactile contact. The fNIRS data was recorded with a Hitachi ETG4000 fNIRS transcranial optical topography system.
Results:
Epochs of fNIRS data were extracted from each optode around the stimulus presentation (-3 sec – 15 sec) and averaged by brushing type (fast, slow) and hemisphere for each participant. High-risk infants, in comparison to low-risk infants, showed increased responses to fast brushing 4-5 seconds after the beginning of the stimulation over the left temporal area. In response to slow brushing, optodes covering the right temporal scalp measured a larger response in high risk infants approximately 12 seconds after the brushing began. Follow-up analyses will include comparisons of slow and fast touch across risk.
Conclusions:
This is the first known study to examine neural responses to a tactile social perception task in infants at-risk for ASD. We found that infants at high- and low-risk of developing ASD have differential sensitivity to social, as well as nonsocial, tactile stimuli. The type of social touch utilized in our experiment has been shown to uniquely stimulate a specific group of unmyelinated nerve cells called CT afferents. These receptors indirectly project to the insular cortex, which is thought to connect sensory systems to emotional processing centers of the brain. Our results suggest that areas of the temporal cortex (potentially superior temporal cortex), which is known to respond to visual social cues, may also play a role in the processing of tactile social information; however, further research is needed to better understand this process.

Shining light on neural dynamics of cognitive flexibility in early childhood.

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We use NIRS to probe the neural dynamics of cognitive flexibility in early childhood. The Dimensional Change Card Sort (DCCS) task requires children to switch between shape and color rules when sorting cards. Three-year-olds typically perseverate, but 4-year-olds can switch rules. Previous studies using NIRS have shown that the development of flexible rule-use is associated with changes in the strength of activation in lateral frontal cortex. Three-year-olds show weak frontal cortex activation, but 4-year-olds show strong frontal cortex activation (Moriguchi & Hiraki, 2009). This suggests that the development of flexible rule-use relies on the maturation of frontal cortex. However, despite an immature frontal cortex, 3-year-olds can reliably switch rules when conflict is absent (No-Conflict version) during the pre-switch phase.

We use a model-based approach to examine the source of 3-year-olds success in this version. Specifically, Dynamic Field Theory (DFT) is a neuro-computational framework that has previously been used to simulate these developmental changes in behavior and neural activation (Buss & Spencer, 2014). The model predicts that 3-year-olds who perseverate in the standard task should show stronger frontal activation when they switch rules in a No-Conflict version. This is due to the interaction between posterior cortical systems involved in object representation and frontal systems involved in dimensional attention. When conflict is absent during the pre-switch phase, the object representation system forms memory traces linking visual features to spatial locations which overlap with the rule mapping for the post-switch phase. The object representation system, then, sends a strong bottom-up signal to frontal areas involved in dimensional attention.

We tested this prediction using NIRS with 3- and 4-year-olds. As predicted, perseverators showed stronger frontal activation when switching in the No-Conflict version compared to when they perseverated in the standard task. Developmental differences were also observed between children who perseverated and children who switched rules. Perseverators showed diffuse activation across multiple frontal channels, but Switchers showed focal activation on a single frontal channel as well as activation in parietal and temporal areas. This suggests that, in addition to changes in the strength of frontal activation, the development of flexible rule-use also involves changes in a broader network of cortical regions that are involved in flexible rule-use. Importantly, this also suggests that activation of frontal cortex depends on more than its own developmental state. Finally, this points toward a developmental mechanism by which posterior cortical systems can provide a learning signal for dimensional representations in frontal cortex.

Acquisition of Adjectives in 5-year Old Children: fNIRS Suggests Stronger Reliance on Pragmatic Cues in Bilingual Compared to Monolingual Children.

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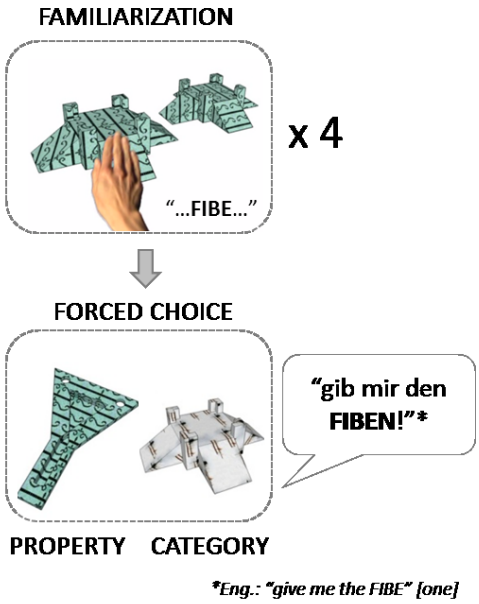
During language acquisition adjectives represent a particularly challenging word class. To learn their function as a property indicator, the shape bias (i.e. novel words are assumed to refer to a whole object) must be overridden. Besides word learning principles (1), syntactic and pragmatic cues (e.g. descriptive gestures) may support this step in language development (2). For the learning of novel nouns pragmatic cues have been shown to be a more efficient help for bilingual than monolingual children (3). In the current study we predicted a similar result for the learning of novel adjectives.



We studied 60 children at the age of 5 years: 32 bilingual children exposed to German and Spanish from birth (BFLA, bilingual first language acquisition (4); n= 32) and 28 monolingual German-speaking children (MFLA, monolingual first language acquisition; n = 28). Participants were confronted with novel words referring to novel objects with novel surface properties. In a playful video-game environment a novel object identifiable by shape (CATEGORY) and surface (PROPERTY) was paired with the novel word four times. The pragmatic cue consisted of a human hand stroking the novel object's surface to indicate property reference (familiarization, see Figure). In the ensuing forced choice task the child had to choose between two objects: one PROPERTY and one CATEGORY match object (lower part of Figure). Apart from the behavioral assessment, fNIRS (9x14 source-detectors, NIRx Germany) monitored changes in cerebral oxygenation over bilateral fronto-temporo-parietal areas to allow for a first glance at the underlying neuronal processing supporting this form of novel word learning in bi- and monolingual children.

Behavioral results did not show any statistically significant difference between BLFA- and MLFA-children. However, fNIRS disclosed an increase over the right temporal ROI, which was statistically significantly stronger in BLFA when compared to MLFA. This temporal activation is in line with previous work suggesting a role of the temporal cortex (STS) in gesture integration (5).

The fNIRS results may indicate that BFLA children attend more strongly to pragmatic cues in the learning of novel adjectives than MFLA children. Thus, by investigating the neuronal underpinnings of children's language development with fNIRS, behavioral data in research on language development for the challenging word class of adjectives was greatly enriched.

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Prefrontal Cortex Hemodynamics and Age: A Pilot Study Using Functional Near Infrared Spectroscopy in Children

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Abstract

Cerebral hemodynamics result from dynamic cognitive processes and underlying physiological processes, both of which are captured by functional near infrared spectroscopy (fNIRS). Applying filters for specific frequency bands related to specific physiological processes (i.e., respiration and autoregulation) provides distinction between these two sources. Here, we introduce a novel parameter of Oxygenation Variability—the OV Index—directly obtained from fNIRS data and we demonstrate its use in a group of children. fNIRS data were collected with 17 children (ages 4-8 years), while they performed a standard Go-NoGo task. Data were analyzed in two frequency bands—the first attributed to cerebral autoregulation (CA) (0.07-0.1 Hz) and the second to respiration (0.2-0.3 Hz). Results indicate differences in patterns of oscillations of oxygen saturation (SO2) between bands. Specifically, there was much higher variability for the autoregulation band than for respiration across subjects. In addition, these pilot data reveal a dynamic relationship between age and OV index. Specifically, OV index increased with age between 4 to 6 years and decreased with age between 6 and 8 years. These findings provide preliminary evidence of the utility of the OV index and are the first to describe the relationship between cerebral autoregulation and age in children using fNIRS methodology.

Developmental Changes in Visual Working Memory Revealed by Image-Based fNIRS Analyses

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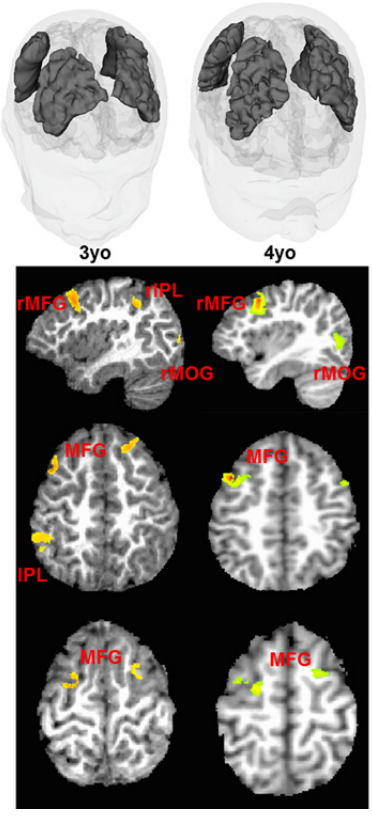
Working memory (WM) is a core cognitive system with a highly limited capacity. WM capacity limitations are associated with individual differences in a host of cognitive functions, and WM deficits have been observed in a variety of clinical populations. Given these influences, understanding the development of WM capacity limits has broad implications and may be critical to intervention efforts with at-risk children.

To investigate the early development of visual working memory (VWM), 3- and 4-year-olds completed a change detection task. Participants were shown a sample array of 1-3 colors, there was a 1 second delay, and then a test array was presented. Participants had to determine if the sample and test arrays were the same or different. Across two sessions, participants completed 24 'different' and 24 'same' trials at each set size. We recorded fNIRS activity from frontal, parietal, and temporal-occipital areas using a 40-channel TechEn CW6 machine.

To track functional changes in brain activity, we conducted image-based fNIRS analyses using the following protocol: (1) we digitized optode locations for each session and registered an age-specific atlas to these locations using AtlasViewer software; (2) we generated probability distributions of photon migration for each source-detector pair using Monte Carlo photon migration simulations; (3) we computed the intersection image across the two sessions (top panel of figure); (4) we processed the fNIRS data for each session using tPCA; (5) we modeled the hemodynamic timecourse using deconvolution techniques (OLS) to compute a β value for each channel for each condition for both HbO_2 and HbR; (6) we created a voxel-based functional brain image (HbO_2, HbR) for each session and condition by weighting these β values by the probability distributions for each channel and summing the per-voxel β values. We then analyzed these data at the group level using AFNI, applying a familywise correction (3dClustSim).



The figure shows group-level results from analyses of 9 3-year-olds and 7 4-year-olds. The brain images show clusters with statistically robust set size main effects, indicating an increase in the strength of the hemodynamic response as the memory load increased (a common effect in the adult fMRI literature on VWM). The sagittal views show significant activation in MOG and MFG at both ages. Note that 4yo showed robust parietal activation, but not differential activation across SS as was found in IPL with 3yo. The axial views in row 3 show common r-MFG activation, but l-MFG activity is differentially localized. This was not the case across the board: row 4 shows common bilateral MFG activity.

We correlated HbO^2 in these clusters with behavioral performance. For 3yo, rMFG (r=.64, p<.06) and rIPL (r=.68, p<.05) correlated with % correct at SS3. For 4yo, rMFG activation correlated with % correct at SS3 (r=.78, p<.05). **These data show the first image-based view of how the VWM network changes in early development.**

Brain activation to human vocalisations and environmental sounds in infancy and its association with later language development

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Being able to recognise human voices in our auditory environment is the first necessary step to speech recognition and language learning. Using functional near infrared spectroscopy (fNIRS) and functional magnetic resonance imaging (fMRI), we have previously shown that an area of the anterior temporal cortex of young infants activates preferentially to human voices in comparison to other environmental sounds (Blasi, Mercure et al, 2011, Lloyd-Fox et al., 2012). Does this cortical sensitivity to human vocalisations in infancy relate to later language development? To address this question, infants were followed longitudinally at two time points. At 4 to 7 months, they participated in an fNIRS study in which brain activity was recorded while they were presented with two categories of sounds: Vocal sounds (human non-speech vocalisations, such as cries, laughter, sneezes, etc), and Non-vocal sounds (non-vocal environmental sounds that babies are likely to be familiar with, such as toy sounds and water sounds). The multi-channel NIRS sensor pads were placed over an area covering part of the temporal and inferior frontal cortices (bilaterally). At 14 months, these infants' primary caregiver completed the MacArthur-Bates Communication Development Inventory (CDI) to assess their receptive and expressive language development. We are reporting data from 48 infants. FNIRS results showed voice-sensitive activation in the anterior temporal cortex. The degree of voice-sensitivity in this region increased with age between 4 and 7 months but did not correlate with CDI scores at 14 months. However, infants with higher vocabulary scores at 14 months showed more widespread activation to vocal and non-vocal sounds at 4 to 7 months along the superior temporal sulcus. These results suggest that a neural reactivity to sounds in infancy, rather than voice-sensitivity, may lead to better language development in toddlerhood.

A Blasi, E Mercure, S Lloyd-Fox, A Thomson, M Brammer, D Sauter, Q Deeley, G J Barker, V Renvall, S Deoni, D Gasston], SCR Williams, MH. Johnson, A Simmons & DGM MurphyCurrent Biology 21, 1–5, July 26, 2011 DOI 10.1016/j.cub.2011.06.009

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Influence of early language experience on brain activation to language: A study of hearing infants with Deaf mothers

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This presentation will introduce a new research project aiming to determine the impact of early language experience on language representation in the brain. We are currently studying hearing infants with deaf parents (HoD) and comparing them to hearing infants with hearing parents (HoH). Despite normal hearing, HoD infants have a very different early experience of speech and language to that of HoH. When the parents' dominant language is a signed language, such as British Sign Language (BSL), their speech and language input differs from that of HoH infants. First, HoD infants have reduced exposure to spoken language in the prenatal and early postnatal period. Many deaf signing individuals use speech to communicate with hearing people, but the extent to which they actually 'voice' this speech and produce sound, as opposed to silently mouth, is extremely variable (Bishop & Hick, 2005). Second, the postnatal experience of HoD infants includes both a language in the visual modality, e.g. BSL, and one in the auditory modality, e.g. English, which can be used by the parents, as well as by hearing relatives and the rest of the hearing community. Since HoD individuals grow up learning two languages, they are compared to HoH individuals growing up learning two spoken languages. Three groups of infants (4-7 months) are recruited: 30 infants from a monolingual English speaking family, 30 infants from a bilingual family in which two spoken languages are frequently used by the parents, 30 infants with deaf parents for whom BSL is the dominant language. We are using functional near infrared spectroscopy (fNIRS) to study brain activation during spoken and sign language perception. Sentences are presented in infant-directed English and French (familiar and unfamiliar spoken languages), as well as in BSL and French Sign Language (familiar and unfamiliar sign languages). Analyses will focus on the preferential activation for a familiar over an unfamiliar language and on left and right hemisphere activation. Hypotheses of how the experience of HoD infants could influence their brain activation to spoken and sign language will be discussed. Preliminary results from 5 HoD infants and 5 HoH infants suggests strong activation to spoken language in the temporal cortex in all groups, which may be more left lateralised in HoH infants than HoD infants. Activation to sign language was found in a more posterior and more restricted area of the temporal cortex in all groups.

Reference

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Left-lateralized responses correlate with familiarization to novel phonotactic regularities in 12 months old infants

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During the first months of life infants begin to increase their sensitivity for regularities in their native language. This also applies to phonotactic constraints, a set of combinatorial rules for the potential clustering of phonemes in a given language (*1*). Phonotactic rules are relevant for word learning (*2*) since they may modulate lexical access and may additionally help to segment the continuous auditory stream (*3*). For phonemic and prosodic variations it has been shown that the discrimination at the word level lead to lateralized responses at ~ 12 months of age, while evidence for discrimination of sound structure seems to evolve at an earlier stage (*4,5*).

While most studies have looked into the spontaneous evolution of linguistic capacities the present study addressed the question whether and how neuronal response to a phonotactic contrast changes in response to a training intervention. 12-month-old infants were repeatedly exposed to pseudowords of native and non-native phonotactic regularities. 25 infants underwent a passive listening experiment consisting of a pretest, a training, and a posttest, repeated on three consecutive days. During the pre- and posttest monosyllabic pseudowords (PW) were auditorily presented: 50% complying with German phonotactics (i.e., native PW), and 50% complying with Slovak phonotactics (i.e., non-native PW). We selected Slovak phonotactic rules for non-native pseudowords since Slovak is characterized by a wider variety of attested consonant clusters at word onset and therefore allows for a strong contrast to the infants' native language (German). During passive listening (familiarization), half of the native and non-native pseudowords were repeated six times and acoustically presented in a pseudo-randomized order. All pseudowords were presented in infant-directed-speech by a bilingual speaker to ensure that toddlers listened to a largely 'natural' language input not confounded by speech mode or phonotactic production competence of the speaker. During the whole experiment silent videos were shown to maintain active subjects' attention. To assess event related brain responses during pre- and posttest as well as during training, cerebral oxygenation changes were monitored by fNIRS over bilateral fronto-temporo-parietal areas (cw-imager, 16 channels, NIRx -Europe, Berlin Germany)

Results show an increase in activation (increase in oxy-Hb) for trained native and non-native regularities on the second day of training. This suggests early learning effects due to the repetitive exposure even outside a meaningful linguistic context. Interestingly untrained native regularities showed a similar effect, potentially indicating generalization effects. Regarding the question on the underlying neuronal substrates for such learning, all these changes were left-lateralized. This may indicate that infants start to process speech–like input in a linguistic way, as evidenced by leftward lateralization, previously demonstrated for adults using very similar material and methodology (6)

(1) Trask, London: Routledge (1996); (2) Rossi et al. Brain & Lang (2013); (3) McQueen, J Mem Lang (1998); (4) Minagawa-Kawai et al. J Neurosci. 2007; (5) Sato et al. Japan J Logop Phoniatr. 2003; (6) Rossi et al., J Cog Neurosci (2011)

The processing of faces across non-rigid facial transformation develops at 7 month of age: A fNIRS-adaptation study

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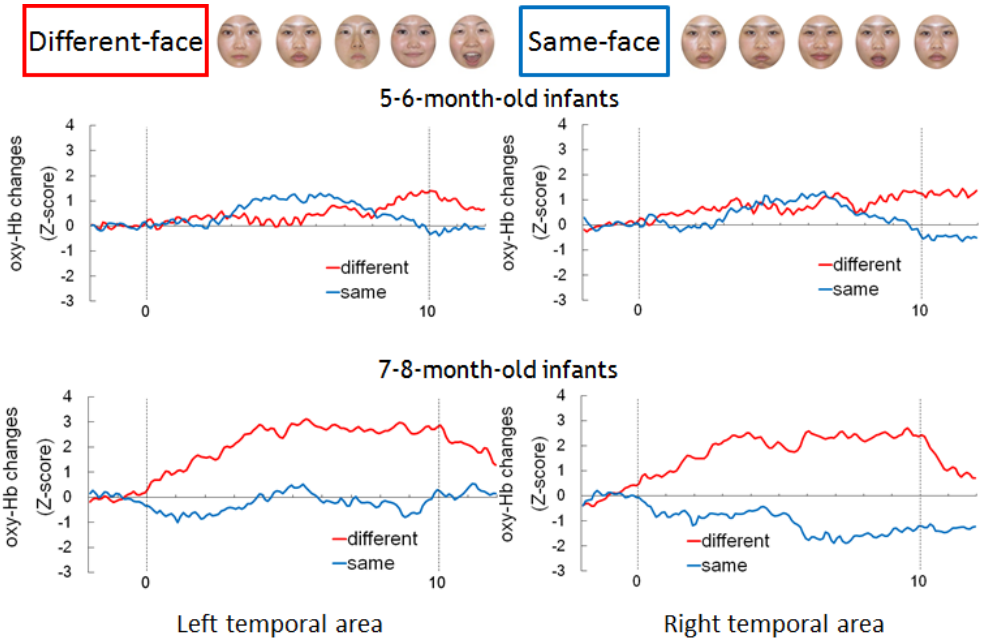
The aim in the current study was to investigate whether infants' temporal areas process facial identity across the non-rigid transformation of facial features by using fNIRS-adaptation paradigm.

Neural adaptation refers to the attenuation of brain activity by the repeated presentation of an identical stimulus compared to that of different stimuli (e.g., Grill-Spector et al., 1999; Andrews & Ewbank, 2004). By measuring the recovery from adaptation to stimulus changes, the nature of representation in a specific cortical area can be assessed. By applying this technique to infant NIRS measurement, we have examined face processing in infants' temporal areas (Kobayashi et al., 2011, 2012). We revealed that (1) infants' temporal areas are involved in processing of facial identity, (2) size-invariant processing develops by 5 months of age, (3) the ability to process facial identity in a view-invariant manner develops around 7 months after birth.

In this study, we compared hemodynamic changes of 5- to 6-month-olds and 7- to 8-month-olds during the 10 sec presentation of an identical face and of different faces with non-rigid facial transformation. We found that 7- to 8-month-olds, but not 5- to 6-month-olds, showed attenuation of oxy-Hb (adaptation) in the channels around the T5 and T6 position to the presentation of the same face rather than that of different faces, regardless of non-rigid facial changes. Our results suggest that the processing of facial identity across non-rigid facial transformation develops around 7 months after birth.



The Infant Occipital Cortex Responds to a Predictive Cross-Modal Stimulus: An fNIRS Study of 6-month-olds

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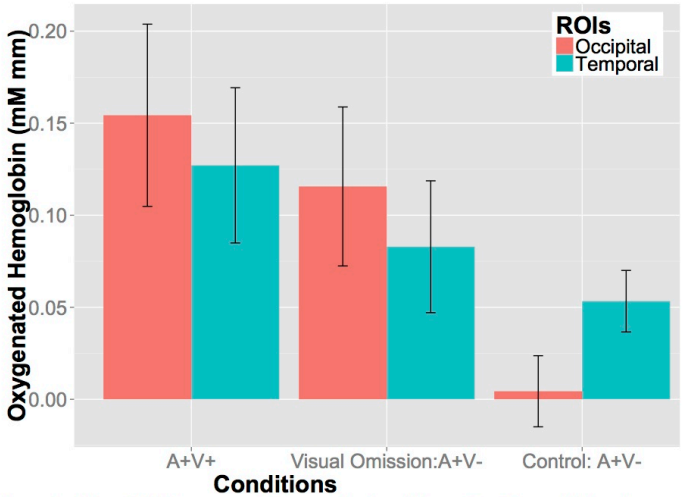
It is unknown which neural systems in the infant brain translate experience into perceptual development. We employed fNIRS and MR co-registration to unambiguously record neural activity in the perceptual cortices (occipital/temporal) as infants learned and responded to violations in cross-modal (auditory/visual) statistical information.

Studies of learning (e.g., statistical, associative) typically present novel stimuli to assess the outcome of exposure to stimuli. However, the neural signals elicited by novel test stimuli confound novelty responses with neural responses to increased prediction error or other learning-associated responses. This is especially true in perceptual cortices where repetition or familiarity affects neural responses. To address this confound, we employed a novel behavioral paradigm: After a period of familiarization where a sound always predicts a visual event (statistically consistent trials, A+V+), infants viewed *unexpected visual omission trials* (A+V-) where the predictive auditory stimulus was *not* followed by the expected visual stimulus. The unexpected absence of a stimulus can not elicit a neural response based on a change from a familiar to a novel stimulus, but rather must be an adaptive change in perceptual cortex resulting from statistical learning.

Recordings from 15 6-month-olds revealed robust and similar increases in activity in the occipital cortex during both statistically consistent (A+V+) and unexpected visual omission trials (A+V-), suggesting that the occipital cortex has adapted its function as a result of learning the A+V+ pairings. Recordings in 16 additional infants confirmed that the presentation of the same stimuli as an unexpected visual omission (A+V-), but without prior learning of the visual expectation, results in no response in the occipital cortex (mean fNIRS responses 5-9 seconds after trial onset presented in Figure below). Thus, the infant *occipital* cortex only responds to an *auditory* stimulus when an infant has learned that it predicts a visual stimulus.



The Neural Development of Children's Spontaneous Deception:
A Functional Near-infrared Spectroscopy (fNIRS) Study

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The neural mechanisms underlying children's spontaneous deception are entirely unknown. Here, we used functional near-infrared spectroscopy (fNIRS) methodology to investigate the neural correlates of children's spontaneous deceptive behavior. We specifically focused on whether or not spontaneous deception would engage a network of neural regions similar to that found in adults' studies (Greene& Paxon, 2009; Ding et al., 2013 & Ding et al., 2014). Fifty-nine children between 7 and 12 years of age participated (M_{age} = 8.90; *SD* = 1.22; 27 males). Their deceptive behaviors were elicited using a guessing game. In the game, children could guess incorrectly but falsely claim being correct (incorrect-dishonest) or tell the truth (incorrect-honest) as well as control trials where they guessed correctly and told the truth (correct-honest). The underlying cortical regions for the NIRS channels were identified by co-registering the NIRS channels placed on each individual on an MRI from a set of MRIs taken from Chinese children. Results showed that: 1) The incorrect-dishonest trials elicited significantly larger changes in [oxy-Hb] concentration than the incorrect-honest trials in the left middle frontal gyrus(MFG) for younger children, and the left superior frontal gyrus(SFG) for older children, suggesting that children's lying engendered significantly more [oxy-Hb] activities in the frontal area than truth-telling; 2) The correct-honest trials elicited significantly larger [oxy-Hb] changes in the left SFG than incorrect-honest trials for younger children but in the left angular gyrus and the right middle occipital gyrus for older children; 3) Unlike adults, there was no significant difference of [oxy-Hb] changes between correct-honest and incorrect-dishonest trials for both younger and older children. Results revealed that, like adults, executive functioning and the reward network play an important role in children's spontaneous deception. However, unlike adults, differentiated self-evaluations in terms of dishonestly gained points vs. honestly gained points may be yet to reach the adult level by early adolescence.

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Neural correlates of own- and other-race face recognition in preschoolers: A functional near-infrared spectroscopy (fNIRS) study

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Previous studies revealed a neural other-race effect (NORE) paralleling the behavioral other-race effect (we recognize own-race faces better than other-race faces). The existence of NORE suggests that adults' asymmetrical experience with own- and other-race faces have a direct impact not only on their behavior but also on their neural responses. However, the developmental origin of the NORE is still unknown except for a recent fNIRS study elementary school children (Ding et al., 2014). The present study extended the work by Ding et al. (2014) by investigating the neural correlates of preschoolers' own- and other-race face processing using fNIRS. An old-new paradigm was used to assess 3- to 6-year-old preschooler's recognition ability of own- and other-race faces (N=67, Mean Age: 5.1± 0.7 Years). The underlying cortical regions for the NIRS channels were identified by co-registering the NIRS channels placed on each individual on an MRI from a set of MRIs taken from Chinese children. FNIRS data revealed that own-race faces elicited significantly greater [oxy-Hb] changes than other-race faces in the left middle frontal gyrus (LMFG) and the left middle occipital gyrus (LMOG). The [oxy-Hb] activity differences between own- and other-race faces, or the NORE, was significantly positively correlated with age in the LMFG, but negatively correlated with age in the left MOG. Moreover, these areas had strong functional connectivity with a large swath of the cortical regions in terms of the size of NORE. The connectivities of the LMFG to other cortical regions became more concentrated and limited to fewer channels as age increased. These results taken together suggest that similar to school aged children and adults, preschoolers devote different amounts of neural resources to processing own- and other-race faces but the size of NORE and associated regional functional connectivity undergo developmental changes.

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Age-dependence of emotional face processing in infants as measured with near-infrared spectroscopy

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Abstract: The goal of this work is to elucidate the neural basis of the development of emotional face processing in infants over the first year of life. Prior work has shown that infants after but not before 7 months of age show enhanced attention to fearful faces as opposed to happy faces. Event-related potentials have shown an increased neural response to fearful faces also for older infants, however the poor spatial localization capability of EEG has left unanswered questions. In this study, near-infrared spectroscopy (NIRS) was used to measure infants' brain activity during the presentation of happy, angry and fearful faces. Separate groups of 5- (n = 16) and 7- (n = 16) month-old infants were tested with a 46-channel NIRS system that recorded brain activity over the frontal, temporal, and parietal cortex. The oxyhemoglobin responses to each emotional condition were calculated. Subjects at 5 months showed increases in oxyhemoglobin concentration in the right superior temporal cortex to fearful ($p<0.01$) and angry ($p<0.01$) faces, but not happy faces. Subjects at 7 months showed responses to fearful faces in the right superior temporal region ($p<0.01$) and left frontal region ($p<0.01$). Angry faces presented at 7 months corresponded to a negative change in oxyhemoglobin in the right sensorimotor cortex. No statistically significant responses to happy faces were found. The stimulus-related change in heart rate was also calculated from the NIRS signals as a measure of attention. Heart rate for all ages and conditions decreased with stimulus presentation, indicating the infants orienting to the stimuli. These findings suggest that the neural architecture of facial emotion processing in infants is age-dependent.

Bilingualism alters children's prefrontal activation during a non-verbal attention task

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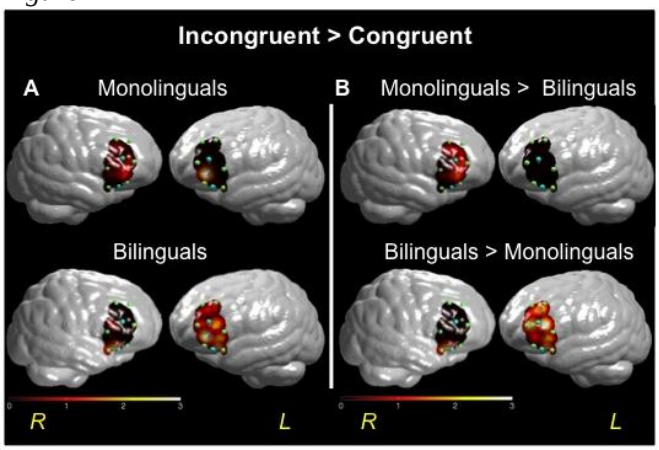
Does early bilingual exposure alter children's neural organization of cognitive processes? Bilingualism theories suggest that the need to selectively attend and alternate between two competing linguistic inputs fosters an overall improvement of selective attention mechanisms in young bilinguals—an improvement likely supported by the prefrontal cortex (Bialystok, 2001). While growing research yields inconclusive results on the notion of cognitive advantage via early bilingualism, little is still known about the impact of bilingualism on children's frontal lobe maturation. Hence, the present study used functional Near-Infrared Spectroscopy (fNIRS) to investigate whether early dual-language exposure alters bilingual children's frontal lobe engagement during a non-verbal task of selective attention.

METHOD: Thirteen Spanish-English bilingual and fourteen English-monolingual children (M = 9 years-old, range= 7 to 12) completed the Attentional Network Task (ANT; 2 control conditions [neutral and congruent] and 1 experimental [incongruent]). ANT requires participants to selectively attend and inhibit conflicting and non-conflicting information.
A TechEN-CW6 system with 690 and 830 nm wavelengths was used. The setup included 4 emitters of near-infrared light and 12 detectors spaced 2.7 cm apart, yielding 14 data channels sampled at 10-Hz (7 channels per hemisphere). We examined brain activation of selective attention in bilateral prefrontal cortex regions: inferior, middle and superior frontal gyri. The probe localization was established using the international 10-10 transcranial system positioning (Fz, Cz and pre-auricular were measured for each participant and the two lower sources were anchored at F7 and F8).

RESULTS: Language groups did not differ in ANT accuracy or response time performance. Neuroimaging results revealed that children activated bilateral prefrontal regions during the incongruent relative to control conditions (Figure 1A). Direct comparisons between the groups revealed hemispheric differences of brain activation: bilinguals had greater left-than-right activation (Figure 1B), and overall significantly greater left hemisphere activation relative to monolinguals. Additionally, bilinguals' brain activation correlated to language abilities suggesting that neural differences between the groups may be due to early-life bilingual experiences.

CONCLUSIONS: The greater recruitment of the left hemisphere (the hemisphere known to be critical for language abilities) in bilingual children suggests that early dual-language experiences may indeed alter children's neurodevelopmental mechanisms of cognitive development. In particular, extensive bilingual experiences may strengthen the computational capabilities of children's left hemisphere, which may thus become more efficient during non-verbal tasks of selective attention and possibly other cognitive functions. The present findings carry powerful implications for understanding the impact of early language experiences on neural plasticity and to inform theories of early cognitive development.

Figure 1



What is that baby thinking? The development of an fNIRS measure of live parent-infant interaction

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Tightly controlled experimental paradigms have greatly increased our knowledge of the neurological correlates of infant social development; however, due primarily to methodological challenges, to what degree these findings reflect neural responses during actual social interaction is not yet known. In comparison to other neuroimaging methods, functional near-infrared spectroscopy (fNIRS) systems have the advantage of permitting a higher degree of movement and comfort level, allowing infant participants to be awake and relatively active during data collection. This provides a promising opportunity to uniquely measure neural responses during live social interaction.

We are developing a task that capitalizes on the flexibility of the fNIRS approach, which measures event-related neural responses to a naturalistic measure of parent-infant interaction. During this task (see Figure), infants engage in a 5-minute face-to-face interaction with their primary caregiver while seated in an infant seat across from their parent and wearing infant fNIRS headgear (optodes covering areas of the temporal lobe involved in processing social information). For the interaction period, parents are instructed to play with their child as they

30-s pre-baseline: No interaction

5-minutes: Parent-infant interaction

30-s post-baseline: No interaction

normally would at home. The interaction is preceded and followed by 30-second baseline periods with no social interaction. The infant and parent's behaviors are video recorded for later behavioral coding. Key infant and parent social behaviors, including affect, gaze, vocalizations, and touch will then be micro-coded on a frame-by-frame basis. We plan to utilize these codes to denote independent social events, which we will link in time to fNIRS measurement of the hemodynamic response. We can then examine whether these events predict, or are predicted by, neural responses in the right and left temporal regions.

We have begun collecting pilot data on this task. Initial examination of data from the first two participants, both nine months old, indicated little evidence of motion artifacts, successful acquisition of fNIRS and behavioral data, and little apparent interference of the fNIRS headgear on the infants' ability to engage in social interaction. For this presentation, we will present on the details of this measure and initial findings from our pilot sample. We will further include the advantages and challenges of our approach and recommendations for researchers interested in utilizing fNIRS during naturalistic social interaction.

Processing time-compressed speech in the newborn brain: the role of scale-invariant statistics

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Speech is a special auditory signal for humans, processed in functionally specialized brain areas and preferentially attended to from birth or even prenatally (Pena et al. 2003, Vouloumanos & Werker 2007). However, what makes speech special is still not fully understood. In this study, we propose to take a new perspective on this classical and fundamental question, reconsidering it from the perspective of the theory of efficient neural coding (Barlow 1961). According to this hypothesis, the mammalian perceptual systems have evolved to encode environmental stimuli in the most optimal manner, as defined by information theory (Rieke et al., 1995). Consequently, the neural code used by the perceptual systems should match the statistical structure of environmental stimuli, which has indeed found to be the case for visual and some auditory stimuli (Simoncelli and Olshausen 2001). This predicts that newborns might recognize speech by its statistical structure. Importantly, many environmental stimuli, including speech, are characterized by a scale invariant or fractal structure. For auditory stimuli such as speech, scale-invariance is most relevant in the temporal dimension (Voss and Clarke, 1975). To test whether newborns encode speech in a scale-invariant manner, tolerating the time-compression of speech up to a certain level (~40%), as adults do (Pallier et al., 1998; Sebastian-Gallés et al., 2000), in a near-infrared spectroscopy experiment, we presented normal and accelerated speech to twenty-three newborns. Stimuli were presented (Figure 1A) in blocks that either contained speech at one of three levels of acceleration (non-alternating blocks: (i) normal, (ii) compressed to 60% of its original duration, intelligible for adults or (iii) compressed to 30%, non-intelligible for adults) or in blocks alternating normal and compressed speech samples (alternating blocks). Optical probes were placed on the newborns' head bilaterally on the fronto-temporal, temporal and temporo-parietal areas (Figure 1B). Results show that newborns process 60% compression, but not 30% compression, similarly to normal speech when the three different types of non-alternating blocks are compared (Figure 1C), but can nevertheless discriminate between normal and compressed speech, as an increased response to alternating as opposed to non-alternating blocks suggests (Figure 1D). Further, the fact that this discrimination is more pronounced in the RH than in the LH implies that speech prosody and rhythm might underlie its scale-invariance, converging with previous behavioral findings in adults (Pallier et al., 1998; Sebastian-Gallés et al., 2000). These results show that newborns are able to encode the temporal scale invariance of speech.

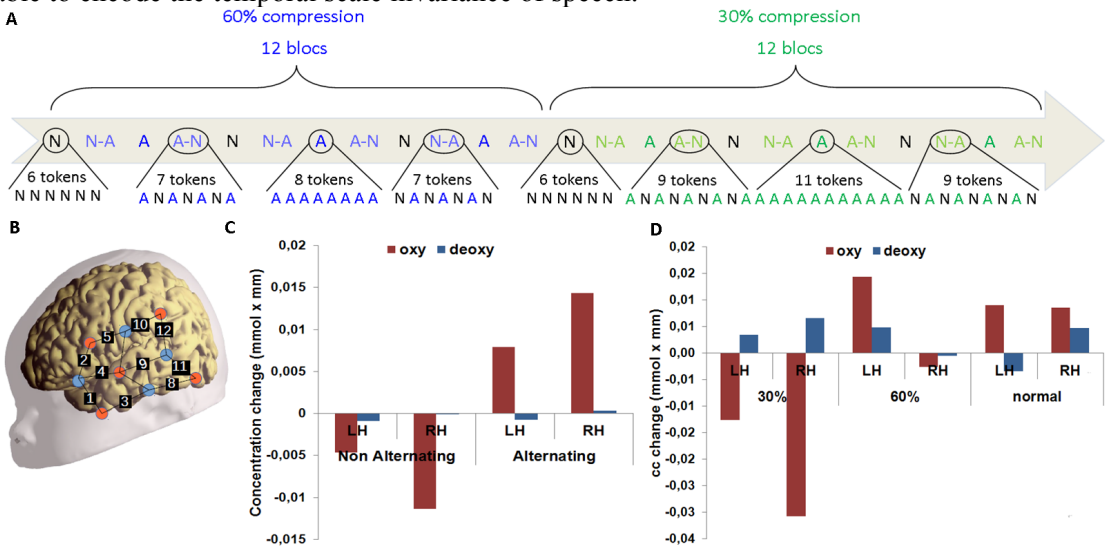

Figure 1. A) Experimental design, B) Probe placement, C) Grand Average of Non-Alternating Blocks, D) Grand Average of Alternating and Non-Alternating Blocks

Different Language Learning Settings Alter the Processing of Phonotactics in Infancy: a Combined EEG and fNIRS Study

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Background:
Infants' speech perception tunes in to the mother tongue within the first year of life (Sebastián-Gallés, 2006).Studies have shown that the sensitivity to prosodic (Mehler et al., 1988) and phonemic features (Minagawa-Kawai et al., 2007) emerges as early as 3 months. Here we focus on phonotactics, a prelexical regularity, which governs the possible combinations of phonemes in a word or syllable in a given language. Going beyond a cross sectional approach testing linguistic abilities at a certain age we here probe the sensitivity to native and non-native phonotactic cues in 6-month-old infants to then inquire into the the changes in neuronal responses due to three kinds of training-interventions, all performed over 3 days: (i) a passive listening training and (ii, iii) two different kinds of semantic training.

Methods:
3 groups of 6-month-old German infants underwent a pretest, training, and posttest on 3 consecutive days. During the pretest and posttest we acoustically presented pseudo-words which were phonotactically legal or illegal with respect to German phonotactic rules. The passive listening training consisted of a pure acoustic presentation of the pseudo-words. The semantic trainings provided a semantic context instead. The pseudo-words were either combined with pictures of real objects or with pictures of pseudo-objects. For the latter tow interventions the training followed the principles of statistical learning. Brain responses were monitored by means of event-related brain potentials (ERPs) and functional near-infrared spectroscopy (fNIRS; BrainScout, NIRx Europe, Berlin). Sources and detectors of the dual wavelengths cw-monitor were arranged in a pattern allowing for registration of 16 channels covering fronto-temporo-parietal areas, bilaterally.

Results and Conclusions:
fNIRS results revealed different short-term (pre-test vs. post-test on each day) and long-term (day 1, day 2, day 3) learning effects for the 3 different training settings. Both semantic trainings elicited **short-term learning effects** leading to an increase of oxy-Hb and a decrease of deoxy-Hb from pretest to posttest on each day. The effects were most prominent for trained legal and trained illegal pseudo-words. The short-term activation changes appeared bilaterally for the training with real objects but shifted to the left hemisphere for the training with pseudo-objects. Interestingly, within the passive listening training *untrained* pseudo-words caused strongest short-term effects with a decrease of oxy-Hb and an increase of deoxy-Hb from pre- to posttest on both hemispheres. An increase of activation from day1 to day3 for trained legal and trained illegal pseudo-words in both hemispheres indicated **long-term learning effects** for the training with pseudo-objects. In contrast, the passive listening training lead to a significant decrease of activation for untrained legal and illegal pseudo-words from day1 to day3. No long-term learning effects appeared within the training with real objects.
The findings indicate a high degree of brain plasticity in 6 months old infants in response to an intervention targeting a subtle rule based pre-lexical regularity. Notably changes in the processing of novel verbal material occurred on both time lines short-term and long-term. Beyond the changes regarding phonotactic processing our results confirm a strong influence of the learning scenario on word learning in infancy.

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Re-test reliability of fNIRS with infants

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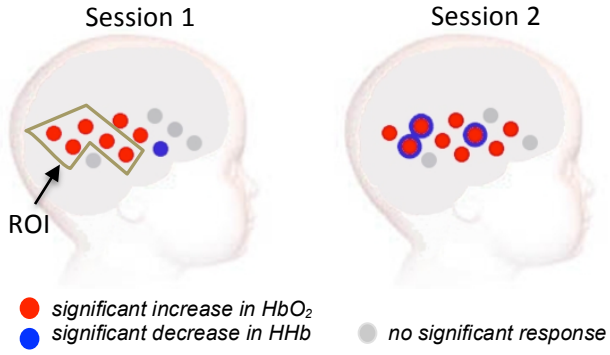
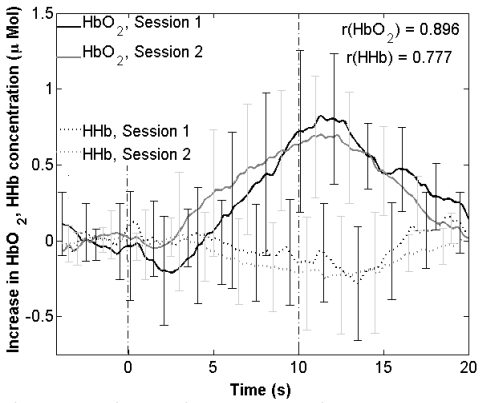
There has been a rapid rise in the number of functional near infrared spectroscopy (fNIRS) studies for human developmental research over the past decade. Most recently research in this field has shifted towards performing prospective longitudinal comparisons with other measures of development, with a view to identifying individual differences in at risk infants. Central to this work is the identification of factors influencing the reliability of fNIRS measures, as the ability to detect individual differences will be compromised if the reliability of the method is questionable. In the current work we investigated replicability at *group* and *individual* level of; (1) the amplitude of the activation-related signal change, (2) spatial distribution of cortical activation and (3) the overlap of averaged measured haemodynamic time courses between two data acquisition sessions. We utilized data from a longitudinal cohort of 13 infants who participated in an fNIRS study on social perception at 4-8 months and, again, at 12-16 months of age. Infants wore custom-built 12-channel fNIRS headgear over the right hemisphere, which was aligned with 10-20 coordinates using external anatomical landmarks as reference. Oxy- and deoxy-haemoglobin (HbO_2 and HHb) changes were used as measures of brain activation to the auditory+visual social stimuli from a baseline of silent non-social visual stimuli.



Activation maps to the auditory-visual social condition vs baseline.



HbO_2 and HHb averaged across ROI channels and participants per session.

Our participants achieved a similar level of compliance with the study at both sessions and there were no significant discrepancies in headgear placement. Our results show a high degree of reliability in signal change and spatial mapping across sessions (spatial overlap was 0.94 and average signal change within an ROI was r = 0.90 for HbO_2 and r = 0.78 for HHb). At participant level, spatial overlap was acceptable (> 0.5 on average across infants) although signal reliability varied between participants. This first study of test-retest reliability of fNIRS in infants shows encouraging results, particularly for group based analysis.

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Syllable Processing in Infants: Uncovering the Temporal Organization of Perisylvian Brain Regions

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The ability to discriminate syllables is an essential component in language processing. There is a growing body of evidence demonstrating that infants are not only capable of discriminating basic syllable changes, but also that the brain regions involved are similar to that seen in adults. The goal of the present study was to investigate the temporal organization of these structures in infants. The event-related optical signal (EROS) has been shown in adults to provide localized maps of brain activation with temporal resolution on the order of milliseconds, corresponding to the neuronal activity typically measured with event-related electrical potentials. Here, we apply this technology for the first time to infants. Eighteen healthy, full-term, 4 month old infants participated in a passive auditory (/bē/ and /bō/) oddball (80/20 probability) experiment. We recorded EROS from 160 channels covering bilateral temporal and lateral frontal cortical areas. All syllables, independent of probability, lead to bilateral activation of auditory cortex starting around 100 ms followed, at a much later interval (600 ms), by left lateralized activity in inferior frontal cortex near Broca's area. When comparing deviant (low probability) syllables to standards, the earliest differences emerged around 300 ms in anterior superior temporal gyrus (STG) bilaterally (right hemisphere preceding left). This was followed by bilateral posterior STG, again with right hemisphere activation preceding left hemisphere activation and then finally left lateralized supramarginal gyrus. This activation pattern is similar, but with delayed latencies, to that found in adults. In sum, this study demonstrates the feasibility of EROS to provide information about the temporal organization of perisylvian brain regions recruited when 4 month old infants process syllables, and suggests that EROS may be a useful tool for investigating neurodevelopmental changes with age.

fNIRS in Rural Gambia: Studies of Cognitive Function from Birth to 24 Months of Age

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Appropriate nutrition in the first 1000 days of life is essential for optimal brain development and function. Approximately 165 million children worldwide are undernourished, and the ramifications for neurocognitive development are poorly understood. Global health initiatives seeking to track neurocognitive development have typically used standardised behavioural assessments as outcome measures of nutritional interventions. Although useful, these assessments can only be used to detect the effects of nutritional status once they have reached the point of observable behaviour, thus reducing the efficacy of targeted early intervention strategies. Further, the use of these techniques requires considerable cultural adaptation, as they are typically designed and normed on Western populations. The aim of this study was to demonstrate the use of optical imaging as an assessment tool for cognitive function in the first two years of life for nutrition based studies in a resource poor setting.

We transported a custom-built UCL topography system to a field station in rural West Africa to study infants from four age groups (0-2month-olds, n = 23; 4-8 month-olds, n = 24; 9-13 month olds, n = 26; 18-24 month-olds, n = 20). Infants wore custom-built fNIRS headgear consisting of an array over the right hemisphere, containing a total of 18 channels (source-detector separations; 12 at 2cm and 6 at 4.5cm) with wavelengths of 780nm and 850nm. fNIRS was used to measure brain activation to visual and auditory social and non-social stimuli. Significant activation was seen during auditory social (e.g., laughter) compared to auditory non-social (e.g., rattles) conditions - as well as to visual social (human peek-a-boo) compared to visual non-social (transport images) conditions - in channels localised over the right posterior temporal hemisphere. In addition to the fNIRS measurements, all infants underwent growth measurements (i.e., anthropometry), and some infants underwent behavioural assessment using a culturally adapted version of the Mullen Scales of Early Learning.

The results of this study suggest that vocal selectivity can be used to differentiate neurodevelopmental trends in visual and auditory processing during the critical first 1000 days of life. Importantly, this study also confirms the viability of fNIRS as a tool to objectively measure cognitive function from birth in a resource poor setting, and provides a solution to the cultural adaptation required by behavioural assessment.

Title: Changes in motor cortex activity of infants' reaching and stepping patterns
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Introduction: Infants develop patterns of neural activations as they repeat cycles of perceiving and acting, enabling them to achieve their goals. Theoretically, during the early cycles of reaching, sitting, crawling and walking, movements are inefficient and associated with diffused activity within and across a number of cortical areas. As infants gain experience, efficient neuromotor responses emerge. To date, the neural bases for the emergence of functional motor skills have yet to be verified. The purpose of this study was to use fNIRS to investigate the changes in motor cortex activity as infants perform reaching for a toy and stepping while supported over a treadmill.
Methods: Two groups of typically developing infants, 6 younger (mean age 26.1 ± 3.5 weeks) and 6 older (mean age 51.9 ± 1.7 weeks) completed both reaching and stepping conditions. *Reaching:* Infants were secured into a customized seat and presented toys within reach at midline. After each reach, we presented a video for rest phase for 20 seconds. *Stepping:* Infants were supported under the arms in an upright position to enable stepping on the treadmill for 30 seconds. For the rest phase infants were held near the chest for 30 seconds.

We used continuous-wave fNIRS (CW6, TechEn Inc) with 4 dual-wavelength (690 & 830 nm) sources and 8 detectors (center around Cz using the international 10-20 system) creating 12 channels covering the bilateral motor cortex (Figure 1). Distance between sources and detectors was 25mm. Data were pre-processed and filtered using Homer2 (Huppert et al., 2009) with a wavelet-based motion correction applied (Molavi et al., 2012). We then compared rest with task to detect any significant activation using a t-test.

Figure 1. Estimated location of headgear.

Results: All infants completed 10 successful trials in both reaching and stepping. During reaching, younger infants showed 7 active channels distributed bilaterally, while older infants showed only 4 active channels unilaterally.

Both groups of infants showed both unimanual and bimanual reaches. Younger infants did not show any difference in activation patterns between the two types of reaches. Older infants, however, showed more bilateral activation during bimanual reaches, and unilateral activation during unimanual reaches.

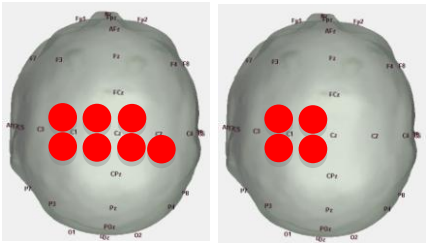

Figure 2. Location of active channels during reaching for a) younger and b) older infants.

For stepping, younger infants showed 10 active channels distributed bilaterally, while older showed 7 active channels distributed bilaterally.

Conclusions: We were able to successfully use fNIRS to detect changes in hemodynamic activity related to reaching and stepping. Younger infants showed dispersed areas of activation compared to older infants in both skills. Our data support our hypotheses that infants infants with more developed skills refine cortical involvement in patterned behavior through self-initiated efforts to achieve the motor outcomes.

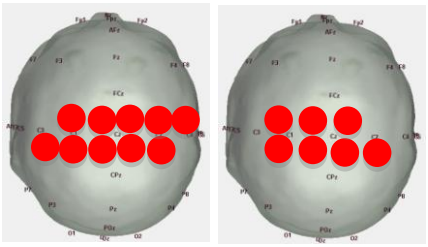

Figure 3. Location of active channels during stepping for a) younger and b) older infants.

Functional Organization of Object Processing Areas in the Infant Brain

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A great deal is known about the functional organization of cortical networks that mediate visual object processing in the adult. The current research is part of a growing effort to identify the functional maturation of these pathways in the developing brain. Functional near-infrared spectroscopy (fNIRS) was used to investigate activation of the infant cortex during the processing of featural information (shape) and spatiotemporal information (speed of motion) during the first year of life. Infants aged 3 to 6 months (Experiment 1, $N = 51$), 7 to 8 months (Experiment 2, $N = 51$), and 10 to 12 months (Experiments 3 and 4, $N = 52$ and $N = 53$) were shown one of three events: shape difference, speed discontinuity, or control (Fig. 1). Neuroimaging data were collected in four cortical locations in the left hemisphere: occipital, posterior parietal, anterior temporal, and posterior temporal areas (Fig. 2).

Three main findings emerged. *First,* processing of the speed-discontinuity event activated posterior parietal cortex in all age groups, revealing early emerging and stable responses to spatiotemporal information in dorsal areas during the first year. *Second,* processing of the shape-difference event activated parietal cortex in the younger but not the two older to age groups, indicating that prior to about 7 months dorsal areas are involved in the analysis of object shape in this task. A number of possible explanations for this result are considered (e.g., young infants depend on motion-carried information in their analysis of 3D form and/or processing of object form is embodied). *Third*, activation was obtained in anterior temporal cortex only in conditions in which infants individuated the objects, providing converging evidence for the critical role that anterior temporal cortex plays in the individuation process during infancy. However, there was one condition in which object individuation did not result in anterior temporal activation: this area was not activated in the oldest age group in response to the speed-discontinuity. This null result was unexpected. Additional studies confirmed that older, like younger, infants detect the discontinuity of speed and interpret the event as involving two objects (i.e., individuate the objects on the basis of spatiotemporal information). Several reasons for why engagement in the individuation process during this event did not result in parietal activation in the older infants are considered.

Together, these results reveal functional plasticity of the infant cortex and suggest reorganization of object processing pathways during the first year. Hypotheses about the nature of this reorganization will be discussed.

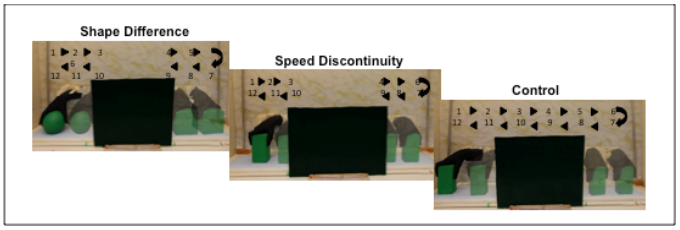

Fig. 1. The shape difference, speed discontinuity, and control test events of the current experiments. Each cycle of the test event was 12 s and infants saw 2 complete cycles during each test trial. Hemodynamic responses (HbO, HbR, HbT) were obtained during each event.

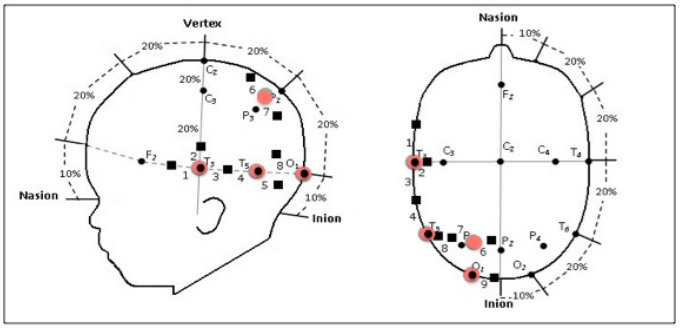

Fig. 2. Configuration of the sources (red dots) and detectors (black squares) and the nine corresponing channels (numbers) from which optical imaging data were collected. Optodes were was placed in relation to the 10-20 International EEG sytem. One source was placed on or near O1, T5, T3, and P3. Four cortical areas were covered: occipital cortex, posterior temporal cortex, anterior temporal cortex, and posterior parietal cortex, respectively. HbO responses were analyzed.

The neural basis of speech and reading in developing readers: an fNIRS study

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Poor phoneme representations are recurrently marked as a cause for deficits in reading development. Current theory suggests that the required phonological reorganization and neuroplasticity depend on speech perceptual/motor systems (Guenther, Ghosh, & Tourville, 2006). Individual differences in phonological awareness predict activity patterns in the left hemisphere superior temporal and occipito-temporal gyri and inferior frontal gyrus for both speech-perception and reading (Frost et al., 2009). The underlying neural networks involved in speech and reading in developing readers largely remain to be elucidated. fNIRS provides an optimal opportunity to map brain activity in young children. This study aims to shed light on which neural networks are involved in speech and reading and how these networks overlap in developing readers.

In this study we recruited 32 grade-1 children (15 girls) to participate in an fNIRS study to map speech and reading activation. Furthermore, we collected behavioural measures of word decoding, phonological awareness, letter knowledge, vocabulary and rapid naming. During the fNIRS, children wore bilateral 5x3 probes of which the lowest central optode was centered over T3 and T4 to map temporal, inferior parietal, inferior frontal and motor areas. Imaging data is acquired using the UCL optical topography system (Everdell et al., 2005). The stimuli consisted of 33 auditory (speech perception) and 33 visual (reading) words and nonwords. Stimulus presentation proceeded as follows: a sign indicated whether the trial was auditory/visual, 7 seconds fixation cross, 6 repeats of the same stimulus (1 second each; 100ms ISI), 7 seconds of silent video animation. One oddball (auditory/visual stimulus differing in one phoneme/grapheme) was presented in 9 trials. A button had to be pressed in case of an oddball in order to keep the children engaged.

Light intensity data was converted to hemoglobin data, the NIRS channel locations were estimated using 3D digitizer data and statistical analysis was performed using NIRS-SPM. A general linear model was applied to calculate which channels were significantly activated during speech and/or reading. Results will be discussed within a framework of well-known speech brain areas (e.g. Broca's and Wernicke's area), as well as typically activated areas for reading (e.g. Angular Gyrus). This study tries to further clarify the neurobiological mechanisms on how speech and reading are related.

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Distinct temporal properties of cortical hubs in the language network of infants

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The cortical network for language processing consists of the frontal, temporal, and parietal regions of the brain. While it is probable that an early precursor of this network exists in the infant brain, the characteristics of the network during development have not been fully investigated. In the present study, the spatiotemporal organization of this functional network was examined in the infant brain. Twenty full-term healthy infants (104–123 days old) participated in this study. All infants were asleep during testing, and cortical activation was measured using 94-channel near-infrared spectroscopy (NIRS). Briefly, Japanese speech sounds (duration: ~4 s) were presented to infants every 10 or 20 s (63 sentences over 920 s). We then calculated correlation coefficients between a continuous time course of oxygenated hemoglobin (oxy-Hb) signals, obtained from a single channel, and that of all other channels. Continuous data were filtered using two band-pass filters (0.009–0.02 or 0.04–0.2 Hz) prior to analysis. Based on these correlation coefficients, we calculated eigenvector centrality values. These analyses revealed that the left inferior frontal and left auditory regions had high eigenvector centrality values in the lower frequency band. In contrast, the bilateral frontal and temporoparietal regions showed greater eigenvector centrality values in the higher frequency band, which may correspond to frequencies related to hemodynamic responses to speech sounds. The direct comparison of the values between the two bands revealed a ventro-dorsal distinction in the left frontal region. Our findings suggest that the left frontal and temporoparietal regions of infants are cortical hubs of the language network. While the dorsolateral prefrontal and temporoparietal regions form a dorsal pathway in which ongoing language information is processed, the left ventral frontal hub might support processes that occur in the longer time range.

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Brain Response to Reading Tasks and Reading Training in Dyslexia as Measured by fNIRS

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A person with dyslexia may have problems in areas of the brain that help interpret written language. As a result, individuals experience difficulties in fluent decoding of the printed materials and in reading comprehension. In a study conducted by NIH for 20+ years, the prevalence of reading disorders was found to be ~ 20% in children[1]. If reading disorders remain undiagnosed and untreated, it affects the economic, social and emotional life of the individual. Use of advanced brain imaging technologies provided tremendous progress in the diagnostic domain. However, knowledge on the remediation aspects of reading disabilities is still limited. Using the evidence on the brain's ability to adapt (plasticity) it is conceivable that with an adequate intervention program, the brain of the dyslexics may improve for the better. Hence, the current study aims to develop effective, reliable, objective and individualized diagnosis and intervention tool for long term reading skills enhancement in dyslexics. We attempt to do so by integrating behavioral and brain based measures, with the use of state of the art reading training, namely reading acceleration program (RAP, based on reading acceleration phenomenon developed by Dr. Zvia Breznitz[2]) and a noninvasive, safe, easy to use, portable and affordable neuroimaging modality based on functional near infrared spectroscopy (fNIRS).

In this ongoing study, native English speaking children, dyslexic and typical readers of age 8-10 years old are recruited. All participants undergo an initial session during which paper and pencil tasks (i.e. Gray Oral Reading Test (GORT)) are performed for the purpose of screening and baseline evaluation. Next, a brain imaging session is conducted. fNIRS measurements are collected while participants perform two computerized reading related tasks: passage reading and lexical decision task (LDT, requires classification of visual stimuli as words or pseudo-words[3]). Additional 2 sessions are performed 3 months later, with the same tasks as done during the first and the second sessions, to provide measures of reading performance changes. During the three months period between those sessions, the group of dyslexic readers is trained using RAP.

So far 7 children with dyslexia and 1 typically reading child were recruited. All finished the pre-training evaluation sessions, while 4 children within the dyslexic group finished the training and the post-training evaluation sessions as well. fNIRS measurements were collected from the 2 channels on the left and 2 channels on the right dorsolateral prefrontal cortices. At first, hemodynamic responses in terms of changes in oxygenated hemoglobin (HbO2) as measures by fNIRS to word and pseudo-word conditions in LDT are analyzed for different channels (left and right), participants (dyslexic and typical readers) and pre- and post-training outcomes. The initial paper and pencil test evaluations of the dyslexic participants resulted in very low percentile scores in GORT fluency and comprehension tests as compared to the typical reader. In the post-training paper and pencil test evaluations, there were improvements in the fluency of two dyslexic readers and the comprehension of the other two dyslexic readers based on GORT percentile scores. Correspondingly, in fNIRS measures, initially the trend in HbO2 for word and pseudoword conditions of the dyslexic readers were opposite of the typical one. Following the training, fNIRS measurements of three dyslexic readers were more in line with those of the typical reader. There was one extremely deficient dyslexic reader, for whom RAP training did not result in much difference in fNIRS measurements. These very preliminary outcomes may indicate that changes in the reading skills of dyslexic individuals may be improved with the use of RAP, while the changes in brain processing during reading can be measured with fNIRS. These results will be verified and studied in depth once more dyslexic and typical readers are recruited in the study.

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Acute neuropharmacological effects of atomoxetine and methylphenidate on children with attention deficit/hyperactivity disorder as assessed using fNIRS

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Attention Deficit Hyperactivity Disorder (ADHD) is one of the most prevalent developmental disorders. Symptoms of ADHD typically develop during early elementary school years. The non-stimulant drug, atomoxetine (ATX) as well as the stimulant drug, methylphenidate (MPH) have been recommended as primary medications. One promising approach for objectively assessing the efficacy of either medication for ADHD children is the exploration of distinct biological markers and their testing with a noninvasive neuroimaging modality. However, it is often difficult to assess neuroactivation patterns during locomotor tasks with fMRI-based neuroimaging, and this can often cause problems in the neuro-functional assessment of school-aged ADHD children with hyperactivity. Conversely, fNIRS is suitable for clinical diagnosis of ADHD children, especially those at young ages. fNIRS can offer robust advantages such as its compactness, affordable price, tolerance to body motion and accessibility, which has allowed it to be applied for clinical assessment of ADHD children. In a series of studies, we explore the neural substrate for effects of ATX and MPH on inhibitory and attention controls in school-aged ADHD children using fNIRS. We monitored the oxy-hemoglobin signal changes of ADHD children (6 to 14 years old) performing go/no-go or oddball tasks before and 1.5 h after ATX, MPH or placebo administration, in a randomized, double-blind, placebo-controlled, crossover design. We also included age- and gender-matched normal controls without medication. In the control subjects, the go/no-go task recruited the right inferior and middle prefrontal gyri (IFG/MFG), and this activation was absent in pre-medicated ADHD children. The reduction of right IFG/MFG activation was acutely normalized after ATX and MPH administration but not placebo administration in ADHD children. In the control subjects, the oddball task recruited the right IFG/MFG and the inferior parietal cortex. The right prefrontal activation was normalized after ATX and MPH administration in ADHD children, but the right inferior parietal normalization was specific to ATX. These results led us to conclude that fNIRS successfully visualized differential neuropharmacological effects of ATX and MPH to up-regulate the noradrenaline and dopamine systems in the inhibitory and attentional networks in the brains of ADHD children. Thus, the right prefrontal and inferior parietal activations would serve as an objective neuro-functional biomarker to indicate the effectiveness of drug administration on ADHD children.

Dynamics of functional connectivity changes and connectivity strength development in healthy children and adults

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Abstract: Human brain is a dynamic and complex network. The studies of functional connectivity (FC) revealed that the function of the human brain undergo complex changes across development from children to adults. Regrettably, those studies generally assumed that the strength of interaction between two regions was constant throughout the scanning duration (termed static FC), whereas ignored the temporal dynamics of FC. In this study, we explored developmental changes in dynamic FC between children (N=18, ages 6-9 years) and adults (N=18,ages 21-27years) by examining spontaneous fluctuations in brain activity, using fNIRS. We set up 46 channels over the frontal, temporal, parietal, and occipital regions of the participant brain. We adopted a sliding time-window correlation approach to evaluate the whole-brain FC dynamics. We found that: **(1)** averaged dynamic FC variability has significant difference between children and adults (p=0.005), while the averaged static FC strength showed no difference between these both groups (Fig.1); **(2)** the nodal degree (i.e., nodal averaged FC variability) showed regional dependency in the course of development and the frontal regions showed primarily decreased FC variability in the two hemispheres(Figs.2A and B); **(3)** compared to children, most edges in adults showed significant decreased FC variability(Figs.2A and B), whereas most edges with increased static FC in adults are mainly involved with frontal regions and decreased FC in parietal regions(Figs.2C and D). our analysis of connectivity dynamics provides, to our knowledge, the first whole-brain characterization of dynamic FC differences in development.

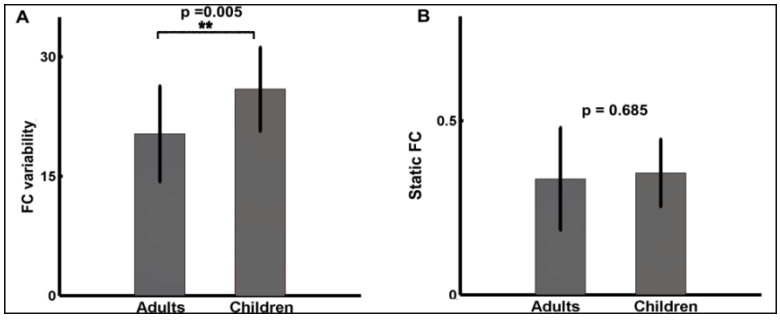

Figure1. (A) Group differences in averaged FC variability across edges between groups. (B) Group differences in averaged static FC across edges between groups.

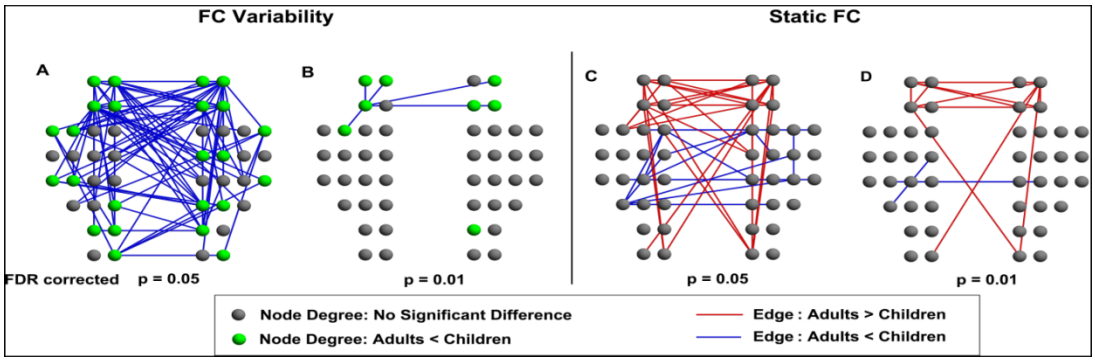

Figure2. (A) Compared to children, significantly decreased nodes and edges from FC variability in adults (FDR corrected, p = 0.05). (B)Similar to A, FDR corrected p = 0.01. (C) Compared to children, significantly decreased (blue) and increased (red) edge (FDR corrected p = 0.05) from static FC in adults. (D)Similar to figure C, FDR corrected p = 0.01.

Development of phase difference between cerebral oxy- and deoxy-hemoglobin fluctuations during the first half year of life

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Spontaneous low-frequency oscillations (less than 0.1 Hz) of cerebral hemodynamics recorded by fNIRS have revealed the development of functional connectivity of the cortex in young infants (Homae et al. 2010; White et al. 2011; Imai et al. 2014). While in-phase oscillations in either of oxy- or deoxy-hemoglobin (Hb) at distant channels reflect network properties of the synchronous activity of the cortical regions, phase relationships between oxy- and deoxy-Hb at the same channel should reflect blood flow and tissue oxygenation in relation to the neurovascular coupling. The phase differences between oxy- and deoxy-Hb signals of spontaneous fluctuations were reported in the cortex of sleeping infants around term age (Taga et al. 2000, Imai et al. 2014). However, the developmental changes in the phase differences have not been well studied. In the present study, we used data of quietly sleeping infants with 0, 3, and 6 months of age (N=15, 21, and 16, respectively) measured at 94 channels over the frontal, temporal, parietal, and occipital cortices (Homae et al. 2010) to perform analyses of phase synchronization between oxy- and deoxy-Hb signals. The result revealed that the channel averaged phase differences were close to in-phase (5.38 [rad]) in 0 months of age but were close to anti-phase (3.71 and 3.76 [rad]) in 3 and 6 months of age, respectively. Modeling studies has suggested that intermediate phase differences observed in NIRS signals can result from the superposition of signals from arterioles, capillaries and venules (Fantini 2002; Boas et al. 2008). While in-phase oscillations largely reflect blood volume changes induced by arterioles dilation, anti-phase oscillations reflect the dynamics of blood flow, blood volume and oxygen extraction in the capillaries and venules. We speculate that the developmental changes in the phase difference between NIRS signals may reflect capillary angiogenesis in concert with synaptogenesis in the developing cortex within the first 3 months of age.

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Using fNIRS to study the effects of nutrition on cognitive development in infants: A pilot study on working memory in infants in rural Africa and UK

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Inappropriate nutrition during fetal and early postnatal life can cause detrimental and persistent central nervous system alterations and deficits in behavioral functioning into childhood and adulthood [1,2]. Two of the well-documented deficiencies associated with poor nutrition in infancy are suboptimal hippocampus-based memory functioning and deficiencies in frontostriatal-mediated executive functions [3]. These deficiencies are generally only detected once the affected cognitive functions reach the point of observable behavior, usually during the second year of life or later, limiting the possibility of intervention at an earlier stage. In this pilot project, we aimed to study the cortical correlates of working memory in infants with the aim to establish whether fNIRS could provide a tool for earlier detection of potential cognitive deficits due to undernutrition. We used an *object permanence* paradigm, a task testing the ability to create and hold a mental schema of an object in mind, when it is no longer visually accessible, tapping into both executive functions and working memory. We have collected data using fNIRS in 3 age groups in a population at risk for undernutrition in rural Africa (9-13 months, 12-16 months and 18-24 months) and are currently collecting data in an age equivalent group of infants in UK. Preliminary findings (see Figure 1 for results from the 12-16mths in Africa) and their potential implications as well as future applications and limitations of fNIRS for use in studies of nutrition and brain development will be discussed.

Figure 1. Participants taking part in the study (left), the stimuli used in the working memory paradigm (middle) and the location of the significant group responses in Group 4 for the 3 and 6 second delay of the object in the box (orange) and 6 second delay only (green) (right).

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Cerebral Hemodynamics and Metabolism Responses to Somatosensory Stimulations in Premature Neonates by Near-infrared Spectroscopy

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Twelve percent of live births in the United States are premature, resulting in high risk of adverse long-term neurological impairments[1]. Functional near-infrared spectroscopy (fNIRS) measures local brain activity in response to a specific task or stimulation. Being portable and non-invasive, it is particularly useful for studying brain functional responses in young infants[2]. Although the use of fNIRS is relevant and rapidly growing, current fNIRS systems (continuous wave (CWNIRS)) are only able to quantify hemoglobin changes. In our lab, we have developed advanced fNIRS methods to overcome current limitations by adding quantification of baseline hemoglobin concentrations using frequency domain NIRS (FDNIRS), as well as changes in cerebral blood flow (CBF) using diffuse correlation spectroscopy (DCS), and from the combination of the three systems we derive baseline and functional measures of cerebral oxygen metabolism ($CMRO_2$). This multimodal approach transcends the prevailing limitations of each stand-alone modality and hence, it promises to yield more synergistic and prognostic results. In the previous study, we have demonstrated the ability of advanced fNIRS to measure evoked changes hemoglobin and CBF separately in premature infants[3]. In this study, we further improve our technology in order to acquire hemoglobin concentrations and CBF simultaneously.

Up to date, we have enrolled four premature infants (GA: 25.3-32.3 wks) at Brigham and Women's Hospital with Institutional Review Board approvals and after parental informed consent. We performed weekly measurements at earliest of 32 weeks postmenstrual ages (PMAs) until they discharged from the hospital. We placed a custom fNIRS probe over the parietal area and performed somatosensory stimulations which we gently stroked the infant's palm with a soft toothbrush. For each measurement differential pathlength factors and baseline hemoglobin obtained with FDNIRS were used to convert CWNIRS data to relative changes of HbO and HbR. We also modified Homer, a MATLAB data analysis GUI developed in-house[4,5] to simultaneously analyze both CWNIRS and DCS functional data to quantify relative vascular and metabolic change (rSO_2, rOEF, rCBF and $rCMRO_2$) [3].

As a first-pass analysis, we have verified the consistency of the CWNIRS and DCS measures by comparing the intensity changes measured (DCS) and calculated (CWNIRS) at the same wavelength (785 nm). In 3 premature neonates, we observed the typical neonatal pattern of positive rHbO and negative rHbR, similar as [3]. As in adults, the amplitude of rCBF is larger than the hemoglobin changes. These preliminary results show consistency in the functional responses over weekly measures on the same subject and differences in the responses between the different gestational ages. In one premature neonate measured at the age between 2.5-4.5 wks, we observed inverted post-stimulus hemodynamic responses with increased $rCMRO_2$. This infant had extremely low baseline hemoglobin concentration (HbT) as measured by FDNIRS and extremely low hematocrit during all three measurements sessions. This preliminary finding is in agreement with our previous observation [4], where we noticed a strong correlation between baseline hemoglobin concentration and sign of the hemodynamic responses. We attributed the negative responses to the fact that due to immaturity of the cerebral vascular system in newborns, the locally available oxygen supply is not always sufficient to exceed oxygen demand. These results highlight the need to quantify baseline HbT in order to correctly interpret vascular functional responses as well as measure $CMRO_2$ changes directly as a more robust measure of neuronal activity. This study demonstrated the feasibility of simultaneous CWNIRS-DCS measures and advantages over CWNIRS alone. Advanced fNIRS measurements offer a new way to assess neonate's neuronal development.

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Developmental and Condition-related Changes in the Prefrontal Cortex Activity during Rest

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Abstract: The prefrontal cortex (PFC) plays an important role in cognitive process related to executive function, but is also active during resting states. Quantifying prefrontal cortex activity during resting states provides a baseline for interpreting task-induced brain activity. Researchers commonly use resting conditions where participants are prompted to stare at a screen (eyes open) or close their eyes (eyes closed). Are these two conditions equivalent representations of baseline resting state? Further, does prefrontal cortex activity during these conditions change as a function of development? The aim of this study was to examine differences in prefrontal cortex activity between eyes open and eyes closed conditions during resting states in children and adults to provide a rationale of proper selection of baseline condition in future research. Total of 36 participants in 3 age groups were recruited in this study including twenty-four adults, 5 12-15 years old children, and 7 8-11 years old children. Concentrations of oxygenated hemoglobin (Δoxy-Hb) were obtained using functional near-infrared spectroscopy (fNIRS) in eyes closed (EC) and eyes open (EO) conditions, 3 minutes each. Contrasts were tested to compare the differences of Δoxy-Hb between eyes open and eyes closed conditions. The EC condition had significantly higher Δoxy-Hb than EO when all groups were combined ($t(17.268) = 3.021$, $p = .008$). When comparing Δoxy-Hb between eyes conditions within each group, the younger group had significantly higher Δoxy-Hb in EC than EO ($t(9.459) = 2.734$, $p = .022$). Based on these results, the EO condition may be a better baseline condition, particularly in studies with younger children, since it has less activity in the PFC that could interfere with interpretation of task-induced activity.

Developmental changes in executive functions during the first years of primary school – a longitudinal study using functional near-infrared spectroscopy.

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Self-regulation involves controlling ones own cognitions, emotions, and behavior. A closely related concept is that of executive functions (EF), involving such cognitive component processes as shifting, inhibition and updating of working memory contents. Self-regulation and EF play an important role for academic achievement (Blair, 2002). However, the exact structure of EF is still controversially discussed, and the brain mechanisms underlying their development are among the central topics of developmental cognitive neuroscience research.

In this study, we examined the development of executive functions during the transition from Kindergarten to primary school. We hypothesized on the one hand that inhibition and shifting have different developmental courses at both the behavioral and neuronal levels. Secondly, we tested whether three subcomponents of inhibition, as discussed in the literature, could be dissociated in terms of behavioral or neuronal development. We performed a longitudinal study with children entering primary school (group 1) and children at the beginning of the second year of primary school (group 2) with the second measurement point being one year after the first one in both groups. We used a NIRx NIRScout system with 32 emitters and 40 sensors to investigate neuronal activation in frontal and parietal regions during child-friendly versions of several prototypical paradigms measuring EF, i.e., the Go/Nogo task, the fish flanker task, the day/night Stroop task for for measuring different aspects of inhibition. In addition, a dimensional change card sorting task was used to measure shifting. All tasks were presented in block designs. Data were pre-processed using different functions from Homer2, and then exported into NIRS-SPM format for further analysis. At the conference, we will present the results as well as our integration into current discussions of the development of executive functions.

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fNIRS imaging of pediatric spatial working memory

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Introduction. Working memory is an essential aspect of human cognitive development. Defined as the processes that guide behavior toward one's goal, based on internal representations of actual and anticipated cues, working memory is not a single ability, but a series of complex skill [1, 2]. These skills involve perception, discrimination, encoding, maintenance, recognition, retrieval, and integration of stimuli and are hypothesized to mature and assimilate across development. The purpose of this study was to investigate the role of the lateral prefrontal cortex (LPFC) in children and to examine changes in brain activity correlated with developmental age.

Methods. Subjects were 3-5 year-old children (N=57; mean=4.43, SD=.93, range=3.0-5.83) recruited through local advertising. A parent or legal guardian provided written informed consent for each child subject. All recruitment and experimental procedures were approved by the local IRB.

Children were seated at a touch-screen computer at a child-sized desk for a spatial working memory task. They were introduced to a cartoon character named Moochie the Monkey and told that Moochie likes to hide his bananas in trees. Their job was to remember where Moochie hides his bananas. Six palm trees were presented on the screen for the duration of each trial. For each trial, Moochie first appeared, holding his bananas, on one of the six trees (2 seconds). This was followed by either a long (6 second) or short (2 second) delay period in which Moochie disappeared, requiring the child to hold his location in working memory. After the delay period, red question marks appeared on the screen (3 seconds) prompting children to touch the tree in which the bananas were hidden.

As described by Perlman and colleagues (Perlman et al. 2014) non-invasive optical imaging was performed with a CW6 real-time fNIRS system (Techen Inc, Milford, MA). In this study, a total of four light source emitter positions each containing a 690nm (12mW) and 830nm (8mW) laser light and eight detectors were used. The inter-sensor distance was 3.2cm. Sensors were mounted into a custom-built head cap constructed from neoprene and silicone, which was comfortably worn by the participant.

Results. Group-level ANOVA based analysis was used to look at average brain activity across the group and areas interacting with age as a covariate. As shown in figure 1, we found activation in the right frontal and left LPFC areas. Activation in these areas increased with the age of the subjects.

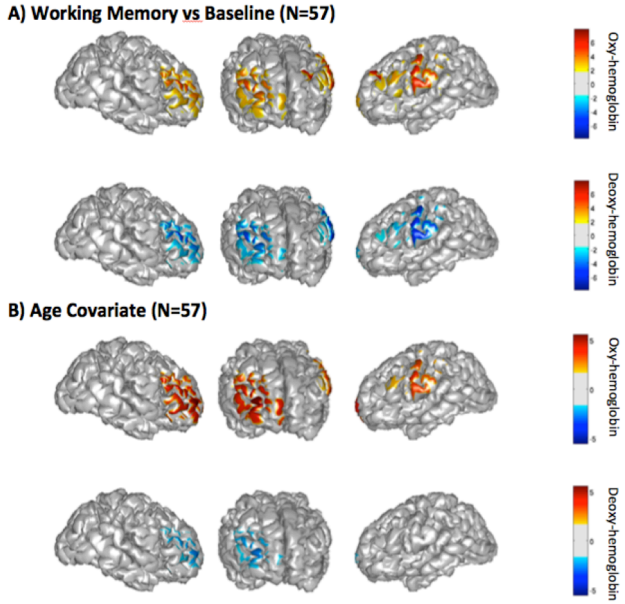

Figure 1. FNIRS images of oxy- and deoxy-hemoglobin are shown for the average brain activity (effect) and age-covariate in the group-level ANOVA analysis

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Neural Representations for Spoken Language are Influenced by the Development of Reading

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How does the developing brain process spoken language as children transition from pre-readers to emergent readers? Developing readers are proficient users of spoken language. Indeed, a child's awareness and ability to manipulate the sound units of their language, phonological processing, is strongly predictive of later reading ability. The "classic" language areas in the left hemisphere, including the left Inferior Frontal Gyrus (LIFG) and the left Superior Temporal Gyrus (STG), are crucially involved in relating phonological information to printed text, phonological segmentation during reading, and word retrieval. Here, we asked whether there are developmental changes in the pattern of neural activation in the brain's language circuitry during processing of spoken language. To test this, we compared neural activation patterns for spoken word processing among younger pre-readers and older emergent-readers.

Methods. This ongoing study consists of five younger pre-readers (ages 3.5-5 years; preschool) and six older emergent-readers (5-6 years; first grade). Children completed a battery of English language, reading and cognitive tasks. Children heard spoken language stimuli (words and pronounceable nonwords) while simultaneously undergoing fNIRS brain imaging (Hitachi-ETG-4000). Like fMRI, fNIRS measures hemodynamic change but has key advantages for studying language across the lifespan: e.g., it is quiet, portable, tolerates movement. We used NIRS-SPM to compare neural activation patterns for word vs. nonword conditions across our two groups (pre-readers, emergent-readers).

Preliminary Results. We observed differences in the pattern of neural activation for words and nonwords, with notable differences between pre-readers and emergent readers. Pre-readers showed greater activation in the left STG for nonwords versus words (Figure 1). However, emergent readers showed greater activation for nonwords versus words in the left IFG (Figure 2).

The present study highlights changes in neural activation patterns for spoken language during the development of reading. Pre-readers showed greater recruitment of phonological processing regions (STG), but emergent readers showed greater recruitment of regions associated with lexical access, morphology, and syntax (LIFG). This shift in neural activation follows children's transition from phonological processing to orthographic lexical processing and reveals ways in which the acquisition of reading may modulate spoken language processing during development.

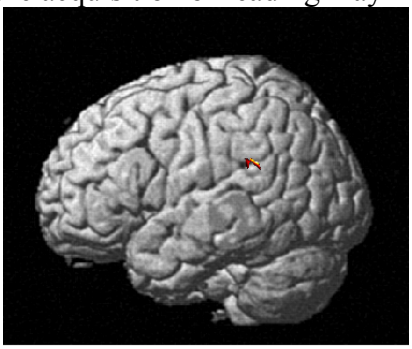

Figure 1. Pre-readers show greater activation for nonwords versus words in the left STG (p=.05, uncorrected).

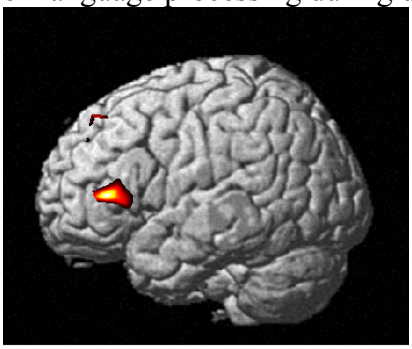

Figure 2. Emergent readers show greater activation for nonwords versus words in the left IFG (p=.05, uncorrected)

Impact of Visual Signed Language Exposure and Phonological Language Tissue Development: Evidence from fNIRS neuroimaging of language processing in deaf individuals with cochlear implants

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For deaf individuals with cochlear implants, the specific impact of differences in early life language experience on auditory tissue and related spoken language development remain controversial,[1-4] with a prevailing view being that early exposure to a signed language negatively impacts healthy auditory cortical maturation and spoken language development.[5-6] As a unique window on human cortical reorganization and neural plasticity, here we ask whether the age of exposure (AoE) to a visual signed language impacts "classic" left-hemisphere spoken language systems in deaf individuals with CIs.

Two hypotheses are tested. (H1: AoE) *Early* language exposure (early AoE), both signed and spoken, facilitates normal neural development for language processing. The prediction here is that CI individuals with early, but not later, signed language exposure should recruit classic left-hemisphere language areas associated with typical language processing. Alternatively, (H2: modality) only *spoken language* exposure will facilitate normal neural development for language processing. Here the prediction is that only spoken language experience yields typical neural language processing. By contrast, early AoE with a signed language yields a disruption to typical development, in which CI individuals with early and later signed language exposure do not recruit left-hemisphere language areas.

Methods. In this study, CI individuals (mean age of cochlear implantation: 8 yr) with either early (≤4yr) or late (≥5yr) AoE with a visual signed language read aloud single English words while undergoing fNIRS neuroimaging (Hitachi ETG-4000). fNIRS neuroimaging advances the capability to safely conduct neuroimaging on cochlear implant users.

Preliminary Results. The normal development of neural tissue for language processing is supported by early exposure to a signed language, whereas later language exposure resulted in atypical language processing, thereby supporting H1. The results address the field's controversial claims by disambiguating the impact of age and modality on the development of the neural systems underlying language. It provides intriguing contrary evidence to widely held beliefs about the deleterious impact of early signed languages on auditory tissue development, and it provides new insights into the role of early visual signed language exposure on phonological language processing tissue development.

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Differences in Activation to Biological and Mechanical Motion in the Infant Temporal Cortex

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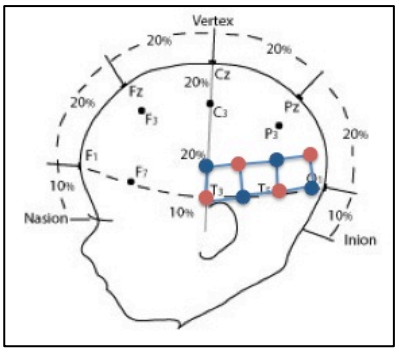
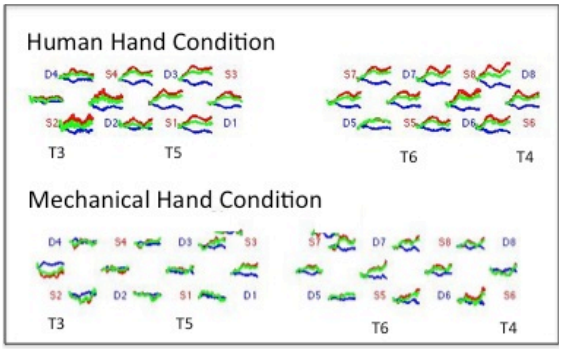
Introduction: From the early days of life infants prefer visual displays containing biological motion (e.g., point light displays of human walkers) as compared to other types of motion (e.g., scrambled or inverted displays of human walkers). There is also evidence that early in the first year infants distinguish between human and mechanical entities and have different expectations for the way that they should move and interact. These findings raise questions about whether there are distinct, early emerging systems for the processing of human and mechanical motion, similar to those observed in the adult. To address this question, the current research uses functional near-infrared spectroscopy (fNIRS) to assess patterns of cortical activation to events involving human and mechanical entities.

Design: Infants aged 7 to 9 months were tested in one of four conditions formed by crossing hand type (human or mechanical) and event type (functional or articulated motion). In the functional motion event infants saw pound and pour events (a hand used a tool to pound a nail or scoop and pour rice) on alternating trials. The articulated motion events were identical to the functional motion events except that the tools did not come in contact with the nail or rice. About an equal number of infants were assigned to each condition: human hand, functional motion (n = 16); human hand, articulated motion (n = 17); mechanical hand, functional motion (n =14); mechanical hand, articulated motion (n = 13). All events were presented in a puppet-stage apparatus. Infants saw 12 trials (15 s each), and each trial was preceded by a 10 s baseline period during which a curtain was lowered to occlude the apparatus stage. Prior to test, infants were fitted with a custom-made headgear (Figure 1). Changes in HbO, compared to baseline, were averaged over 8-15 s of each trial; then averaged over trials and participants to obtain a grand average for each group.

Results and Discussion: We grouped the channels into three meaningful regions of interest (ROI): posterior temporal, inferior temporal, and superior temporal (Figure 1). *First*, analyses of mean HbO responses indicate widespread bilateral activation in temporal cortical ROIs in the human hand conditions. In contrast, in the mechanical hand conditions, HbO responses were not significantly different from zero. This suggests greater sensitivity to events performed by human than mechanical hands in the temporal cortex. *Second*, when comparing the functional versus articulated motion events performed by the human hand, the inferior temporal ROI shows significantly greater activation to functional than articulated motion events. This suggests a specialized subset of channels sensitive to these types of functional events. *Third*, no significant differences were obtained when comparing (a) functional versus articulated motion events performed with the mechanical hand or (b) articulated motion performed by the human versus mechanical hand. This leads us to believe that these temporal regions are specialized for processing human motion, particularly if the motions are functionally relevant when involving tools. Together, these data suggest both that the type of hand (human or mechanical) and the type of event in which the hand is engaged (function or articulated motion) influence the pattern of cortical activation obtained.

Figure 1. (Left) International 10-20 system. Only the left hemisphere is displayed. The right hemisphere is organized identically but is labeled with even (rather than odd) numbers. The red dots are sources and the blue dots are detectors. Figure 2. (Right) Mean HbO curves at each of the 20 channels for infants in the human hand and mechanical hand conditions. The red letter-number pairs are sources and the blue letter-number pairs are detectors.





Using fNIRS and preferential looking to examine the early development of visual working memory

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Visual working memory (VWM) is a core cognitive system with a highly limited capacity. These limitations have a profound impact on the development of a broad range of cognitive abilities[1]. The present study investigated the neural correlates of the development of VWM in infancy using Functional Near-Infrared Spectroscopy (fNIRS). We recorded optical neuroimaging data while 1- and 2-year-olds completed a preferential looking task[2]. During the task, infants were presented with two side-by-side flickering displays composed of an array of colored squares. In one display, one of the items changes after a brief delay. Preference is calculated as the proportion of time that the infant spends looking at the changing stream. Near-infrared sources and detectors were placed over the frontal and parietal cortex bilaterally. Preliminary analyses revealed that participants showed an increase in activation as the working memory load increased from 2 to 6 items within the VWM network that included right frontal and parietal for 1-year-olds and left frontal and bilateral parietal for 2-year-olds. Moreover, left frontal activation correlated with the change preference score at SS4 ($r(6)=.88$, $p<.05$) for 2-year-olds. These results provide a first-look at the neural processes that underlie the development of VWM in infancy.

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5. Neurocognition (Adults)

Activation of the prefrontal cortex while performing a task at Preferred Slow Pace and Metronome Slow Pace: A functional near-infrared spectroscopy study

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Abstract

【Introduction】Individuals have a Preferred Pace by which they perform voluntary repetitive movements[1)]. Previous studies reported that activation of the prefrontal cortex was greater with self-initiated than with externally triggered movements[2) 3)]. The purpose of the present study is to compare activation of the prefrontal cortex when subjects perform a task at Preferred Slow Pace (PSP, self-initiated condition) or Metronome Slow Pace (MSP, externally triggered condition) in a natural environment using functional near-infrared spectroscopy (fNIRS).

【Methods】Twenty-two healthy right-handed subjects participated in the present study. This study was approved by the Institutional Review Board of Gunma University. We employed 42-channel fNIRS system (LABNIRS, Shimadzu corp.) to detect cortical activation. In the PSP task, subjects performed the task like walking slowly. Subjects had to decide when to initiate movements and maintain their PSP. Subjects performed MSP task at the pace of that almost matched their PSP rate. The task paradigm was a periodic block design with rest (20 s) and task (30 s) periods. Each task was repeated 3 times.

【Analysis】We used oxy-Hb in further statistical analyses. A baseline correlation was performed prior to statistical analyses. We approximately divided fNIRS channel locations into the frontopolar prefrontal cortex, dorsolateral prefrontal cortex, and ventrolateral prefrontal cortex. We considered the channel to have been significantly activated when the GLM analysis with Bonferroni correction was significant ($p<0.0001$) and the *t*-value was more than 10. And the oxy-Hb integral value of the PSP task was compared with that of the MSP task at each region using a pared *t*-test. The IBM SPSS Statistics 21 software was used for analysis and the level of significance was set at $p<0.10$.

【Results】Activation of the left ventrolateral prefrontal cortex was significantly greater during the PSP task than during the MSP task.

【Discussion】The ventrolateral prefrontal cortex has been associated with working memory[4)]. The results suggest that performing the PSP task required the use of information about previous response timing in working memory. In addition, subjects may have felt that the PSP task was more difficult and required a greater mental effort because PSP was not their Preferred Pace.

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fNIRS reveals cross-modal reorganisation in auditory cortex following deafness

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Introduction: Studies using functional magnetic resonance imaging (fMRI), electro-encephalography (EEG) and magnetoencephalography (MEG) suggest that deafness is associated with cross-modal reorganisation within auditory cortex [1]. This reorganisation may influence restoration of hearing with a cochlear implant (CI) [2], but this hypothesis is difficult to test since most recording techniques are plagued by implant-related magnetic and/or electrical artefacts. No such artefacts are associated with neuroimaging recordings using functional near-infrared spectroscopy (fNIRS) or positron emission tomography (PET). However, the latter is unsafe for studies in certain populations, or for repeated use. Thus, our group uses fNIRS to study CI-related cross-modal plasticity. Recently we investigated auditory cortex responses to visual and somatosensory stimulation in 29 profoundly-deaf (mean age 41±11 years) and 30 normal-hearing (mean age 34±13 years) adult participants.

Methods: Auditory stimuli took the form of 10 Hz amplitude modulated and unmodulated broadband noise, visual stimuli consisted of white dots on a black background moving with either random or coherent motion and somatosensory stimuli were 10 Hz or 20 Hz sinusoidal vibrations presented to the palms and fingers of both hands. Each of the 6 stimulus conditions was presented for 20 s and repeated 5 times in a pseudo-random order interleaved with a variable rest period (25 – 45 s). Functional NIRS data were acquired using a 24-channel Hitachi ETG4000 system.

Results & Discussion: Temporal lobe responses to auditory stimulation were larger in normally-hearing individuals compared with the profoundly-deaf group. Visual and somatosensory responses were larger in profoundly-deaf participants compared with the hearing control group, particularly over the right hemisphere (see Figure). These data support the suggestion that auditory deprivation is associated with cross-modal reorganisation in brain regions involved in auditory processing. Ongoing studies aim to assess longitudinal cortical responses to sensory stimulation in profoundly-deaf individuals prior to and following cochlear implantation for correlation with speech perception ability with a CI. We hypothesise that functional neuroimaging may provide a useful prognostic indicator and/or objective measure of CI outcome.

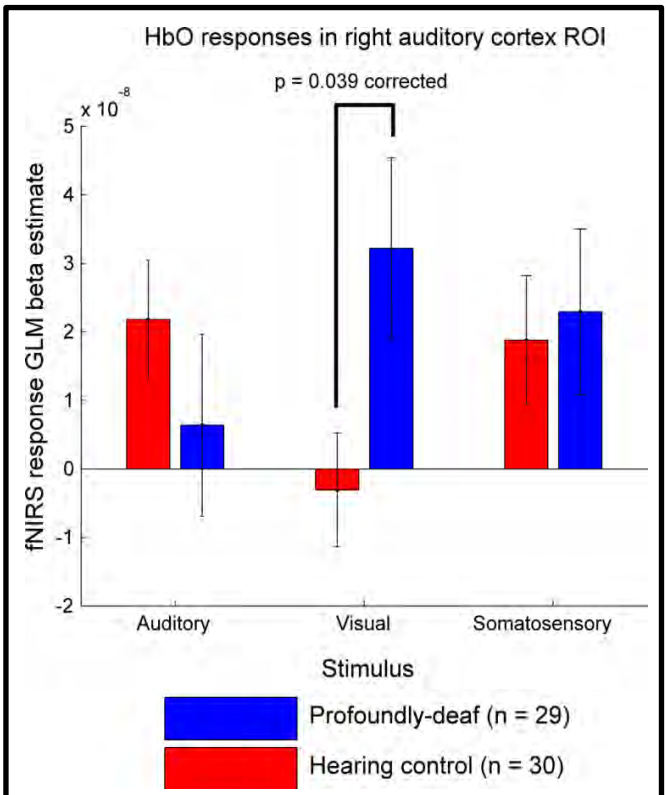

Figure: Mean (± standard error) general linear model estimates of fNIRS response in auditory, visual and somatosensory modalities. Difference in visual responses is significant at the group level.

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Functional brain imaging during simulated driving using hyperspectral functional near-infrared spectroscopy

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Background: Functional NIRS has been used to measure brain activity during driving [1]. The hyperspectral fNIRS is the most sensitive type of fNIRS due to the ample dynamic spectral information that allows for the extraction of functional cerebral signals using novel signal processing techniques [2,3]. Driving involves mostly posterior brain networks; however, a recent study has shown that pre-frontal cortex is significantly activated during distracted driving, for example, driving while talking on a hands free device [4].

Objective: We investigated the activity of the prefrontal cortex during driving with distractions. Since a previous study using functional MRI has shown increased activity in the prefrontal cortex during distracted driving [4] we expected fNIRS to show increases in oxy-hemoglobin concentration.

Materials and Methods: To measure the changes in the brain tissue chromophore concentrations, the optodes were placed on the head over the F7 and F8 positions of the 10/20 system using an EEG cap. We used a driving simulator with a fully functional steering wheel and pedals with two different driving scenarios on 16 adult (aged 20-30) right-handed participants. Two stabilized tungsten halogen light sources and QE65000 spectrometers (Ocean Optics, FL) were used to record the diffused light spectra on both hemispheres simultaneously. Participants were distracted while driving by asking true/false questions. Recorded data were de-trended and denoised using the independent component analysis. Changes in the concentrations of oxy-hemoglobin (HbO2) and deoxy-hemoglobin (Hb) were obtained using a hyperspectral fitting algorithm, and the time intervals related to each event were isolated. Straight driving was considered as baseline. To assess the effects of distractions all measurements during undistracted driving were compared with the same situation along with distraction.

Results: For all right handed participants the left prefrontal cortex showed stronger activation than the right side during distracted driving [4]. During straight driving without distractions, no significant changes in HbO_2 were observed. During driving tasks such as "making a left turn in traffic" and "right turns" the HbO_2 level decreased. During similar driving tasks, but with distraction, the increases in HbO_2 concentration were observed. During "left turn in traffic with distraction", "left turn with stop sign and distraction", "straight driving with distraction" and also "right turn with distraction" the concentration of HbO_2 increased. During the accident avoidance HbO_2 in the F7 area (left hemisphere) decreased.

Conclusion: Our findings confirm that during driving the prefrontal cortex can be significantly activated due to distractions thus, inhibiting visual attention [4]. The hyperspectral fNIRS offers excellent sensitivity to assess brain activity during driving.

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Title: “Can you hear me? An fNIRS study on the auditory recovery after cochlear implantation”

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Hearing and language restoration with cochlear implant (CI) ultimately hinges on the brain’s ability to adapt to a new way of hearing – processing the CI’s signal as sound. Because of CI’s poor compatibility with traditional neuroimaging methods, little is known about the brain’s organization for language and hearing in CI recipients. Functional near infrared spectroscopy (fNIRS) offers an innovative solution for imaging the impact of CI on brain’s language and hearing functions. The aim of this study was to evaluate the fNIRS as method for detecting brain activity in CI recipients. Ten adult CI recipients (M: 52.7±17.3 years) and ten normal hearing (NH) adults (M: 50.6±17.2 years) completed two language and hearing auditory tasks during fNIRS imaging. In the rhyme and tone judgment task, participants heard two words (i.e., cat/hat) or two sounds and indicated if they rhymed or matched. In the passage and long tone listening task, participants listened to short passages and tones of the same duration. CI recipients showed a lower accuracy but similar reaction time as compared to normally-hearing controls during rhyme and tone judgment tasks. Overall, CI and NH controls exhibited a similar pattern of brain activation for language and non-verbal auditory tasks. Our results have demonstrated that CI adult recipients showed increased hemodynamic response in cortical regions responsible for language and auditory processes, establishing that fNIRS is effective tool for monitoring hearing and language recovery with CI. Further investigation by fNIRS may help us better understand brain plasticity following cochlear implantation and might be especially critical for improving therapeutic approaches to child language acquisition with CI.

Using fNIRS to Characterize of Human Influential Factors: Towards Models of Quality of Experience Perception for Text-to-Speech Systems

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Introduction: With the thriving speech communications industry, the global market for speech technology is going through a phase of rapid growth and a recent market analysis report predicts the speech technology market to cross $31.3 billion dollars by 2017. Technologies such as, automatic speech recognition (ASR), speaker verification (SV) and text-to-speech (TTS) (i.e., synthesized speech) will form the major component of this market. Therefore, there is a greater push by the industry and researchers towards evaluating the quality of these technologies through concepts like Quality-of-Experience (QoE). QoE takes a user centred approach towards characterising the quality of a product, which ultimately leads to its greater acceptability. For most of the last decade, experts have focused on the development of methods for objective characterisation of QoE, so as to expedite the process of its quantification. However, a recent expert panel pointed out that the existing objective methods lack insights from the so-called 'Human Influence Factors' (HIFs) which characterize users' emotional states, preference, attention and their other variant or invariant characteristics. But the basic constructs of HIFs are not directly observable and take form inside the users' brain. Thus, there is a shift towards probing the brain activity using technologies such as electroencephalography (EEG) or functional near infrared spectroscopy (fNIRS) to understand and characterize the HIFs and ultimately, develop better objective QoE quantification techniques. In this paper we present the results of an ongoing study which leverages the advantages of fNIRS to characterize the HIFs dominant in synthesized speech QoE.

Methodology: Eight fluent English speakers (4 females) were recruited to participate in the study. The stimuli consisted of 16 natural and 28 synthesised speech samples (average length = 20s), which were presented to the participants through insert-earphones. These 44 stimuli consisted of 4 different sentences recorded with 4 different female natural speech and 7 different synthesized speech voices. After listening to each voice sample, the participants were asked to rate the quality of the speech signals using the 5-point continuous rating scales which accounted for overall impression, voice pleasantness, comprehension, emotion, intonation, listening effort, naturalness, speaking rate and acceptance of the voice sample. At the beginning of each stimulus, a 15 seconds rest period was added to allow for oxygenated (HbO)/deoxygenated (HbR) haemoglobin concentration levels to return to baseline before the stimulus was presented. A NIRx NIRScout system consisting of 16 sources (850 and 760 nm) and 24 detectors, was used with an optode topology arranged to probe the major brain regions. The raw signals were corrected for low frequency drifts and systemic artefacts, and converted to HbO/HbR concentration levels using the NIRS-SPM toolbox. Finally, various features such as HbO peak, HbR valleys and area under the HbO curve (AUC_{HbO}) were extracted from the clean signals.

Results: Preliminary Pearson correlation analysis has shown some of the left and right temporal regions of the brain to be moderately significantly correlated with the subjective ratings. Among the above mentioned ratings, 'voice pleasantness' showed the maximum correlation ($r_{pearson} = 0.47$) with the AUC_{HbO} for the channel located in the left temporal region and 'naturalness' showed maximum correlation ($r_{pearson} = 0.40$) with the AUC_{HbO} for the channel located in the right temporal region. This suggests that there is an increase in HbO concentrations in the temporal regions of the brain with better speech quality.

HEMODYNAMIC RESPONSE IN PRIMARY SENSORIMOTOR CORTEX TO DIFFERENT MECHANICAL STIMULATIONS OF THE LOWER BACK AS MEASURED BY FNIRS

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Introduction
There is little evidence about cortical mechanisms underlying somatosensory processing of the lower back. Such knowledge would allow for deeper insights into maladaptive changes of sensorimotor brain systems in chronic low back pain patients (CLBP). In a novel approach, repetitive mechanical stimuli were applied to the lower back of healthy subjects while recording brain activity by means of functional near infra-red spectroscopy (fNIRS).

Aim
The present study aimed to validate the fNIRS-technique for measuring cortical activation in the primary sensorimotor cortex by applying different non-painful and painful mechanosensory stimulation of the lower back in healthy subjects.

Methods
18 healthy subjects (8 females) with a mean age of 40 years (SD 16.8, range 23-66 years) participated in this study. The pressure stimulation consisted of posterior-anterior (PA) pressure exerted with a thumb grip perpendicularly to the spinous processes: This manual technique is commonly used in investigation and treatment of the lumbar spine. The pressure force was controlled by a sensor attached to the subjects' spinous process. To assess the sensitivity of the fNIRS, different pressure forces covering non-painful and painful ranges were applied in a pseudo-randomized order. Each stimulus was administered 17 times with duration of 5s and an inter-stimulus interval of 10s. Data acquisition was performed using NIRSport 8x8 (NIRx Medizintechnik GmbH). Data analysis was conducted using nirsLAB and IBM SPSS Statistics 19.

Results
Preliminary results revealed robust bilateral hemodynamic responses in the primary sensorimotor area. A main effect of painful and the non-painful pressure forces was found in repeated measures ANOVA's. Moreover, painful stimulation elicited stronger hemodynamic response than non-painful stimulation.

Conclusion
This study shows the feasibility of fNIRS as a novel approach for measuring cortical hemodynamic response to painful and non-painful mechanosensory stimulation of the lower back in healthy participants. The acquired data will serve as a baseline for further investigations in CLBP subjects to disentangle maladaptive neuroplastic changes in primary sensorimotor cortex.

Prefrontal activation is predictive of working-memory training gain in elderly

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Objectives: Older adults show more bilateral prefrontal activation during cognitive performance than younger adults, who typically show unilateral activation [1]. This over-recruitment has been interpreted as compensation for declining structure and function of the brain [2]. The aim of our research project is to gain insight into the relationship between increased aging-related prefrontal activation and individual behavioral performance. In this study, we investigated whether prefrontal compensatory mechanisms could be strengthened by working-memory (WM) training in healthy elderly and patients with Mild Cognitive Impairment (MCI).

Methods: Participants were 23 healthy older adults (70.1 ± 5.4 years, MMSE = 29.3 ± 1.0) and 17 amnestic MCI patients (67.4 ± 4.8 years, MMSE = 27.1 ± 2.3). The online adaptive WM training Cogmed QM (commercially available software) consisted of twelve verbal and spatial exercises. Participants completed 25 training sessions of 45 minutes. Before and after training, participants performed four versions of a verbal n-back task with varying levels of WM load: 0- (low load), 1-, 2-, and 3-back (high load). During task performance, oxygenated ([O_2Hb]) and deoxygenated ([HHb]) hemoglobin concentration changes were registered by two fNIRS channels located over the left and right prefrontal cortex.

Results: WM training resulted in improved performance on the 0-back task (healthy elderly and MCI) and the 1-back task (MCI). At group level, no training effects were found in prefrontal activation. However, prefrontal activation during pre-training measurements was found to be related to behavioral performance and predictive of behavioral training gain. Stronger activation was related to worse behavioral outcome during 0-back and 1-back performance. These correlations were also found for post-training measurements. Furthermore, in healthy elderly, stronger activation during 0-back performance was predictive of lower behavioral training gain on this task ([HHb] left $r = .477$, $p = .029$; [HHb] right $r = .524$, $p = .015$). Finally, in healthy elderly, a stronger increase in activation from 0-back to 3-back performance was predictive of a stronger behavioral training gain on the 3-back task. ([O_2Hb] left $r = .495$, $p = .022$; [HHb] right $r = -.474$, $p = .030$).

Conclusions: We did not find evidence for WM training-related changes in prefrontal activation as measured with fNIRS. However, prefrontal activation patterns were predictive of behavioral performance level and behavioral training gain. Our study supports the compensatory view of aging-related prefrontal over-recruitment; low performers need to recruit more neural resources at low levels of cognitive load in order to maintain task performance. In addition, individuals who show larger neural reserve might be able to benefit from cognitive training. More research is needed to establish individual factors that are predictive of cognitive training gain.

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Influence of Reading Habits on Brain Plasticity for Discourse Comprehension in Aging: NIRS contribution

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Abstract

Brain plasticity through aging, like in the cognitive reserve theory, is often described as a way for elderly adults to compensate the cognitive loss often reported. Many factors seem to act upon this plasticity like education or occupation. Even if discourse comprehension is very important to human communication, how it evolves through aging is not much studied. The present study looks at influence of reading habits through the life on brain plasticity by the way of a discourse comprehension task. NIRS techniques were used to allow a more natural, and quiet, reading environment while processing the task. Two groups of native French speakers, 16 young adults and 16 elderly adults, participated in this task. They read short stories and answered true or false probes after each one. They also completed a questionnaire about their reading habits through their life. The results show no correlation between reading habits and brain activity in the younger group. In the elderly group, the results show that the more experienced elderly readers had higher activation in the superior left region of the prefrontal cortex while they were reading the stories but lower activation in the same region when they were retrieving the information to answer the probe when compared with less experienced elderly readers. Therefore, the more experienced elderly readers seem to have built strategies to compensate the effect of aging on reading. They seemingly put more effort to acquire and maintain the information needed to answer, but this effort makes answer easier. Since, more they nurture their reading skills through their lifetime, more they seem to adapt the brain effort needed to process adequate text's comprehension while reading. These results reinforce the hypothesis that brain plasticity is promoted by cognitive activities throughout the lifespan.

The right encoding strategy: a near-infrared spectroscopy study on the lateralized activation for own and other race faces.

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Face perception is based on a holistic approach, so that not only the single elements (eyes, mouth, nose) are detected, but also the global shape and second order relationships as the distances between the elements (Behrmann, Richler, Avidan & Kimchi, 2013). This strategy, however, does not seem to work equally for all types of faces: behavioral studies demonstrated that other-race faces are perceived more analytically than own-race faces (Michel, Caldara & Rossion, 2006). At the neural level, both holistic and analytical face processing were found to elicit a lateralized activation: the holistic processing is localized on the right hemisphere, while the analytical processing is localized in the left hemisphere (Rossion et al. 2000).

In this study we used functional Near-Infrared Spectroscopy (fNIRS) to investigate the neural correlates of own and other race processing styles. Neural responses from twenty-seven Caucasian participants were collected while they were presented with Caucasian and African faces in a passing view procedure. Activation in the occipito-temporal areas (BA 18, 19, 37, 39) for oxy- (HbO) hemoglobin showed a significant main effect for race, with a greater activation for own-race faces, and an interaction between race and hemisphere. Bonferroni corrected contrasts on the peak values of the HbO hemodynamic responses revealed that other race faces elicit a comparable response in both hemispheres. On the contrary, activation for own race faces is significantly higher in the right hemisphere, where, indeed, the two groups of stimuli produce a different neural response. Data from the recognition task also confirmed the own race recognition advantage.

Our results tend to confirm the existence of different processing for own and other race faces. The neural differences between the two categories seem localized in the right hemisphere and can be probably attributed to the lack of holistic processing for the other race faces stimuli.

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Frontal brain activation during emotional Stroop task in individuals at risk for schizophrenia and bipolar disorder using fNIRS.

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Background: The emotional Stroop task is used to assess the processing of emotional words in an attentional process. In this task the participants have to name, as fast as possible, a color of an emotionally charged word presented in colored letters. The interference is measured as prolonged reaction times (RTs) while naming colors of emotionally relevant words compared to neutral ones. On a behavioral level prolonged RTs, especially for negative words, were found in healthy individuals and various psychiatric patients groups [1]. Patients with schizophrenia and bipolar disorder show increased RTs for disorder relevant words, that is for words related to paranoid and depressive symptoms respectively [2]. Furthermore, a recent imaging study has linked decreased activation in the dorsolateral and medial prefrontal cortex (PFC) during the emotional Stroop task with increased anxiety sensitivity [3]. Based on these findings we expected to observe lower frontal brain activity in individuals at risk for schizophrenia and bipolar disorder compared to the healthy controls.
Methods: A total of 151 participants were included in the analysis and assigned to the following four groups: at risk for bipolar disorder (BIP; n=16), at high risk for schizophrenia (HR; n=41), at ultra high risk for schizophrenia (UHR; n=48), and healthy controls (HC; n=46). The emotional Stroop task was presented on a computer screen during which the frontal brain activity was measured using a 52-channel fNIRS. The task was composed of each 10 positive, negative and neutral words, each of them in four colors (red, yellow, blue and green). Frontal brain activity was compared between all the groups, for all channels. Furthermore, a subsequent analysis of activation in medial and bilateral dorsolateral PFC was performed.
Results: The preliminary results show significantly higher overall frontal activity, measured by increased O_2Hb, for all categories of words for HC compared to all the experimental groups ($t>3$, $p<0.05$). The subsequent analysis of the PFC revealed significantly lower O_2Hb levels in UHR compared to HC in the right dorsolateral PFC but only for the negative words ($t_{(102)}=2.97$, $p<0.05$).
Conclusions: This is the first study investigating frontal brain activity during emotional Stroop task in individuals at risk for schizophrenia and bipolar disorder. Significantly lower activation in the right dorsolateral PFC for the negative words in the UHR group was in line with our initial hypothesis and previous findings, which associate lower activity in the dorsolateral PFC with higher activation of amygdala and increased fear sensitivity [3]. Our findings could indicate that individuals at ultra-high risk for schizophrenia show higher fear sensitivity and tendency to over-interpret potentially harmful stimuli. Nevertheless, further and more detailed analysis of this phenomenon is still needed to confirm its stability as a potential bio-marker.

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Project Title: Test-Retest Reliability of fNIRS: Evidence from a Cognitive Working Memory Task

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Abstract: A high level of test-retest reliability in functional neuroimaging is essential for understanding cognitive research results and developing clinical assessment methods. Given the limited mobility and high costs associated with functional magnetic resonance imaging (fMRI), functional near-infrared spectroscopy (fNIRS) represents an exciting alternative for evaluating neural activity (Fishburn *et al.,* 2014). However, to date, little published work has evaluated the reproducibility of the NIRS signal. Furthermore, the existing investigations focus solely on sensory, motor and resting state conditions, rather than cognitive results (e.g., Plichta et al., 2006; Strangman et al., 2006; Niu et al., 2013). The current study examined the test-retest reliability of fNIRS on a cognitive working memory task. Specifically, a group of healthy young adults (N=7, M_{age}=20.0) was assessed repeatedly over a two-week period with a 2- and 3-back task. A ten-channel TechEn Cw6 NIRS system was used, with probes placed according to the 10-20 system over F5 and F7 in the left frontal lobe and F6 and F8 in the right frontal lobe. At the group level, paired Student's t-tests were used to compare [HbO] at time 1 (mean) to time 4 (mean), with no significant difference detected for the 2- or 3-back tasks (p = 0.39, p = 0.81, respectively) (Figure 1). Intraclass correlation coefficients (ICC) were also calculated and fair to good reliability was found for both tasks (ICC = 0.52 and 0.51, respectively). The current results are consistent with recent findings by Plichta *et al.* (2012), who used a similar task to investigate the reliability of the hemodynamic response using fMRI. Notably, the current study indicates that fNIRS is a reliable technique for examining cognition, as observed in a task of working memory.

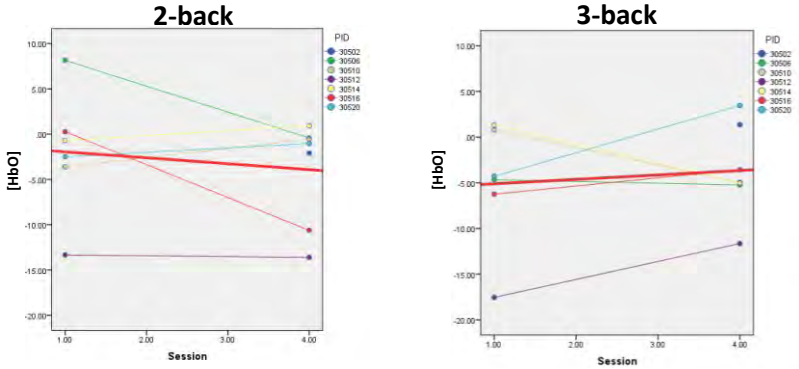

Figure 1. Panel plot of [HbO] changes across two sessions for the 2- and 3-back working memory task.

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A Problem-Solving Task Specialized for Functional Neuroimaging: Validation of the Scarborough Adaptation of the Tower of London (S-TOL) Using Near-Infrared Spectroscopy

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Problem-solving is an executive function subserved by a network of neural structures of which the dorsolateral prefrontal cortex (DLPFC) is central. Whereas several studies have evaluated the role of the DLPFC in problem-solving, few standardized tasks have been developed specifically for use with functional neuroimaging. The current study adapted a measure with established validity for the assessment of problem-solving abilities to design a test more suitable for functional neuroimaging protocols. The Scarborough adaptation of the Tower of London (S-TOL) was administered to 38 healthy adults while hemodynamic oxygenation of the PFC was measured using 16-channel continuous-wave functional near-infrared spectroscopy (fNIRS). Compared to a baseline condition, problems that required two or three steps to achieve a goal configuration were associated with higher activation in the left DLPFC and deactivation in the medial PFC. Individuals scoring higher in trait deliberation showed consistently higher activation in the left DLPFC regardless of task difficulty, whereas individuals lower in this trait displayed less activation when solving simple problems. Based on these results, the S-TOL may serve as a standardized task to evaluate problem-solving abilities in functional neuroimaging studies.

Neural correlates of processing elastic moving faces:
A functional near-infrared spectroscopy (fNIRS) study

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Most of our understandings about face processing are derived from studies using static face pictures as stimuli. It is unclear to what extent this knowledge can be generalized to face processing in the real world situations where faces are moving. Recent behavioral studies showed that moving faces optimize face processing efficiency by facilitating part-based face processing as opposed to static faces (Xiao et al., 2012 & 2013). This study using functional near-inferred spectroscopy (fNIRS) methodology explored the neural mechanisms underlying this moving face effect in face processing. We predicted that presenting moving faces would engender enhanced cortical neural activities in the primary visual and posterior temporal cortices.

Thirty-one adults participated in the present study. The classic Composite Face Effect was used to examine holistic versus part-based face processing. In the dynamic condition, participants first learned a 2-second silent moving face video, depicting chewing and blinking movements in the learning phase. In the testing phase, a static composite test face was presented. The test face consisted of upper and lower face halves from different people, displayed either aligned or misaligned. Participants decided whether the upper half was the same person as the one they just learned. The static condition was identical to the dynamic one, except that the learned faces were static pictures. A ETG-4000 (Hitachi Medical Co., Japan) was used to acquire and record fNIRS data in the temporal and occipital regions. The time course of [oxy-Hb] changes of each channel was first low-pass filtered (HRF) and high-pass filtered (Wavelet-MDL) to respectively remove low-frequency noise and high-frequency noise such as the drift and the noise induced by breathing and motion. Then, the filtered time courses were baseline-corrected. We converted the 3D spatial location data obtained from the 3D digitizer to obtain cortical positions of our NIRS channels on an estimated MNI space.

We found the robust behavioral composite face effect whereby the misaligned faces were better recognized than the aligned ones and learning moving faces led to better recognition than learning static faces. fNIR results revealed a significant greater cortical [oxy-Hb] responses in the middle temporal gyrus for watching moving faces than static faces. This finding is in accord with previous fMRI findings that the posterior temporal region is involved in processing dynamic aspect of facial information (Pitcher et al., 2011; Schultz et al., 2013). In addition, learning moving faces influenced the cortical neural responses for processing aligned and misaligned composite faces in the primary visual cortex. More specifically, learning moving faces led to decreased [oxy-Hb] responses to process aligned composite faces (beta = -0.08) but increased responses to misaligned composite faces (beta = 0.11). However, static faces led to similar amount of [oxy-Hb] activation for aligned (beta = 0.08) and misaligned composite faces (beta = 0.06). This neural effect due to facial motion suggests that facial movement might exert a top-down influence on visual processing in the primary visual cortex, by inhibiting holistic processing when viewing aligned composite faces. These findings taken together suggest that facial movements not just engender greater cortical activities, but also affect how facial information is processed, which may be critical for optimal face processing in the real world.

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The strategy and motivational influences on the beneficial effect of neurostimulation: a tDCS and fNIRS study

Transcranial direct current stimulation (tDCS) is a noninvasive technique in which small amounts of current are passed through the cortex in order to change the resting potential of underlying neural populations. Depending on the tDCS protocol used, task performance may be enhanced or suppressed. Importantly, other factors, such as education, age, genetics, appear to modulate tDCS effects. Our previous findings demonstrated that tDCS can improve working memory (WM) performance in individuals with *high WM capacity*. Therefore, we wanted to explore some possible reasons that might play a role in this individual difference. In Experiment 1 and 2 we investigated why low WM capacity participants do not benefit or have reduced performance after tDCS. To quantify the underlying changes induced by tDCS, w measured the blood flow using functional near infrared spectroscopy (fNIRS). We measured the blood flow before the participants received the stimulation as a baseline measurement. Then we used fNIRS again, after the stimulation during the WM task. In Experiments 1 and 2 we examined how strategy use and motivation level facilitate tDCS effects in high and low WM capacity groups. The results demonstrated that active strategy use does not facilitate tDCS effects in low WM capacity participants. Conversely, the high WM capacity participants showed improved performance. Furthermore, we found that only the high WM capacity participants had an increase in oxygenated blood flow following anodal tDCS regardless of strategy use. In Experiment 2 we found that motivation level promoted enhanced performance across tDCS conditions for both high and low WM capacity groups. Interestingly, only the low WM capacity participants had an increase in oxygenated blood flow across all motivation and tDCS conditions. The results from these experiments have important implications for future successful use of tDCS in both clinical and healthy populations. Incorporating fNIRS measurements extends our understanding of mechanism as we were able to better understand tDCS-induced changes in blood flow to stimulated sites.

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Using fNIRS to compare immersion vs. translation approaches for second language learning

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Learning a second language (L2) is increasingly becoming indispensable in order to communicate in our global society. Yet learning a L2 presents a challenge for many individuals, especially when this skill is acquired during adulthood. Identifying best methods for L2 learning is therefore necessary to facilitate new language learners. A previous behavioral study (Chen, 2013) suggested that the immersion approach, rather than the translation approach, facilitates better L2 learning in children, but that the two approaches are equally effective for adults. **Objectives.** This study aims to compare the neural responses of immersion versus translation L2 word learning approaches in adult learners using functional Near-Infrared Spectroscopy (fNIRS). **Method.** 18 monolingual English-speaking participants (age range 18 – 27, 6 males) were asked to learn four Chinese words, two for each presentation method. During the training phase participants listened to a sentence presented with a target word [e.g., ("球"/*qiu2*; ball)] in Mandarin Chinese. For half of the words, this sentence was presented again, but in English (i.e., using a translation approach). For the other half of the words, the sentence was again presented in Chinese (immersion approach). Each sentence was accompanied by a scene in which an actor dressed in a Teletubby costume performed an action on an object (e.g., pushing a ball) that corresponded to the target word. During the testing phase, participants were shown two scenes simultaneously (one matching the target word and the other not) and were instructed to indicate which scene matched the audio. **Results.** There were no significant differences in accuracy or reaction time between the two learning approaches during the testing phase. However, a generalized estimating equation (GEE) model indicated that there was a significant main effect of learning approach on oxy-hemoglobin response in the left inferior frontal regions. While no significant difference was found in the training phase, less activation was found in the immersion than the translation approach during the testing phase. **Conclusions.** Our results suggest that while there is no explicit behavioral evidence for an advantage of the immersion approach for short-term word learning in adult learners, the immersion approach may recruit fewer brain resources during L2 learning and word retrieval, leading to potentially improved learning for larger amounts of material. These findings shed light on the neural mechanisms of L2 word learning and provide insights for better understanding of L2 acquisition.

Language and Categorization in Monolingual and Bilingual Mandarin Speakers' Brains

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Typical items of a category (e.g., robin) are categorized faster and more accurately than atypical items of a category (e.g., penguin). In this study, we examined how and whether bilingual (English- vs. Mandarin-dominant) and monolingual Mandarin speakers would be influenced by both the cues available in Mandarin and the relative lack of cues available in English object names to examine neural correlates of the typicality effect. To accomplish this, functional Near Infrared Spectroscopic (*fNIRs*) imaging data were collected in eight bilingual English-dominant speakers, six bilingual Mandarin-dominant speakers, and nine monolingual Mandarin speakers during a category judgment task. Participants were asked whether a picture (e.g., a passenger car) was an example of the concept represented by the preceding word (e.g, "vehicle"). Both the typicality (typical vs. atypical member of a category) and type of linguistic cue to the category name (morphological vs. orthographic) were manipulated.

Across all three groups, and replicating behavioral results for both English and Mandarin speakers, typical items of a concept were responded to faster than atypical items, regardless of the type of linguistic cue in the item names. For the fNIRs data, generalized estimating equation (GEE) models revealed an interaction between typicality and linguistic cue ($p=0.002$), a marginally significant main effect of typicality ($p<0.10$), and an interaction between group and typicality ($p<0.10$). Consistent with fMRI and ERP results with monolingual Mandarin Chinese speakers, atypical items had increased oxy-hemoglobin response relative to typical items for items with orthographic cues; there was no such difference in items with morphological cues. Consistent with fMRI and ERP results with monolingual English speakers, bilingual English-dominant speakers had increased oxy-hemoglobin response to atypical items, relative to typical items when making category judgments in Chinese. There was no such typicality effect in the brain responses of bilingual Mandarin-dominant speakers and monolingual Mandarin speakers, suggesting that these speakers may use linguistic cues that are prevalent in their dominant language to override the typicality effect in this categorization task.

Our results suggested that both the structure and the everyday use of language impact the extent to which basic cognitive processes such as categorization rely on features of the categories themselves vs. the linguistic terms used to describe members of those categories.

Auditory Processing in the Cerebellum: An Examination Using fNIRS

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Oral presentation, Neurocognition (adults)

Molinari et al. (2008) reported that the primary contribution of the cerebellum to auditory perception is sequence detection in acoustic stimuli. Contrary views, however, suggest the cerebellum is primarily responsible for more global analysis of timing in both motor and cognitive tasks (Lewandowska, Piatkowska-Janko, Bogorodzki, Wolak, & Szelag, 2010).

Bregman and Campbell (1971) observed that the human auditory system processed complex auditory environments comprising multiple sound sources into "streams". Auditory stream analysis describes the perception of sound sequences as belonging together or separately. The relevant stream is formed by clustering similar auditory events based on common perceptual features. From this point of view, it is possible that the cerebellum is involved in perceptual organization of acoustic stimuli by providing an analysis of temporal information in auditory environments. Yabe et al. (2001) suggests that because acoustic similarities play a major role in determining the grouping of the sounds, auditory stream segregation can prevent masking between consecutive stimuli, and thus contribute to auditory perception. Recent cerebellar lesion studies indicate that right cerebellar damage impairs the sequencing of verbal stimuli (Leggio et al., 2008). Given the equivocal views in the literature (e.g., Lewandowska, et al, 2010), the aim of this study is to identify the cerebellar involvement in the formation of a complex auditory perceptual grouping tasks.

Thirteen (N = 13) right-handed male subjects aged 18-55 with normal hearing participated to this study. All participants underwent hearing screening to assure normal thresholds of hearing (25 dB HL or better at 250 Hz – 4000 Hz). Participants listened three auditory stimuli comprising a cycle of six tones: (1) a slow multi-frequency tone sequence, (2) a fast multi-frequency tone sequence, and (3) a fast monotone with a single repeated frequency at the same repetition rate as the fast multi-frequency stimulus. Participants reported hearing only one single auditory stream after listening a slow multi-frequency tone. Whereas the fast multi-frequency tone lead participants to perceive two separate auditory streams. The single frequency fast monotone was used to differentiate stream formation from timing analysis. Cerebellar responses to these three tone sequences were recorded using the Biopac fNIR100 16-channel fNIRS device.

Preliminary data analysis showed significant activation in the right cerebellar hemisphere in response to the different stimuli. Specifically, cerebellar responses to slow and fast tones were different illustrating that different perceptual grouping of auditory stimuli produced different cerebellar responses. However, there was less difference between fast multi-frequency tone and a single monotone repeated at the same repetition rate suggesting that the cerebellum is also involved in the analysis of acoustic timing cues that give rise to perceptual differences. Overall, results showed that cerebellum plays an important role in both sequence detection and timing with different degrees. This suggests that along with motor timing, cerebellum is also important for complex grouping tasks that are essential for the cognitive aspect of an auditory perception.

Effects of anodal high-definition transcranial direct current stimulation on bilateral sensorimotor cortex activation during sequential finger movements: an fNIRS study

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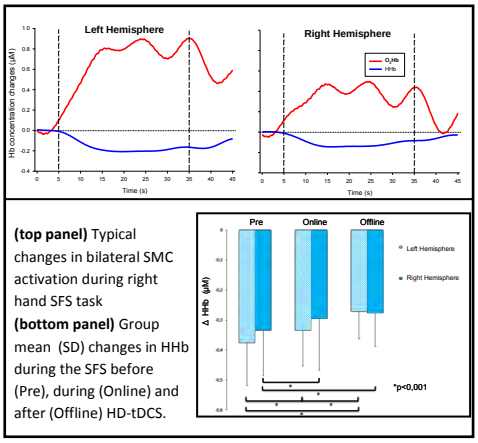
Introduction. Transcranial direct current stimulation (tDCS) is a non-invasive electrical brain stimulation technique that applies mild (1-2mA) direct currents over time (10-20min) via the scalp to increase or decrease neuronal excitability (1). The subsequent changes in spontaneous neuronal firing rates, coupled with synaptic neuroplasticity, contribute to the intra-(Online) and post-(Offline) stimulation effects, respectively (1). Recently, anodal high-definition (HD)-tDCS (2mA, 20min) targeting the primary sensorimotor cortex (SMC) was shown to induce "Offline" increases in resting corticospinal excitability (2). However, it is not clear how "Online" and "Offline" HD-tDCS modulate SMC activation during a motor task. An indirect marker of task related cortical activation is the subsequent increase in the regional blood flow and oxygenation (i.e., neurovascular coupling). Functional near infrared spectroscopy (fNIRS) measures several physiological parameters related to cortical blood flow and oxygenation including measurements of changes in oxygenated-O_2Hb and deoxygenated-HHb haemoglobin (Hb) concentrations. Therefore, the aim of this study was to utilise fNIRS neuroimaging to measure bilateral SMC activation during a simple finger sequence (SFS) task in order to determine the "Online" and "Offline" effects of anodal HD-tDCS targeting the SMC.



(top panel) Typical changes in bilateral SMC activation during right hand SFS task
(bottom panel) Group mean (SD) changes in HHb during the SFS before (Pre), during (Online) and after (Offline) HD-tDCS.

Methods. Before (Pre), at 10 min during (Online), and 3 min after (Offline) anodal HD-tDCS (2mA, 20min, Startim®, Neuroelectrics) targeting the left SMC (anode-C3), 8 healthy right handed subjects performed a self paced SFS task at 2-3Hz with their right and left hand in an alternating blocked design (30-s task and 30-s rest, repeated 5 times). During the SFS task, a multichannel NIRS system (Oxymon MkIII, Artinis Medical Systems) measured O_2Hb and HHb concentration changes from the left and right SMC.

Results/Discussion: Before HD-tDCS, the right and left hand SFS task induced a typical cortical haemodynamic response (i.e., increase in O_2Hb and decrease in HHb) in the bilateral SMC, with a greater response in the contralateral hemisphere to the hand performing the task (see figure top panel). The main new finding of this study was a significant reduction in bilateral SMC activation (based on smaller changes in HHb) for a similar motor output (SFS task) in the "Online" and "Offline" conditions compared to the Pre condition (see figure bottom panel). These findings could be related to a greater efficiency of neuronal transmission (3) in the bilateral SMC (i.e., less synaptic input for the same neuronal output) that reduced SFS task induced blood flow in the bilateral SMC and thus produced smaller changes in fNIRS-derived HHb.

Conclusion. This study has shown for the first time that both "Online" and "Offline" anodal HD-tDCS reduced bilateral SMC activation to perform a motor task. Despite the attempt at focal stimulation to the left SMC by HD-tDCS, the effects were bilateral, probably because intervening in one part of a distributed system has effects on many nodes in the system.

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Assessing emotions through Near Infrared Spectroscopy

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Abstract

This abstract present two studies on DLPFC activation (Brodmann areas 9 and 46) during viewing of scenes with different emotional and sexual content. Here, we introduce a new paradigm in the study of emotional processes, emphasizing the role of affective dimensions in DLPFC and their influence on the neuroimaging of evoked hemodynamic changes. Two affective dimensions have been studied, arousal (exciting or calming) and valence (positive or negative). The content of the scenes ranged from mutilation, repulsive acts, and violence to walking along the street, cartoons, and scenes with explicit sex. The results showed that the representation of the stimulus remains in the prefrontal cortex, even when the stimulus is no longer present. The second study explored DLPFC structures involved in the processing of films with and without sexual content. DLPFC plays a specific role in working memory to guide the inhibition or elicitation of sexual action. We measured stimulus response during direct viewing of the stimulus and for a short time after stimulus cessation, and recorded the temporal course of activation in DLPFC. Changes in pre-frontal concentrations of oxygenated haemoglobin (oxyHb) were measured during the two experimental conditions ("on" and "off" periods). At the end of the presentation, participants were asked to rate each scene from 1 to 9 on a 2-dimensional scale. We found that exposure to a sexually explicit scene produced strong overshoot in DLPFC, while exposure to a non-sexual scene did not. We also found that the hemodynamic response to visual sexual stimuli differed between genders, with men registering higher oxyHb levels in DLPFC than women. Compared to baselines, both genders showed significant overshoot in response to the sexual stimulus, although men showed higher activation in absolute values. These studies demonstrate the feasibility of examining brain activation/sexual response relationships using fNIRS, highlighting its utility as a reliable tool for research on cognitive as well as emotional processes. Its high temporal resolution facilitates research of cerebral processes in their most dynamic and lasting form.

Title: Impact of Mayer waves on motor cortical excitability explored by a combination of NIRS-TMS

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Context and goal: Mayer waves are periodic variations of blood pressure (0.1Hz) brought about by oscillations in baroreceptor and chemoreceptor reflex control systems and detectable in fNIRS signals. While the presence of these waves at cerebral level is generally considered as a simple high-pass of peripheral hemodynamic variations, some data suggest that they may play a role in cerebral auto regulation mechanisms. Particularly, it has been demonstrated that the rise of brain pressure following the increase of arterial blood pressure is superior by 40 to 50 %, suggesting a dynamic component. In addition, it has been noted that the phase between arterial and cerebral Mayer waves is altered following a stroke and can vary from one hemisphere to the other. However, the impact of Mayer waves on functional neurophysiology has never been investigated. Therefore, the goal of this study was to determine the impact of Mayer waves on motor cortical excitability.

Method: 14 subjects participated in this experiment. After identifying the portion of the motor cortex which activates the FDI for each hemisphere and placed the optodes of the fNIRS on the corresponding hotspots, the cortical portion of interest was stimulated by single pulse TMS while subjects maintained a constant contraction of FDI, targeted at 30% of their maximum force. The stimulation intensity of the TMS was adjusted depending on the experimenter delivering pulses before each block of 20 trials so that the amplitude of the MEPS reaches the motor threshold. Within each block, the pulses were sent randomly during the high or low phase of Mayer waves (double blind).

Results: Preliminary analyzes indicate that stimulation delivered during the high phases of Mayer waves induced MEPs higher by 5% to those obtained during the low phase. However, these results do not reach statistical significance.

Conclusion: the phase of the Mayer waves does not seem to influence significantly the motor cortical excitability for low stimulation intensities. Further experiments are currently underway to determine whether these results can be extended to higher stimulation intensities.

Prefrontal Activation during Tower of Hanoi in Healthy Participants.

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The prefrontal cortex plays an important role in executive functions which include cognitive processes such as decision making, working memory, planning, inhibition of responses, and cognitive flexibility. Tower of Hanoi (TOH) is a commonly used tool to assess executive function and has demonstrated sensitivity to PFC dysfunction. However, limited neuroimaging evidence is available to support the contribution of the PFC in TOH. The aim of this study was to examine the level of task-induced activity in the PFC when participants performed TOH. Nine healthy adults (3 males, 6 females, mean age = 20.5 years old) participated in the study. Concentration of oxygenated hemoglobin (Δoxy-Hb) was obtained during 1) resting (REST), 2) TOH, and 3) a simple tapping task in which the hand movement was similar to the movement during TOH (TAP). Paired t-test was used to compare differences between conditions. A significant higher Δoxy-Hb in TOH was found when compared to REST, $t(8) = -2.438$, $p = .041$, and TAP, $t(8) = -2.427$, $p = .041$. No significant difference was found between REST and TAP, $t(8) = .506$, $p = .627$. There was a higher activation in the PFC when participants performed TOH but not the tapping task indicated the activation in the PFC was resulted from the executive elements of TOH. The result was in line with the previous finding that TOH can be used to measure executive function.

Exploring the Link Between Big Five Personality Traits and Motor Inhibitory Control Using Functional Near-Infrared Spectroscopy (fNIRS)

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Understanding the neural circuits that are involved in inhibitory control has been the subject of a considerable number of studies to date, and specific regions of the prefrontal cortex (PFC) have been implicated as essential to this cognitive function. Although the neural basis of inhibitory control is reasonably well established, the role that individual differences in personality may play in influencing cortical activity associated with this ability remains largely unexplored. Therefore, the present study sought to explore the association between the Five-Factor Model (FFM) of personality traits and the neural correlates of motor response inhibition within the PFC. We obtained self-report ratings of FFM personality traits from 108 healthy adults and hemodynamic oxygenation in the PFC was recorded using a 16-channel continuous-wave fNIRS system while participants completed a standardized Go/No-Go task. Results indicated that Neuroticism and Openness to Experience were associated with attenuated activity in the lateral PFC, regions that have been implicated in emotion and behavioural control. Conversely, Agreeableness, Conscientiousness and Extraversion were associated with greater activation in the lateral PFC. Results also demonstrated that high levels of Openness to Experience were associated with decreases in activation within the medial PFC, a region linked to task engagement and self-monitoring; the converse trend was associated with higher levels of Agreeableness. These findings suggest that individual differences in specific personality traits may underlie engagement of distinct prefrontal systems involved in motor inhibitory control.

Exploring Behavioural Performance and Cortical Haemodynamic Response Differences in Executive Function for Older Adults Varying in Mobility

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Falls are a leading cause of injuries resulting in limitations to everyday routine activities, with recent estimates suggesting that 63% of Canadian senior citizens have suffered at least one fall. Early identification of those at risk for falls, as well as intervention strategies to reduce fall risk, are needed. Of the potential mechanisms associated with fall risk, deficits in executive function (EF) have been linked prospectively to fall status, with poor EF performers up to three times more likely to fall than high EF performers. Although behavioural measures have been useful for differentiating fall status, differences in functional brain activity (e.g., haemodynamic response) may provide further insight into the cognitive underpinnings related to falls and allow for earlier identification of those at risk.

Here, we report on the relationship between EF and fall status using measures of sensorimotor speed (SRT), cognitive interference (MSIT) and inhibition (Flanker) in two groups of older adults (65+); those who had had a fall within the last year (high-risk), and those who had not (low-risk). We used a multichannel, continuous-wave optical imaging system (CW6) developed by TechEn. The system contained an array of 8 sources (4 at 690nm, 4 at 830nm) and 8 detectors, for a total of 10 channels (source detector separations = 8 at 3cm and 2 at 1.5cm). The array was positioned over bilateral prefrontal cortex, and target brain regions were established a priori using Homer 2 software.

We found group differences such that the low-risk group showed haemodynamic response function (HRF) patterns typical of cognitively intact healthy adults in channels localized over dorsolateral prefrontal cortex (DLPFC) during the more executively demanding conditions of the EF tasks. In contrast, the high-risk group did not show differential activation between task conditions, suggesting they were not recruiting DLPFC to cope with the executively demanding aspects of the tasks. A similar pattern was observed in the behavioural data such that high-risk group performed more poorly during the executively demanding aspects of the tasks, relative to the low-risk group.

Overall, these results are in keeping with assertions that diminished executive control is related to fall status. Importantly, the group differences observed in DLPFC activation may ultimately precede those observed in behaviour, which may facilitate an earlier identification of those at risk for falls. A combination of behavioural and optical imaging assessment may provide sensitive insights into the efficacy of targeted intervention strategies. Additionally, in the cognitive ageing literature, intraindividual variability (IIV) across behavioural, functional brain, and physiological modalities have emerged as alternatives to central tendency that are more sensitive to CNS integrity. The correspondence of IIV across modalities is therefore of interest, as it may help facilitate a better understanding of the mechanisms associated with age-related CNS change. Future research will examine the correspondence of IIV across behavioural, functional brain and physiological modalities to help inform mechanisms of CNS integrity.

Speaker-listener persuasion: an fNIRS study of message propagation

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Successful message propagation depends on both the intention of a speaker to spread a message and their conception of how that message will be received by others. Previous fMRI studies[1,2] have collected neural data during an initial exposure to original content (i.e. pilot TV shows and novel products), along with post-exposure ratings and video recommendations of the content. This work suggests that greater activity in mentalizing regions during idea exposure characterizes speakers who are subsequently more successful at propagating their messages. With the ability to simultaneously record time-locked video and neural activity, functional near-infrared spectroscopy (fNIRS) affords the potential to understand the neural mechanisms of recommendation propagation and other dynamic social interactions.

In this study, which uses 30 mobile games applications as content, participants (n=25) were asked to watch either seed videos or video recommendations recorded by previous participants, make a rating of their intention to recommend the game, and then record their own video recommendation for each game, all while their neural activity was simultaneously recorded using fNIRS. The initial seed recommendation videos were controlled for enthusiasm (high vs. low) and valence (positive vs. neutral vs. negative), allowing us to examine how these features elicited neural activity in an initial group of listeners, and how that neural activity then propagated from the initial group to subsequent listeners, along a chain formed by speaker-listener dyads. Each dyad is structured as part of a propagation chain, such that the first-order participant in the chain watches the original, controlled content of the seed videos and the second-order participant watches the video recommendation recorded by the first.

Using past fMRI research, we define the mPFC, dmPFC and bilateral TPJ as a priori regions of interest, and hypothesize that more successful recommendation propagation depends upon greater activity in these mentalizing regions. We include the Theory of Mind localizer[3] as a task to confirm mentalizing activity in the TPJ, and find significant activation in the right TPJ during the perspective-taking condition ($t(297)=3.30$, $p < 0.01$). Initial results from the video recommendation task agree with previous fMRI results, showing that a speaker's right TPJ activity during their initial exposure to the game application video significantly predicts the subsequent listener's rating of the game application ($t(274) = 2.036$, $p <0.05$). Our analysis methods leverage the correspondence between neural activity as participants are exposed to ideas, and then subsequently deliver those ideas, as well as analysis of correspondence in neural activity between speaker-listener dyads. Additional behavioral and fNIRS data from the propagation chains will be reported, with a focus on how these results inform our understanding of the psychology of successful communication.

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Using functional Near-infrared Spectroscopy (fNIRS) to examine the neural correlates of spontaneous improvisation and creativity in a word-guessing game of Pictionary

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Abstract: Creativity, typically defined as the ability to create novel and useful outcomes, is considered as the driving force behind all human progress. It is, thus, no surprise that creativity is widely recognized as an essential skill for interpersonal, psychological, as well as entrepreneurial success[1]. Given the wide import of this cognitive faculty, understanding the neural correlates of creativity is vital to develop novel interventions to in turn foster creativity across lifespan. Sixty years since J. P. Guilford's seminal lecture on the importance to examine creativity[2], studying the brain processes underlying creative thinking is still a challenge[3]. This challenge has been mainly attributed to the inherent elusiveness of the construct itself and the lack of neuroimaging paradigms that allow participants to express their creative potential in an unrestricted manner[3]. Recent neuroimaging studies, however, have begun to explore new avenues for studying the neural basis of applied creativity. For example, by focusing on artists and musicians, researchers have examined the neural correlates of artistic creativity and musical improvisation in experts, thereby revealing a role of prefrontal cortices during creative thinking[4-6]. Although an intriguing finding, it is unclear whether similar brain processes would be involved when non-artists are engaged in comparable creative thinking tasks. To examine the brain processes underlying spontaneous improvisation, and by extension applied creativity, in non-artist healthy adults, we developed a novel fNIRS paradigm based on a word-guessing game of Pictionary[TM,7]. For this task, participants (N=28, 15F, mean age=27.64 years) drew a given word (action or verb) to the best of their ability using a drawing tablet in 30 seconds, with the caveat that others would later try to guess the word by their drawing alone. To control for the basic motor and visuospatial aspect of the word-drawing condition, participants drew a control word ("zigzag") in the second condition for the same duration. Overall, there were 10 blocks per condition, with 30 seconds for each block and a random jitter of 10-15 seconds between each block. The rationale for developing this novel word-guessing fNIRS task was two-fold: (a) to assess applied improvisation and creative skills in the context of a social game, as opposed to using some imaginary problem; and (b) by using a drawing tablet, participants expressed their creative abilities in a relatively direct and unrestricted fashion, as opposed to pressing a button or "thinking" creatively. While participants were engaged in the word-guessing task, a Hitachi Medical System (ETG-4000) with a standard 3x11 optical array probe set (52 channels) was positioned across their forehead, covering bilateral frontal and partial temporal/inferior parietal cortices, to collect data at 10Hz. We hypothesized that by contrasting the oxy-hemoglobin (Hbo) concentrations during word-drawing with zigzag-drawing condition, we could reveal the neural correlates of spontaneous improvisation and creativity. Using standard preprocessing and group-level GLM analysis, word-drawing versus zigzag-drawing contrast revealed a significant ($p<0.05$) increase in Hbo concentrations across the right superior frontal and middle- and left-prefrontal areas, suggesting a role of these areas during spontaneous improvisation and creativity. Further, the beta-estimates of word-drawing condition over the middle-prefrontal cortex were observed to be directly related to higher scores on the Creative Achievement Questionnaire (CAQ[8]; $r=0.42$, $p<0.05$), suggesting that the more the creative capacity of a participant the higher is the engagement of middle-prefrontal cortex during the word-drawing condition. Altogether, we anticipate that these results advance our understanding of the neural basis of creativity in order to guide future efforts for developing interventions to foster creativity.

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fNIRS study of numerical cognition in adults.

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The building blocks of mathematical ability are knowing numbers and equations as well as being able to process approximate magnitudes. How can we best study the neural underpinnings of these mathematical abilities in children and adults using functional Near Infrared Spectroscopy? **Objectives**: Develop a functional localizer method for identifying neural networks for the two subtypes of numerical cognition in the brain. **Method**: 30 adult participants were asked to judge varying quantities expressed via number (digits), amount (dots) and size (shape) during fNIRS imaging. fNIRS probes were placed on participants' bilateral frontal, temporal-parietal and occipital regions. **Results.** The experimental method was effective at localizing brain regions engaged in numerical processing in frontal and parietal cortexes. The next step is to extend this method to the study of young children **Conclusion**: Children's brains undergo rapid and dynamic reorganization in both anatomy and function. Localizer methods bring new ways for improving fNIRS methodology for studying higher cognitive function in young children. Present study offers new insights into using a localizer method to study numerical cognition.

Inter-personal functional connectivity during interaction tasks

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Introduction: In this study, functional NIRS was used to measure intra- and inter-person functional connectivity during a dual-person interactive cognitive task. Functional connectivity analysis was preformed on fNIRS data collected simultaneously on pairs of subjects while preforming independent and together tasks. Resting state connections between subjects were shown to statistically increase during the joint task conditions.

Methods: A total of 15 pairs of individuals (N=30) were scanned using a continuous wave NIRS system. During scans, individuals participated in 2-minute blocks of alternating resting/relaxation periods and an independent or cooperative work on a puzzle game. The puzzle game (Tangos) consisted of trying to reconstruct puzzle pieces of varied shapes and sizes to match the silhouette of an object presented on a card. Subjects completed as many puzzles as possible (usually 0-1) in a 2-minute period while working alone or in pairs. During paired interactions, the participants worked jointly on the same puzzle.

During scanning, each subject wore a 8-detector/6-source NIRS cap which covered the bilateral frontal and right posterior parietal (spatial) regions of the brain. Data was sampled at 20Hz at 690nm and 830nm.

Analysis of resting state signals was preformed using a structured vector equations (SVEC) model that included p-th order autoregressive and cross terms. Permutation testing on the likelihood of the models against unpaired datasets was used to estimate connected networks. As shown in figure 1, we found that serial correlations in noise resulting from slow drifts in physiology results in significant false-discovery of resting state connections that is corrected by the SVEC model.

Results: Inter-subject connections were present only when the subjects jointly participated in the puzzle task. During independent tasks or resting state (relaxation) tasks, only intra-subject correlations are observed.

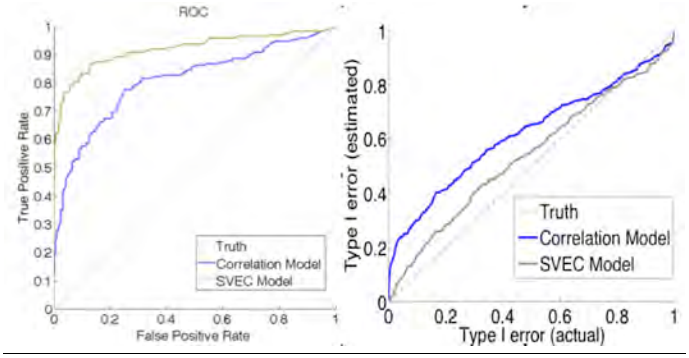

Figure 1. Simulations were preformed to examine the sensitivity and specificity of resting state fNIRS analysis. Due to serially correlated errors and over-sampling of the slow hemodynamic response, a high degree of false-positives are observed. Auto-regressive models of the noise structure is proposed to reduce these errors.

fNIRS imaging of motor learning during upright stepping

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Introduction. Functional NIRS allows imaging of brain activity during ambulatory and upright movement tasks. In this study, NIRS was used to investigate changes in brain activity associated with motor learning during a foot stepping task.

Methods: Functional NIRS was used during a motor learning task which involved repetitions of a sequence of four stepping moves (e.g. {Left/Left/Right/Left}). This pattern was repeated seven times per block and alternated with blocks of control tasks in which a random sequence was presented. Each control block had a different sequence. 4-5x 6-minute scans consisting of 6 blocks each were repeated while recording fNIRS and foot pressure/reaction time. A total of N=16 healthy subjects participated in the study. Structural MRI was additionally obtained on all subjects.

FNIRS signals were recoded from a probe that covered bilateral frontal, premotor, and motor regions and consisted of 18-detectors and 12- CW NIRS light sources.

FNIRS analysis was preformed using a parametrically modulated general linear model. The average reaction time over the 7 repeated sequences for the control and learning blocks is shown in figure 1 and was used as a modulator of the hemodynamic response to examine areas of the brain, which changed over the trials. An iterative weighted least-squares model with auto-regressive whitening [1] was used to estimate brain activation during the stepping task.

Results: The average reaction time for the stepping task is shown in figure 1. During the learning task (red), the reaction time decreased over the first 1-4 trials. No statistical changes were observed in the reaction times for the control task. Estimated NIRS brain activity is shown in figure 2 for the learning verses control condition and the parametrically modulated regressor term. Brain activity in the motor area was observed to decrease with repetitions of the task (e.g. positively correlated with the decrease in reaction time). Areas of the right frontal cortex increased activation.

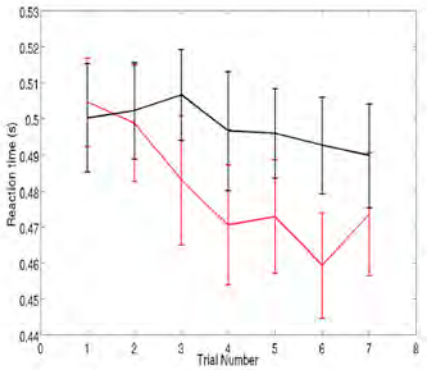

Figure 1. Average reaction times for the learning (red) and control (black) conditions from the N=16 subjects. Foot/stepping reaction time decreased with repeated trials.

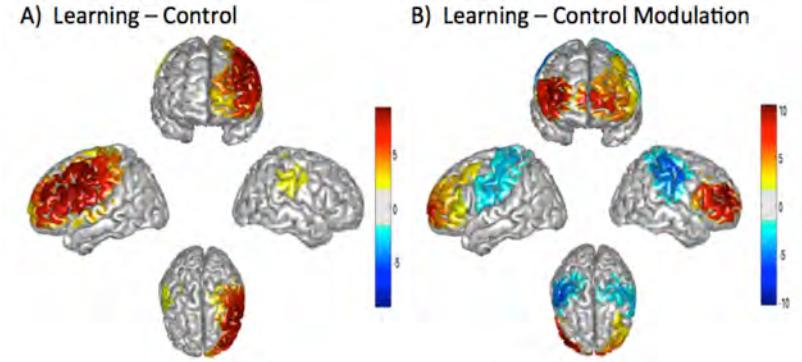

Figure 2. Estimated brain activity (oxy-hemoglobin effect size) is shown for the learning verse control conditions (panel A). Panel B shows the correlation with the parametric regressor model (reaction time) and shows decreases in motor activity and increases in frontal involvement with repetitions of the task.

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Functional NIRS imaging during vestibular balance prosthesis

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Introduction. Because falls are a leading cause of costly and debilitating injury, especially among older adults, the development of a sensory aid for balance has become of interest, with clear clinical and economic importance. Previous clinical and laboratory studies have demonstrated that vibrotactile feedback (VTF) can improve postural stability as quantified by reductions of overall body sway during VTF. However, when users are asked to engage in other cognitive tasks while undergoing VTF, interference between the task and VTF is observed; this effect is especially pronounced among older adults, who exhibit increased reaction times and less postural sway reduction during dual task experiments with VTF [2].

Methods: Continuous wave NIRS was recorded during upright balance under various sensory conditions (eyes open/closed and fixed/sway referenced flooring). VTF feedback was applied during sensory organization testing.

Results: Increases in brain activity were observed in the superior temporal gyrus and temporal-parietal areas of the brain during sensory tasks that forced reliance on vestibular information. During VTF stimulation, activation increased in the left temporal area (figure 3).

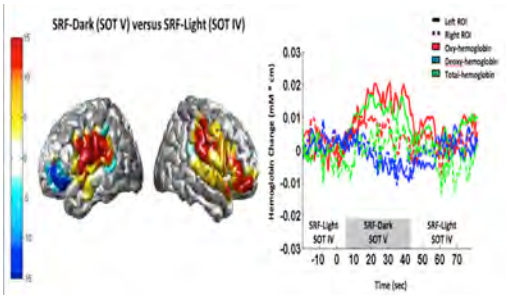

Figure 1. FNIRS shows increases in the temporo-parietal area during computerized posturography testing in healthy volunteers. The images above show oxy-hemoglobin statistical maps of the increase in brain activity when the posture condition is changed from a sway-referenced floor (SRF) in the light (SOT IV) to a SRF in the dark (SOT V) (N=15; [1]).

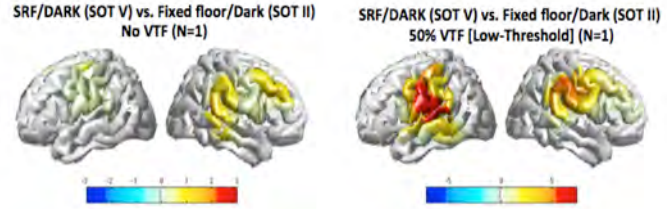

Figure 2. Comparison of brain activity in posturography testing (SOT V-SOT II) with (right) and without (left) VTF feedback.

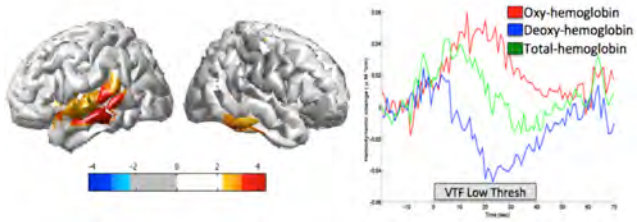

Figure 3. Brain activity changes directly evoked by changing the VTF stimulator from high to low threshold while standing eyes-closed/SRF (SOT V).

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Temporal lobe responses to auditory expressions: An fNIRS study of music and voice processing

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Studies using fMRI have revealed differential responses to specific types of human expressions — such as speech, nonlinguistic vocalizations, and music — along the temporal lobe. The aim of this study was to replicate these findings using functional near infrared spectroscopy. Healthy young adults passively listened to blocks of short auditory stimuli consisting of either speech (brief sentences spoken in different languages) or musical excerpts (played by piano or violin) while we recorded both oxy- and deoxygenated cerebral blood concentrations using a Brainsight NIRS 32-channel system set to a sampling rate of 20 Hz. The duration of each stimulus was 1.5 sec on average, and they were grouped in blocks of 20 seconds. The experiment consisted of 4 runs of 8 blocks of each category, as well as 8 blocks of silence (total duration of a run was 8 minutes). A comparison between each experimental condition with silence confirmed that several of the channels overlying auditory regions within the temporal lobe captured significant auditory-evoked responses. A direct comparison between conditions revealed, in most of these channels, a stronger response to speech than to music. These results are consistent with those we previously obtained in fMRI with the same stimuli and confirm the feasibility of using NIRS to investigate temporal lobe responses to complex auditory stimuli

Abstract: fNIRS 2014

Title: Cortical correlates of updating processes in working memory: a fNIRS investigation

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Functional Near-Infrared Spectroscopy (fNIRS) is a non-invasive imaging method that allows measuring hemodynamic changes at the cortical level. Functional NIRS has gained interest as a potential alternative to fMRI given the high correlation between Oxyhemoglobin (HbO) changes recorded using fNIRS and the fMRI BOLD signal that reflects the differential between Oxygenated and Deoxygenated hemoglobin, i.e HbT [1]. Furthermore, fNIRS features facility and flexibility of use combined with safety, making it a versatile tool [2]. In the present study, we examined brain activity associated with the updating process in working memory using a N-back paradigm. Working memory reflects the ongoing, active maintenance and manipulation of limited amounts of information. Cortical brain activity was recorded in 12 young healthy adults using a multichannel fNIRS system (BrainSight, v2.3b12). Oxy- and deoxy-hemodynamic activity, as estimated by changes in light diffusion attenuation, was measured at two wavelengths: 685 and 830 nm. The configuration of the optodes featured 8 sources and 16 detectors, clustered over four main areas, i.e. the prefrontal and parietal regions in the left and right hemispheres. Continuous signals were digitalized at a sample rate of 10 Hz, and the spatial position of optodes was accurately set up using a 3-D coordinates system coupled with a Polaris localization system. Data analysis was computed off-line using the Matlab (V.11) programming environment and HOmer toolbox (3). During the experimental procedure, participants were presented with an alternative succession of two conditions, repeated 5 times. In both conditions, letters were successively displayed on screen. In the easiest (N0) condition, participants had simply to press a key each time the letter "X" was presented. In the updating working memory condition (N2), participants were instructed to press the key only when the letter displayed on the screen was the same that the letter presented two positions before. Higher cognitive demands in the N2 than the N0 condition, associated with higher updating demands should be related with increased brain activity in key areas. Accordingly, preliminary results disclosed increased HbO levels during the working memory task (N2 > N0), especially in parietal cortices. These results are in agreement with a growing literature [4-5] that propose fNIRS as a suitable and pragmatic mechanism to study brain activity related to working memory paradigms.

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Title: Decoding vigilance with NIRS

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Preference: poster presentation

Topic area: Neurocognition (adults)

Abstract:

Sustained, attention is associated with variations and decrements in performance. Such fluctuations in vigilance can be a risk factor especially during dangerous attention demanding activities. Functional MRI studies have shown that attentional performance is correlated with BOLD-signals, especially in parietal and prefrontal cortical regions (Weissman 2006). An interesting question is whether these BOLD-signals could be measured in real-world scenarios, say to warn in a dangerous workplace whenever a subjects' vigilance is low. Because fMRI lacks the mobility needed for such applications, we tested whether the monitoring of vigilance might be possible using Near-Infrared Spectroscopy (NIRS). NIRS is a highly mobile technique that measures hemodynamics in the surface of the brain. We demonstrate that non-invasive NIRS signals correlate with vigilance. These signals carry enough information to decode subjects' reaction times at a single trial level (see Figure 1).

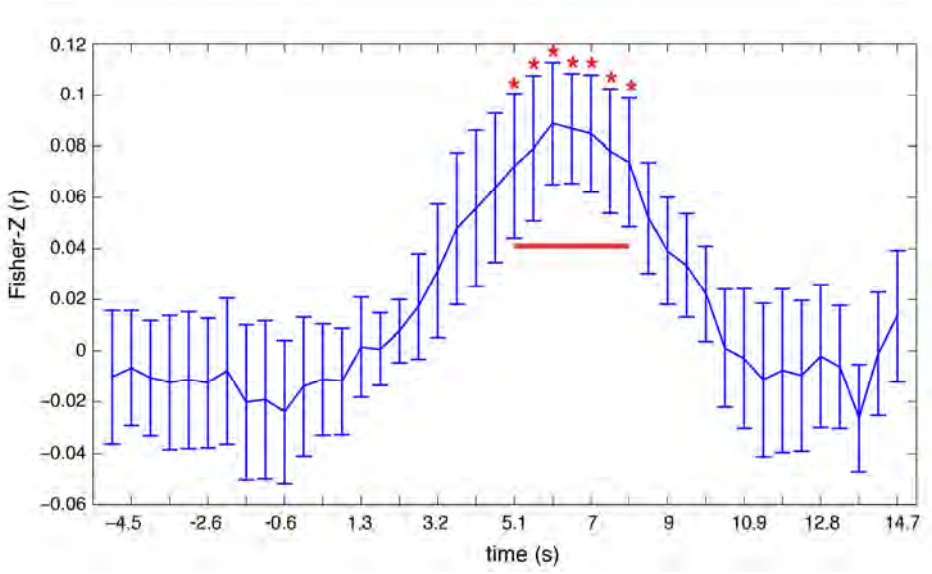

Figure 1: Decoding of response times, which reflect the subjects' vigilance on a single trial level, from NIRS signals. Timeline of the averaged accuracy (averaged Fisher-Z normalized correlation) of the prediction of subjects' single trial reaction times. During the time points that are marked with red asterisks (the time window that is highlighted with the red bar) decoding was significant ($p<0.05$; t-test on the Fisher-Z normalized correlation) above chance level.

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6. Neonatal and Pediatrics

FNIRS-based Evaluation of Cortical Plasticity in Children with Cerebral Palsy Undergoing Constraint-Induced Movement Therapy

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Abstract
We demonstrate the utility of functional near-infrared spectroscopy (fNIRS) for evaluating sensorimotor cortex plasticity induced in children with hemiparetic cerebral palsy (CP) that underwent constraint-induced movement therapy (CIMT). Sensorimotor cortex activation patterns were studied in eight children with CP (10.4 ± 1.4 years old) performing a finger-tapping task before, immediately after, and six months after therapy. Measurements were also performed on eight age-matched healthy controls (10.3 ± 1.4 years old) at the same time points. Spatial metrics of activation (laterality index and activation area), temporal ones (time-to-peak over duration) and resting-state functional connectivity were tested as potential fNIRS-based biomarkers for assessing the effects of therapy. It was shown that immediately after therapy both the laterality index and total activation area in the lesioned brain hemisphere increased, while overall connectivity strength between sensorimotor centers decreased compared to pre-therapy. These trends reflected a normalization of sensorimotor activation patterns immediately post-therapy, resembling measurements on healthy controls, but relapsed at six months post-therapy. Interestingly, in contrast to all other fNIRS metrics tested, the ratio of activation time-to-peak over activation duration for all sensorimotor centers during finger tapping displayed significant improvements after therapy that persisted six months later. Taken together, these results indicate that although the local temporal hemodynamic response of each sensorimotor center sustained a longer term normalization, the interaction between sensorimotor centers only normalized in the short term, but then relapsed. The measured fNIRS-based metrics reflecting changes in sensorimotor network normalization with time had consistent trends with corresponding clinical manual ability assessment scores for these subjects.

Keywords: functional near-infrared spectroscopy (fNIRS); cerebral palsy (CP); constraint-induced movement therapy (CIMT); sensory-motor cortex; resting-state functional connectivity.

Contribution of deep- and shallow-layer hemodynamics to fNIRS signals in infants' heads

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While neuroimaging studies based on functional near-infrared spectroscopy (fNIRS) have revealed the developmental processes of the functional activation and connectivity in the brains of infants, very few studies have examined the quantitative contributions of deep- (cerebral) and shallow-tissue (superficial) layers to fNIRS signals in infants. In this study, a methodology[1] for separating the effects of these layers on fNIRS signals was used for previously obtained fNIRS data[2] on nine three-month-old infants. The hemodynamic changes over their bilateral temporal cortices was measured while they were sleeping by using an fNIRS system with multiple source-detector (S-D) distances while presenting speech stimuli or no sounds (silence). The separation method[1] uses a time-delayed decorrelation independent component analysis (TDD-ICA) for multi-distance channels and separates each independent component into deep- and shallow-subcomponents on the basis of the dependence of the deep- and shallow-layer signal amplitudes on S-D distance. Deep and shallow signals are reconstructed by using the linear sum of the sub-components of all independent components. The key assumption is that the partial optical path length of the deep layer linearly increases as the S-D distance increases from a threshold, whereas that of the shallow layer does not change. In advance, we validated this assumption and obtained a structure-dependent threshold for three-month-old infants. As a result, fNIRS signals obtained from the infants' heads reflected the deep layer more than the shallow layer when an appropriate S-D distance such as 20 or 30 mm was used. Moreover, the deep-layer contributions were large under both speech and no-stimulus conditions. A subsequent left-right connectivity analysis under the no-stimulus condition showed that bilateral correlation coefficients for original- and deep-layer signals did not differ from each other, whereas they were larger than those for the shallow layer.

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A novel 4D neonatal head model for diffuse optical imaging of preterm to term newborns: where to find it and how to use it?

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Image reconstruction in diffuse optical tomography (DOT) is more accurate when individual MRI data are available to be used both as spatial priors in the forward problem solution and for the visualization of the reconstructed changes in oxy- and deoxy-hemoglobin. However, the need to acquire anatomical data for each participant undermines many of the advantages of diffuse optical techniques (i.e. portability and applicability to challenging populations, such as preterm neonates). To overcome this issue, the use of registered atlases to model the individual anatomy is becoming commonplace [1]. Whilst for the adult population different standard head models have been proposed and validated [2], little has been done for the neonatal population. DOT techniques are particularly suitable for studies on preterm and term babies and have the potential to provide important clinical information. The growth and maturation of the infant brain is very fast and babies born at different post-menstrual ages (PMA) will have morphologically different brains. Therefore, carefully aged matched head models are required to produce DOT images as accurately as possible and to increase the interpretability of DOT data in the neonatal population.

Here, we present a novel 4D neonatal head model, which, for each week from 29 to 44 weeks PMA, provides all the structural data required by the user to perform image reconstruction with DOT data [4]. Users can apply this model to optimize probe location, register data to cortical locations and optimize image reconstruction. The model allows maximal flexibility to the user in the choice of the method of solving the forward and inverse problems. The package is freely available online at www.ucl.ac.uk/medphys/research/4dneonatalmodel and is accessible also in the Homer2 fNIRS analysis package [3]. For each age the following is provided (Fig.1): i) a multi-layered tissue mask (extra-cerebral tissues (ECT), cerebrospinal fluid (CSF), grey matter (GM), white matter (WM), cerebellum and brainstem), ii) a high-density volumetric head mesh, iii) GM, WM and scalp surface meshes, iv) cranial landmarks and 10-5 positions on the scalp surface.

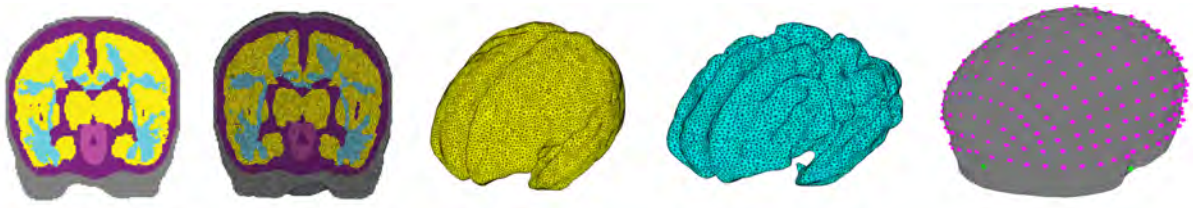

Fig.1: examples of tissue mask, volumetric head mesh, grey matter and white matter surface meshes and scalp surface mesh with 10-5 positions superposed for different selected ages.

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Are babies born with left-hemisphere language dominance? An fNIRS study.

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ABSTRACT

The age at which babies start showing a left hemisphere functional specialization for language remains a matter of controversy. Do newborns already show a hemispheric specialization for language discrimination? Twenty-seven one-day-old infants from francophone parents in Quebec underwent functional near-infrared spectroscopy (fNIRS) to assess whether the neonate brain shows left hemisphere dominance for native language. Fourteen full-term newborns (7 boys, 7 girls) listened to a story read in the language spoken at home (French) and in a foreign language (Arabic). All readings (forward speech conditions) were done by the same speaker. To determine if hemispheric dominance reflects the use of prosodic cues, a second group of 13 full-term newborns (8 boys, 5 girls) were tested with the same utterances played backwards (backward speech conditions). A nonparametric permutation test was applied to find the time points (0 to 30 s) that would show significant differences between the left and right temporal regions for each of the forward and backward speech conditions. Results revealed significantly higher oxyhemoglobin (HbO2) concentration in the left than in the right temporal region when neonates were hearing the story in the French forward condition ($p = 0.001$). Both forward Arabic and backward French elicited a significantly higher right hemisphere activation ($p = 0.007$ and $p = 0.025$, respectively) whereas the backward Arabic condition elicited a bilateral activation (right hemisphere = .0005 mol/L, left hemisphere = .0004 mol/L). We interpreted that within the first few hours after birth, newborns of French speaking parents showed left hemisphere dominance in processing prosodic cues that are language specific. These results confirmed that hemispheric specialization for language and prosodic processing is present at birth.

In vivo measurement of cerebral mitochondrial metabolism using broadband near infrared spectroscopy following neonatal stroke

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Introduction: Neonatal stroke encompasses ischaemic and haemorrhagic cerebral injuries. Near infrared spectroscopy (NIRS) can assess cerebral oxygenation, haemodynamics and metabolism continuously, using concentration changes of haemoglobin and cytochrome-c-oxidase (CCO). CCO is the terminal electron acceptor in the mitochondrial electron transfer chain (ETC) and plays a crucial role in mitochondrial oxidative metabolism and ATP synthesis.
Aim: To compare between the injured (left) and non-injured (right) side of the brain following neonatal stroke, using broadband NIRS measurement of CCO.
Method: We studied a term newborn infant (40+6 weeks) admitted with clinical seizures that started at 9hrs of age on the right side. EEG revealed repeated seizure episodes originating from left hemisphere. NIRS measurements were started at 24 hrs of age (seizures stopped 7hrs prior to the study after medications). One NIRS channel was placed on either side of the forehead. $\Delta[HbO_2]$, Δ[HHb] and Δ[oxCCO] were collected and Δ[HbT] ($\Delta[HbT]=\Delta[HbO_2]+\Delta[HHb]$) and Δ[HbDiff] ($\Delta[HbDiff]=(\Delta[HbO_2]-\Delta[HHb])$) were derived. Systemic data was collected and synchronised with the NIRS.
Results: Transient haemodynamic and metabolic changes with drop in $\Delta[HbO_2]$, Δ[HHb] and Δ[oxCCO] were noted on both sides without significant changes in systemic observations (Fig 1). A drop in Δ[HbT] more than 2μM was marked as an 'event' and 16 events were noted during 3 hour study period. Similar events have been described before following seizures[a]. A significant difference was noted between two sides in both cerebral metabolism (measured by Δ[oxCCO]) and oxygenation (measured by Δ[HbDiff]). During the events, maximum change in $\Delta[HbO_2]$, Δ[HbT], Δ[HbDiff] and Δ[oxCCO] were different between two sides ($p<0.0001$). Δ[oxCCO] responded differently to changes in Δ[HbDiff] between the left side (slope 0.64, r^2 0.50) and right side (slope -0.21, r^2 0.05) (Figure 2).

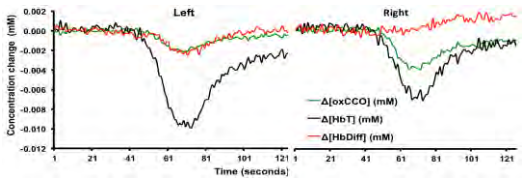

Fig 1. One event showing Δ[HbT], Δ[HbDiff] and Δ[oxCCO].

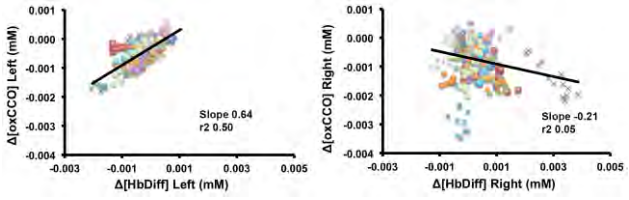

Fig 2. Δ[oxCCO] on both sides in response to Δ[HbDiff]

Conclusion: A clear asymmetry was noted in the spontaneous haemodynamic and metabolic responses between the injured left side and the right side. Cerebral oxygenation (measured as HbDiff) and cerebral metabolism (measured as oxCCO) were highly coupled on the injured side (left). Following stroke, a decrease in blood flow leads to a decrease in both substrate supply and oxygenation on the injured side[b]. They have opposite effects on Δ[oxCCO], this explains the limited change in Δ[oxCCO] on the injured left side. Restricted Δ[oxCCO] on the injured side of the brain may reflect persistent abnormal mitochondrial metabolism following unilateral seizures and reduced ATP turnover. Such unilateral reduced energy state has been described using ^{31}P MRS[c]. Increase in energy demand is known to give rise to unpredictable changes in the redox states of ETC metabolites[b]. MRI findings on day 5 confirmed neonatal stroke and asymmetric brain injury.
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A new broadband NIRS system for in-vivo measurements of cerebral cytochrome-c-oxidase changes in neonatal brain injury

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Perinatal hypoxic-ischaemic encephalopathy (HIE) is associated with severe neurodevelopmental problems and mortality. There is an urgent need for real time in-vivo measurements of brain tissue oxygenation and oxygen utilization for effective clinical assessment of neonates with HIE. We have developed a new dual-channel broadband near-infrared spectroscopy (NIRS) system that monitors brain tissue concentration changes in oxy- and deoxy-haemoglobin (HbO_2 and HHb) and the oxidation state of cytochrome-c-oxidase (oxCCO) (Fig.1(a)). Cytochrome-c-oxidase (CCO) is a mitochondrial enzyme and we have previously demonstrated that the changes in oxCCO correlate with biomarkers of metabolism in animals [1] and humans [2].

We have demonstrated the use of the system in a cohort of 6 newborn infants with HIE for continuous measurement periods of up to 5 days. NIRS data was collected from above the frontal lobe on the left and right hemispheres simultaneously with systemic data to allow multimodal data analysis (see Fig.1.(b)). We analysed the NIRS variables in response to global pathophysiological events and we focused our analysis to spontaneous oxygen desaturations. We identified changes from the NIRS variables during 236 oxygen desaturations from 212 hours of data with a change from the baseline to nadir of -12±3%. There was a decrease in NIRS-measured oxygen delivery ($\Delta[HbD]=\Delta[HbO_2]-\Delta[HHb]$) and Δ[oxCCO] measurements, -3.0±1.7μM and -0.22±0.11μM respectively, and an increase in NIRS-measured haemoglobin changes ($\Delta[HbT]=\Delta[HbO_2]+\Delta[HHb]$), 0.85±0.58μM, across all subjects. We have shown that the relationship between Δ[HbD] and Δ[oxCCO] during these desaturation events was significantly associated with a magnetic resonance spectroscopy measured biomarker of injury severity ($r=0.91$, $p<0.01$).

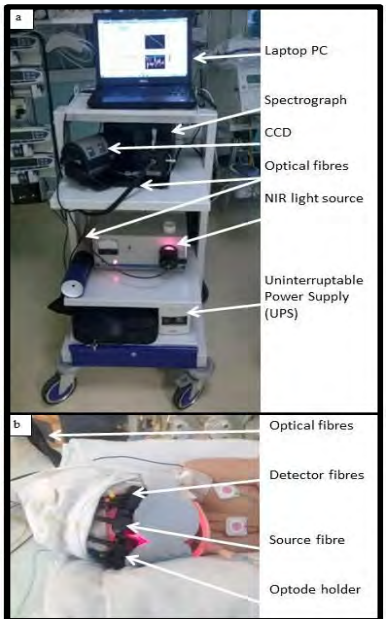

Fig. 1: (a) Components of NIRS system. **(b)** Subject during measurement with optode positions.

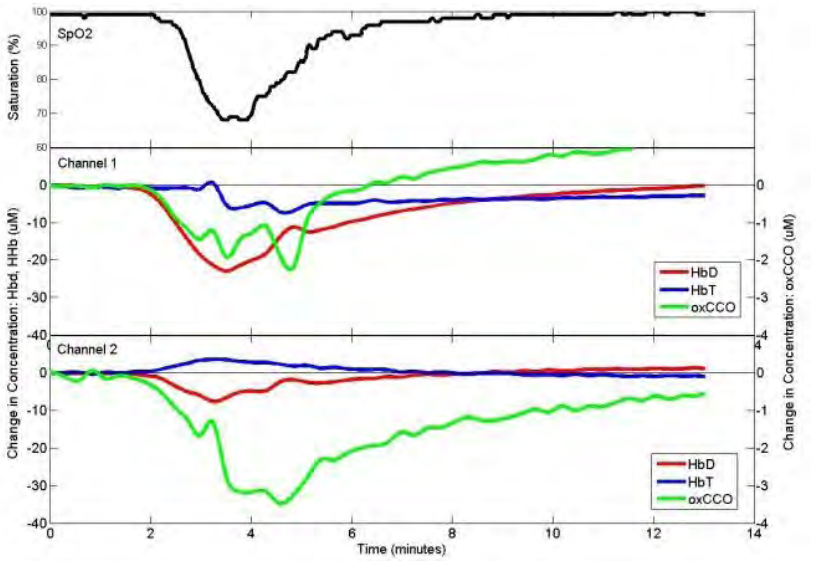

Fig. 2: Example of large SpO_2 desaturation and the response of Δ[HbD], Δ[HbT] and Δ[oxCCO] in the frontal lobe in each hemisphere (left and right respectively).

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Neonates' hemodynamic responses to linguistic phonetic differences as a predictor of later language development

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Preterm infants may experience various cognitive deficits such as impaired motor skills and language delay as they grow up. While early detection and intervention is crucial to offset the developmental impairments, there is little evidence on how such developmental impairments can be detected with reliable behavioral and neuronal markers. To better understand the relationship between early neurocognitive traits and developmental outcomes, we are currently performing a longitudinal prospective cohort study examining behavior and brain function from birth to 3 years of age. This is a preliminary report from this cohort. We examined whether cerebral responses to linguistic contrasts are related to the development of motor and cognitive skills, and language abilities. Longitudinal data obtained from 14 term infants and 13 preterm infants were used in this analysis. Cerebral responses to phonemic and prosodic contrasts were measured using NIRS at 33 to 40 weeks (corrected gestational age). We analyzed the hemodynamic response function (HRF) for multiple channels and laterality indices of the auditory area. In a follow-up test, we assessed infants' general development using the Kyoto Scale of Psychological Development (KSPD) and MacArthur-Bates Communicative Developmental Inventories (CDI). Results of correlation analyses revealed significant correlations between the HRF typicality score for the phonemic contrast and CDI score at 9 and 12 months of age. The HRF typicality score significantly correlated with KSPD language-social score. To control for possible effects of gestation, birth weight and corrected gestational age on the HRF typicality score, we performed partial correlation analyses. The correlation between HRF typicality score for phonemic contrast and CDI score at 12 months of age remained statistically significant. These results indicate that neonatal cerebral sensitivity to phonemic differences, but not prosodic differences, could predict language development at 12 months of age. This suggests this type of neural marker can be utilized to screen neonates for possible language delays.

Can low or high cerebral oxygenation be prevented in preterm infants? A multicenter randomized controlled phase II trial using NIRS

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Brain injury in preterm infants is a major cause of mild to severe long term neurodisability, with suboptimal cerebral oxygenation (i.e. too high or too low) implicated in this form of injury. Near-infrared spectrometry (NIRS) continuously non-invasively measures tissue oxygen saturation (StO_2) and can be applied to determine the cerebral oxygenation. The aim of this study was to determine, whether it is possible to reduce the burden of too high or too low cerebral StO_2, by measuring StO_2 by NIRS and following guidelines to adjust the StO_2, if the values are outside a normal range. The hypothesis was that this burden could be halved.

The study design was a multicenter randomized controlled phase II trial. A total of 166 preterm infants (<28 weeks gestation) were included in the trial from 8 neonatal units across Europe. All infants had continuous NIRS measurements for 72 hours. In all infants cerebral StO_2 was measured by NIRS. 86 infants were randomized to the treatment group: their measured StO_2 was visible and if the StO_2 values were outside the normal range, the clinician considered a set of guidelines to adjust several parameters to bring the StO_2 into a normal range. 80 infants were randomized to the control group: here the StO_2 was measured too, but the values were not displayed and the infants were treated according to the local hospital's standards.

The two groups of infants were comparable (mean gestational age intervention group: 26.6 weeks, control: 26.8 weeks). The burden of maloxygenation was approximately halved in the intervention group compared to the control group (p=0.0009).

In conclusion, it is possible to reduce the burden of cerebral maloxygenation in preterm infants by measuring cerebral StO_2 by NIRS and following specific guidelines. A future larger trial should address whether a lower burden is associated with a reduction in death and neurodisability in this vulnerable population group.

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Pre-operative cerebral hemodynamics from birth until surgery in infants with critical congenital heart disease

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Introduction—Infants with critical congenital heart disease (CHD) exhibit a high prevalence of hypoxic-ischemic white matter injury, termed periventricular leukomalacia (PVL). Recent work has shown that the risk for PVL in these infants is dependent on the waiting time from birth to surgery. Understanding the changing cerebral physiology during this vulnerable preoperative period may lead to new therapeutic algorithms aimed at prevention.

Methods—Term neonates with critical CHD were recruited for this study. Frequency domain diffuse optical spectroscopy and diffuse correlation spectroscopy were employed to noninvasively quantify cerebral tissue oxygen saturation (StO_2). Daily StO_2 measurements were made from day of recruitment until the day of surgery. A mixed-effects model was used to account for within-subject correlation due to repeated measures for each patient and to assess the effect of cardiac diagnosis on changes in StO2 over time.

Results—We studied 26 neonates with critical CHD. The subjects were placed in 3 groups depending on their cardiac diagnosis: hypoplastic left heart syndrome (HLHS, N=8), transposition of the great arteries (TGA, N=11), or other diagnoses (N=7). In a linear mixed-effects model, time after birth was significantly predictive of StO_2 ($p<0.01$), with StO_2 decreasing as a function of time from birth.

Conclusions—We observed decreasing StO_2 from birth until surgery in all groups. These results suggest that reported increases in risk for PVL with time-to-surgery could be due to decreasing cerebral oxygenation.

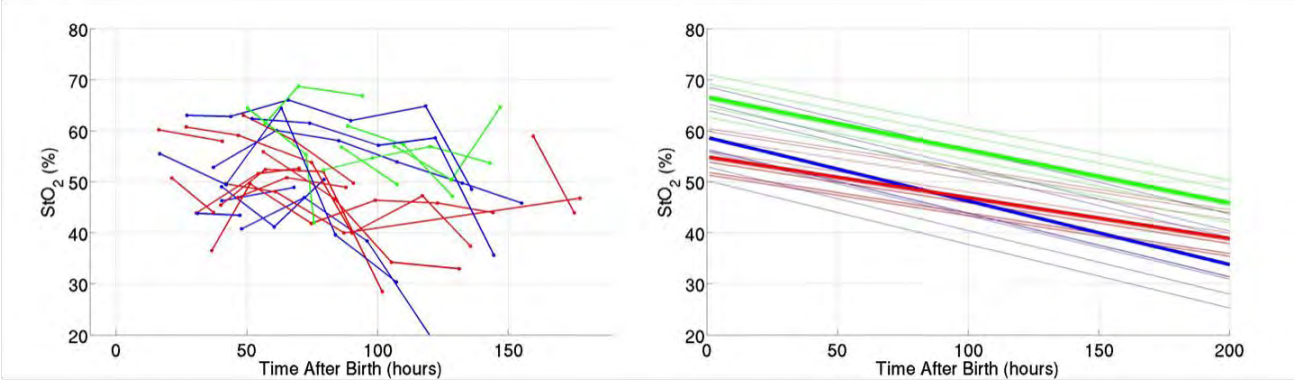

Figure 1: Daily measurements of StO_2 from birth until surgery (left) and fitted lines from a mixed-effects model of pre-operative StO_2 with a subject-specific intercept (right). Color represents groups by cardiac diagnosis: HLHS (blue), TGA (red) or other (green). In the right plot, thin lines represent individual subject modeled trajectories and thick lines represent trajectories for the entire group.

Simultaneous EEG and fNIRS recordings in neonates and children

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Brain function can and should be analyzed in its complexity to clarify the interactions between neural and vascular systems by characterizing their electrical and hemodynamic modulations, respectively.

The multimodal nonivasive EEG-fNIRS approach provides this opportunity in both preterm infants and children, normal and pathologic.

This multimodal approach allows to characterize the nature of the implementation of neural networks during development, particularly in premature infants, and to specify how it can be affected in various pathological situations. Through this type of analysis, adaptation of neural networks to external and internal stimuli, in normal and pathological situations can be better understood.

Using exogenous stimuli, this multimodal approach enabled us to clarify the temporal dynamics (EEG) and spatial (fNIRS) capabilities of the immature preterm brain to discriminate phonemes and voices from 28 weeks gestational age, at a time when the sensory afferents start their connections with neurons of the cortical plate. In some pathological conditions, such as intraventricular hemorrhage, this now clinical approach can be used to identify the brain adaptability when one of the two compartments (neural and/or vascular) is altered.

Among the endogenous stimulation, epilepsy represents a model of choice for the analysis of neuronal and vascular interactions. Whatever interictal epileptic spikes or seizures, they both rely on complex neural mechanisms that result in pathological hypersynchronization of pyramidal neurons. Multimodal approach in newborn and children allowed us to more precisely specify in their entirety, neural and vascular, the pathophysiological mechanisms underlying or secondary to these hypersynchronisations, whatever it concerns modulation of blood volume and/or neurovascular coupling.
Beside studies in neonates and children, we performed preclinical approaches using animal models with direct cortical surface analysis to better assess the physical and physiological mechanisms underlying the optical signals, thus avoiding inherent problematic due to studies in humans.

The combined approach EEG-NIRS become a temporal and spatial investigation valuable tool for normal maturation and brain dysfunction analysis, notably in the pediatric populations, in which we lack predictive and diagnostic tools

Bedside functional connectivity mapping of the developing brain

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Introduction

Diffuse optical tomography (DOT) is a portable imaging modality that provides the ability to perform early and continuous monitoring of brain function in infants. Its methodology overcomes many of the technical and logistical challenges of performing magnetic resonance imaging investigations in neonates. The initial step to establishing functional connectivity DOT (fcDOT) as a bedside tool for real-time monitoring of cerebral function in neonates is to define normal fcDOT patterns in healthy, term infants and validate results against the gold standard of functional connectivity magnetic resonance imaging. In this work, we demonstrate results from non-concurrent fcDOT and fcMRI maps obtained in a cohort of healthy, full-term neonates scanned within the first days of life.

Methods

Nine infants (GA at birth: 39-41 weeks) were recruited from the Newborn Nursery within the first 48 hours of life. Non-concurrent MRI and DOT data sets were obtained within one day. Functional MRI data acquisition was performed on a Siemens 3-T scanner (TR/TE 2910/28 ms, voxel size 2.4x2.4x2.4 mm^3). Resting-state DOT data was collected over 30 minutes using an imaging cap of 32 sources and 34 detectors (Fig. 1a). Optical measurements were converted into volumetric reconstructions of HbO_2 and HbR. Seed correlation analysis was used to create resting-state maps for DOT and fMRI data sets in reference to predefined seeds (Fig. 1b).

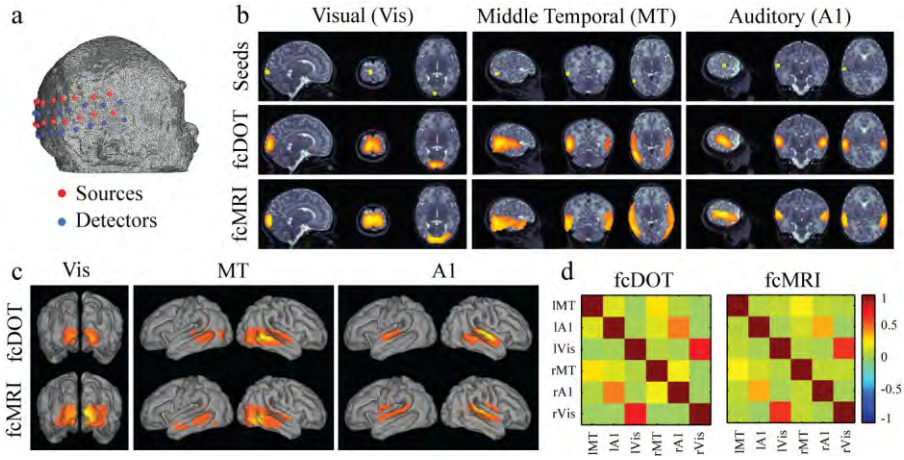

Figure 1: (a) The imaging cap covers the occipital and temporal regions of the infant's head. (b) Resting-state functional connectivity maps obtained for a single infant using three different pairs of seeds (visual, MT and auditory seeds). (c) Average correlation maps for a group of nine infants. (d) Seed-to-seed correlation matrices for fcDOT and fcMRI group maps. Seeds are organized from left (l) to right (r).

Results

fcDOT identified multiple resting-state networks in term neonates. The spatial extension of these networks is consistent with the maps obtained using fcMRI at the individual (Fig. 1b) and group levels (Fig. 1c). Correlation matrices obtained using each modality confirms that these maps are quantitatively comparable (Fig. 1d).

Conclusions

Due to its portability, fcDOT is well-suited for continuous monitoring of brain function at rest. Here we demonstrate that our fcDOT system generates resting-state maps exhibiting strong agreement with non-concurrent fcMRI maps in identical subjects. These results represent a critical step towards establishing a normative data set necessary for studying resting-state networks in high-risk neonates at the bedside.

Accuracy of slab model recovery of S_tO_2 and HbT values in neonates with frequency modulated (FM-) NIRS

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Introduction: The purpose of this study was to assess the magnitude of errors introduced in recovered tissue oxygen saturation (S_tO_2) and total hemoglobin (HbT) values due to modeling the head as a semi-infinite, homogenous medium (i.e., slab model). Previous work has investigated the accuracy of recovered absorption values under this assumption, but has only made an indirect assessment of errors in physiological parameters [1]. Simulations on homogenous spheres were also performed to characterize the effects of curvature/finite volume.

Methods: FM-NIRS data were simulated by computing light propagation through volumetric images via Monte Carlo Extreme software [2]. Absorption, scattering, S_tO_2, and HbT values recovered using the "slab model" were compared with simulated values. Simulations were performed for spheres of varying radius (20-120 mm) to characterize the effects of curvature/finite volume. Simulations were also performed on a segmented structural magnetic resonance image (MRI) from a 24 day old, full term neonate. Optical properties of the scalp, skull, and cerebrospinal fluid (CSF) were fixed to literature values [3-6], while brain properties were varied based on S_tO_2 (0-100%) and HbT (20-120 μM).

Results: Curvature induced underestimation of absorption, scattering, S_tO_2, and HbT. For radii of curvature ranging from 40-70 mm, errors in S_tO_2 were minimal (<2%), while errors in absorption, scattering, and HbT were more severe (8-15%, 15-29%, and 9-15%, respectively). Within a physiological range of 40-90% S_tO_2 and 40-80 μM, errors in absorption, scattering, S_tO_2, and HbT ranged from 1-25%, 30-60%, 1-15% and 1-15%, respectively, in the neonate model. The combined effects from the influences of the scalp, skull, curvature, and CSF were found to vary with physiological state (S_tO_2 and HbT) and source-detector distance.

Conclusion: Typical errors in S_tO_2 and HbT ranged from 1-15% in neonates without morphological abnormalities.

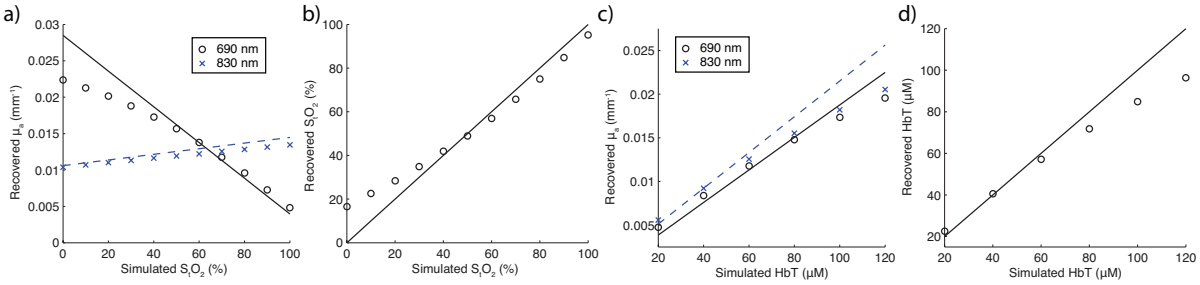

Figure 1. Errors in a neonate model. (a) Recovered absorption values for varying brain StO2 for 690 nm (O's) and 830 nm (X's) compared to simulated values (solid line for 690 nm, dashed line for 830 nm). (b) Recovered StO2 values (O's) compared to simulated values (solid line). (c) Recovered absorption values for varying brain HbT for 690 nm (O's) and 830 nm (X's) compared to simulated values (solid line for 690 nm, dashed line for 830 nm). (d) Recovered HbT values (O's) compared to simulated values (solid line).

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Clinical Evidence of Ventricular Contamination in a NIRS Study of Post-Hemorrhagic Hydrocephalus in Preterm Infants

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Intraventricular hemorrhage (IVH) remains a common problem associated with preterm birth, leading to life-long neurological sequelae, such as cerebral palsy. The prognosis is worsened by post-hemorrhagic hydrocephalus (PHH), which occurs in 10-30% of patients. There is currently no means of accurately predicting PHH, and interventions, such as ventricular tapping to remove cerebrospinal fluid (CSF), are based on clinical signs of elevated intracranial pressure (ICP), along with increases in head circumference and ultrasound (US) metrics of ventricular growth. These assessments are known to lack sensitivity, which can delay intervention. The overall aim of this project is to improve PHH management using three-dimensional US to measure increases in ventricular volume[1] and NIRS to determine if cerebral blood flow is reduced by concurrent increases in ICP. However, the accuracy of NIRS may be affected by signal contamination from enlarged ventricles, especially if there are blood breakdown products in the CSF following IVH[2]. In this study, spectra were acquired from PHH infants and CSF samples obtained during ventricular tapping to investigate this potential source of error.

Methods

Data were acquired from preterm neonates with IVH selected for a ventricular tap based on clinical evidence of PHH. Broadband reflectance spectra were measured using an in-house developed NIRS system and two fiber bundles positioned 3-cm apart over the frontoparietal region. Absorption spectra were acquired from 1-ml CSF samples acquired during tapping. Each sample was placed in a cuvette and analyzed using the same NIRS system.

Results

Seven IVH patients have been enrolled, of which CSF spectra were required from four. Figure 1 illustrates spectra from one infant with bilateral grade III IVH who underwent three taps (labeled dark, yellow and light yellow for their visual appearance) spaced 1 wk apart. The mean spectrum from a group of preterm infants without PHH is shown for reference. All spectra were normalized to absorbance at 800 nm. Figure 2 illustrates CSF spectra from the same infant, again labeled by appearance, normalized to 980 nm.

Figure 1

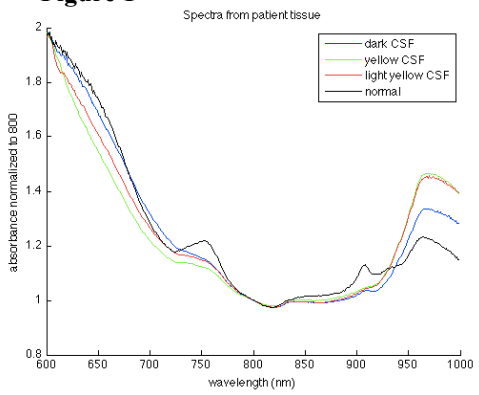
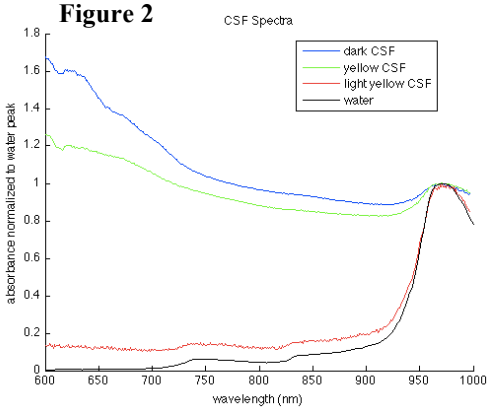


Figure 2



Discussion

Changes in reflectance spectra shown in Fig. 1 were typical, in particular increased absorption at 980 nm due to higher water concentration and a diminished deoxyhemoglobin feature at 760 nm. The latter is understandable since CSF after IVH will contain a mixture of oxyhemoglobin, bilirubin and methemoglobin, all of which have broad absorption characteristics, which is also reflected in the CSF spectra. A considerable variation in cortical thickness was measured by US (1.5 to 0.3 cm), indicating that accurate NIRS measurements will also require correcting for partial volume errors. It should be possible to correct for this error and the presence of blood breakdown products using a combination of spatial priors from US and broadband NIRS.

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Effects of Somatic Stimulation on Human Neonatal Fronto-Parietal Cerebral Cortex using Functional Near-Infrared Spectroscopy

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Introduction: Characteristics of functional near infrared spectroscopy (fNIRS) signal changes associated with lateralization in newborn brain development are unclear. Our objectives were to perform NIRS in unsedated neonates at the bedside and characterize the oxy-hemoglobin (HbO) and deoxy-hemoglobin (Hb) concentration changes in bilateral fronto-parietal cortex. We hypothesized that bilateral concentration changes will occur in these brain regions of interest upon somatic stimulation for certain stimuli.

Methods: Six neonates (born at 33.9 ± 2.7 wks gestation, evaluated at 43.5 ± 2.7 wks post menstrual age, 3.9 ±0.6 kg) underwent fNIRS with two different source-detector arrangements. Somatic stimulation paradigm was conducted by tapping the palmar and plantar areas bilaterally (left and right independently) and included intervals of oro-motor stimuli (i.e. pacifier). Post processing was done using Homer2 and code written in MATLAB (www.mathworks.com). The raw data was converted into the .nirs format and motion artifacts were removed with the wavelet filter described by Malovi et al 2012 using an IQR value of 0.1. The data was then filtered with a bandpass filter (0.02 to 0.75 Hz) based on existing research. Tasks were averaged across all patients of each cap configuration for analysis. The signals were then zeroed by subtracting the mean of the values of t<0. Hemodynamic responses were determined by visually inspecting the averaged signal and chosen for channels that showed a typical response curve and increase of 0.08 uM or more from stimulation start. Baseline value, maximum value, latency, and response duration were marked down for each channel that showed a response. Statistical analysis was performed on this data to determine if there were differences between stimulus type and cap layout. A total of 47 somatic stimuli were provided and the following physiological variables were analyzed bilaterally: response latency and duration, magnitude of changes in HbO and Hb, and brain lateralization. Three patients were analyzed with a 4x8 source detector setup, and three using an 8x16 setup.

Results: Between both cap configurations, responses were seen for all stimuli types, but parity between channels was not seen. Channels that showed activation for one stimulus were not activated for another among and between configurations. Oro-motor and foot tapping does show activation in the fronto-parietal cortex.

Conclusion: We have shown that between cap configurations activation can be viewed for certain motor function tasks, but similar channels are not activated for all the tasks. Foot tapping and oro-motor stimuli have also been shown to trigger activation in the fronto-parietal cortex and can help understand connectivity in neonates in the clinical setting.

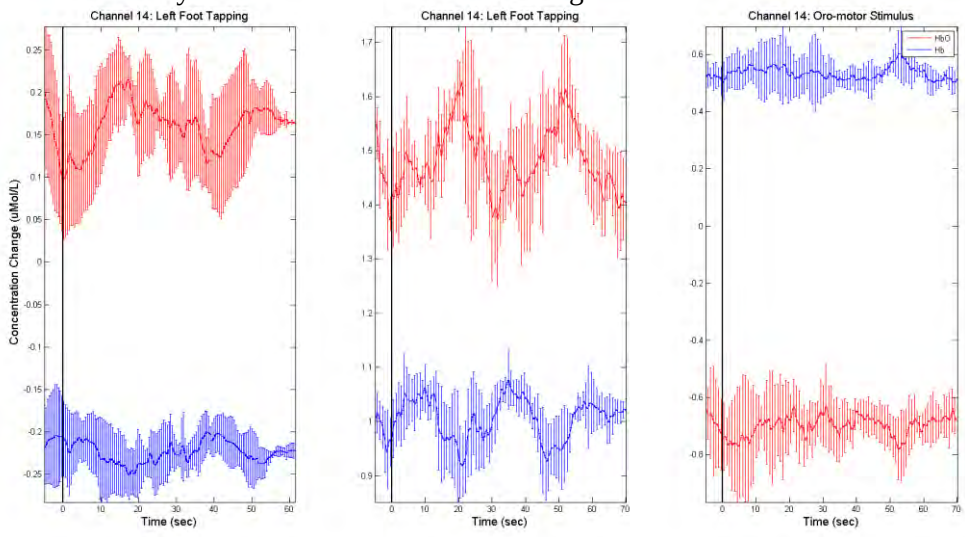

Fig. 1: Displays the hemodynamic responses to different stimulus given to each group for an averaged channel. Left foot tapping for the 4x8 (left) and for the 8x16 (middle) group, and oro-motor stimulus for the 8x16 (right) group.

Depressed Cerebral Blood Flow Response to Hypercapnia in Children with Obstructive Sleep Apnea Syndrome

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Aims: Obstructive sleep apnea syndrome (OSAS) is characterized by episodes of repetitive upper airway collapse during sleep, resulting in intermittent hypercapnia, hypoxemia, and frequent arousals from sleep. Children with OSAS are chronically exposed to hypercapnia during sleep and consequently may have abnormal cerebral blood flow (CBF) regulation. Induced hypercapnia is a standard procedure for assessing cerebrovascular reactivity (CVR) by measuring relative CBF change during the challenge. We hypothesized that children with OSAS have abnormal CVR during wakefulness, compared to snorers and controls.

Methods: We utilized diffuse correlation spectroscopy to non-invasively and directly monitor cerebral hemodynamics during induced hypercapnia. CVR was assessed in awake children with OSAS, snoring, and age-matched healthy controls. During induced hypercarbia, respiratory rate, inspiratory and expiratory flow, end tidal CO_2, and pulse oximetry, were recorded continuously (no significant differences). To isolate and quantify the effects of hypercapnia, we compared the peak of a temporally smoothed rCBF to a pre-hypercapnic baseline. Wilcoxon rank sum test was used for two-group comparisons.

Results: The fractional change in cerebral blood flow relative to a pre-hypercapnic baseline was significantly higher in healthy controls (213.6%, N=6) compared to children with OSAS (155.2%, $p = 0.018$, N=9) or snorers (149.3%, $p = 0.02$, N=8).

Conclusions: Noninvasive optical measurements of hypercapnic reactivity may provide significant insight into the physiopathology of OSAS in children. Further, this technique could be used clinically to assess the level of habituation to hypercarbia, potentially leading to further understanding of central nervous system complications of OSAS.

Interhemispheric connectivity is disrupted in primary motor cortex of pediatric post-concussion syndrome patients

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Post-concussion syndrome (PCS) occurs in 30% of pediatric patients who have sustained a mild Traumatic Brain Injury (mTBI). In the pediatric population symptoms tend to be prolonged and affect critical brain development. Treatments are being developed, but are difficult to assess given the lack of measures to quantitatively monitor concussion and there is no accepted imaging metric to monitor recovery. Functional Near Infrared Spectroscopy (fNIRS) can detect inter- and within- hemisphere coherence as an indicator of functional communication. We hypothesized that there is a reduction in coherence as a marker of inter-brain communication in pediatric PCS patients with chronic symptoms.

Methods

17 PCS patients (age 15.3±0, mean±S.D, 8 males) and 8 healthy controls (age 14±0.8, 5 males) were recruited through the Alberta Children's Hospital Brain Injury Clinic. fNIRS data were recorded using a CW5 TechEn mapping system from the motor cortices during a 5 minute resting state recording was following by a 5 minute task alternating between 30s resting and 15s tapping. The reference frequency seed was the left side fiber pair showing the maximum response to finger tapping in the right hand. Motor network connectivity was measured using coherence analysis. Coherence analysis was completed using using total- and oxy-hemoglobin activation for resting state and finger tapping datasets using average values over ipsilateral and contralateral hemisphere. The

Results

In oxyhemoglobin, resting state and task activation coherence was significantly reduced between the left and right hemisphere in PCS patients ($p=0.01$). In total-hemoglobin there is a significant difference in both resting state and task activation ($p>0.01$ and $p>0.05$ respectively).

Conclusion

There is a significant reduction in functional coherence in the PCS patients which may reflect functional impairment in major connecting fibre tracts. fNIRS provides a new non-invasive method to assess brain function in PCS and mTBI patients. Such fNIRS technology provides new opportunities to study brain function associated with brain injury and disease.

7. Clinical Applications

Persistent post-concussive symptoms are accompanied by decreased functional brain oxygenation

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Abstract

Mild traumatic brain injuries are common incidents in sports and there is a growing list of (prominent) athletes who had to end their careers prematurely due to persistent post-concussive symptoms. Diagnostic methods are considered a major concern in determining when an athlete is ready to return to training and competition. In the present study we examined previously reported controversies of brain activation patterns during memory tasks in prefrontal brain regions using functional NearInfraRed Spectroscopy (fNIRS). Seventeen concussed volunteers and eight non-concussed control subjects matched in age participated in the study. Participants were first assessed by a clinical examination, the Sport Concussion Assessment Tool 2 (SCAT2), and subsequently underwent fNIRS measurements to investigate the hemodynamic response of prefrontal brain regions during a working memory task. The results demonstrated decreased working memory performance amongst concussed subjects with post-concussive symptoms, which were accompanied by decreased brain oxygenation above prefrontal brain regions of both hemispheres. The oxygenation of the dorsolateral prefrontal cortex (DLPFC) of the left hemisphere correlated negatively with the severity of post-concussive symptoms. The dorsolateral prefrontal cortex of the right hemisphere showed decreased brain oxygenation for the concussed group suffering from post-concussive symptoms when compared to the concussed group with minor symptomatology and the healthy control group during the visual abstract memory task design. While the left hemispheric DLPFC was closely related to symptom severity, the right DLPFC showed decreased oxygenation on tasks relying on hemispherically specialized functions amongst participants suffering from post-concussive symptoms. We conclude that fNIRS is a valid method to investigate persistent concussive syndromes demonstrating a relationship between decreased brain oxygenation, low performance on working memory tasks, and increased symptom severity scores after experienced mild traumatic brain injuries.

Habituation of brain activation during painful and non-painful electrical stimulation: a functional near infra-red spectroscopy study.

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Postsurgical chronic pain is commonly attributed to neuropathic pain arising from iatrogenic injury to major peripheral nerves during surgery and affects approximately 30% of all surgical patients. Nociceptive signaling to the brain during surgery may contribute significantly to perioperative stress and can have a profound effect in the perioperative period. Moreover the neural processing associated with painful stimuli (nociception) may be maintained or even enhanced under anesthesia. At present there is no objective, repeatable measure of pain or the efficacy of analgesia in the anesthetized patients. Such a measure is urgently needed to guide surgical anesthesia and reduce post-operative sequelae.

Methods: The study was approved by the IRB of the Massachusetts General Hospital. Data were collected using a multichannel imager (CW6 system) operating at 690 and 830 nm (TechEn Inc. MA, USA). The probe contained 11 sources and 16 detectors (~3 cm distance apart from the source) and 11 short separation detectors (~1 cm distance apart from the source). 11 healthy subjects were included in the study (right handed, male, 28 ± 5 (mean±std) years old). Each subject gave informed written consent prior to the experiments. Prior to the actual experiment, electrical stimulation was applied to each subject's left thumb through electrodes with a 5 Hz electrical stimulator (Neurometer CPT, Neurotron, Baltimore, MD) to determine current levels that elicited subjective ratings of 3/10 (innocuous) and 7/10 (noxious) from each subject. These current values were used in the actual experiment.

Results: The changes in HbO and HbR as a response to noxious stimuli significantly decreased in the second three minutes as compared the first three minutes of the experiment (paired t-test, $p < 0.01$ for each hemoglobin species). There was no significant difference in the hemodynamic response to innocuous stimuli from the first to the second three minute period (paired t-test, $p > 0.50$). The hemodynamic response to innocuous and noxious stimuli in the first three minutes was also compared. The HbO response to noxious stimuli was significantly higher than the response to innocuous stimuli (paired t-test, $p < 0.01$). The magnitude of the HbR response to noxious stimuli was also significantly higher than the response to the innocuous stimuli (paired t-test, $p < 0.01$).

Conclusion: Post-surgical chronic pain can be avoided with the use of a robust pain biomarker during surgery. Our results support that fNIRS has a strong potential to guide anesthesia during surgery by providing a direct and objective measure of pain which will potentially decrease the number of such cases.

Semiautomatic application for task-related component analysis (TRCA) to extract task-related signal changes from fNIRS signal: Clinical applications.

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The intracarotid amobarbital test or Wada procedure has been used in the test of language lateralization. This procedure introduce amobarbital via internal carotid arteries invasively to block a language function and is typically used to assess language lateralization prior to brain surgery. While this test is highly accurate, this is uncomfortable for the patients. Therefore, it is critical that non-invasive and accurate alternative tests of language lateralization are developed [1]. Functional near-infrared spectroscopy (fNIRS) is a technique that measures hemodynamic brain responses by passing light through the superficial tissue of the head to cerebral cortex. Previously, we demonstrated that fNIRS can be used to assess language lateralization [2]. A current limitation is that the contamination of the signal from superficial tissue layers and sensitivity to motion artifacts, which while controllable in the lab environment, may prove more problematic in a clinical setting. To overcome these issues, we recently introduced a task-related component analysis (TRCA) to extract task-related signal changes from measurement signals of fNIRS. This method uses a reproducibility of repeated measurement signals as an index of task relatedness. Under this method, extraneous artifacts are eliminated by summing up the measurement signals from each channel with adequate coefficients. In a sample of 17 participants, we compared NIRS decoding of language lateralization with that obtained from the Wada procedure. The results showed identical lateralization of fNIRS and the Wada procedure in 15 participants. We conclude that fNIRS combined with TRCA provides a promising test of language lateralization. The fNIRS test of language lateralization we developed online as a plugin for Platform for Optical Topography Tools software developed by Central Research Laboratory, HITACHI.

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Hemodynamic changes in cortical sensorimotor systems following hand and orofacial motor tasks and pulsed cutaneous stimulation.

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Background: The integrity of the cerebral cortex can be assessed by measuring its responsiveness to repetitive sensory and motor stimulation. This neurophysiologic feature is known as neural adaptation, and is thought to enhance learning and detection of environmental stimuli. The adaptation of hemodynamic responses to motor and sensory experiences in hand and face are of particular interest—as these are structures most commonly used in human communication—and proper delivery of oxy-hemoglobin to primary motor (M1) and somatosensory (S1) cortices is essential for functional cortical activation.

Objective: To examine the hemodynamic differences between hand and face cortical representations during motor and passive somatosensory conditions, as measured with functional near-infrared spectroscopy (fNIRS). The recorded data will be used to create a computational model of cortical adaptation for future neurodiagnostic and neurotherapeutic applications.

Methods: The ongoing study design includes 20 neurotypical adults, ages 19-30. A TechEn CW6 device was used for fNIRS data acquisition. A 4x3 optode montage with 2 short separation measurements (8 mm) was placed over left M1 and S1 to sample hemodynamic activity following repeated hand and orofacial motor activity and repeated pneumotactile stimulation. The two motor conditions consisted of a repetitive hand grip ("light squeeze"), and repetition of a voiceless bilabial syllable ("pa"), each at 2 Hz (30 sec ON/60 sec OFF, repeat 10x). For the passive sensory conditions, a Galileo™ Somatosensory stimulator was programmed to generate a biphasic pneumatic pulse train (-80 to 140 cmH_2O, 50-ms pulse width, 9 ms rise/fall time, pulse rate 2 Hz, 30 sec ON/60 sec OFF, repeat 10x) applied through TAC-Cells placed on the glabrous right hand and lower face near right oral angle. The order of conditions was counterbalanced among participants, each lasting 15 minutes. A custom processing stream built in Homer2 was used to remove motion artifact, regress physiological interference (via short separation optodes) out of data, and calculate group hemodynamic response functions (HRFs) across all channels. The 3 most representative channels over face and hand M1 and S1 were chosen for analysis. Oxy- and deoxyhemoglobin concentrations (HbO and HbR) were averaged over 10 trial blocks relative to 30-second stimulus ON periods with a 10-second pre-stimulus window, and a 30-second post-stimulus window.

Results: Preliminary results are from 3 females (mean= 22 yrs). As expected, motor activity of either the lip or hand was associated with a predominant HbO response localized to M1, whereas the passive somatosensory stimulation conditions resulted in predominant HbO responses in S1. Lip motor activity yielded significantly greater mean concentration levels of HbO in face M1 than hand motor activity in hand M1 ($t[1500]=196.62$, $p< .000$), as well as greater mean levels of HbO in face S1 than hand S1 ($t[1500]=83.51$, $p<.000$), during the 30 second stimulation periods. Oppositely, somatosensory stimulation of the hand yielded significantly greater mean HbO concentration levels in hand S1 than did the same stimulation of the face in face S1 ($t[1500]=5.43$, $p< .000$), during the 30 second stimulation periods. Adaptation patterns differed across both structures, most notably during passive somatosensory conditions. Also, a significant increase in HbO directly after stimulus offset was seen. This "cortical refill" was strikingly apparent after both motor and sensory tasks in the face, and less so for the hand.

Conclusions: Many significant differences were found in hand and face M1 and S1 across the different motor and sensory conditions, including distinctive HRFs, adaptation patterns, and cortical refill responses. These differential effects are likely due to differences in regional arterial/venous anatomy, cortical vascular beds, extent and orientation of somatotopy, task dynamics, and mechanoreceptor typing in hand and face.
Supported in part by the Barkley Trust (Barlow).

Diffuse optical characterization of the microvascular cerebral blood flow during obstructive sleep apnea events

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Chronic obstructive Sleep Apnea (OSA) has hemodynamic consequences leading to an increased risk of cerebrovascular and cardiovascular diseases [1]. The measurement of the apnea-induced microvascular cerebral blood flow (CBF) has the potential to reveal the relationship between OSA and cerebrovascular diseases [2]. However, traditional methods are very difficult to utilize in this setting since bed-side, longitudinal, continuous measurements are required to characterize the CBF during each episode of apnea. To that end, we have explored the feasibility of diffuse correlation spectroscopy (DCS) [3] to follow the apnea induced microvascular CBF throughout the whole night sleep and characterize the CBF changes during each individual apnea episode.

The concurrent optical and Polysomnography (PSG) data, from 16 patients with severe OSA, were acquired during the whole night sleep. DCS probe was placed on the right hemisphere on the fore-head. The percent relative CBF change $\Delta rCBF$ was defined as: $\Delta rCBF = (\frac{CBF}{CBF_{bl}} - 1) \times 100)$, where CBF_{bl} is the average of twenty (20) seconds before every individual apnea start. A total of 1043 OSA events where identified, recorded and were then parameterized for further analysis. The first step was to group them according to the type of apnea, then according to apnea duration and according to the sleep stage. Overall, similar CBF patterns were observed for OSA events with different lengths consisting of a drop in CBF after the apnea start, followed by a CBF peak after the apnea termination. The depth of the drop and the peak were dependent on the apnea duration. By isolating apneas that were separated by a long duration from the previous apnea, we were able to prove our hypothesis that the drop is due to the effects after the termination of the previous apnea. Notably, these microvascular CBF changes measured by DCS are similar to those of Cerebral Blood Flow Velocity, measured by Doppler Ultrasound [4]. These repetitive, significant periods of hypo-perfusion after the OSA termination in combination with hypoxic periods after the OSA termination may explain the high risk for cerebral infarction and permanent brain damage for OSA patients. We will present our $\Delta rCBF$ results in more detail. In addition, we will compare our average and per-apnea based $\Delta rCBF$ measures with sleep parameters, from PSG, and other clinically relevant parameters, and further discuss potential of diffuse optics in Sleep laboratory settings.

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Novel application of Support Vector Machines to classify hemodynamic response obtained by multi-channel NIRS measurement

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To extract the information from the data acquired using multi-channel NIRS, selecting the informative channels is important. Recently we found that children with attention-deficit / hyperactivity disorder (ADHD) and children with autism spectrum disorder (ASD) showed different hemodynamic responses during viewing the face image of their own mother. If we could find the informative channels to classify these hemodynamic data into ADHD or ASD, we would be able to predict to which diagnostic group an unknown participant belongs.

In the present study, we applied a support vector machine (SVM) [1] to search exhaustively the optimal channels for classifying the hemodynamic data of these two groups. The SVM found the optimal subset of channels in each data set and successfully classified the ADHD data from the ASD data. For the 24-dimensional hemodynamic data, two optimal subsets classified the hemodynamic data with 84% classification accuracy, while the subset contained all 24 channels classified with 62% classification accuracy. On the other hand, two existing methods, least absolute shrinkage and selection operator (LASSO) [2] and sparse logistic regression (LSR) [3], Yamashita et al., 2008), classified with 30% and 66%. These results indicate the potential application of our novel method for classifying the hemodynamic data into two groups and revealing the combinations of channels that efficiently differentiate the two groups.

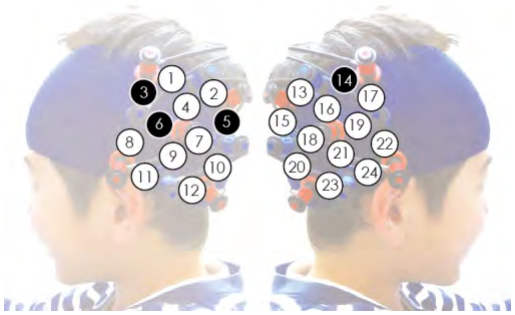

Figure. The position of the channels included the best 50 subsets which classify ASD and ADHD with higher accuracy.

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Diagnosis of focus side in intractable mesial temporal lobe epilepsy by fNIRS during spontaneous seizure

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(Purpose)

To localize the epileptic focus is the most important purpose of the presurgical evaluation in patients with medically intractable partial seizure.

Functional near-infrared spectroscopy (fNIRS) is a light based neuroimaging technology for continuous and non-invasive measurement of oxygenated (OxyHb), deoxygenated (Deoxy Hb) with high temporal resolution which allows monitoring regional cerebral blood volume (rCBV) changes during long term video-EEG monitoring in epileptic patients as well as in daily living conditions. The present study will attempt to reveal the usefulness of fNIRS simultaneously recorded with EEG to detect the correct focus side of intractable mesial temporal lobe epilepsy (mTLE) in preoperative evaluation.

(Methods)

Sequential fNIRS recording was performed along with long term video-EEG monitoring. Twelve CPS (complex partial seizure) with/without GTS (generalized tonic clonic seizure) attacks of Eight patients underwent selective amygdalohippocampectomy for intractable mTLE after the diagnostic procedure were recorded during fNIRS recording. We used the 22 channel NIRS system (ETG 4000; Hitachi Medical Corporation, Tokyo, Japan), with infrared light with two wave length of 695 and 830nm. We measured the change in Oxy and Deoxy Hb after on-set of seizure and caliculated laterality index of 3 channels in temporal region to compare with the correct epileptogenic side judged by EEG. We also measured the duration of clinical semiology, EEG and fNIRS changes during seizure. We compared each other and correlation with the change of fNIRS.

(Result)

Laterality index of 11/12 in OxHb and 9/12 in DeoxyHb showed increase on the correct epileptogenic side. There was a strong positive correlation between increase in OxHb and DeoxyHb. Duration of EEG and fNIRS changes showed negative correlation with extent of OxHb increase.

(Conclusion)

fNIRS is non-invasive useful tool for determining epileptogenic side of intractable MTLE patient.

Functional near infrared spectroscopy evaluated brain representation of acute dental pain in the somatosensory and prefrontal cortex

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Dentin hypersensitivity is a very common clinical problem that is characterized by short, acute pain arising from typically non-noxious stimuli. This situation is often caused by gingival recession exposing patent dentinal tubules of the tooth secondary to abrasion, erosion, corrosion or periodontal treatment. In this study, we used functional near-infrared spectroscopy (fNIRS) to assess the activity in the somatosensory and frontal cortical regions of a patient with dentin hypersensitive. Twenty participants with hypersensitive tooth (14 female) completed two fNIRS testing sessions in a portable dental chair. Control non-painful mechanical stimuli followed by noxious cold stimulation with controlled temperature applied to the hypersensitive tooth were performed in the two sessions. The collected data in both sessions were band-pass filtered, and then converted to hemoglobin concentration change data (oxygenated and de-oxygenated) for further analysis. The data from the first session were used as a localizer, indicating the region of interest in the second session.

Percussion led to a relative high activation on the contralateral somatosensory cortex (SI) in the orofacial homuncular region compared to the ipsilatateral side. Moreover, the cold pain stimulation on hypersensitive tooth evoked a two-peak response in course of time on the contralateral sensory cortex, where the first peak occurred before pain feel showing the cold sense related response, while the second peak appeared after pain feel showing the pain associated response. In addition, we noticed increase activity in prefrontal cortical areas that are usually associated with cognitive and behavioral processing, including anxiety.

These findings may lead in the future to more objective and immediate assessment of pain processing, directly from the brain, during dental/surgical procedures, for instance with special needs patients. This technology can also be used as a standardization for clinical effectiveness of dentin hypersensitivity medication.

Usefulness of double density fNIRS (DD-fNIRS) for the diagnosis of neocortical epilepsy focus

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Purpose

Functional near-infrared spectroscopy (fNIRS) is one of the non-invasive functional brain mapping methods. The advantages of this method are its portability and higher tolerance for body movements. On the other hand, the largest disadvantage of fNIRS resides in its low spatial resolution. The spatial resolution of fNIRS is estimated to be 20mm to 25mm, making it difficult to detect the activated area as small as one gyrus-width, which is about 10-15mm. To overcome this problem we developed double density fNIRS (DD-fNIRS) probe design.

For the patient with intractable epilepsy, an accurate diagnosis of the epilepsy focus is inevitable in order to get good outcome in a surgical intervention. For this purpose, we developed and investigated the utility of ictal DD-fNIRS recording as a new functional mapping technique in the presurgical diagnosis of epilepsy focus, especially in neocortical epilepsy.

The purpose of this study is to clarify the usefulness of the ictal DD-fNIRS in neocortical epilepsy focus diagnosis.

Method

DD-fNIRS has special emitting and detecting optrode set. Two pairs of optrode sets (emitting optrode and detecting optrode separated in 30mm in conventional fNIRS) are placed overlapping each other where the optrode of the second pair is placed between the first one. This makes measuring points placed 15mm apart each other in place of 30mm apart in conventional design. In this study we used ETG 4000 (Hitachi Medical Corporation, Tokyo, Japan) for DD-fNIRS.

Ictal video-EEG monitoring (VEEG) is the most reliable and important examination to diagnose epilepsy focus for the patient with intractable epilepsy. We have applied ictal DD-fNIRS simultaneously recorded with VEEG for two patients with neocortical intractable epilepsy. DD-fNIRS data has analyzed and superimposed with individual MRI image by 3D-magnetic digitizer.

Results

Both patients had had operation of subdural electrodes placement for chronic subdural EEG recording after non-invasive pre-surgical examination such as ictal DD-fNIRS, VEEG, Iomazenil-SPECT (IMZ-SPECT) and magnetoencephalography (MEG). The epileptic focus diagnosed by ictal DD-fNIRS was quite similar to the lesion diagnosed by ictal subdural EEG recording. One patient has been already past more than two years after resection of epilepsy focus and no seizure has been described, another patient has been about 3 months after focus resection and seizure free.

Conclusion

DD-fNIRS is useful to diagnose epilepsy focus for the patient with neocortical intractable epilepsy.

The effect of obstructive sleep apnoea syndrome on the microvascular cerebral blood flow response to orthostatic stress

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The obstructive sleep apnoea-hypoapnoea syndrome (OSAS) is a cardiovascular risk factor that leads to increased cardiovascular morbidity and mortality [1]. The OSAS diagnosis is performed by a sleep study which measures respiratory events such as apneas and hypoapneas, the mean nocturnal O_2 saturation (mean SpO_2%) and the oxygen desaturation index 4% (ODI4%). The severity of the syndrome is defined by the apnea-hypopnea index (AHI) (number of apnea and hypoapnea events/sleep hour). The increased risk of strokes in OSA patients is believe to be related to impairments or alterations of cerebrovascular reactivity (CVR) or cerebral autoregulation [2, 3]. Diffuse correlation spectroscopy (DCS) is a technique that allows non-invasive measurements of the cerebral hemodynamics in humans by measuring microvascular cerebral blood flow (CBF) [4, 5]. We have used diffuse correlation spectroscopy (DCS) to measure the cerebral vasoreactivity in a group of 83 subjects. 69 of them were OSA diagnosed patients: 29 Mild, 12 Moderate and 28 Severes. The remaining 14 conformed a control group of healthy subjects. To that end we have utilized a protocol involving orthostatic stress induced by changing the head-of-bed (HOB) angle in the following steps: 0° to 30° to 0° to 20° to −8° to 0°. Our hypothesis was that OSA patients from different groups of severity will show different responses and that the CVR may correlate with respiratory parameters such as the mean SpO_2% or the ODI4%. We will present a complete analysis of this data, by delivering the mean values of rCBF for each group at a given (HOB) angle and exploring the correlations of rCBF with other clinical and demographic parameters and the potential clinical applications of the technology.

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Graph Theoretical Approach to Functional Connectivity in Schizophrenia

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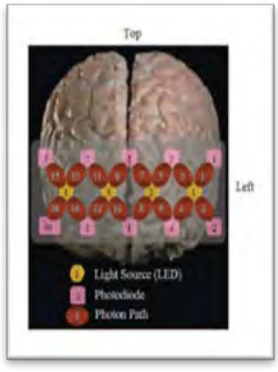
Introduction: In this study, we aimed to investigate the change in the global efficiency of the functional connectivity patterns in the prefrontal cortex (PFC) emerging during a modified version of the color-word matching Stroop task. This task consists of three different stimulus conditions: Neutral (N), Congruent (C) and Incongruent (IC). A continuous wave 16 channels functional near-infrared spectroscopy (fNIRS) device (ARGES Cerebro, Hemosoft Inc., Turkey) was used to measure the changes of HbO2 concentrations from 12 healthy volunteers and 16 schizophrenia subjects. The probe was placed on the forehead with approximate cortical sampling regions as depicted in Figure 1.

Methods: Wavelet based partial correlation (WPC) analysis allows us to observe the functional similarity between PFC regions based on activity in a defined frequency interval in each stimuli. WPC was computed for the frequency interval of [0.003 to 0.08] Hz. We considered the channels as a set of vertices V and computed the WPC between each pair of channels. WPC coefficients were assigned as weights on the set of edges E, leading to an undirected complete weighted graph G= (V, E). Global Efficiency (GE) can be evaluated for wide range of networks, including weighted graphs. The formal definition is as follows: $E_{global} = \frac{1}{N(N-1)} \sum_{i \neq j \in G} \frac{1}{L_{ij}}$ where N is the number of nodes in the network, Lij is the shortest path length between nodes i and j.

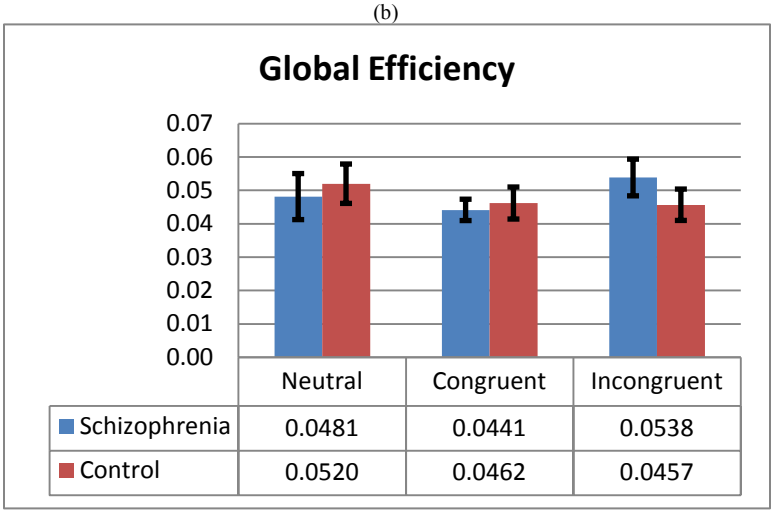
Results: We have considered 10% of strongest connections in each network. GE values were computed for each stimulus condition. Path length is inversely related to the GE of a network for the transfer of information between nodes by multiple parallel paths.

Conclusions: GE exhibits a stable decrease in healthy controls showing an attempt of the brain regions to promote a sparser connectivity with long-spanning connections while the same adaptability cannot be observed for schizophrenia patients. This is in line with the hypothesis that schizophrenia is a disorder of connectivity between components of large-scale brain networks.



(a)

(b)



	Neutral	Congruent	Incongruent
Schizophrenia	0.0481	0.0441	0.0538
Control	0.0520	0.0462	0.0457

Figure1: (a) Placement of the fNIRS probe on the PFC, (b) GE scores for different question types

Active vs. assisted vs. passive finger movements - a hemodynamic comparison of premotor and motor cortex activity

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Background: Robotic technologies to (re-)learn and train specific movements are emerging in rehabilitation centers for patients with neuromotor disorders. Many of those technologies come with a fully guided mode or with an assistive mode, where patients are supported in an "as much as necessary, as little as possible"-fashion. However, it is unclear how such guidance strategies influence (pre-)motor cortex activations compared to voluntary unguided performed movements. Therefore, the aim of this study is to investigate differences in motor and premotor cortex activations between unguided, assisted and fully guided robot-supported finger-bending movements.

Methods: We intend to measure 15 healthy individuals with a 16 channel continuous wave functional near-infrared imaging system (NIRSport, NIRx, USA). The probe layout is bilaterally focused on positions C3/C4 and FC3/FC4 of the 10-20 system. The non-dominant hand is mounted to an actuated finger rehabilitation robot (Amadeo, Tyromotion, Austria, Figure 1) and 3 different modes of index finger bending are applied: *Passive*: The finger is moved by the robot at 1Hz; *Assistive*: The subject bends his finger and is being supported by the robot (1Hz); and *Active*: The subject moves his finger himself without guidance of the robot (self-paced, instruction to bend and extend at 1Hz). All conditions are randomized, each condition is performed 10 times and each stimulus phase of 20s is followed by a resting phase of 30s. The measurement starts with a resting period of 3min. To quantify physical activity, electromyography of the M. flexor digitorum superficialis is recorded simultaneously.

Results: Will be presented at the meeting.

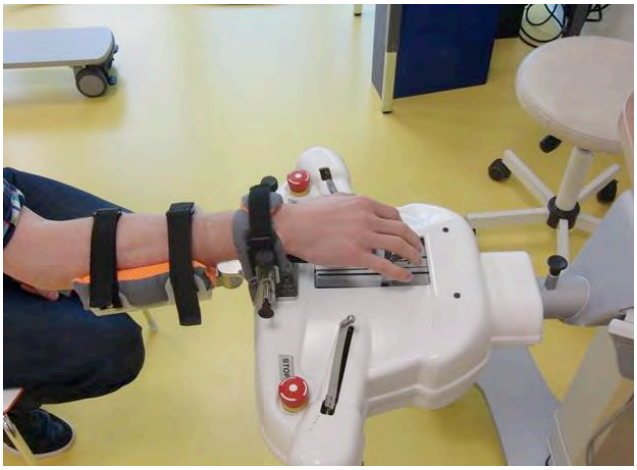

Figure 1: Finger rehabilitation robot

Real-time mapping of optode-scalp optical coupling for optimized placement of fNIRS headgear

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Functional near-infrared spectroscopy (fNIRS) relies on efficient light delivery and collection through the scalp. This is attained by placing optodes (i.e., optical fibers or discrete optical sources/detectors) in good contact with the scalp, usually after parting the hair over each location, then securing the optodes on headgear to guarantee their stability during the experiment. Carefully placing dozens of optodes in preparation for an fNIRS experiment can take a considerable amount of time, particularly with subjects where achieving good optical coupling to the scalp is difficult due to thick and/or dark hair. Although long preparation is generally acceptable in a research environment, it is a penalizing factor in clinical settings or in special populations where the patients' cooperation can be adversely affected by fatigue and/or intolerance to prolonged wearing of the headgear (e.g., elderly or pediatric populations). Such preparation would be substantially reduced by an fNIRS headgear that has all the fibers built in, thus allowing the experimenter to adjust only those few individual fibers that resulted in poor scalp contact.

In response to this need for an optimized and rapid headgear placement, we propose to exploit a measure of the optical coupling between each optode and the scalp, termed *scalp coupling index* (SCI). The detection of intracranial systemic (cardiac) pulsations in a raw fNIRS signal (i.e., source-detector pairing) usually indicates that both emitting and collecting optodes are in good contact with the scalp. Considering that fNIRS systems deliver light at two wavelengths from each emitting optode, the SCI of an optical channel is defined as the zero-lag value of the cross-correlation between the two co-located photodetected signals, after band-pass filtering (0.5÷2.5 Hz) and normalization. In ideal conditions, two identical signals would yield an SCI equal to 1, whereas pulsation-free signals would result in a null SCI. Therefore, SCI provides an easily interpretable estimation of the quality of the optodes-scalp contact, reflecting also the signal-to-noise ratio (SNR) of an optical channel.

In our previous investigation[1], we scanned 19 subjects with a 40-optodes system (NIRScout, NIRx Medical Technologies) and used SCI as a post-hoc metric for excluding channels with poor SNR from further processing. Interestingly, an analysis performed on the same dataset revealed that most optical channels had an acceptable SNR (SCI>0.75) upon initial placement of the integrated optical headgear and obtaining the best possible experimental setup would have required the adjustment of a limited number of optodes, i.e. on average, 10±7 (mean±STD) out of 40 optodes yielded a poor SCI. Therefore, SCI is useful for *a priori* location of optical channels affected by poor scalp contact of their optodes during the subject's preparation. Relating several optical channels with poor SCI that originates from individual optodes with poor scalp contact requires a simple logic transformation based on the optical layout of the experiment. SCI can be calculated in real-time on hundreds of optical channels for displaying an optodes-scalp coupling map during the patient's preparation, hence allowing rapid optimization of the optical setup of the fNIRS experiment. This approach is analogous to measuring the impedance and the offset of each electrode prior to EEG experiments to locate those that have insufficient electrical conductivity. The proposed method has the potential to maximize the quality of the collected data for offline analysis and to substantially reduce the patients' visit time, and it is being successfully tested in our experimental activity on cochlear implant patients at the Stanford Hospital System.

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Title: Cortical Activation During Swallowing, Cortical Suppression During Vibrotactile Stimulation Alone

Background and Purpose: Animal studies have demonstrated an increase in brain stem control of swallowing with stimulation of afferents in the superior laryngeal nerve. In awake humans swallowing likely involves a coordination of cortical and brain stem control. In this study, a vibrator was placed on the skin overlying the thyroid cartilage to stimulate the laryngeal tissue non-invasively in healthy volunteers and increase swallowing. Our purpose was to determine what vibratory frequencies would optimally induce swallowing and whether cortical responses occurred in response to laryngeal stimulation independent of swallowing. Continuous wave functional near-infrared spectroscopy was used to record cortical changes in blood oxygenation levels (HbO2) over the motor and sensory cortices on the right and left hemispheres in 10 healthy right-handed volunteers.

Methods: Brainsight software was used with MRIs from individual participants and MNI coordinates to position emitters over the pre-motor and parietal cortices on the right and left sides; detectors were positioned 3 cm from emitters on the oral motor M1 and oral sensory S1 cortices. Thirty 10-second epochs of stimulation were presented during 20-minutes in random order across subjects for 6 conditions: no stimulation (control), 30, 70, 110 and 150 Hz stimulation and hybrid condition (combining 70 and 110 Hz). Both 4 Hz pulsed and continuous stimulation were presented during the hybrid stimulation condition. After artifact rejection and deletion of epochs containing swallows, event-related averaging was conducted for each subject over the 20-30 trials for each of the 4 detector locations during each condition. Recordings containing spontaneous swallows without stimulation were also event-related averaged for each subject across conditions to examine for cortical responses to spontaneous swallowing..

Results: Hybrid motor stimulation increased swallowing by 100-300%, to a greater degree than 30 Hz, 110 Hz, or 150 Hz stimulation alone ($p < .004$). Continuous and pulsed hybrid and 70 Hz stimulation equally increased swallowing.

The effect of condition on changes in cortical activity varied by whether there were relative increases or decreases in HbO2 ($F=12.82$, $p=.002$). Positive cortical responses occurred during swallowing as well as when a swallow occurred during vibratory stimulation. Negative cortical responses occurred during vibratory stimulation only (without swallowing), suggesting that sensory stimulation alone may have a suppressive effect on cortical physiology although swallowing increased presumably due to activation of brain stem central patterning for swallowing. .

Conclusion: The results suggest that vibratory stimulation will have a suppressive effect at the cortex while enhancing swallowing at the brain stem level. In contrast, during spontaneous swallowing the cortical and brain stem systems are co-activated.

Brain perfusion assessment by time-resolved monitoring of inflow and washout of ICG in patients with disorders of cerebral circulation

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Usefulness of the methodology of bedside brain perfusion assessment based on optical monitoring of inflow of a contrast agent was extensively validated in last years [1,2]. Indocyanine green (ICG) was applied in these studies. This dye is a relatively safe and non-toxic contrast agent [3] revealing high absorption and fluorescence emission in near infrared wavelength range [4].
Recently, we reported that the inflow of ICG can be monitored with the use of time-resolved technique at the bedside in the intensive care unit during treatment of patients with posttraumatic brain injury. We showed that the time courses of the statistical moments of measured distributions of times of flight of photons (DTOFs) and distributions of times of arrival of fluorescence photons (DTAs) can be used for differentiation of patients with different degree of brain perfusion disorder [2]. In these studies we used multichannel time-resolved system operating at wavelength of 760 nm which allows for simultaneous monitoring of diffuse reflectance and fluorescence signals from 8 source-detector pairs [5]. The setup is based on semiconductor lasers generating picoseconds light pulses and time-correlated single photon counting for acquisition of DTOFs and DTAs.
In the present contribution we will present results of analysis of the washout of ICG after its intravenous injection. We will show that the dynamics of the return of the signals to the initial level may depend on the function of the blood-brain barrier. After intravenous ICG injection the signals of statistical moments of DTOFs and DTAs change rapidly in the ICG inflow phase. Subsequently, in the washout phase, the signals return to the initial level. It was observed, that in healthy subjects the signals return relatively quickly to the initial level (dropping below 20% of the maximum 3 min long period after the maximum) whereas in patients with blood-brain barrier disruption the return is delayed (the signals drop only above 50% of the maximum). In patients with brain edema and brain death the signal return ratio was between 20 and 40%. It was also observed that these ratios differ when different statistical moments of DTOFs and DTAs are analyzed.
Results of this study show that the optical signals monitored during ICG washout phase may be useful in assessment of the condition of the blood brain barrier in patients with severe cerebral perfusion disorders. We conclude that combined assessment of the ICG inflow kinetics (which depends on brain perfusion) and ICG washout (which predominantly depends on the condition of the blood-brain barrier) may provide more detailed information on the brain condition.

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Subthalamic nucleus high frequency stimulation reduces – almost immediately - primary sensorimotor and prefrontal dorsolateral cortical activity whatever the patient is at rest or performing a motor task: a fNIRS study

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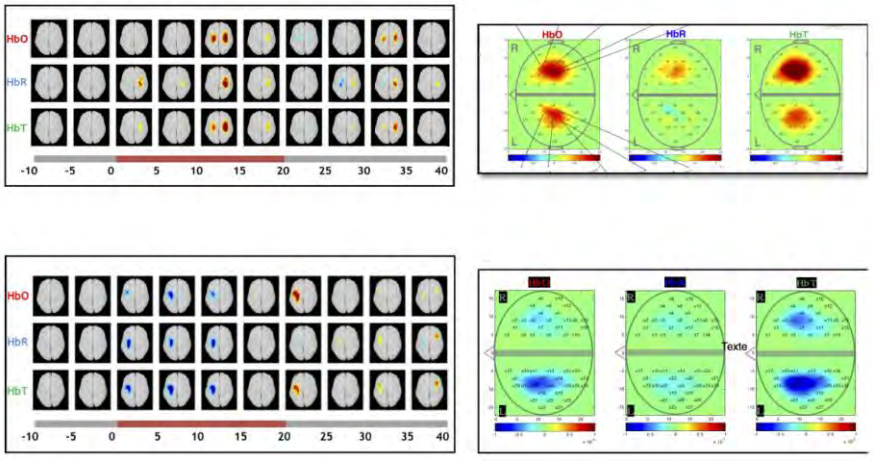
Deep brain stimulation of SubThalamic Nucleus (STN-DBS) is an effective treatment for idiopatic Parkinson disease. However, the efficacy of STN-DBS relies on unclear mechanisms. In this study, using optical imaging, we evaluated the cortical hemodynamic changes induced by STN-DBS.

We performed a functional optical imaging study using Near-InfraRed Spectroscopy (fNIRS) in 7 parkinsonian patients after STN-DBS. We measured bilateral local cortical hemodynamic changes under "On" and "Off" stimulation conditions at rest and during a motor task (hand movement). Relative concentration changes of oxyheamoglobin (HbO), deoxyhaemoglobin (dHb), and total Haemoglobin (tHb) were continuously analysed.

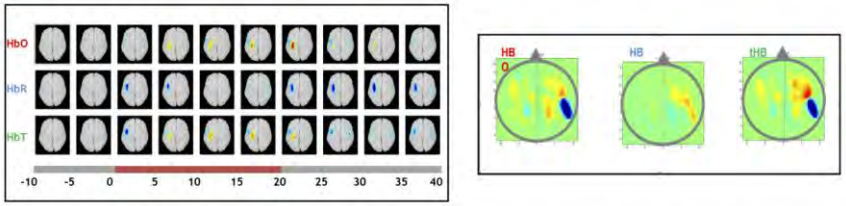
In STN-DBS "off" condition Oxy-Hb and tHb increased immediately in respect of motor and pre motor dorsolateral cortical area after the onset of the motor task. In STN-DBS "on" condition without realisation of any movement, a decrease in HbO and tHb within the 5 first seconds of stimulation, maintained during all the time of stimulation is objectified in relation to sensori-motor area and dorsolateral cortex for all patients. During motor task and STN-DBS "On" condition, a specific increase of HbO -ie cortical activation- of motor cortex and pre-motor cortex is objectivized whereas other cortical regions still presented decrease of HbO in 5 patients. There was a significant reduction of the increase of HbO during the motor task suring "off" STN-DBS condition for all patients.

This study provides new arguments in favour of STN-DBS main cortical effect, which is to reduce regional cerebral blood flow in the primary sensorimotor and premotor dorsolateral cortex areas. Our study advocates that STN-DBS neuromodulation output is always the same whatever is the cortical activity and appears almost immediately after the stimulation has started.

On the left is illustrated the dynamic (every 5 secondes) relative concentration changes of HbO , HbR and tHb - On the right is illustrate the mean relative concentration changes of HbO, HbR and tHb during the realization of the task



B) STN-DBS « On » - Patient at Rest
You can see a decrease of both HbO and tHb almost immediately after the beginning after the STN-DBS has started in regard of sensori-motor and frontal dorso-lateral cortical area



C) STN-DBS « On » - Motor Task
During STN-DBS « on » a specific increase of HbO - ie cortical activation- of sensori-motor and pre motor cortex is objectified whereas other cortical regions still presented decrease of HbO.

This advocates that main effect of STN-DBS neuromodulation is to reduce cortical hemodynamic in regard of sensori-motor and frontal dorsolateral whatever is the cortical activity

Title: Human auditory and adjacent non-auditory cortical areas are hypermetabolic in tinnitus patients as measured by fNIRS.

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Tinnitus is the phantom perception of sound in the absence of a physical sound stimulus. The underlying etiology of tinnitus perception is not currently clear, yet basic mechanisms pinpoint hyperactivity neuronal activity within the central auditory pathways, including the primary auditory cortex (A1). The aim of this study was to measure metabolic activity within A1 and surrounding auditory cortex under conditions of auditory stimulation and silence in patients with tinnitus as compared to non-tinnitus controls using functional Near-Infrared Spectroscopy (fNIRS). Patients with bilateral subjective tinnitus with near normal hearing and non-tinnitus controls were tested during a passive auditory listening task. Hemodynamic activity was monitored over the fronto-temporal cortex under episodic periods of auditory stimulation with a 750 Hz or 8000 Hz tone, broadband noise and silence. Preliminary results demonstrated a greater activation over the auditory cortex in patients with tinnitus compared to controls during periods of silence and auditory stimulation with a 750 Hz tone while less activation was found during broadband noise. No significant differences in the activation were found between the auditory and non-auditory brain areas in patients with tinnitus. These preliminary data demonstrate that both auditory and adjacent, non-auditory cortices are hypermetabolic in tinnitus patients suggesting that these anatomic areas may be contributing underlying tinnitus perception. This finding using fNIRS as a non-invasive tool may be an important first step in the diagnosis and management of this pervasive problem.

Cortical Contributions to Gait Control in Freely Moving Humans.

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Background: Upright gait is a human faculty which may have contributed to the evolutionary advantage (Niemitz, 2010). Beyond that it is of undisputable relevance for independent and socially integrated living as reflected in the fact that gait rehabilitation is one of the prime goals in long-term care for patients with acquired brain lesions. Understanding the neuronal underpinnings of gait control by neuro-imaging may be a first step towards "neurophysiologically-evidenced" treatment strategies (Jahn & Zwergal, 2010). Since techniques such as fMRI and PET require immobilization of the participant, fNIRS has been used to complement existing high resolution data (Enzinger et al., 2008) by low resolution cortical activation maps in ecologically valid scenarios (Miyai et al., 2001; Perrey, 2014). While most previous fNIRS studies on gait used setups on tread-mills (patient stationary with regard to the imaging device) we have recently shown the feasibility of fNIRS in outdoor unconstraint locomotion (Piper et al., 2013). Therefore the present study addresses the question whether cortical gait control can be mapped in unconstraint walking. • **Methods:** 11 young healthy participants performed a walking paradigm comprising 4 conditions of gait varying regularity (REG) of the steps and locomotion (LOCO; i.e. stationary vs. forward movement): $STAT^{REG}$, $STAT^{IRR}$, MOV^{REG}, MOV^{IRR}. The steps were paced by a metronome, and the conditions were announced prior to each block by earphones. Changes in cortical oxygenation were monitored by a portable fNIRS dual wavelength cw-imager (NIRSport, NIRx Medical Techologies). Each trial lasted 30s, and jittered resting periods (no gait movements, Ø 20s) separated the trials. 10 trials of each condition were performed in a pseudo-randomized order. Data were analyzed off-line, using a Beer-Lambert next-neighbor approach. Artefact correction, filtering and GLM-based analysis were performed by NiLAB (in-house analysis software). • **Results and Discussion:** Comparing all conditions vs. rest a large central area showed statistically significant decreases in deoxy-Hb while the increases in oxy-Hb were seen more laterally. A 2x2 ANOVA (REG x LOCO) showed a strong main effect of regularity (IRR>REG) in oxy-Hb and deoxy-Hb and a more circumscribed main effect for the factor LOCO selectively in deoxy-Hb readings. Interestingly, in a right lateralized area a significant interaction was seen showing that regularity has an inverse effect on MOV versus STAT. The largest changes were seen for MOV^{IRR} in line with the expectation, that irregular forward walking is most demanding for the conscious control of pace and equilibrium. In sum the data show that cortical control of unconstraint gait can be monitored by fNIRS. This can be used to investigate the effect of training to then inquire into the cortical contributions during gait rehabilitation. The main effect of locomotion was most prominent during the first phase of the moving. To modulate the cortical contribution previous studies have used paradigms which include different complexities of gait. Precision stepping (Koenraadt et al. 2013) and backwards walking (Kurz et al. 2012) were investigated in a treadmill-based experimental design. Furthermore cognitive tasks, performed during treadmill walking were shown to enhance (pre)frontal activation potentially reflecting the additional executive challenge (Holtzer et al., 2011). Challenging acquired balance-control another study used a video game simulating skiing to investigate cortical networks supporting such a task (Karim et al., 2012). Extending this work we here focus on the option to investigate gait in a more ecologically valid scenario. Besides the ecological validity it shuld be noted that treadmill walking may require special adaptation.

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Title: Personalized simultaneous EEG-NIRS to assess the neurovascular coupling in focal epilepsy

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Background: The activity of the epileptic focus produces interictal epileptic discharges (IEDs) that are associated with metabolic-vascular changes (Heers, 2014). We employed simultaneous EEG-NIRS acquisitions to study the neurovascular coupling at the time of IEDs, aiming at validating the feasibility of prolonged EEG-NIRS scans, to characterize the Hemodynamic Response (HR) to IEDs and to localize it on the cortex. *Methods*: We recruited four patients with neocortical focal epilepsy and performed EEG-NIRS recording (up to 5 hours) targeting the epileptic zone and its homologous contralateral region. To maximize the accuracy and sensitivity, we positioned the optodes according to an optimal montage (Machado, 2013) informed by previous multimodal investigations (MEG, fMRI) and glued them on the scalp using collodion (Yücel, 2014). Simultaneous EEG allowed to mark IEDs, only discharges occurring 35s apart each other were selected. Such events were used as trigger to average HbR and HbO time-courses and to identify the HR to IEDs. Finally HbO and HbR responses were localized along the cortical surface using a Restricted Maximum Likelihood method, with minimum norm prior. *Results:* All patients tolerated well the procedure and no side effects were reported. For IEDs whose duration ranged from 70ms to 2s, the overall HR peaked at about 15s (range 10-20s). All patients showed a bilateral HbR decrease, three out of four a bilateral HbO increase, one a bilateral HbO decrease. 3D reconstructions confirmed large HR within the epileptic focus and within the contralateral homologous region. *Discussion:* Individualized and prolonged EEG-NIRS is a powerful method to study hemodynamic coupling in epilepsy. IEDs are associated with a slow and bilateral HR which is very long-lasting when compared to physiological HR. HbO increases paired to HbR decreases resemble an expected positive BOLD response while HbO and HbR decreases suggest a more surprisingly reduction of regional cerebral blood volume. Such long effect has strong implications for HR modelling and is probably related to an impaired neurovascular coupling.
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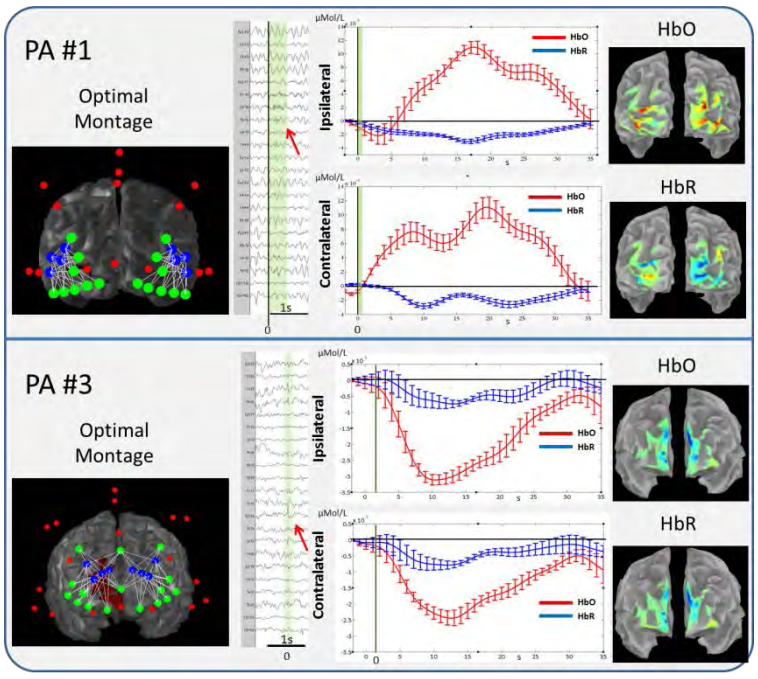

Figure1. Summary of PA#1 and PA#3 results. From left to right: optimal montage computed on single patient level, EEG IEDs (Occipital Burst of Rapid Activity for PA#1 and frontal spikes for PA#3), hemodynamic response at sensor level averaging all the NIRS pairs for each side, HR tomographic reconstruction on brain surface in the 0-30s time-window. PA#1 shows a clear HbO increase and HbR decrease. PA#3 shows a reduction of regional blood volume with HbO and HbR decrease. Despite the direction of HR modulation, for all patient the effect is bilateral and long-lasting, as shown for PA#1 and PA#3

Pre-surgical investigation of reading epilepsy using multimodal neuroimaging

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Reading epilepsy is a rare type of reflex epilepsy in which seizures are provoked by reading (1). In a previous study (2), we investigated a 42 year-old male patient with reading epilepsy using clinical assessments and continuous video-electroencephalography (EEG). Results showed that reading-induced spikes were localized mainly in the left and bilateral frontocentral regions and that the spike frequency significantly increased with the involvement of the phonological reading pathway. In the present study, functional near-infrared spectroscopy (fNIRS), functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG) each combined with simultaneous EEG recordings were used to localize the epileptogenic zone as part of the pre-surgical evaluation of this patient.

The participant read irregular words and non-words presented in a block-design paradigm during EEG-fNIRS, EEG-fMRI and EEG-MEG recordings. Articulation was overt during fNIRS and covert during MEG and fMRI recordings. fNIRS recordings were obtained using 16 NIRS detectors and 55 sources covering the frontal, temporal, parietal and occipital lobes bilaterally. Haemoglobin concentration variations were calculated using the Modified Beer Lambert Law. fMRI acquisitions (399 volumes) were performed with a 1.5T MRI system using a standard head coil and data were processed using SPM 8. MEG was acquired with a CTF-VSM whole-head 271-sensor MEG system; equivalent current dipole analysis was conducted for spike source localization. EEG recordings were simultaneously acquired with each of these techniques with electrodes placed according to the 10-20 system.

Spike analyses revealed an epileptic focus in the left pre-central gyrus in fNIRS, fMRI and MEG recordings, thus confirming the localization of epileptic focus across the three neuroimaging techniques. There was no difference in spike localization between covert (MEG and fMRI) and overt reading (fNIRS), nor between irregular word and non-word reading-induced spikes.

This case report illustrates that multi-channel fNIRS has the potential to contribute favorably to the pre-surgical investigation of patients with particular types of epilepsy such as reading epilepsy.

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Coherent Hemodynamics Spectroscopy – Advances in Methodology and Clinical Applications

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Coherent Hemodynamics Spectroscopy (CHS) is a technique based on inducing cerebral hemodynamic oscillations at multiple frequencies, measuring them with near-infrared spectroscopy (NIRS), and analyzing them with a hemodynamic model to obtain physiological information such as blood transit times in the microvasculature and the autoregulation cutoff frequency. Here we are presenting the latest development in CHS methodology as well as initial clinical applications.

Coherent Hemodynamics Spectroscopy

NIRS can measure cerebral oxy- (O) and deoxy- (D) hemoglobin concentrations, where the underlying sources of these signals are changes in cerebral blood volume (CBV), cerebral blood flow (CBF), and metabolic rate of oxygen ($CMRO_2$). We have recently introduced a hemodynamic model, which, in conjunction with measurements of induced hemodynamic oscillations at multiple frequencies, led to a technique we have named Coherent Hemodynamics Spectroscopy (CHS). For CHS, we have demonstrated that hemodynamic oscillations can be induced, one frequency at a time, and the phase and amplitude relationship of those hemodynamic oscillations can be described with the novel hemodynamic model. As a result, physiological parameters, such as the blood transit times in the microvasculature and the autoregulation cutoff frequency can be obtained. We have already shown that CHS is applicable in the clinical setting of the hemodialysis unit. In a study on patients undergoing dialysis, where cerebral hemodynamic oscillations were induced by periodic inflation and deflation of a pneumatic thigh cuff, we found a longer capillary transit time, indicating a reduced cerebral blood flow, in patients compared to healthy controls. While CHS spectra can be obtained by inducing oscillations at multiple frequencies, the sequential measurement of oscillatory hemodynamics at each frequency results in relatively long measurement times and in CHS spectra whose individual data points at each frequency are measured at different times. Here we introduce a new method of inducing cerebral hemodynamic perturbations from which all of the frequency information needed for CHS is obtained simultaneously. This method is based on inducing a sudden change in the systemic mean arterial blood pressure (MAP), and consequently in $O(t)$, $D(t)$, and $T(t)$, by a fast deflation of two thigh cuff after they have been kept inflated for 2 min at a pressure of 200 mmHg. This step-like response of the cerebral hemodynamics features a frequency information content that is suitable for CHS, and we demonstrate that CHS spectra can be obtained at once from the data collected over a period of ~20 s after the sudden release of the thigh cuff pressure.

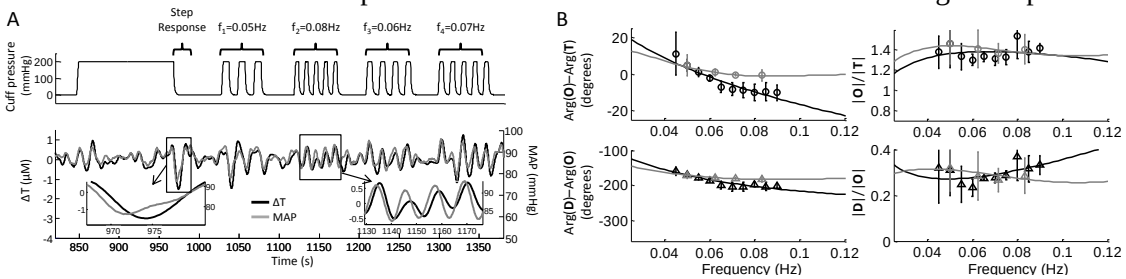

Figure 1. (A)Temporal trace of cuff pressure (top figure) and MAP (bottom figure) for one step response and one set of periodic inflations. (B) CHS spectra for one subject based on the step response (black markers) and the periodic inflation (grey markers).

This approach does not require sequential measurements of hemodynamic oscillations at multiple frequencies, and we show that cerebral hemodynamics measured from a single step change in MAP and from sequential MAP oscillations at multiple frequencies result in the same CHS spectra (Figure 1) to within measurement errors. We will further demonstrate that dynamic measurements of autoregulation are possible with this approach and will show the application to altered autoregulation in healthy volunteers during hyperventilation as well as measurements on patients in the neurocritical care unit.

Cortical mechanisms underlying sensorimotor enhancement induced by light haptic touch during locomotion

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Abstract

Background: Haptic cues such as those provided through light touch in the fingertip have been shown to improve postural stability during gait in post stroke individuals. Recent studies utilizing EEG demonstrate that both the motor cortex and the corticospinal tract contribute directly to muscle activation in lower limbs during steady-state treadmill walking. However, cortical hemodynamic activities associated with changes in locomotor function in response to light haptic touch remains unclear. The primary objective of this study is to utilize functional Near-Infrared Spectroscopy (fNIRS) to investigate the effects of haptic touch during self-paced treadmill locomotion in post-stroke participants and healthy subjects walking at matching slow speeds.

Methods: We have currently examined 7 healthy control subjects and 1 stroke participant. fNIRS measurement was performed using the Hitachi ETG-4000 (44-channel) system. The experimental protocol included repeated block trials consisting of two alternating blocks of standing and walking at a comfortable self-selected speed in stroke participants and slow matching speed in healthy controls. Subjects participated in a total of three walking trials, where the haptic touch condition was randomly alternated with no haptic touch condition. The cortical hemodynamic response was quantified in four different phases: (1) preparation (2) acceleration, (3) steady-state walk, and (4) deceleration. Primary outcome measures included changes in oxygenated hemoglobin concentrations at these four phases with respect to quiet standing, and the average gait speed attained, with and without haptic touch.

Results: Light haptic touch during slow speed walking in healthy controls did not show any significant changes in gait speed as well as in cortical activity. In contrast, individuals with stroke had a significant increase in gait speed in the haptic touch condition compared to the no haptic touch condition. This increase was associated with an increased activation of the lateral sensorimotor cortex of the affected hemisphere. In addition, changes in laterality index with light haptic touch demonstrated improved cortical symmetry during walking.

Conclusion: Improved symmetry of cortical activation of sensorimotor regions associated with enhanced locomotor ability post stroke provides preliminary evidence of promoting sensorimotor enhancement with haptic feedback during locomotion, as a novel intervention of gait rehabilitation post stroke.

Bioadequate electromagnetic therapy efficiency estimation using tissue oximetry

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Because of wide spread occurrence of vascular diseases of lower extremities, the problems of diagnostics, treatment and rehabilitation of patients with these pathologies are relevant and have the important social implication. Among vascular diseases of lower extremities there are widely distributed diseases such as chronic venous insufficiency, chronic obliterating diseases of arteries, and also diabetic microangiopathy. They are characterized by pathology of regional hemodynamics and microcirculation. Improvement of regional hemodynamics can be obtained with the help of bioadequate electromagnetic (EM) therapy. Low intensity electromagnetic field with the fixed amplitude-frequency characteristics induces recovery of microcirculatory blood flow that causes metabolic reactions in organs and tissues. Nowadays it is an important complex task to estimate blood microcirculation parameters qualitatively, to estimate efficiency of electromagnetic influence and personal reaction in order to determine parameters of bioadequate electromagnetic stimulation individually for every patient during physiotherapeutic session.

Usually electrical impedance rheography monitors are used for diagnostics of lower extremities circulation. But any changes of blood flow parameters in arterial or venous vascular department are inseparably linked with changes of microcirculatory parameters.

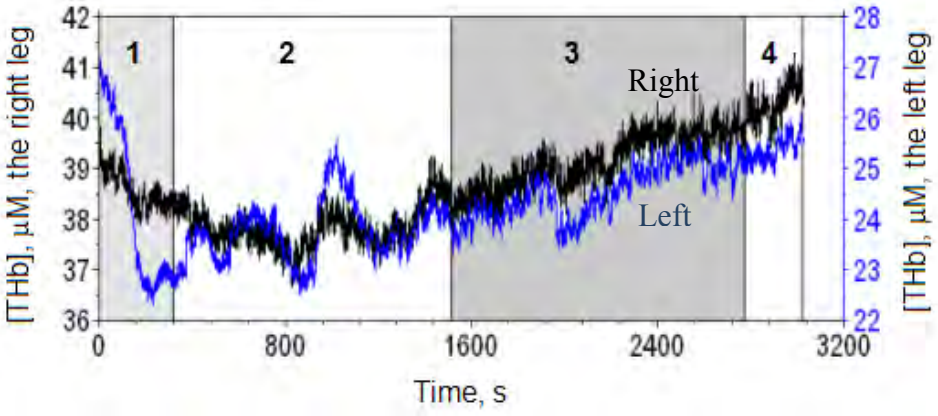

Fig. Changes in total hemoglobin concentration ([THb]) observed by the tissue oximeter "OxiplexTS" (ISS, Inc.) on lower limbs of a patient with diabetes and atherosclerosis during applied EM stimulation. The marks "2" and "3" indicate venous and arterial regimes of EM therapy. The marks "1" and "4" correspond to the time periods without stimulation; the orthostatic changes are seen during period "1"

The tissue oximetry method was chosen for monitoring during EM therapy among the variety of tools such as laser Doppler flowmetry, high-frequency USD-scanning, photoplethysmography. The carried out research have demonstrated the efficiency of the additional diagnostic tool application especially in a case of combined pathologies.

Investigation of Hemodynamic Changes during General Anesthesia via Functional Near Infrared Spectroscopy

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Introduction: Anesthesia is used during surgery to suppress movement, memory and awareness. Positron emission tomography studies have shown that anesthetics produce unconsciousness in humans by suppression of neuronal activity in the brain[1]. Also, concentration changes of oxygenated (HbO2) and deoxygenated (Hb) hemoglobin under general anesthesia were found using functional near infrared spectroscopy (fNIRS)[2,3] which led to further direct analysis in the operating room[4,5]. The primary goal in the clinical study outlined here is to demonstrate the feasibility of using hemodynamic activity based features as measured by fNIRS for the classification of awake and anesthetized states.

Methods: fNIRS data was collected in the operating room continuously during 50 surgical procedures requiring general anesthesia. Two probes consisting of one light source with built in LEDs at 730 and 850nm wavelengths and two light detectors were placed on the subject's forehead over each eyebrow prior to the induction of anesthesia. During each procedure physiological parameters, type and concentration of anesthetic drugs (sevoflurane and desflurane) and position changes were recorded. This initial evaluation explored in 21 procedures the statistical differences in mean HbO2 and Hb as measured from the right dorsolateral prefrontal cortex between maintenance (one minute of data obtained before the initiation of wound closure) and emergence phases (at two time points: i) one minute of data after anesthetic gas concentration reached zero and ii) one minute of data immediately preceding the first attempt of movement). In addition, the discrimination capacity between maintenance and emergence phases was evaluated using a support vector machine (SVM) with a radial basis function (RBF) kernel in 10 cases of sevoflurane anesthesia. The classifier was trained using the previously described minute intervals.

Results: The maintenance and emergence groups were evaluated by the non-parametric Friedman test for repeated measures. There were statistically significant differences (α=0.05) between the 3 time periods in Hb ($\chi2(2)$=14.000, p=0.001) and HbO2 ($\chi2(2)$=6.952, p=0.031). Post hoc analysis by Wilcoxon signed-rank test was conducted with a Bonferroni correction applied (p<0.017). Significant differences were found between the maintenance and the emergence phases (case ii) in Hb (Z=-3.215, p=0.001, Power=92%) and HbO2 (Z=-3.11, p=0.002, Power=88%).

Using labeled data for the maintenance and emergence phases, an SVM based classifier with an RBF kernel was trained and tested by the leave one out method. The fNIRS feature vector was composed of 1 minute averages of Hb, HbO2, Hb+HbO2, Hb/HbO2, and standard deviation of HbO2. The best classification was obtained between maintenance and emergence phase (case ii) with an accuracy of 90%. The classification accuracy between maintenance and emergence phase (case i) was found to be 80%.

Conclusion: These preliminary results are promising and provide indications on the feasibility of fNIRS for the discrimination between the stages of anesthesia. In order to fully study classification performance and predictive capability of fNIRS, more data under various conditions will need to be further analyzed.

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Imaging acute stroke at the bedside using High-Density DOT

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Objective: During the first hours after stroke onset, brain injury evolves rapidly. Ischemic stroke, the major stroke subtype, typically begins with the occlusion of an artery in the brain, which triggers a complex cascade of events including anoxic depolarization, excitotoxicity, spreading depression, and in some cases, reperfusion or recruitment of collateral flow. While MRI and CT provide clinicians with snapshots of structural status, a bedside functional imaging modality could provide more frequent assays to better understand the progression of stroke and potentially inform clinical decisions.

Methods: We have developed a portable high-density DOT system (Fig. 1a) which can perform bedside imaging of sensory and motor areas in the occipital, parietal, auditory, and frontal cortices (Fig. 1b). We have used the MRI-validated fcDOT analysis [1] as a lesion indicator (Fig. 1c-h) and developed fcDOT metrics to investigate stroke severity. We also acquired the NIHSS (NIH Stroke Scale) as a behavioral metric of stroke-induced functional deficit. All research was approved by the Human Research Protection Office at Washington University School of Medicine.

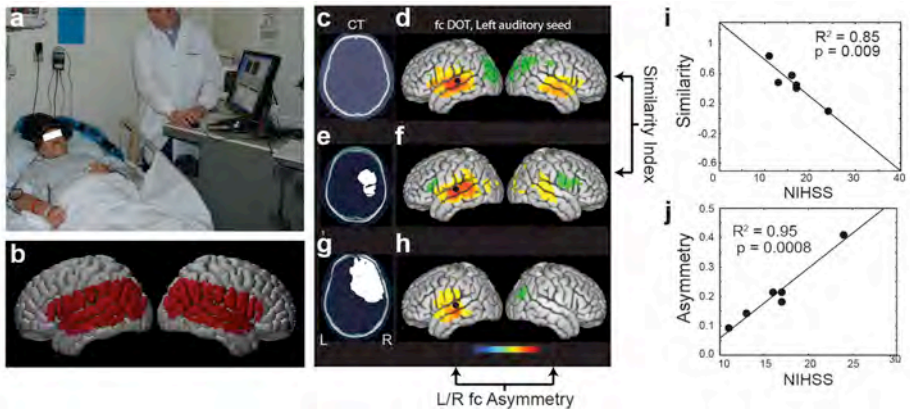

Figure 1. (**a**) fcDOT in the ICU on a patient recovering from an acute stroke. **(b)** Field of view of imaging cap projected onto the cortex. CT and fcDOT for (**c-d**) a healthy subject, (**e-f**) a moderate stroke subject and a (**g-h**) severe stroke subject. The infarcts are represented by binary masks (**c,e,g**). The alterations in fc patterns are correlated with the severity of stroke injury. An asymmetry index quantifies how different the maps are opposite sides of the head (**i**) and shows strong correlation to the NIHSS across 6 subjects. A similarity index quantifies how similar any two fc maps are and also shows a strong correlation to the NIHSS (**j**).

Results: fcDOT metrics such as Similarity (Fig 1i) and Asymmetry (Fig. 1j) are correlated with behavioral measures of stroke severity and may be used to track progression and recovery from stroke.

Discussion: HD-DOT could potentially serve as a bedside monitoring tool to help inform clinical decisions in the initial hours of stroke recovery.

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Functional connectivity of the occipital region based on recurrence plot

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Introduction: Have you ever experienced that you have got clearer vision when you put your glasses on?
Of course, the attention enhance your accommodation, however, more detailed images help you to see more clearly. In this study, we aimed to investigate the functional connectivity changes in occipital area between the conditions without the glasses and with glasses on.

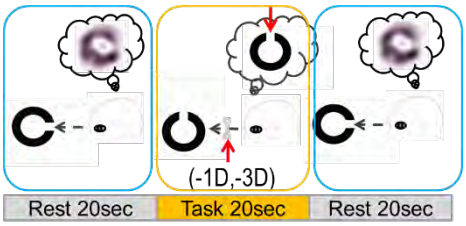

Figure 1: Experimental design

Subjects and Methods: Two healthy volunteers with mild myopia participated in the experiment. Both of them had neither visual nor neurological disorder. They wear glasses (about -3D) daily. The experiments were done avoiding the overcorrection. Binocular visual acuity is listed below.
Subject1: BV=0.1p (0.1 x -1D) (0.9p x -3D)
Subject2: BV=0.1p (0.1 x -1D) (1.0 x -3D)

One session consists of pretask, task and posttask, each duration is 20 seconds length (Figure 1). In every session, task was performed with concave lenses and rest without them. Sessions were repeated five times in each experiment. Subjects were asked to input the direction of the gap through experiment with key pad. The response time and the answers input were recorded. We examined on concave lenses of the different powers (-1D,-3D) and three different stimulus sizes (0.1, 0.4, 0.7).

Table 1: Behavioral data

• Subject #1

		0.1		0.4		0.7	
		RT	AR	RT	AR	RT	AR
−1D	rest	2.67	0.77	4.55	0.25	3.77	0.19
	task	2.50	1.00	3.33	0.27	4.55	0.09
−3D	rest	3.13	0.61	3.45	0.40	3.33	0.23
	task	2.78	0.94	2.27	0.98	2.86	0.99

• Subject #2

		0.1		0.4		0.7	
		RT	AR	RT	AR	RT	AR
−1D	rest	1.57	0.81	1.46	0.28	1.53	0.24
	task	1.54	0.98	1.64	0.40	2.04	0.21
−3D	rest	1.19	0.91	1.25	0.31	1.11	0.21
	task	0.94	0.98	0.96	1.00	1.23	0.99

Foire-3000(Shimadzu Corporation, Kyoto, Japan) was used to monitor changes in the oxygenated hemoglobin concentration. Landolt's rings were used as visual stimuli, the sizes of those are correspond to 0.1, 0.4 and 0.7 in visual acuity. The gap directions are up, down, right and left.

The percentage of stimulus answered correctly (PSAC) is considered into three categories (chance level, partial, visible). For the boundary of chance level and partial, we applied binomial test at the 5% significant level and tested the null hypothesis H_0: The percentage of stimulus answered correctly (PSAC) is chance level. For the boundary of partial and visible, we adopted 0.8.

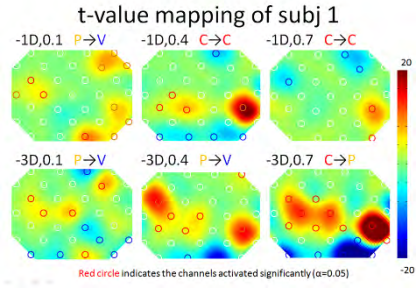

Figure 2: Activation map of sbj1

We placed 4*5 probes in the occipital area. NIRS-SPM was used to detect the projection of channels on the cortical surface. Using 3D digitizer data, probabilistic registration can be calculated on the MNI space without MRI [1]. We calculated the average data in channels corresponding to V1, V2 and V3. To detect the functional connectivity between them, we adopted recurrence plot and joint recurrence plot [2] [3].

Results: Behavioral data is shown in table 1. 1) When the category improves, the number of significantly activated channels increases. 2) At the same time, as the size of stimuli is getting smaller, activated channels shifts V3 to V1. 3) Compared the case of one step improvement of the category with that of two steps, beta value and t value of the latter is bigger than former.4) When the lenses are on, functional connectivity between V2 and V3 are appeared.

Conclusion: Suitable Correction of the eye brings quality of vision. On the other hand, lack of correction or overcorrection of glasses sometimes causes asthenia, headache, and productivity decline and so on. These results could contribute to qualify and quantify the correction of the eye.

Reference: [1]NIRS-SPM: http://bispl.weebly.com/nirs-spm.html#/
[2] N. Marwan et al., Physics Reports, 438, 237-329, 2007.
[3]Y. Hirata & K. Aihara, Phys. Rev. E 81, 016203, 2010.
[4] K. Iwayama et al., Scientific Reports, Vol. 2, 423, 2012.

Functional connectivity of the occipital region based on recurrence plot

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Introduction: Have you ever experienced that you have got clearer vision when you put your glasses on?
Of course, the attention enhance your accommodation, however, more detailed images help you to see more clearly. In this study, we aimed to investigate the functional connectivity changes in occipital area between the conditions without the glasses and with glasses on.

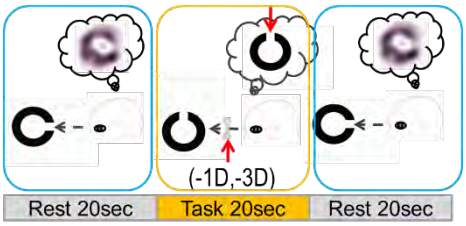


Figure 1: Experimental design

Subjects and Methods: Two healthy volunteers with mild myopia participated in the experiment. Both of them had neither visual nor neurological disorder. They wear glasses (about -3D) daily. The experiments were done avoiding the overcorrection. Binocular visual acuity is listed below.
Subject1: BV=0.1p (0.1 x -1D) (0.9p x -3D)
Subject2: BV=0.1p (0.1 x -1D) (1.0 x -3D)

One session consists of pretask, task and posttask, each duration is 20 seconds length (Figure 1). In every session, task was performed with concave lenses and rest without them. Sessions were repeated five times in each experiment. Subjects were asked to input the direction of the gap through experiment with key pad. The response time and the answers input were recorded. We examined on concave lenses of the different powers (-1D,-3D) and three different stimulus sizes (0.1, 0.4, 0.7).

Table 1: Behavioral data

• Subject #1

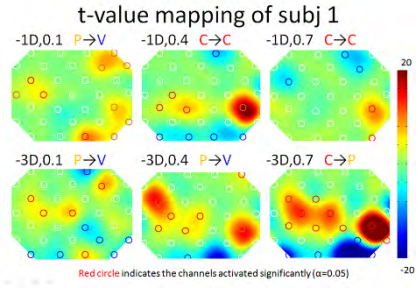
		0.1		0.4		0.7	
		RT	AR	RT	AR	RT	AR
−1D	rest	2.67	0.77	4.55	0.25	3.77	0.19
	task	2.50	1.00	3.33	0.27	4.55	0.09
−3D	rest	3.13	0.61	3.45	0.40	3.33	0.23
	task	2.78	0.94	2.27	0.98	2.86	0.99

• Subject #2

		0.1		0.4		0.7	
		RT	AR	RT	AR	RT	AR
−1D	rest	1.57	0.81	1.46	0.28	1.53	0.24
	task	1.54	0.98	1.64	0.40	2.04	0.21
−3D	rest	1.19	0.91	1.25	0.31	1.11	0.21
	task	0.94	0.98	0.96	1.00	1.23	0.99

Foire-3000(Shimadzu Corporation, Kyoto, Japan) was used to monitor changes in the oxygenated hemoglobin concentration. Landolt's rings were used as visual stimuli, the sizes of those are correspond to 0.1, 0.4 and 0.7 in visual acuity. The gap directions are up, down, right and left.

The percentage of stimulus answered correctly (PSAC) is considered into three categories (chance level, partial, visible). For the boundary of chance level and partial, we applied binomial test at the 5% significant level and tested the null hypothesis H_0: The percentage of stimulus answered correctly (PSAC) is chance level. For the boundary of partial and visible, we adopted 0.8.



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Epileptic seizure detection in fNIRS signals using a supervised classifier

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[a]Department of Electrical Engineering, École Polytechnique de Montréal, Canada; [b]Montreal Heart Institute;
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1. BACKGROUND

Functional near infrared spectroscopy (fNIRS) is a non-invasive, non-ionizing neuroimaging technique capable of monitoring cortical hemodynamic changes. Recent studies have shown that fNIRS can assess cortical hemodynamic changes associated with seizures, paving the way to a potential application in monitoring critically ill patients at risk for seizures. fNIRS could potentially help both in the detection of seizures and the assessment of their impact on brain oxygenation.

2. AIM

The objective of this study is to explore the feasibility of using fNIRS as a tool for automatic seizure detection. To the best of our knowledge this is the first study of fNIRS in epileptic seizure detection.

3. METHODS

One 49-year old male patient, with drug-resistant left temporal lobe epilepsy was chosen from a previous EEG-fNIRS study. Data were recorded over a period of ~82 minutes. Wavelengths at 690 and 830nm were recorded through 133 optical channels, covering bilateral frontotemporal regions. fNIRS data was pre-processed with a MATLAB toolbox developed in-house to get concentration changes of oxy- and deoxy-hemoglobin (HbO_2 and HbR, respectively).

The selected set of features consisted solely of amplitude changes of HbO_2 and HbR time traces, rescaled to have zero mean and unit variance. These features were given as inputs to the classifier every second. The supervised classifier chosen in this work was partial least squares discriminant analysis (PLS-DA), because it is well suited to perform regression on multicolinear explanatory variables with a discrete dependent variable.

The performance of the classifier was determined in terms of sensitivity (the proportion of actual seizures identified as such), specificity (the proportion of non-epileptic activity correctly identified) and positive predictive value (PPV, the proportion of predicted seizures that are actual epileptic ictus), which were computed by averaging the results of ten 10-fold cross-validation runs. In each one of the runs, the data was split into 10 approximately equal partitions, and each in turn was used for training while the remainder is used for testing. Features were simulated with signal-to-noise ratio (SNR) ranging from 10^{-1} to 10^{7} in order to determine the minimum SNR that would yield results comparable to a state-of-the-art classifier.

4. RESULTS

Five seizures were labeled by a clinical neurophysiologist and reviewed by an epileptologist. Average seizure duration was 82 s. The overall PPV attained by the classifier was 70.8%, while sensitivity reached 86.9% and specificity was 96.6%. Figure 1 shows the classification results: there is only one isolated false positive and no such false negative, implying that all misdetections happened at the beginning or end of seizures. The minimum SNR that yielded robust results was ~0.3, one order of magnitude smaller than the estimated SNR of the NIRS recordings. Preprocessing and prediction of the testing data using a calibrated model took an average of ~290ms on a desktop computer (Intel Xeon CPU, clock rate 2.27GHz, and RAM memory of 24 GB).

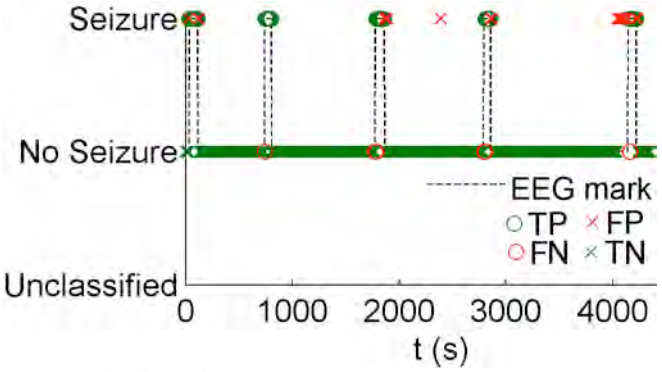


Figure 1. Classification results

5. DISCUSSION AND CONCLUSIONS

Our preliminary findings support the use of fNIRS as a completely non-invasive tool to detect epileptic seizures; however more features and classification methods need to be investigated, in order to perform better than a state-of-the-art supervised algorithm. The computation time suggests that a real-time implementation is feasible for the proposed approach.

The concurrent use of electro-encephalography (EEG) and fNIRS will be explored in future work, since these methodologies complement each other, one assessing directly brain activity and the latter sensing the oxygenation changes. The results suggest that the discrepancies in performance observed here were mostly due to the hemodynamics of seizures actually following a different time course from the EEG manifestations.

Exploration of the Potential Clinical Applications of Near Infrared Spectroscopy (NIRS) in the Area of Pain Management

Kambiz Pourrezaei, *Ahmad Pourshoghi. Zeinab Barati, Issa Zakeri , Daryl Omire-Mayor, Ardy Wong, Minakshi Mohanty, Kanghee Lee*
Biomedical Engineering Department, Drexel University, Philadelphia, PA 19104

A significant portion of society suffers from chronic pain. In the United States, the incidence of pain is more than diabetes, heart diseases and cancer combined. According to the Institute of Medicine of the National Academies Report, the prevalence of chronic pain in adult Americans was at least 100 million in 2011. In particular, this problem is more prevalent among older adults to a large degree due to the aging process. Potent and effective opioids have been helpful in treating acute pain; however, for chronic pain, their long-term usage could result in losing their effectiveness and ultimately lead to addiction. In recent years, self-management pain interventions such as meditation, group therapy and biofeedback have been proposed as alternative solutions to medication.

In the last few years, we have investigated the potential utility of NIRS as a tool for monitoring individuals' responses to painful stimuli. In particular, we have done extensive studies of healthy subjects' hemodynamic response to painful thermal and mechanical stimuli by NIRS. Our current study involves using machine-learning analysis to classify the fNIR data in response to painful stimuli.

The most recent study in this lab investigated the feasibility of employing fNIRS as an objective assessment of migraines in humans and the efficacy of drug infusions used to treat these patients. 41 patients took part in a non-blinded trial using 3 medications; Magnesium (Mg), Sodium Valproate, (Depacon) and Dihydroergotamine (DHE). 34 patients were female, 7 were male. They had an average age of 49.2±9.5 (results shown below).

In the presentation of this investigative work, we will briefly review brain imaging of pain by fMRI and fNIRS followed by an in-depth presentation of the work in our laboratory. We will also discuss techniques for assessing pain among patients with chronic back pain and those suffering from congestive heart failure.

Figure 1: Near Channel (skin)

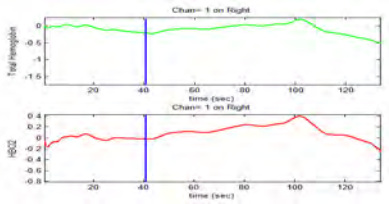
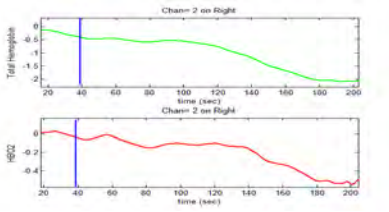


Figure 2: Far Channel (deep)



Near Channel	Depacon	Magnesium
Mean	0.030	0.031
Standard Deviation	0.004	0.004
P-value	0.478	

Far Channel	Depacon	Magnesium
Mean	0.125	0.022
Standard Deviation	0.070	0.001
P-value	0.050	

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Figures 1 and 2 (blood flow change comparison between drug infusions as measured by fNIRS) accompanied by their tables show that there is significant difference between blood flow changes in the 2 drugs (as displayed by the slope changes) in the far channels, whereas the near channels show no significant change.

8. Other

REDUCED HAEMODYNAMIC RESPONSE IN THE AGEING VISUAL CORTEX

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Presenting author: Laura Ward (Laura.McKernan@gcu.ac.uk)

The effect of healthy ageing on cortical activation is still be fully explored, yet it is crucial to understand basic visual processes which influence perceptual experiences. Physiologically the occipital cortex is relatively robust to grey matter density loss and shrinkage (Sowell et al., 2003). Yet, the specific impact of age-related changes on visual functioning remains under study. This research aimed to elucidate whether the haemodynamic response (HDR) of the visual cortex varied as a result of healthy ageing. Optically healthy participants were presented with basic passive visual stimulation (reversing checkerboard). Functional Near-Infrared Spectroscopy (fNIRS) was used to measure absolute changes in oxygenated [HbO] and deoxygenated [HbR] haemoglobin concentrations in the occipital cortices. A frequency domain multi-distance method (FD-MD) system was used with a dual channel fNIRS system (OxiplexTS™, ISS Inc.). Full ophthalmic screening was implemented to identify two normal age groups; young adults (n=12, mean age 21 ± 3 years) and old adults (n=13, mean age 71 ± 7 years). Utilising a slow event-related design, participants viewed a full field reversing checkerboard with contrast and check size manipulations (15 and 30" of arc, 50% and 100% contrast). Both groups showed the characteristic response of increased [HbO] and decreased [HbR] during visual stimulation (Figure 1). However, old adults produced significantly varied HDR and often had comparable levels of [HbO] and [HbR] during both stimulus presentation and baseline resting state. Young adults had significantly greater concentrations of both chromophores in every investigation regardless of stimulus used ($p<0.05$; see Figure 2). Effect sizes were remarkably strong – the average variance associated with age for [HbO] was 91% and [HbR] 93%. These results indicate that in passive viewing of basic checkerboard stimulation, without any cognitive input, there is an age-related decline in the HDR. Moreover, regardless of stimulus parameters such as contrast, the HDR is characterised by age. In concurrence with present neuroimaging literature, we conclude that the visual HDR decreases as healthy ageing proceeds.

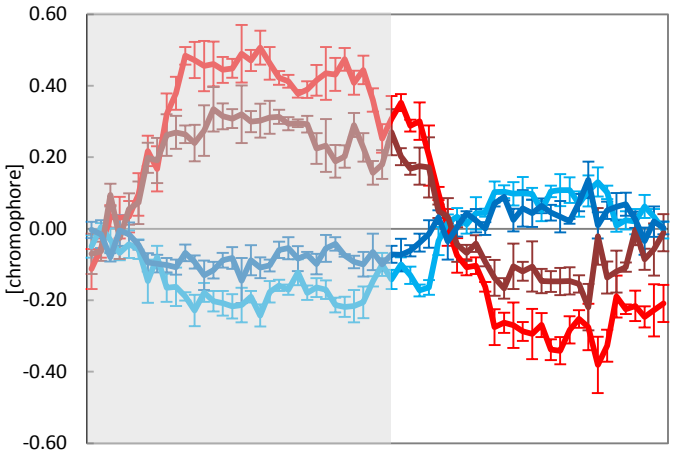

Figure (1) Average response cycle during visual stimulation (grey) comparing young (bright) and old (dark) group haemodynamic response of [HbO] (red) and [HbR] (blue).

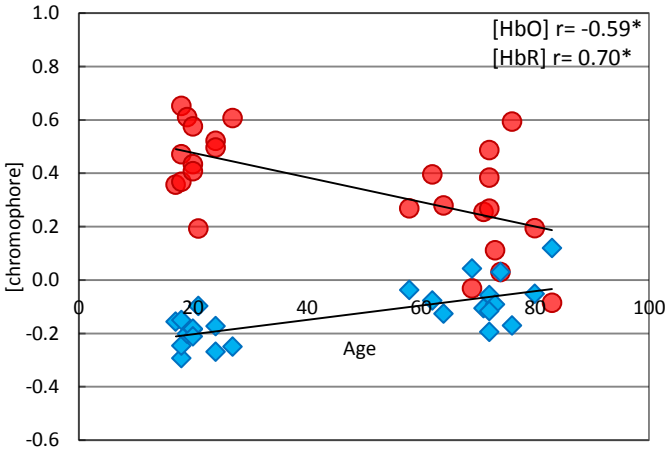

Figure (2) Scatterplot demonstrating individual grand averages to checkerboard stimulation for [HbO] (red) and [HbR] (blue) for entire sample (n=25). *Correlations are significant at $p<0.01$.

Abstract fNIRS 2014, 9-12 October, Montreal

Combined EEG–fNIRS investigation of hierarchical rule learning in 5-month-old infants

Marina Winkler[1,2], Jutta L. Mueller[2,3], Angela D. Friederici[2], Stefan P. Koch[4,5], Claudia Männel[2]

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[1]*International Max Planck Research School on Neuroscience of Communication, Leipzig;* [2]*Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig;* [3]*Institute of Cognitive Science, Osnabrück;*[4]*Charité Universitätsmedizin, Berlin;* [5]*Berlin Neuroimaging Center (BNIC), Berlin*

Human language crucially involves the ability to process hierarchical grammar structures. However, it is still unclear when and how during development this ability is acquired. Recent research has shown remarkable language learning abilities in young infants [1,2], being able to learn simple rules between non-adjacent elements by as early as 3 months of age [3]. The aim of the present study was to examine, whether infants could also acquire more complex, hierarchical rules between elements of center-embedded sequences. The sequences, consisting of pure tones, were presented to 5-months old infants in a passive listening oddball paradigm, while EEG and fNIRS were simultaneously recorded to allow for precise temporal as well as spatial analyses of infants' neural responses to hierarchical grammar learning. The electrophysiological results show event-related mismatch responses to the deviant sequences containing rule violations, which indicates, that the infants have successfully learned the underlying hierarchical rules presented to them. The electrophysiological and the hemodynamic results will be presented.

[1] Gervain, J., Macagno, F., Cogoi, S., Pena, M., Mehler, J. (2008). The neonate brain detects speech structure. PNAS, 105(37): 14222–14227.

[2] Friederici, A. D., Mueller, J. L., Oberecker, R. (2011). Precursors to natural grammar learning: Preliminary evidence from 4-month-old infants. PLoS ONE, 6(3): 1–7.

[3] Mueller, J. L., Friederici, A. D., Männel, C. (2012). Auditory perception at the root of language learning. PNAS, 109(39): 15953–15958.

Does Driver Age, Experience and Gender Affect Overtaking Behaviour and Prefrontal Cortex (PFC) Activity?

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Abstract

Fatalities as a result of road traffic collisions consistently highlight an over-representation of young, novice and predominantly male drivers. This trend could be explained by a lack of prefrontal cortex (PFC) maturation, a process which is not complete until age 25. The PFC has been associated with a number of factors, including workload and inhibitory control. These are particularly important in driving since the common crash types of these at risk drivers have been linked to excess risk taking and thus a lack of inhibitory control and driver workload has previously been found to relate to accidents.

This experiment used functional near-infrared spectroscopy (fNIRS) to measure blood oxygenation changes in the PFC during five simulated driving tasks; four overtaking tasks at different traffic densities and one following task. These five tasks were designed to create variations in inhibitory control and workload. Throughout the experiment age, driving experience and gender were systematically manipulated across eight groups of relatively young and inexperienced drivers. The results showed that when driver workload and inhibitory control levels increased, as measured by a revised NASA TLX workload questionnaire, blood oxygenation in the PFC also increased. The age of the driver did not predict PFC activity or the number of overtakes they made during the overtaking tasks however, this may be due to somewhat limited age ranges in the current study. Although there was no relationship found between experience and the number of overtakes males overtook significantly more often than females, providing support for a greater level of risk taking in males which may relate to the increased crash rates seen in these drivers.

Development of time-domain diffuse optical tomography based on a radiative transfer equation and diffusion approximation hybrid

Y. Hoshi[1], E. Okada[2], S. Okawa[3], Y. Tanikawa[4], T. Yoshinaga[5], H. Fujii[6], K. Fujimoto[5], K. Hashimoto[1], S. Kohno[1]

[1]Tokyo Metropolitan Institute of Medical Science, [2]Department of Electronics and Electrical Engineering, Keio University, [3]National Defense Medical College, [4]National Institute of Advanced Industrial Science and Technology, [5] Institute of Health Biosciences, The University of Tokushima, [6] Faculty of Engineering, Hokkaido University (e-mail: hoshi-yk@igakuken.or.jp)

Diffuse optical tomography (DOT) has great potential for the quantitative detection of focal changes in cerebral hemoglobin (Hb). DOT can be performed with continuous wave (CW), time domain, and frequency domain spectroscopy instruments. Recently, high-density CW DOT has been developed and improved brain specificity compared with conventional optical topography. This CW DOT, which is based on linear-single step image reconstruction, provides only qualitative images of measured changes. Although this method is enough for functional neuroimaging, quantitative images of steady-state cerebral Hb are further useful for diagnostic neuroimaging. Thus, we have been developing time-domain DOT based on a non-linear iterative reconstruction scheme.

It has been widely accepted that the radiative transfer equation (RTE) accurately describes photon propagation in biological tissue, while because of its high computation load the diffusion equation (DE) is often used as a forward model. However, the DE is invalid in low-scattering and/or highly absorbing regions and the vicinity of sources, which reduces image quality. One of the most promising alternative approaches is a hybrid model based on the RTE and DE, which has been proposed in frequency domain. Extending the concept of the hybrid model in the steady state to the time domain, here, we propose a space-time hybrid model in random media under refractive-index mismatching. In the proposed model, the RTE and DE regions are separated in space and time by using crossover length (ρ_{DA}) and a crossover time (t_{DA}). ρ_{DA} and t_{DA} were estimated by investigating the time development of light propagation (fluence rates and photon currents) based on the RTE and DE: $\rho_{DA} \sim 10/\mu'_t$ and $t_{DA} \sim 10/\nu\mu'_t$, where μ'_t and ν represent a reduced transport coefficient and light velocity, respectively (Figs. 1 and 2). The accuracy and computational efficiency of the present model were confirmed by a comparison with numerical results based on the RTE.

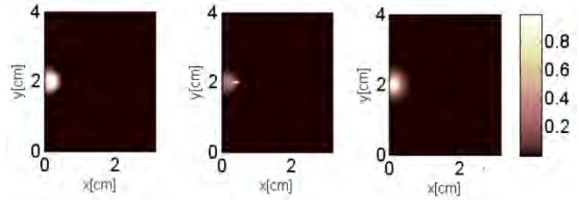

Fig. 1 Spatial distribution of the normalized fluence rate at a given time t = 20 ps shorter than t_{DA} based on the DE (left), the RTE with g = 0.8 and anisotropic source (middle), the RTE with g =0 and anisotropic source (right)

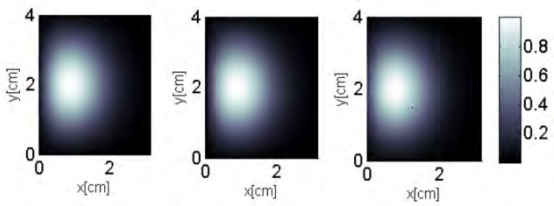

Fig. 2 Spatial distribution of the normalized fluence rate at a given time t = 500 ps longer than t_{DA}. Other details are the same as Fig. 1.

Decision-Making Conflict and the Neural Efficiency Hypothesis of Intelligence: A Functional Near-Infrared Spectroscopy Investigation

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Research on the *neural efficiency hypothesis* of intelligence (NEH) has revealed that the brains of brighter individuals consume less energy when performing easy cognitive tasks but more energy when engaged in difficult mental operations. However, previous studies testing the NEH have relied on cognitive tasks that closely resemble psychometric tests of intelligence, potentially confounding efficiency during intelligence-test performance with neural efficiency *per se*. The present study sought to provide a novel test of the NEH by examining patterns of prefrontal activity while participants completed an experimental paradigm that is qualitatively distinct from the contents of psychometric tests of intelligence. Specifically, participants completed a personal decision-making task (e.g., Which occupation would you prefer, dancer or chemist?) in which they made a series of forced choices according to their subjective preferences. The degree of decisional conflict (i.e., choice difficulty) between the available response options was manipulated on the basis of participants' unique preference ratings for the target stimuli, which were obtained prior to scanning. Evoked oxygenation of the prefrontal cortex was measured using 16-channel continuous-wave functional near-infrared spectroscopy. Consistent with the NEH, intelligence predicted decreased activation of the right inferior frontal gyrus (IFG) during low-conflict situations and increased activation of the right-IFG during high-conflict situations. This pattern of right-IFG activity among brighter individuals was complemented by faster reaction times in high-conflict situations. These results provide new support for the NEH and suggest that the neural efficiency of brighter individuals generalizes to the performance of cognitive tasks that are distinct from intelligence tests.

Temporal-spatial distribution of skin hemoglobin signals on the forehead during a verbal fluency task

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Integrated Neuroscience Research Project, Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

Introduction: Functional near-infrared spectroscopy (fNIRS) is a non-invasive technique for estimating cerebral hemodynamic changes. We have previously reported that the skin blood flow signals during motor task change depending on the task being performed, and the skin blood flow artifacts are removed from original fNIRS signals on the motor area using ICA (Independent Component Analysis) [Kohno, 2007]. In this procedure, it was assumed that the skin blood flow changes are spatially more global than the brain activation. Recently, however, it has been reported that sources of task-evoked systemic signals in fNIRS are co-localized with veins in the scalp [Kirilina, 2012]. Here we explore the temporal-spatial distribution of skin hemoglobin signals on the forehead during a letter-cued verbal fluency task. **Methods:** Sixteen subjects (12males, 4females, mean age/SD: 27.1± 11.0 years.) participated in this study. We used the letter-cued verbal fluency task, during which the word generation was repeated twice in two blocks. Each block consisted of a 60-s-long word-generation period that was preceded for 30 s and followed for 70 s by control periods [Takahashi, 2011]. We first used a multichannel continuous-wave near-infrared imager (FOIRE 3000, Shimadzu Corp.). In order to measure hemoglobin signals from the skin layer, ten source-detector pairs (T1-R1, T2-R2, T3-R3, T4-R4, T5-R5, T6-R6, T7-R7, T8-R8, T9-R9, T10-R10) with a separation of 5 mm were placed on the forehead. In addition, to measure fNIRS signals, which are defined as those arising from both the extracerebral and the cerebral tissue (BA10), two additional detectors (R11, R12) were placed with a source-detector separation (T1-R11, T6-R12) of 40 mm (Fig. 1). Next we used a laser speckle flowmetry (moorFLPI, moor instruments) to measure skin blood flow on the forehead.
Results and Discussion: Though the fNIRS signals were correlated with the skin hemoglobin signals in all the subjects, the correlations with oxygenated hemoglobin changes were stronger than those with deoxygenated hemoglobin changes. In addition, the intra-subject variability on the temporal-spatial distribution of skin hemoglobin signals on the forehead was high (Fig. 2), and the correlation maps between skin hemoglobin signals in some subjects were heterogeneous throughout the forehead (Fig. 3). The heterogeneous blood flow changes were also confirmed by a laser speckle flowmetry (Fig. 4). These results indicate that spatial homogeneity of skin hemoglobin signals on the forehead during a verbal fluency task can't be assumed beyond the range of at least 15 mm.

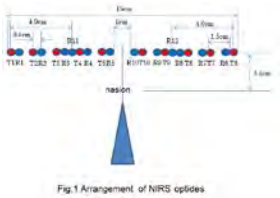

Fig.1 Arrangement of NIRS optides

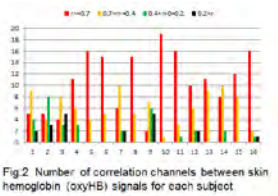
Fig.2 Number of correlation channels between skin hemoglobin (oxyHB) signals for each subject

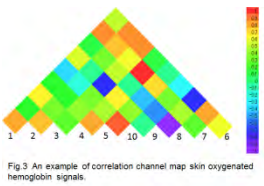
Fig.3 An example of correlation channel map skin oxygenated hemoglobin signals.

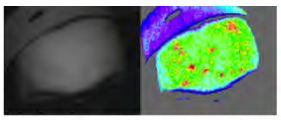
Fig.4 An example of heterogeneous distributed skin blood flow throughout the forehead. Photo image (left) and Flux image (right)

References

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Issues in Functional Near Infrared Spectroscopy

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Abstract

Functional near infrared spectroscopy (fNIRS) is a growing technology that can identify brain activity by measuring changes in regional cerebral blood flow. fNIRS devices provide researchers with a non-invasive method to measure hemodynamic changes within cortical areas of the brain, while providing high task-flexibility and robustness towards motion artifacts. This technology also is vulnerable to various errors, which ought to be understood prior to data collection. The goal of this review is to describe FNIRS technology for the novice user, current uses of the technology, and discuss issues of reliability and validity in measurement.

The development of functional Near-infrared Cortical Imaging (fNCI): the direct cortical hemodynamic mapping of the miniature pig's somatosensory area.

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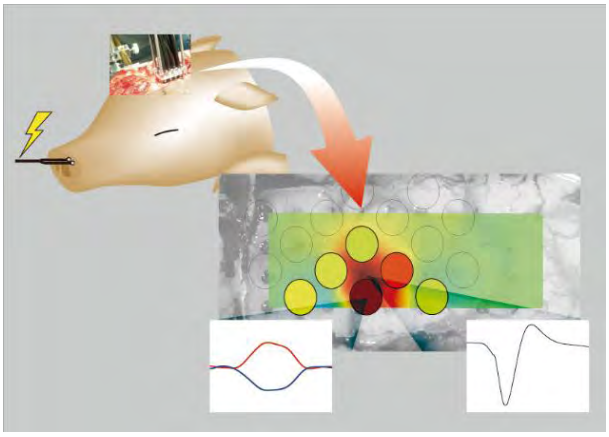
fNIRS is widely used in many research and clinical situations. In the neurosurgery field, sensory evoked potential (SEP) measurement is used to identify functional area or monitor brain activities directly from the cortical surface during craniotomy surgery. However, direct cortical measurement using fNIRS has yet to be realized. Though SEP can measure electrical short range activities well, long lasting hemodynamic conditions cannot be evaluated. Thus, a monitoring method that can measure cortical hemodynamics directly from the brain surface is worth exploring.

To acquire robust information on the hemodynamics of the cortex, we devised a functional Near-infrared Cortical Imaging (fNCI) technique. We demonstrate the first direct functional measurement of temporal and spatial patterns of cortical hemodynamics using the fNCI technique. For fNCI, inter-optode distance was set at 5 mm. This high resolution enabled us to detected the somatotopy of pig nostril sensation, as assessed in comparison with SEP measurements on the same stimulation sites.

In addition to the validation study of fNCI through its comparison to SEP measurements, we will discuss the possibility of down-sizing the measurement module for plausible future clinical application, especially during cortical monitoring during neurosurgery.

The fNCI system realized a direct cortical hemodynamics measurement with a spatial resolution comparable to that of SEP mapping on the rostral region of the pig brain. This animal study provides an important initial step toward realizing functional cortical hemodynamics monitoring during neurosurgery of human brains.



Assessing Cerebral Hemodynamics by Dynamic Contrast-Enhanced Near-Infrared Spectroscopy

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The adaptation of dynamic contrast-enhanced (DCE) methods to computed tomography and magnetic resonance imaging is now used routinely in clinical neuroimaging applications. Near-infrared spectroscopy (NIRS) is also well suited to DCE methodology as data can be acquired with high contrast and temporal resolutions. Using indocyanine green (ICG) as a contrast agent, DCE NIRS has been used at the bedside to monitor cerebral blood flow in stroke patients[1]. However, the utility of DCE NIRS has the potential to extend beyond qualitative assessments if quantitative NIRS approaches are combined with the appropriate kinetic models[2,3]. In this study, we will outline modelling approaches developed to characterize vascular heterogeneity and permeability.

Theory

The relationship between the time-varying concentration of contrast agent in tissue $C_t(t)$ and in arterial blood $C_a(t)$ is given by:

$$C_t(t) = F\left\{\int_0^t C_a(u)du - \int_0^t C_a(u) * h(u)du\right\}$$

where F is blood flow, * represents the convolution operator, and $h(t)$ is the probably distribution function of transit times through the system. For an intravascular contrast agent, the shape of $h(t)$ depends on vascular features such as vessel density, lengths and tortuosity, which can be described in terms of statistical moments. Leakage of contrast agent due to blood-brain barrier disruption will lead to long transit times and it can be quantified by measuring the permeability surface-area product (PS)[4].

Methods

NIRS data were collected using a time-resolved system previously described[2]. Time-of-flight histograms were collected every 0.4 s following the intravenous injection of contrast agent, and $C_a(t)$ was measured simultaneously by pulse dye densitometry (Nihon-Koden, Japan). DCE data were acquired from the brains of six healthy newborn piglets and from tumours implanted subcutaneously on six rats. The latter were used to assess the ability of DCE NIRS to characterize a microvascular system with leaky vessels and greater vascular heterogeneity caused by angiogenesis. Permeability was assessed by collecting data with contrast agents of different molecular weights: ICG (67 kDa) and IRDye 800CW carboxylate (IRD, 1166 Da, LI-COR Biosciences).

Results and Discussion

Fig. 1 presents $h(t)$ curves obtained for ICG from (A) healthy brain and (B) tumour. Since ICG remains in the blood, the greater dispersion observed in (B) reflects a larger distribution of vascular transit times likely due to unstructured vascular growth typical of cancer. The variance of $h(t)$ for tumours was significantly greater than for brain: 90 vs 56 s^2.

PS for ICG in both brain and tumour was negligible, indicating that ICG remained in blood as expected. In contrast, PS for IRD in tumour was 0.051 ± 0.033 ml/g/min, reflecting the retention of the dye in tissue (Fig. 2). These results demonstrate the ability of DCE NIRS to characteristic key features of microvascular circulation, which could be used to assess pathological changes in cerebral hemodynamics.

Figure 1

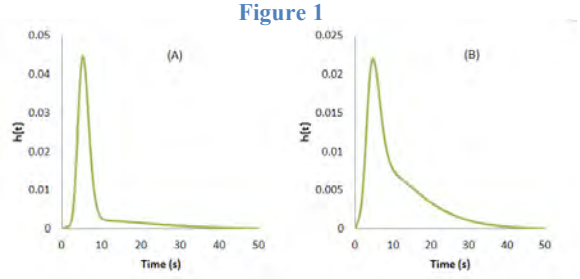
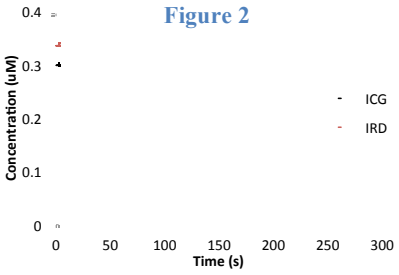


Figure 2



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