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MAP USE IN WILLIAMS SYNDROME: PATTERNS OF SPARING AND VULNERABILITY IN SPATIAL COGNITION

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Abstract

Williams Syndrome (WS) is a rare neurodevelopmental disorder resulting in a unique profile of cognitive abilities, in which spatial cognition is impaired while language and communication remain intact. The present study examines WS patients' sensitivity to core features of Euclidean geometry through a map-reading task. Participants were presented with 4 maps including either: distance, angle, surface length, or a non-geometric landmark cue. After viewing the map, participants were asked to use the symbolic information presented to identify a goal location. In the Landmark condition, WS participants performed at the same level as typically developing (TD) participants, which broadly indicates that this population can understand the symbolic representations used in maps. In each of the geometric conditions, the WS participants performed significantly above chance, but significantly below the TD controls. Both WS and TD participants performed worse when asked to use the spatial information presented in the map as a relational cue compared to a direct cue. There was no effect of sex within the TD sample; however, there was an effect of sex in the WS sample, with males significantly outperforming females. The finding of a sex difference in spatial cognition in WS participants is novel and requires further research. While WS is known for profound deficits in spatial cognition, these results show substantial sparing of core representations of geometry, and vulnerability in more nuanced spatial abilities, such as relational knowledge.

Map Use in Williams Syndrome: Patterns of Sparing and Vulnerability in Spatial Cognition

Individuals with Williams Syndrome (WS) share a unique cognitive profile that includes severely impaired visuospatial abilities paired with intact language and communication (Kozel et al., 2021). This combination of relatively normal functioning coupled with specific deficits in visuospatial processing presents a unique model with which to explore the factors that contribute to typical and atypical development of spatial cognition, such as map-reading abilities. Previous work indicates that individuals with WS have a strong understanding of symbolic representations, which could implicate successful map use, but a weak understanding of spatial relationships, which could result in poor navigation. This paradox leads us to question how individuals with WS might draw on various spatial features, such as Euclidean geometry, in maps to navigate real-world environments.

Etiology

While WS is a complex and multifaceted disorder, its etiology can be clearly traced to a spontaneous deletion of approximately 28 genes on chromosome 7q11.23 (Meyer-Lindenberg et al., 2006). In this way, WS provides a window into the complex relationship between genes and behavior. During meiosis, homologous recombination calls for equivalent portions of the maternal and paternal chromosomes to line up and exchange genetic information in a crossover (Urbán et al., 1996). Misalignment of alleles during meiosis can result in a deletion of genetic information in the copy that is passed on to the germ cell (Urbán et al., 1996). While some deletions affect the future embryo's viability, others simply affect certain aspects of normal functioning. WS is caused by a hemizygous deletion, which means affected individuals have one intact copy and one disordered copy (Frangiskakis et al., 1996). Haploinsufficiency, or unequal proportions of genetic information, ensues: the intact copy does not give rise to enough protein to ensure normal cognitive functioning (Hoogenraad et al., 2002). As such, WS provides valuable information about the relationship between genes, brain structure, and behavior.

The Williams Syndrome Profile

WS has a distinct physical and intellectual presentation. At first glance, one can see that individuals with WS appear to have growth retardation and structural abnormalities within the facial region, including broad foreheads and strabismus, more commonly referred to as crossed eyes (Beuren et al., 1962). Another hallmark of the disorder is cardiovascular issues, which can be found in 80% of patients ("American Academy of Pediatrics: Health care supervision for children with Williams syndrome," 2001). Both structural and cardiovascular abnormalities in WS can be traced to haploinsufficiency for elastin, a protein essential to the extracellular matrix (Morris et al., 2003). Additionally, WS often presents with endocrine imbalances such as hypercalcemia, or excessive blood calcium levels, and complications in the gastrointestinal, neurological, and orthopedic systems (Cherniske et al., 2004). Within this population, chronic medical conditions shorten the life expectancy (Coppus, 2013).

The cognitive profile of WS includes slight to moderate intellectual disability. Previous work on WS indicates the disorder accounts for up to 6% of intellectual disability with a genetic basis (Strømme et al., 2002). More specifically, the WS population exhibits relative strength in language and communication countered by marked deficits in visuospatial processing (Mervis & Klein-Tasman, 2000; Pani et al., 1999). Single-score IQ tests may not properly reflect the cognitive potential of individuals with WS given the documented deficits in visuospatial processing within this population (Mervis et al., 2012). IQ tests draw on visuospatial abilities in addition to verbal and numerical reasoning (Berkowitz & Stern, 2018). Having a single score that reflects both non-spatial and spatial abilities is an oversimplification for WS. Individuals with WS perform within two standard deviations of the mean on verbal and nonverbal reasoning tests, indicating that this population frequently falls within the normal range for some domains of cognitive functioning, albeit on the low end (Mervis & Klein-Tasman, 2000). Similarly, Mervis and John (2010) show that WS patients score within the normal range on verbal and nonverbal reasoning tasks but have significantly lower scores on spatial tasks (Mervis & John, 2010). Such findings contribute to the theory that WS is characterized by intact language and communication, as seen through the verbal reasoning scores, paired with severe deficits in spatial processing, which we explore in more detail in the current study.

Another key aspect of the WS profile is increased social behavior (Jones et al., 2000; Klein-Tasman & Mervis, 2003). Children with WS appear to be more interested in social interactions than their neurotypical peers (Gosch & Pankau, 1994). The marked gregariousness of WS is characterized by social disinhibition: children with WS appear to have little to no reservations about engaging with or even following people they don't know (Gosch & Pankau, 1994). WS patients perform well on face recognition tasks and seem to be particularly sensitive to positive facial stimuli (Gagliardi et al., 2003). Notably, individuals with WS show significant deficits when asked to match facial expressions with emotions, potentially due to the minute changes in facial configurations associated with changing expressions, which could be tied to impaired understanding of spatial relationships, or more likely, another mark of aberrant social processing (Gagliardi et al., 2003). Alternatively, these findings could be explained by a delay in neuronal maturation, which aligns with findings from other cognitive areas that exhibit delayed processing and development (Gagliardi et al., 2003). Individuals with WS struggle to identify and recognize social threats and therefore exhibit low levels of social adaptation (Bellugi et al., 1999).

Even though WS is associated with a cheerful presentation, closer examination reveals high levels of anxiety within this population (Cherniske et al., 2004). To better understand the presence of anxiety within the WS population, researchers look to the amygdala, which reliably produces a fear response when presented with threatening visual stimuli, specifically threatening facial expressions

(Hariri et al., 2002). WS participants showed significantly lower levels of amygdala activation than controls when presented with the same threatening visual stimuli, which could explain the social dishinibition in WS (Meyer-Lindenberg et al., 2005). That said, higher levels of amygdala activation were observed in response to non-social stimuli, which could correspond to the overall higher levels of anxiety within the affected population (Meyer-Lindenberg et al., 2005). fMRI data illustrate decreased blood flow to the orbitofrontal cortex (OFC), an area which appears to be both structurally and functionally affected in WS (Meyer-Lindenberg et al., 2006). The amygdala receives cortical inputs from the OFC, which is an area within the prefrontal cortex that is involved in processing sensory information and active in decision making (Kringelbach, 2005). The OFC has also been linked to social cognition and hedonic processing, such as subjective reward (Kringelbach, 2005). While hypersociability in WS is likely multifaceted, neuroimaging data suggest that the structural and functional differences in the OFC contribute to the atypical social processing that is a hallmark of this disorder.

One factor that allows for heightened social behavior is effective language and communication, a key feature of the cognitive profile of WS (Meyer-Lindenberg et al., 2006). By adulthood, individuals with WS present with fluent language and verbal comprehension (Landau & Ferrara, 2013). Moreover, previous studies indicate that this population understands aspects of linguistic structure, including syntax, semantics, and morphology (Bellugi et al., 1994; Landau & Ferrara, 2013; Musolino et al., 2010). Individuals with WS score much higher on measures of linguistic production and comprehension than participants with other neurodevelopmental disorders, such as Downs Syndrome (Paterson, 2001). In individuals with WS, language production and comprehension are on par with mentally age-matched, typically developing controls (Zukowski, 2009). Analysis of children and adolescents with WS reveals that language acquisition adheres to the same trajectory as typically developing children; however, the process is delayed. For example, neurotypical children show an understanding of syntax at 4 to 5 years of age. The same pattern exists for children WS; however, a developmental delay is present, mirroring the developmental trajectory of other cognitive domains in WS (Musolino et al., 2010). Some researchers propose that among individuals with WS, language is ‘spared’ (Landau & Ferrara, 2013). This concept is misleading, and many researchers have refuted the idea that language is intact in WS (Karmiloff-Smith et al., 1997; Karmiloff-Smith et al., 1998). Within an impaired cognitive system, the knowledge and implementation of language ultimately reaches the low end of the normal range, which leads researchers to conclude that language and communication are spared in relation to other domains, such as spatial cognition (Pani et al., 1999). In other words, individuals with WS perform well on language tasks given that they often have an intellectual disability (Mervis & John, 2008). Because linguistic processing is less impaired than other domains in WS, its relative strength is a central characteristic of the disorder.

Strength in Symbolic Representations

The functional aspects of linguistic communication in WS allow for literacy acquisition, indicating that WS patients have the ability to understand symbolic representations, such as the connection between sounds, symbols, and meaning. While there is conflicting evidence within the current body of work regarding literacy in WS, multiple studies point to strong decoding skills, defined as the ability to integrate the letter-sound relationship when sounding out a word (Levy & Hermon, 2003; Mervis, 2009). That said, there is a wide range of literacy ability within the WS population: A subset of people with WS appear to read at a comparable level to controls, while some cannot read at all (Mervis & Velleman, 2011). Of note, IQ was strongly correlated with reading ability, which parallels the general population (Mervis, 2009). Children with WS who were taught to read by decoding, which uses a systematic, phonetic approach, scored higher in reading comprehension than children with WS who were taught to read using a whole-word approach (Mervis, 2009). While literacy rates vary among this population, strength in decoding abilities points to an underlying understanding of symbolic representations.

Individuals with WS appear to have a strong grasp of symbolic meaning through their understanding of language, as spoken language connects sound to meaning. Written communication, in the form of reading and writing, adds a layer of sophistication as visual symbols come together to represent words, which represent concepts (Sidhu & Pexman, 2018). Moreover, the grammar and syntax of written communication adds further nuance to the conveyed meaning (Sidhu & Pexman, 2018). Literacy, at any level, is a testament to the ability to process symbolic understanding.

As previously discussed, written and verbal communication are strong in WS, underscoring the ability to use and understand symbolic representations. Relatedly, numerical cognition provides an interesting avenue with which to explore symbolic vs non-symbolic understanding in WS. Mathematic abilities draw on two cognitive systems: the approximate number system (ANS), which allows for magnitude comparison without the help of symbolic representations, and a symbolic understanding of quantity, such as a verbal count list or Arabic numerals (Bonny & Lourenco, 2013). Individuals with WS perform well on tasks rooted in symbolic understanding, such as reciting a count list backwards and addition/subtraction problems (Van Herwegen et al., 2020). Moreover, individuals with WS performed better on a verbal magnitude comparison task than a non-symbolic magnitude comparison, providing evidence in support of symbolic understanding within this population (Krajcsi et al., 2009). While individuals with WS appear to have a relatively strong understanding of symbolic representations of mathematical concepts given their intellectual disability, they show particular weakness in areas of mathematical cognition that are intuitive to typically developing individuals, such as ANS-related abilities such as non-symbolic magnitude might pose an interesting challenge for individuals with WS, given that it draws the understanding and use of intuitive spatial representations.

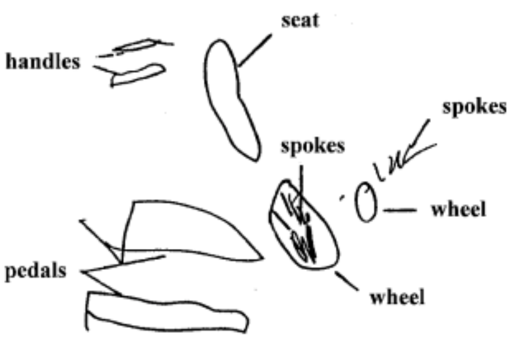
Visuospatial Construction

In the same way that language and numerical cognition can be represented symbolically, spatial properties can also be reduced to 2D visual representations. Visuospatial construction, defined as the ability to breakdown an object or picture into a set of parts in order to recreate it or visually portray it, represents the intersection between spatial abilities and symbolic representations (Farran & Jarrold, 2003; Mervis et al., 1999). For example, humans employ visuospatial cognition when asked to draw a scene, create a model, or assemble furniture, all tasks that require seeing a connection between individual pieces and a whole, a necessary step in creating and understanding symbolic representations (Mervis et al., 1999). While visuospatial construction is an essential cognitive domain, it seems to vary on an individual basis and in relation to intelligence (Mervis et al., 1999).

Impaired visuospatial construction is a hallmark of WS, manifesting in an impaired ability to maintain relationships between singular items, or parts, as they come together to make a whole (Farran & Jarrold, 2003). Visuospatial construction can be measured through drawings, pattern identification and generation, and block design (Frangiskakis et al., 1996). Early studies on adolescents (> 10 years) with WS show how affected individuals fail to reproduce a block pattern that typically developing 6-year-olds are able to reliably reproduce (Bellugi, 1988; Bellugi et al., 1994). The authors note how individuals with WS appear to hyper-focus on the local elements (e.g., the correct color block) at the expense of the global element (e.g., the whole pattern) (Bellugi et al., 1994; Pani et al., 1999). Some researchers attribute this deficit to deviant processing, citing interruptions in the dorsal processing visual stream responsible for encoding spatial relationships, while others argue that it is more similar to a developmental delay (Atkinson et al., 2001; Mervis et al., 1999).

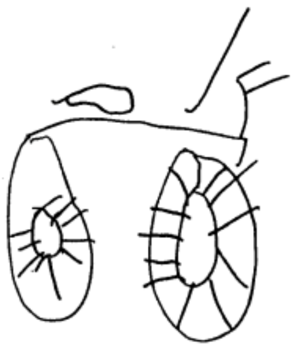
In a longitudinal study, Betrand and Mervis (1996) show how drawing skills in children with WS improve over time. Initial drawings are often unrecognizable. Participants show particular difficulty in connecting objects or parts into the complete scene, and thus struggle to maintain the spatial relationships between objects (Mervis et al., 1999). As seen in Figure 1a, the participant's first drawing reveals an overemphasis of local elements at the expense of the global elements: the individual parts of the bike are present, but the spatial relationships between the parts have been lost, making the picture unrecognizable. Interestingly, the participant spontaneously provided labels for her drawing and can provide a detailed verbal description of the object, highlighting the relative strength in verbal communication and the marked weakness in visuospatial cognition that is foundational to WS (Bertrand & Mervis, 1996; Mervis et al., 1999). The participant's second drawing (Figure 1b) is much improved: the spatial relationships between the local elements are accurate, making the picture recognizable (Mervis et al., 1999). Researchers who note improvement in visuospatial construction over time suggest that the WS progression mirrors the trajectory of a typically developing child, albeit greatly delayed (Bertrand & Mervis, 1996; Mervis et al., 1999). That said, some researchers turn to aberrant neuronal processing to explain the marked deficit in visuospatial processing (Atkinson et al., 2001; Bellugi et al., 1994). From a neurological standpoint, the interruptions in the visual processing stream in the WS model make it so that object recognition is intact, which allows for a hyper-fixation on local elements, but an understanding of the spatial relationships between the objects is disrupted, which results in deficits in global processing (Atkinson et al., 2001). An alternative argument posits that neither local nor global processing is disrupted; instead, individuals with WS struggle to switch back and forth between local and global levels of organization (Pani et al., 1999). In any case, the ability to understand spatial relationships and recreate them or represent them on a 2D plane proves difficult for individuals with WS, indicating that their strength in symbolic representations does not extend to the field of spatial reasoning.

a.



Age: 9 years 7 months

b.



Age: 12 years 11 months

Figure 1. Two drawings of a bicycle by a child with WS at two timepoints. The child was given a piece of paper and pencil and asked to draw a bicycle. The child spontaneously provided labels for the first drawing (a). Visuospatial construction is markedly impaired in WS, but it improves with age (Mervis et al., 1999).

Relational Knowledge: Weakness in Geometric Relationships and Mental Rotation

Vulnerability in visuospatial construction sheds light on potential instability in the foundations of spatial cognition, bringing into question the core understanding of geometric relationships (Atkinson et al., 2001; Foti et al., 2020). A sample of 15 young adults with WS performed poorly when asked to compare or decipher distance, angles, and locations on a table-top task, which shows a clear deficit in comprehension of small-scale geometric relationships (Foti et al., 2020). When asked to recall the spatial properties of symbols and shapes, individuals with WS performed significantly worse than their age- and IQ-matched controls, providing further evidence for deficits in the domain of visuospatial processing, such as allocentric encoding of relational knowledge, which describes the spatial relationships between objects, independent of oneself (Vicari et al., 2005).

Spatial orientation is related to geometric reasoning as it builds on the understanding of the spatial relationships between points, lines, and distances within a form, and requires the observer to shift perspectives. Mental rotation, defined as the ability to perceive a 2D or 3D object and rotate it in space, develops with age and training and draws on a number of spatial skills such as depth perception and size estimation (Moen et al., 2020). As a more sophisticated spatial skill, object-based mental rotation is understandably severely affected in WS, highlighting an impaired ability to understand spatial orientation (Broadbent et al., 2014). Individuals with WS also struggle to recall the spatial configuration among object parts: when asked to reproduce an object or scene, they are able to reconstruct specific shapes but struggle to replicate the angles and distances between shapes that allow the average person to recall or identify familiar objects or scenes (Foti et al., 2020).

The current body of work highlights deficits in particular aspects of spatial cognition, such as relational knowledge and mental rotation. While these skills are clearly impaired in the WS profile, how much, if any, of the foundational components of spatial thought are spared? While it is expected that WS participants perform worse than typically developing participants, how much of the given task can they complete?

Strength in Object Recognition

Interestingly, non-spatial distinguishing visual features may aid WS patients in performing spatial tasks. The characteristic deficits in visuospatial construction are more dramatic in children than adults in the WS population, indicating that some improvements in this area of cognition take place over the course of development (Mervis & Klein-Tasman, 2000; Porter & Dodd, 2011). While children with WS are unable to produce recognizable replications of images they are presented with, they are able to recognize an image across varying levels of distortion, which illustrates the dichotomy between impaired spatial abilities and relatively intact image matching (Landau et al., 2006). This finding of impaired spatial abilities could be explained by selective neurological differences observed in one of the two visual processing streams between WS and typically developing controls.

Neurological Differences: Interruptions in the Dorsal Visual Processing Stream

The juxtaposition between spared object recognition and impaired encoding of spatial relationships points to specific interruptions or malformations within the visual processing system (Meyer-Lindenberg et al., 2006). In primates, the visual cortex supports two diverging pathways that have evolved to receive different types of visual information. The ventral pathway, which moves through the occipitotemporal region, is known as the ‘what’ pathway and is responsible for object recognition while the dorsal pathway, which moves through the occipitoparietal region, is known as the ‘where’ pathway and is responsible for computing an object’s location and spatial features (Ungerleider et al., 1982). WS affects an individual’s ability to understand spatial relationships, which indicates disruptions to the dorsal ‘where’ pathway; however, object recognition, which is localized to the ventral pathway, is relatively intact (Atkinson et al., 2003). In an fMRI comparison between WS and neurotypical controls, Meyer-Linderberg et al. (2004) found distinct hypoactivation in the parietal portion of the dorsal processing stream, and a gray matter volume reduction surrounding the occipitoparietal region, causing an interruption in the dorsal processing stream (Figure 2). The authors posit that such findings provide a neural correlate (Meyer-Lindenberg et al., 2004). Further exploration indicates that the relationship between phenotype and behavior may be confounded by differences in attentional control that are linked to hypoactivation in the frontoparietal region (Atkinson & Braddick, 2011). In sum, the visuospatial processing deficiencies observed in WS may be a result of more than dorsal-stream vulnerability.

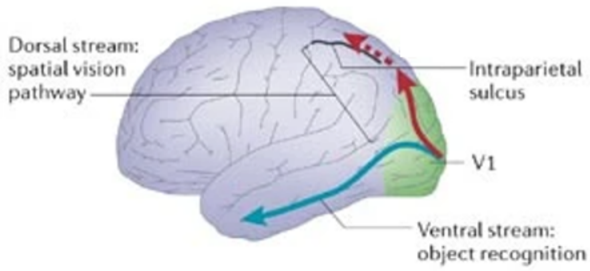


Figure 2. Impaired dorsal stream with intact ventral stream processing in WS. fMRI data shows structural and functional abnormalities around the intraparietal sulcus, which could explain the disruption in the dorsal steam. V1 represents the primary visual cortex (Meyer-Lindenberg et al., 2004).

Researchers look to the hippocampus, which plays a crucial role in spatial thought and navigation, to better understand the nuances of the WS profile.

Functional and metabolic differences have been found between individuals with WS and typically developing individuals; however, no significant differences in volume have been documented (Meyer-Lindenberg et al., 2005). The authors used faces and houses as visual stimuli, as faces preferentially activate the ventral processing stream and houses activate both the dorsal and the ventral processing streams (Grill-Spector, 2003; Meyer-Lindenberg et al., 2005). If hippocampal dysfunction is a result of impairments to dorsal stream processing, activation of the hippocampal formation in response to houses (Meyer-Lindenberg et al., 2005). The control group showed higher levels of activation for faces than houses, while WS participants showed a distinct lack of activation in response to either stimulus (Meyer-Lindenberg et al., 2005). Notably, a difference in bilateral anterior hippocampal formation activation could be seen between the control sample and the WS sample (Meyer-Lindenberg et al., 2005). If the hippocampus were intact but the dorsal processing stream was disrupted, one would see hippocampal formation activation in response to faces but not houses. The lack of activation in response to either stimuli shows hippocampal dysfunction independent from the visual processing streams. (Meyer-Lindenberg et al., 2006). It should be noted that such differences reflect neuronal activation; there is no strong evidence suggesting structural differences (i.e., volume loss) in the hippocampus that could account for impaired processing (Meyer-Lindenberg et al., 2005). Mouse models, which exhibit a WS-specific knockout, support the hypothesis that the WS region is involved in hippocampal function, although it does not seem to affect the structural formation of the hippocampus (Meng et al., 2002; Zhao et al., 2005).

That said, certain reductions in gray matter volume have been observed and documented across WS patients and may contribute to impairments in various cognitive domains (Meyer-Lindenberg et al., 2004). WS patients reliably show reductions in the intraparietal sulcus, around the third ventricle, and orbitofrontal cortex (OFC) (Reiss et al., 2004). The reduced intraparietal sulcal depth could be related to the marked deficits in spatial abilities, given the region's physical position within the dorsal processing stream, which is involved in computing location and spatial relationships (Meyer-Lindenberg et al., 2004). Moreover, functional deficits can be seen in this region as well: two studies cite hypofunction surrounding the affected intraparietal sulcus region (Glabus et al., 2003; Meyer-Lindenberg et al., 2004). The implications of reduced gray matter volume around the third ventricle remain unclear (Meyer-Lindenberg et al., 2006). While most gray matter reductions are associated with cognitive deficits, reductions in the OFC volume may account for poor social adaptation, as seen through hypersociability and high levels of anxiety observed in WS. (Meyer-Lindenberg et al., 2005). In this way, the genetic profile of WS appears to lead to differences in neurological structure and function that correspond in a relatively transparent way to the behavioral phenotype of the disorder.

Navigation in WS

The deficits in visuospatial processing extend beyond symbolic representations into real world navigation. In order to navigate an environment, an individual must gain an understanding of the environmental cues present and their position in relation to such cues (Foti et al., 2020). Successful navigation of an unfamiliar environment draws on egocentric and allocentric information, in which egocentric information describes spatial relationships to one's own position while allocentric information describes spatial relationships between various environmental features (Arleo & Rondi-Reig, 2007). Both cognitive faculties are employed during a navigation task.

The spatial deficits found in WS lead to interesting lapses in navigation behavior. Results from a real-world navigation experiment found that over a 1-kilometer course, individuals with WS perform significantly worse than typically developing individuals and individuals with a mild learning delay (Farran et al., 2010). Notably, the WS cohort performed better with verbal input at different junctions throughout the course, and after multiple trials, which indicates a learning effect (Farran et al., 2010). After verbal cues and additional training, the WS performance was equivalent to the control group. The WS cohort exhibited a poor understanding of spatial relationships between landmarks; while this score was significantly lower than the control, it did not differ significantly from the learning delay cohort, which is surprising given the specific deficit in spatial abilities among individuals with WS (Farran et al., 2010). These findings underscore two aspects of the WS profile: impairments in spatial processing, namely relational knowledge, and the marked strength in verbal communication.

Broadbent et al. (2015) discuss how landmarks could allow for practical navigation in WS, as individuals with WS can draw on object recognition to identify landmarks without employing the relational knowledge that requires an understanding of spatial relationships. Results from a route-learning study show a deterioration in the WS cohort's performance after landmarks were removed (Broadbent et al., 2015). Furthermore, the WS cohort made significantly more errors when learning a new route devoid of landmarks (Broadbent et al., 2015). Taken together, these findings highlight deficits in egocentric encoding of paths. The results also point to a reliance on landmark information, which could be supported by intact object recognition.

Peripersonal environments, in which an individual must navigate a small-scale, contained environment in pursuit of a goal location, pose an interesting challenge to individuals with WS. Foti et al. (2020) utilize a radial arm maze (RAM) task in which one version allows the participant "free choice" as each arm is accessible, while the other version calls on the participant to make a forced choice, as certain arms are physically blocked off. While the search efficacy was reduced in the WS cohort for both conditions, the deficit was greater in the forced choice paradigm as participants with WS made significantly more within-phase errors, which occur when the participant revisits an arm they had previously visited in the same trial, and across-phase errors, which occur when the participant revisits an arm they had visited in an earlier trial. In other words, individuals with WS revisited arms of the maze that they had previously visited and found to be unsuccessful, which reinforces deficits in working memory, or suggests an inability to distinguish different paths from one another in the forced choice task, pointing to a poor understanding of the geometry of the space (Foti et al., 2020). Interestingly, the WS cohort was able to successfully navigate the free choice paradigm, which the authors attribute to relative strength in procedural memory, or egocentric encoding (Foti et al., 2020). The difference between the WS cohort's performance in each condition highlights the distinct deficit in discerning spatial relationships and spatial problem solving. Once again, this disruption can be linked to neurological differences in the dorsal processing stream associated with WS. However, the potential deficit in spatial memory implicated in this study could extend into map-based navigation.

The WS population exhibits poor performance on tasks involving spatial perception and reproduction of spatial relationships, namely in the domain of visuospatial cognition. That said, WS patients appear to have a relatively intact understanding of symbolic representations, as seen through their written communication and numerical cognition. The juxtaposition of vulnerability and sparing in these essential cognitive domains leads us to question how WS patients will perceive spatial symbols and use symbolic representations of space to guide navigation. While certain elements of spatial cognition are conserved across species, other aspects, such as using symbolic information to guide behavior, are uniquely human. Given a map-reading task, WS participants may perform well given their strength in symbolic understanding. Alternatively, the WS cohort may perform poorly given the cognitive deficit observed in visuospatial construction tasks and egocentric navigation.

Map Use in Typically Developing Individuals

Map learning is an area of spatial cognition that could be feasible for individuals with WS, as it includes object recognition and written communication in the form of symbolic representations, two areas of cognition that remain intact in WS. Map-based navigation is a distinctly human behavior as it involves the ability to translate spatial information, such as the relationship between two environmental features, from 2D symbolic representations to 3D spaces. The ability to use maps to navigate large-scale environments emerges early in human development: children ages 3-4 years old appear to use map-based navigation successfully, which suggests an early-rising ability to process information from symbolic representations and apply it to real world environments (Huttenlocher et al., 1999). This concept is further substantiated by data from congenitally blind children who are able to use symbolic representations on a map to guide locomotion and reach a predetermined goal location (Landau, 1986).

Maps traditionally include two categories of information: visual, such as landmarks, and spatial, such as environmental geometry. Children are more successful at reading maps when they include simple geometric shapes and are devoid of complex objects or landmarks (Huang & Spelke, 2015; Shusterman et al., 2008; Winkler-Rhoades et al., 2013). As early as age 3, children are able to perceive distance, one of the most central understandings of spatial relationality, on a map and use that information to navigate an array (Huttenlocher et al., 1999). At the same age, children are also able to use angle information when presented on a map (Vasilyeva & Bowers, 2006). In addition to distance and angle, children as young as 2.5 years understand betweenness (i.e., between two objects) and distance relationships when presented on a map (Winkler-Rhoades et al., 2013). In a study of 5- and 8-year-old children, both age groups successfully used a landmark reference to perceive distance (near vs. far) between the landmark and a target, using that information to navigate (Presson, 1982). When the map was rotated upon presentation, the younger group struggled to apply the symbolic spatial information to the physical environment (Presson, 1982). In this way, the ability to decipher spatial information in maps and apply it to large-scale environments draws on a number of cognitive processes, namely judging distance and angle relationships between target locations. These results show that geometric understanding is more foundational than relational knowledge or mental rotation, both of which appear to develop later in typically developing individuals in map-reading tasks.

While young children exhibit what appears to be intuitive map use, older children display more sophisticated map-reading knowledge, which indicates map-reading skills increase and diversify throughout development (Huang & Spelke, 2015). A comparison between first graders, fifth graders, and college students illustrates how map skills increase dramatically with age (Hardwick et al., 1976). Notably, adults are able to mentally rotate cognitive maps in order to change perspectives, and they make fewer errors when asked to generate maps of new environments (Hardwick et al., 1976; Siegel et al., 1979).

Core Knowledge of Geometry

For centuries, researchers and philosophers have mapped the spatial elements of large-scale environments using symbolic forms. Euclidean geometry is built on symbolic representations of space, highlighting (Spelke et al., 2010). Researchers and philosophers have posited that an understanding of geometry is intuitive to humans (Hatfield, 1990). Recent cross-cultural work reinforces the idea that humans have an innate predisposition to understand geometric relationships. In an Amazonian indigenous group, adults and children were able to differentiate between geometric shapes and understand their symbolic relationships (Dehaene et al., 2006). Thus, even in the absence of formal, or westernized, education that places an emphasis on spatial and mathematical reasoning, humans exhibit an intuitive understanding of the points, lines, and angles that constitute geometry. In fact, children and adults in the Amazonian indigene group performed at a comparable level to American and French children and adults in simple geometric tasks (Izard et al., 2011).

What does it mean to say that geometry is intuitive? When comparing two forms, one innately understands that if the two forms differ, then a difference exists in distance (or length), angle, or orientation (i.e., directionality; Figure 3). Conversely, if two forms have the same distance, angle, and orientation, they are congruent (Spelke et al., 2010).

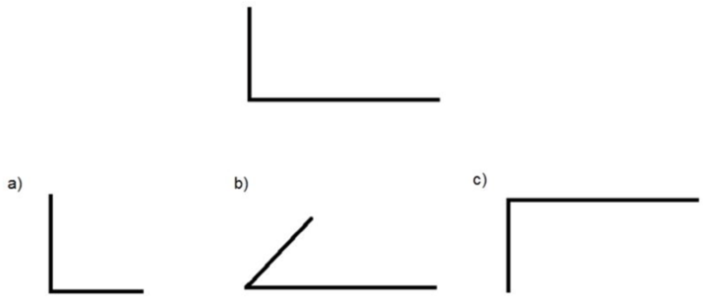


Figure 3. Fundamental properties of Euclidean geometry. If two forms are identical, they can overlap completely. If they are not identical, they differ in length (a), angle (b), or directionality (c) (Klein, 1893).

Geometry as the Foundation for Spatial Cognition

Geometry is one of the most foundational schemas of spatial understanding (Spelke et al., 2010). Both human children and animals primarily rely on geometric information when building a cognitive map and matching it to their environment, indicating that it is the most basic form of representing space (Cheng, 1986; Hermer & Spelke, 1996; Hermer & Spelke, 1994; Lee et al., 2006). Various species such as fish, monkeys, chicks, pigeons and human children use geometry to reorient, or recover the appropriate cognitive map (Gouteux et al., 2001; Kelly et al., 1998; Lee et al., 2006; Sovrano et al., 2002; Vallortigara et al., 1990). Young children prioritize geometric information over landmark information when asked to reorient (Hermer & Spelke, 1996; Hermer & Spelke, 1994). Moreover, humans appear to have an innate ability to understand geometry when represented symbolically (Dehaene et al., 2006; Shusterman et al., 2008). Children use landmarks as a direct indicator of an object's location; however, they are reluctant to use landmarks as a relational cue by which to reorient in a given space (Lee et al., 2006). These findings reinforce the concept that basic Euclidean geometry is arguably the most foundational understanding of space, while relational processing, such as directionality in relation to a landmark, is a more sophisticated process that develops later on.

Given that typically developing children as young as 3 years old use geometric information in the form of distance (Huttenlocher et al., 1999) and angle (Vasilyeva & Bowers, 2006) in various reorientation studies, Lee, Sovrano and Spelke (2012) set out to test 2-year-old children's sensitivity to basic elements of Euclidean geometry individually in a reorientation task. The authors used a range of fragmented rhombic and rectangular environments to test angle, distance, surface length, and direction. The fragmented boundary allowed for the separation of absolute distance from surface length. Their results showed that children successfully used distance and direction to reorient, but failed to use surface length or angles. These findings show that young children incorporate some concepts of Euclidian geometry into reorientation and the formation of cognitive maps, but fail to incorporate others, suggesting the ability to use these concepts improves across development (Lee et al., 2012).

Cell Types Underlying Spatial Sensitivity

Various hippocampal cell types respond to and encode for different spatial properties. Because WS affects hippocampal function, individuals with WS may not show the same sensitivity to core spatial properties as typically developing individuals. Animal research provides substantial information regarding the development of cells attune to certain spatial qualities, such as place cells, head direction cells, boundary cells, and grid cells in the hippocampus (Julian et al., 2018). Such cells allow an individual to determine their own location within an environment and help encode spatial memories (Moser et al., 2015). Place cells, which are active when an animal enters a specific area known as a place field, were first identified in the rat brain (O'Keefe, 1976; O'Keefe & Burgess, 1996; O'Keefe & Dostrovsky, 1971; Taube et al., 1990). Head direction cells exhibit consistent firing in response to directionality which seems to inform navigation (i.e., the ability to “stay on track”) and contribute to memory formation (Taube et al., 1990). Boundary cells fire when an animal approaches the environmental boundary(Lever et al., 2009). Grid cells are active at specific intervals as an animal moves throughout an environment, thus providing a sense of distance (Moser et al., 2014). These findings about the firing properties of different types of hippocampal neurons concretely show sensitivity to different spatial properties that are conceptualized through the geometric relationships of distance, angle, and sense, defined as left-right directionality.

While hippocampal dysfunction has been documented in WS and presumably has implications for navigation behavior, we do not know exactly which spatial perceptions are affected, nor which underlying cell types might be implicated. How much of the core understanding of space is intact in WS, a disorder in which spatial impairments are highlighted throughout the research and clinical narrative?

The Present Study

Theories and empirical evidence about core knowledge of space help establish a framework for exploring which aspects of spatial cognition are spared and which are vulnerable in WS. The present study explored how individuals with WS would perform on a map-reading task and how they would interpret geometric information included in maps. Notably, people with WS show deficits in spatial processing but strength in understanding symbolic representations (Atkinson & Braddick, 2011). Maps include both symbolic information and spatial information. Within spatial cognition, WS patients fare better when asked to process local levels of organization than global ones, a pattern which points to intact object recognition paired with a poor understanding of spatial relationships or relational knowledge (Porter & Coltheart, 2006).

Given that humans appear to have a highly conserved ability to understand geometry, we asked whether individuals with WS would have the ability to perceive geometric information on a map and use that information to navigate real-world arrays. Furthermore, we asked whether WS patients would understand certain geometric relationships better than others, when the spatial relationships included distance, surface length, and angles.

Four conditions were designed to test sensitivity to distance between objects, surface length, (which is denoted by a length of a wall instead of the relational distance between two objects), angles, and a landmark. Each condition had a distinct map and corresponding array. Each map represented a triangular array with one unique corner (A) and two identical corners (B and C). Performance at Target A helps to illuminate direct use of the spatial information, while performance at Target B is indicative of relational knowledge (i.e., left or right of the unique container). Due to intact ventral stream processing, we hypothesized that individuals with WS would perform best when given a map with a landmark feature. We did not have prior hypotheses about the other three conditions, as it is unknown how individuals with WS interpret the core geometric properties of distance, angle, and sense.

Research Questions:

1. Will WS participants succeed on a map-reading task, as indicated by above-chance performance?
    a. Will WS participants perform above chance at Target A, showing that they understand the correspondence between spatial information presented symbolically in a map and the matching real-world array?
    b. Will WS participants perform above chance at Target B, showing the ability to use the spatial information as a relational cue?
2. Will WS participants perform worse in certain conditions than other conditions, exposing specific areas of vulnerability?

Methods

Author Contributions

With the shutdown of in-person child data collection during Covid-19, the project I initially proposed for this master's thesis was not viable. As a result, we contacted collaborators who had data in need of further analysis. Sang Ah Lee and Marilina Mastrogiuseppe graciously shared their data, expressing that there might be subtle patterns that had not been identified. An initial analysis of these data was reported in an undergraduate thesis from Korea Advanced Institute of Science and Technology. The current analyses and interpretation, conducted in partial fulfilment of the MA degree, add to the existing work by adding a linear mixed effects model that accounts for repeated measures, analyzing error patterns, and conducting a more nuanced analysis of sex differences.

Participants

The sample consisted of 26 children and adults with WS (13 female; mean age = 22 years; 2 months, range = 6;6 – 41;9) and 51 typically developing children (24 female; mean age = 7;11, range = 3;8 – 13;0). All participants were from Italy and were tested in 2016.

Typically Developing Children

Typically developing (TD) control children were tested at the Developmental Cognitive Neuroscience Lab of the Center for Mind/Brain

Sciences, University of Trento (Rovereto, Italy). They were recruited either from Rovereto and surrounding areas or by contacting families of children who had previously participated in studies at the lab. Participants were welcomed into the Lab, where toys and books were made available in order to familiarize the child with the environment. Parents were then briefed on the purpose of the study, the length of it and advised to ask any question they might have, and informed consent was obtained. After playing freely for a couple minutes with the experimenter, the child was encouraged to follow him/her in the adjacent experimental room while the parent was invited to watch the live video-recording on the lab's computer. Child and experimenter then moved to the experimental room.

Williams Syndrome Children and Adults

The WS participants belonged to two different Italian Williams Syndrome associations: AGSW (Associazione Genitori Sindrome di Williams) and AFSW (Associazione Famiglie Sindrome di Williams). Families were contacted by telephone or email after parents had agreed to have their child participate in the study. Subjects were tested two different yearly WS retreats in Fano and Peschiera, Italy in 2016. Importantly, in each location the same experimental environment was recreated in terms of room size and landmark positions.

Consent

The study was conducted in accordance with the guidelines of the Human Research Ethics Committee of the University of Trento (internal review board approval No. 2016-005). The experimental protocol was approved by the internal review board, and informed consent was obtained from both the participants and their parents or legal guardians. Participants were rewarded with a little toy of their choosing for participating.

Leiter Brief Intelligence Task

The Leiter Brief Intelligence Task was used to measure the mental age of WS patients. This task is often used to assess the mental age, and cognitive skills, of children with neurodevelopmental disorders such as autism spectrum disorder, ADHD, and general intellectual disability. The assessment is divided into two sections: attention and memory (AM), and visualization and reasoning (VR) (Scattone et al., 2012). Each section includes 10 subtests designed to target specific skills within the discipline, such as recalling a sequence of objects in AM, or forming a complete picture from fragments in VR. The test was administered by an experimenter but included limited verbal instruction to make it accessible for nonverbal participants. The stimulus was presented on an easel. The participant uses colorful cards and foam shapes to respond to the prompt (e.g., complete the form) (Scattone et al., 2012). The participant receives a composite score for each section (Farmer, 2013).

Materials and Procedure

Participants entered a 5-by-3m rectangular room. Four maps were used; each map included a different spatial element: distance, length, angle and landmark. Three cylinders (diameter = 13 cm, height = 13 cm) were placed within the space in a triangular formation; each served as a potential target. One cylinder was unique, separated by a spatial feature that was reflected on the map, while the other two cylinders were nonunique.

Training

The experimenter brought the participant to the starting position located at one end of a rectangular room, in front of a large door. Once the participant was standing in front of the door and facing the room, the experimenter placed a box in front of the child and showed them the drawing of a map (15 x 15 cm) with a single box and a little star drawn on it. The experimenter proceeded to give the instructions verbally: “Look, there is a map with a box and a little star drawn on it. Do you want to put this little toy where the star is on the map?” The procedure was repeated with two boxes of different colors to verify that the child had not placed the toy correctly at the first attempt because it was the only box available. Meanwhile, a second experimenter prepared the setting for one of the 4 layouts. Once the condition was prepared, the child was presented with 4 maps on which the 4 layouts were drawn. At this point the child had to choose the map that corresponded to the conformation of the layout. If they made a mistake, the child was corrected. Pre-testing was done prior to each condition.

Test

The task consisted of placing a toy inside one of the boxes, indicated on the map with a colored star. The experimenter showed the map to the child, pointing to the star while saying, "Look, there's a map with boxes drawn on it, and only inside one of them is a little star. When you feel ready, you can turn around and put this toy in one of the boxes behind you. Pick the box that is represented with the star on the map!" The maps were presented with either a 90- or 270-degree rotation, so the participant had to mentally rotate the map to match the environment. Children were not given feedback on their achievement nor were they warned about map rotation. The experimenter checked to make sure the child did not turn around to look at the map and layout alternately.

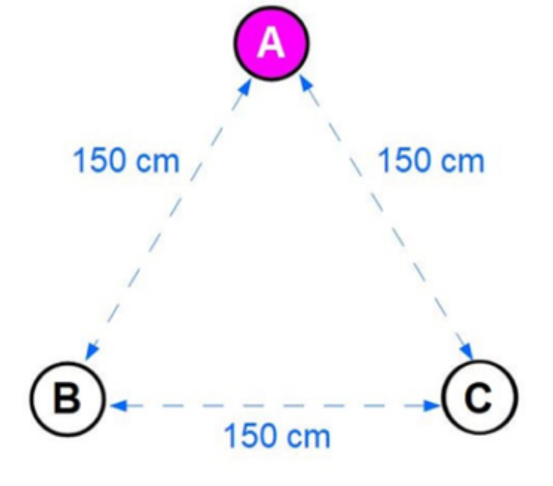
Each participant was given two trials at the unique cylinder (Target A) and two trials at one of the nonunique cylinders (Target B) in each condition. In this way, the two targets call on the participant to use the given information as a direct indicator of the goal location (for Target A) or as an indirect indicator with which to orient to (Target B).

While one experimenter changed the array of the room for each condition, another experimenter conducted a left/right assessment that was scored on a scale from 0 to 8. A mental rotation task was administered to the TD participants but not the WS participants.

Experimental conditions

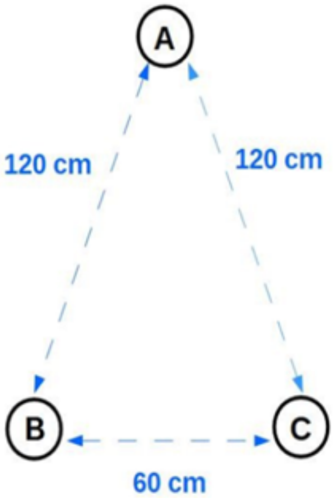
Landmark

In the landmark condition, the unique cylinder (Target A) was a different color from the other two. The color of Target A was the only defining characteristic, and therefore served as a landmark. The three cylinders were equidistant (150 cm) from one another in a triangular formation.



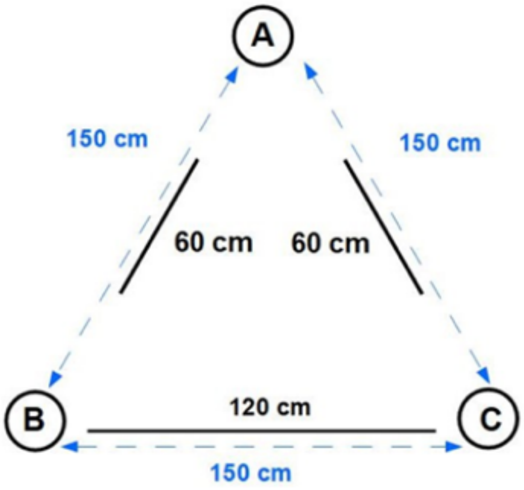
Distance

In the distance condition, Target A was placed farther away (120 cm) from the nonunique Targets B and C (which were 60 cm apart from one another). The defining characteristic for Target A was its distance; the three cylinders were identical.



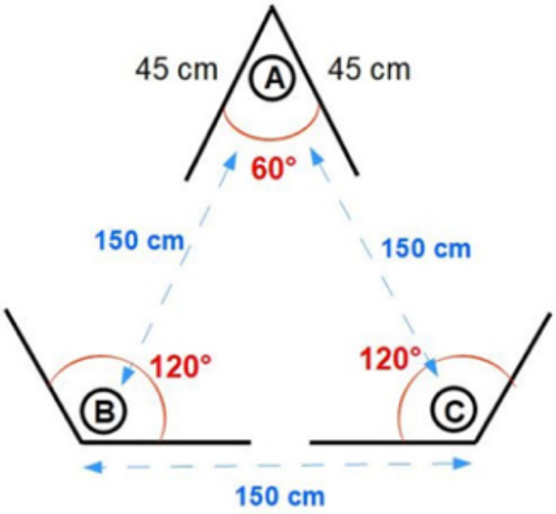
Length

In the length condition, Target A was between by two short walls (length = 60 cm, height = 50 cm) while Targets B and C were between a long wall (length = 120 cm, height = 50 cm) and a short wall. The three cylinders were identical and equidistant (150 cm) from one another; the only defining features were the length of the walls.



Angle

In the angle condition, Target A was backed by walls that formed a 60-degree angle. Targets B and C were backed by walls with the same length and height that formed 120-degree angles. The three cylinders were identical and equidistant (150 cm) from one another; the only defining feature was the angle of the walls.



Data Coding

The experimenter was present throughout and scored the participants' performance live. If the participant was incorrect at Target B, the experimenter noted whether they went to the geometrically equivalent Target C, and consequently made a sense error, or if they went to Target A, signifying confusion of the spatially unique target from the two that were distinguishable by sense (i.e., left-right directionality).

Results

Descriptive statistics for the WS sample and the TD sample are presented in Table 1.

Table 1

Participant demographics

			Chronological Age (years)			Mental Age (years)		
	n	Female	*M*	*SD*	*Range*	*M*	*SD*	*Range*
WS	26	13	22.17	8.68	6.52 – 41.73	6.36	1.19	4.08 – 8.96
TD	51	24	7.94	1.97	3.66 – 12.96	7.94	1.97	3.66 – 12.96

Overall Performance Across Conditions

To see whether participants could relate the spatial information in the maps to the real-world arrays, we compared their performance across conditions to chance, which we considered to be 33.3% given that there were three targets. The TD participants, unsurprisingly, performed above chance in each condition: Angle, M = .78, SD = .41, $t(50)$=15.74, $p < .001$; Distance, M = .72, SD = .45, $t(50)$=12.63, $p < .001$; Landmark, M = .80, SD = .40, $t(50)$=16.68, $p < .001$; Length, M = .78, SD = .41, $t(50)$=15.4, $p < .001$. WS participants also performed above chance in each condition: Angle, M = .58, SD = .49, $t(25)$=5.07, $p < .001$; Distance, M = .53, SD = .50, *t*(25)=4.24, $p < .001$; Landmark, $M = .70$, $SD = .46$, *t*(25)=6.25, $p < .001$; Length, $M = .67$, $SD = .47$, *t*(25)=7.42, $p < .001$. See Figure 4 for a visualization of performance.

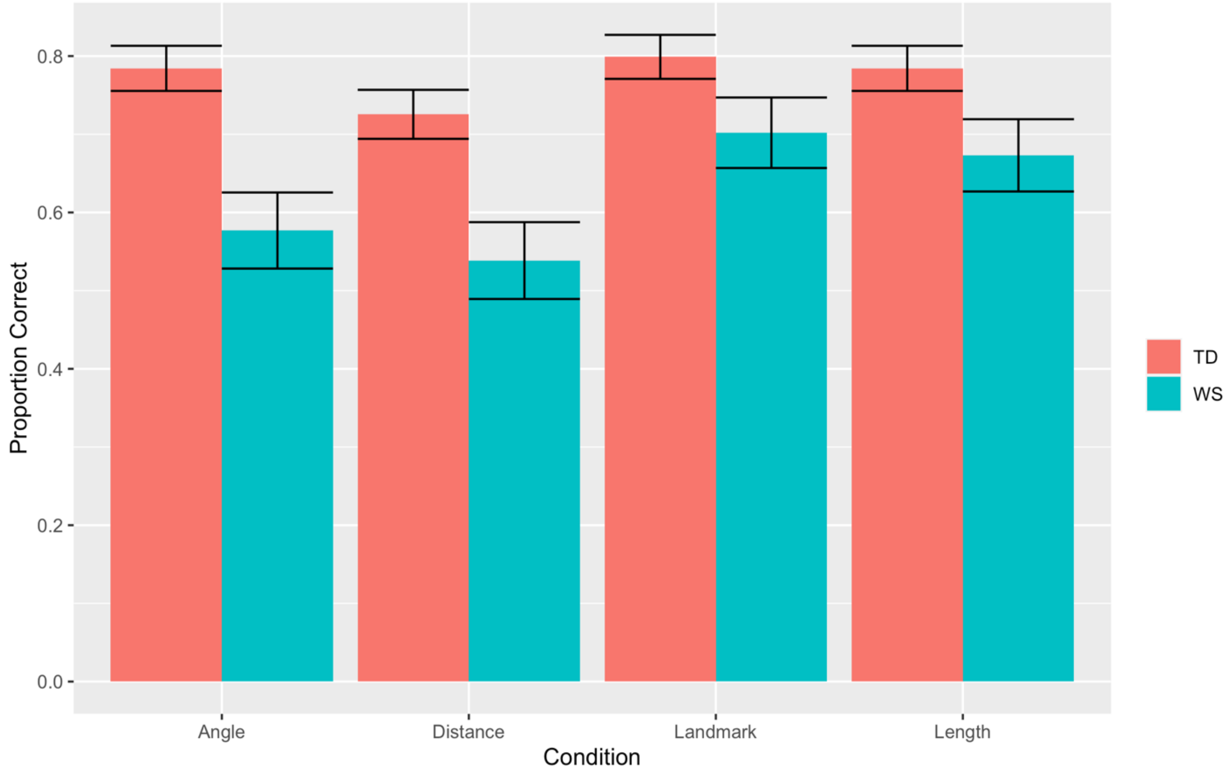


Figure 4. Mean performance by condition and population type. While the WS cohort scores lower than the TD cohort, the performance profile is above chance and relatively similar between the two groups. Error bars represent standard error. TD = typically developing; WS = Williams syndrome.

Performance by Target

We next compared the WS cohort's performance at each Target to chance (Figure 5). We found that WS participants performed above chance at both Targets A and B in each condition except at Distance B: Angle A, *M* = .69, *SD* = .47, *t*(25)=5.61, *p* < .001; Angle B, *M* = .46, *SD* = .50, *t*(25)=1.88, *p* = .03; Distance A, *M* = .63, *SD* = .49, *t*(25)=4.5, *p* < .001; Distance B, *M* = .44, *SD* = .50, *t*(25)=1.61 *p* = .056; Landmark A, *M* = .90, *SD* = .30, *t*(25)=13.9, *p* < .001; Landmark B, *M* = .50, *SD* = .50, *t*(25)=2.43, *p* = .0094; Length A, *M* = .81, *SD* = .40, *t*(25)=8.66, *p* < .001; Length B, *M* = .54, *SD* = .50, *t*(25)=2.99, *p* = .0022.

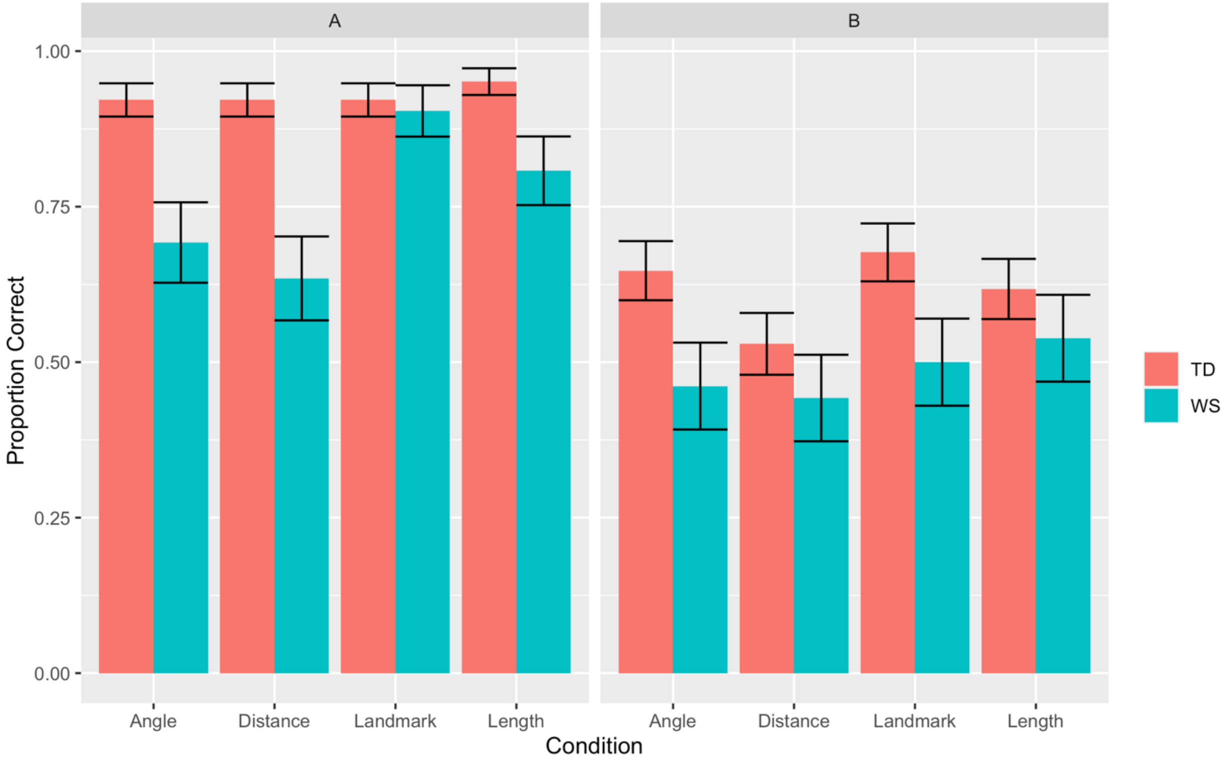


Figure 5. Performance at Target A (left) and B (right) in each condition by population. Participants in both groups perform better at Target A than Target B. TD = typically developing; WS = Williams syndrome.

Results from Mixed Effects Model

Table 2

Coefficient estimates from the linear mixed effects model predicting performance in each experimental condition.

	Coefficient	*SE*	*p(|z|)*
WS	-2.54	0.42	**<.001**
Chronological Age	0.033	0.016	**0.039**
Target B	-2.18	0.22	**<.001**
Sex M	-0.20	0.22	0.36
Angle	-0.33	0.20	0.10
Distance	-0.64	0.20	**0.0015**
Length	-0.13	0.20	0.53
Interactions:			
WS: Target B	0.83	0.32	**0.0090**
WS: Sex M	1.31	0.37	**<.001**

Note. For the condition variable, landmark is the reference category. Comparisons that were significant at the $p<.05$ level are in bold.

We next tested for effects on performance of population (TD vs WS), Condition (Landmark, Distance, Angle, Length), Target (measuring direct or indirect use of the unique feature), sex, and chronological age, as well as mental age. To account for repeated measures, we conducted a linear mixed effects model predicting performance. Predictors included: Population type (TD or WS), Condition, Target, Chronological Age, and Sex as fixed effects, and subject number as a random effect (Table 2). We compared this model to one that included Mental Age as an additional predictor and found that Mental Age did not significantly improve the model fit ($X^2(1) = 0.14$, $p = .71$). The optimizer was set to "bobyqa" to optimally distribute variance.

There was a significant effect of chronological age ($b = 0.033 \pm 0.016$, $p = .03$), with performance increasing as participants got older for both TD and WS participants (Figure 6). It should be noted that the age range was much greater in the WS population (Table 1).

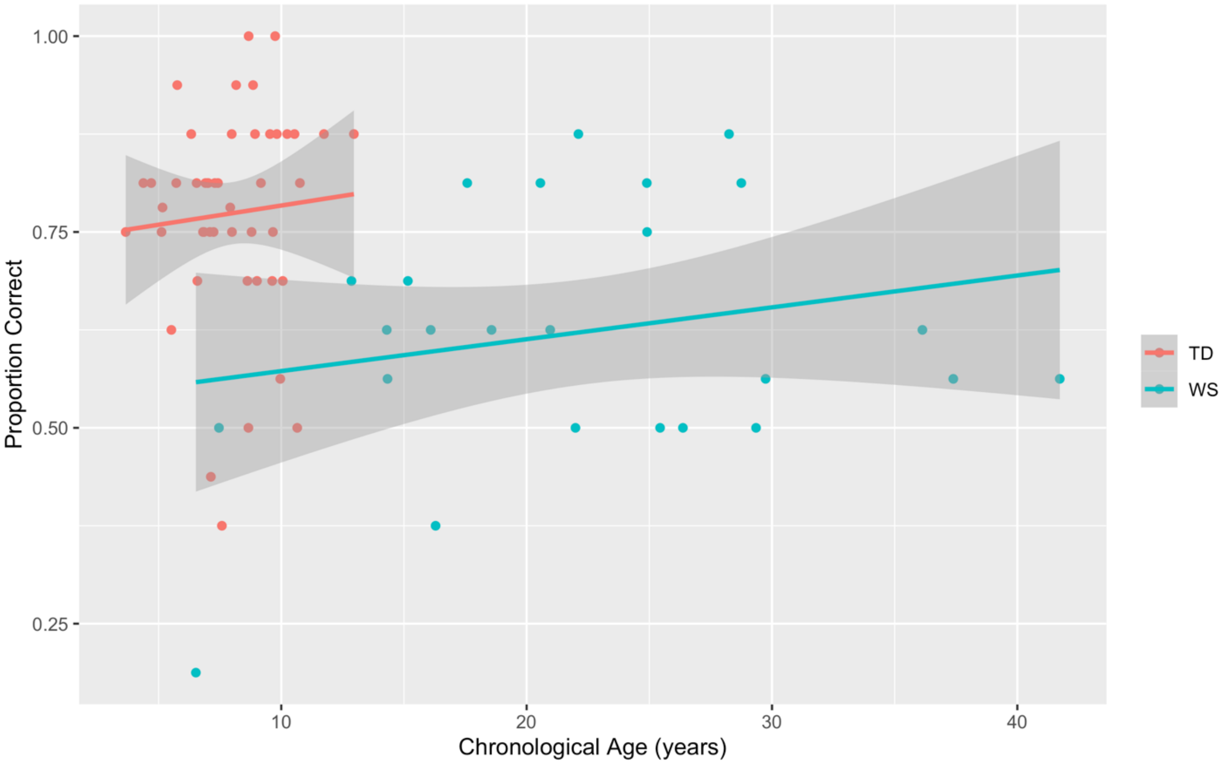


Figure 6. Performance as a function of chronological age for each population. Performance increases with age for both TD and WS participants. The WS cohort spans a greater age range than the TD cohort, but the WS cohort's mental age is comparable to the mean chronological age of the TD cohort. TD = typically developing; WS = Williams syndrome.

There was a significant effect of WS ($b = -2.54 \pm 0.42$, $p < .001$). After finding a significant effect of WS, we used Independent T-Tests to see how WS participants compared to TD controls in each condition. In the Angle condition, WS participants ($M = .58$, $SD = .50$) performed worse than TD participants ($M = .78$, $SD = .41$), $t(177)=3.66$, $p < .001$. In the Distance condition, WS participants ($M = .55$, $SD = .50$)

performed worse than TD participants (*M* = .73, *SD* = .44), *t*(188)=3.21, *p* = .002. In the Landmark condition, WS participants (*M* = .70, *SD* = .46) performed at the same level as TD participants (*M* = .80, *SD* = .40), *t*(184)=1.83 *p* = .07. In the Length condition, WS participants (*M* = .67, *SD* = .47) performed worse than TD participants (*M* = .78, *SD* = .41), *t*(185)=2.04 *p* = .04.

Additionally, Target was a significant predictor of performance (*b* = -2.18 ± 0.22, *p* <.001). Participants performed worse at Target B, the nonunique cylinder, in all the conditions (Figure 5). There was a significant interaction between Target and Population type (*b* = 0.83 ± 0.32, *p* <.009), with WS participants particularly struggling at Target B (Figure 5).

We then used independent t-tests to see how WS participants compared to TD controls at Target B. At Angle B, WS participants (*M* = .46, *SD* = .50) performed worse than TD participants (*M* = .64, *SD* = .48), *t*(99)=2.20, *p* = .03. At Distance B, WS participants (*M* = .44, *SD* = .50) performed comparably to TD participants (*M* = .53, *SD* = .50), *t*(103)=1.02, *p* = .31. At Landmark B, WS participants (*M* = .50, *SD* = .50) performed worse than TD participants (*M* = .68, *SD* = .47), *t*(96)=2.10, *p* = .04. At Length B, WS participants (*M* = .54, *SD* = .50) performed comparably to TD participants (*M* = .62, *SD* = .49), *t*(100)=0.93, *p* = .35.

When analyzing conditions, it should be noted that Landmark was set to be the reference category as it does not include a geometric feature and can act as the control. There was a significant effect of distance (*b* = -0.64 ± 0.20, *p* = .002), indicating that all participants performed worse in the distance condition.

While there was not a general effect of sex, there was a significant interaction between sex and population type ($b = 1.31 \pm 0.37$, $p < .001$). It should be noted that this interaction is present in models that accounted for both chronological and mental age, which are comparable between males and females in the WS sample (Figure 7).

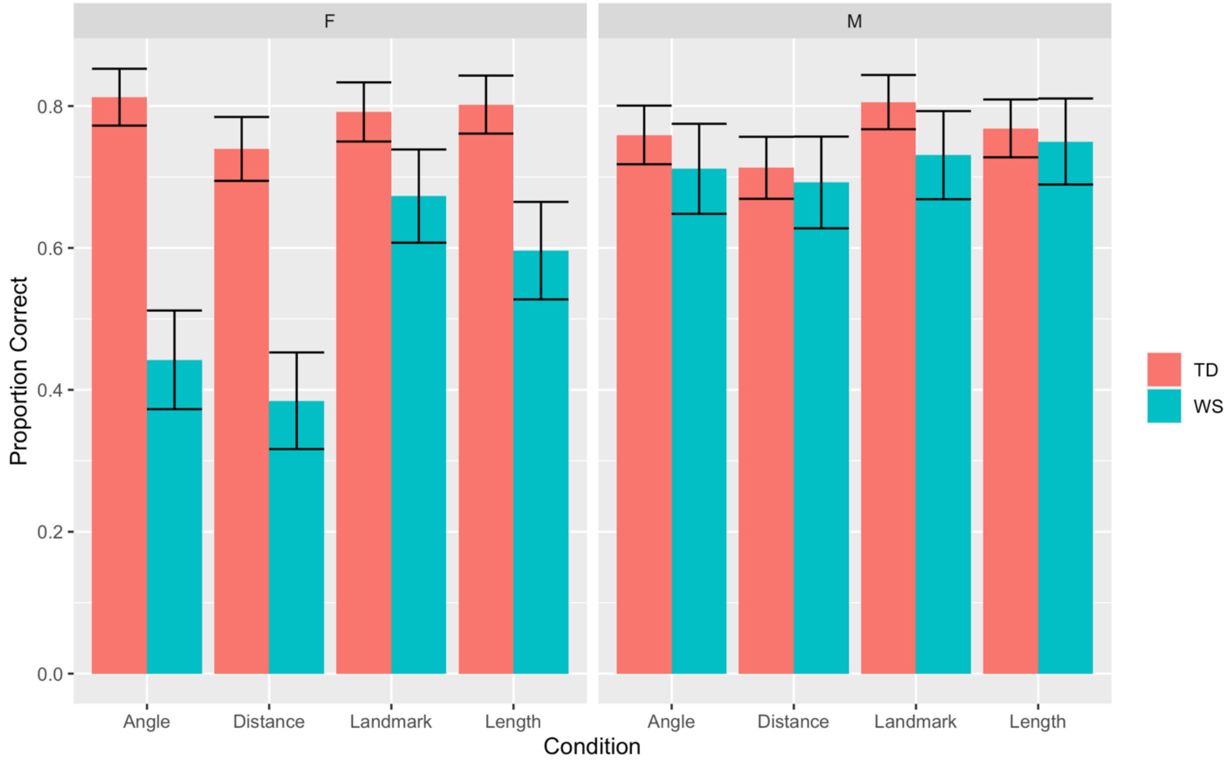


Figure 7. Performance by sex and condition. TD females (left) perform at the same level as TD males (right), while WS females perform at a deficit. Of note, WS males perform at the same level as TD males. TD = typically developing; WS = Williams syndrome.

To better understand the nature of this interaction, we conducted independent-sample t-tests comparing WS females to TD females in each condition. In the Angle condition, WS females (*M* = .44, *SD* = .50) performed worse than TD females (*M* = .81, *SD* = .39), *t*(85)=4.61, *p* < .001. In the Distance condition, WS females (*M* = .38, *SD* = .49) performed worse than TD females (*M* = .74, *SD* = .44), *t*(96)=4.35, *p* < .001. In the Landmark condition, WS females (*M* = .67, *SD* = .47) performed at the same level as TD females (*M* = .79, *SD* = .41), *t*(92)=1.52, *p* = .13. In the Length condition, WS females (*M* = .59, *SD* = .50) performed worse than TD females (*M* = .80, *SD* = .40), *t*(87)=2.58, *p* = .01.

We also conducted independent t-tests comparing WS males to TD males in each condition. In the Angle condition, WS males (*M* = .71, *SD* = .46) performed at the same level as TD males (*M* = .76, *SD* = .43), *t*(95)=0.63, *p* = .53. In the Distance condition, WS males (*M* = .69, *SD* = .47) performed at the same level as TD males (*M* = .71, *SD* = .45), *t*(99)=0.26, *p* = .79. In the Landmark condition, WS males (*M* = .73, *SD* = .45) performed at the same level as TD males (*M* = .81, *SD* = .40), *t*(90)=1.03, *p* = .31. In the Length condition, WS males (*M* = .75, *SD* = .44) performed at the same level as TD males (*M* = .77, *SD* = .42), *t*(98)=0.25, *p* = .80.

Post hoc models were designed to test for additional interactions, but none of the interactions were significant, and a comparison between the original model and more elaborate models showed that adding interactions did not significantly improve the model fit. We tested for interactions between population type and condition and saw no improvement in model fit ($X^2(3) = 2.33$, *p* = .51), between condition and target and saw no improvement ($X^2(3) = 2.72$, $p = .44$), and between target and sex and again saw no improvement ($X^2(1) = 2.35$, $p = .13$).

Analysis of Performance at Target B

Once participants ruled out the unique container (Target A), they had a 50% chance of selecting the correct nonunique container (Target B or C). With that in mind, we compared the proportion correct to 50% to see if participants were able to indirectly use the spatial feature to navigate to the correct nonunique container, or if they were performing at chance (i.e., selecting one of the two nonunique containers at random).

At Target B, TD participants performed above chance in the Angle condition, $M = .65$, $SD = .48$, $t(50)=3.09$, $p = .001$; the Landmark condition, $M = .68$, $SD = .47$, $t(50)=3.79$, $p < .001$; and the Length condition, $M = .62$, $SD = .49$, $t(50)=2.44$ $p = .008$. The only condition in which TD participants performed at chance was distance, $M = .53$, $SD = .50$, $t(50)=.59$, $p = .28$.

Conversely, at Target B, WS participants performed at chance in each condition: Angle, $M = .46$, $SD = .50$, $t(25)= -.55$, $p = .71$; Distance, $M = .44$, $SD = .50$, $t(25)= -.83$, $p = .79$; Landmark, $M = .50$, $SD = .50$, $t(25)= 0.0$, $p = .50$; and Length, $M = .53$, $SD = .50$, $t(25)= .55$, $p = .29$.

Sex Differences by Population and Target

Because there were significant interactions between Population and Target, and between Population and Sex, we decided to analyze performance by sex within the WS cohort exclusively (as there were no significant differences within the TD cohort) (Figure 8). At Target A, WS males performed above chance (33%) in all of the conditions: Angle, *M* = .88, *SD* = .33, *t*(12)=8.68, *p* < .001; Distance, *M* = .81, *SD* = .40, *t*(12)=6.06, *p* < .001; Landmark, *M* = .92, *SD* = .27, *t*(12)=11.13, *p* < .001; and Length, *M* = .92, *SD* = .27, *t*(12)=11.13, *p* < .001. At Target A, WS females performed at chance in Angle (*M* = .50, *SD* = .51, *t*(12)=1.70, *p* = .051) and Distance (*M* = .46, *SD* = .51, *t*(12)=1.32, *p* = .10), and above chance in Landmark (*M* = .88, *SD* = .33, *t*(12)=8.7, *p* < .001) and Length (*M* = .69, *SD* = .47, *t*(12)=3.93, *p* < .001).

At Target B, WS males performed significantly above chance (33%) in all conditions: Angle, *M* = .54, *SD* = .51, *t*(12)=2.09, *p* = .02; Distance, *M* = .58, *SD* = .50, *t*(12)=2.49, *p* = .01; Landmark, *M* = .54, *SD* = .51, *t*(12)=2.09, *p* = .02; and Length, *M* = .58, *SD* = .50, *t*(12)=2.50, *p* = .01. Contrastingly, WS females did not perform above chance at Target B in any of the conditions: Angle, *M* = .38, *SD* = .49, *t*(12)=0.56, *p* = .29; Distance, *M* = .31, *SD* = .47, *t*(12)=-0.24, *p* = .59; Landmark, *M* = .46, *SD* = .51, *t*(12)=1.31, *p* = .10; and Length, *M* = .50, *SD* = .51, *t*(12)=1.70, *p* = .05.

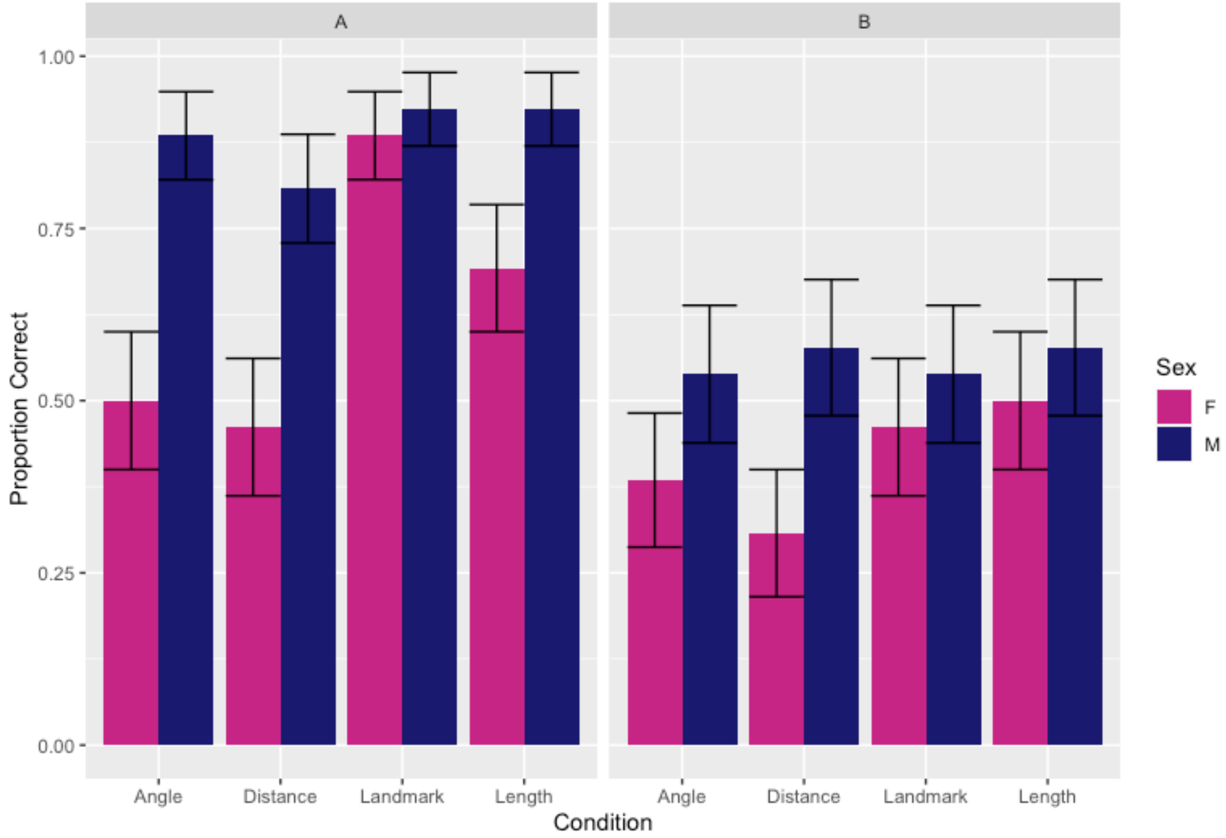


Figure 8. WS cohort's performance by Target, Condition, and sex. WS males perform better than WS females both at Target A (right) and Target B (left). WS females succeed at Landmark A, but struggle with the geometric conditions. TD = typically developing; WS = Williams syndrome.

Error analysis

Given that the structure of the array had two geometrically equivalent locations (Targets B and C), we analyzed the types of errors participants were making at Target B to better understand how they utilized the spatial information presented in the maps (Figure 9). We classified sense errors as going to the geometrically equivalent Target C instead of B, and oddball errors as going to the inequivalent Target A instead of B.

We designed a linear mixed effects model to predict error type (sense or oddball) at Target B. Predictors included: Population Type, Condition, Chronological Age, Sex, and Left/Right score as fixed effects, and subject number as a random effect (Table 3). There were significant effects of WS (*b* = 1.47 ± 0.55, *p* = .0076) and Distance (*b* = 1.32 ± 0.57, *p* =.022). Additional models were run to assess interactions between WS and Condition, and WS and Sex, but neither interaction was significant, and a comparison between models indicated that the model without interactions was the best fit ($X^2(3) = 2.47$, *p* = .65).

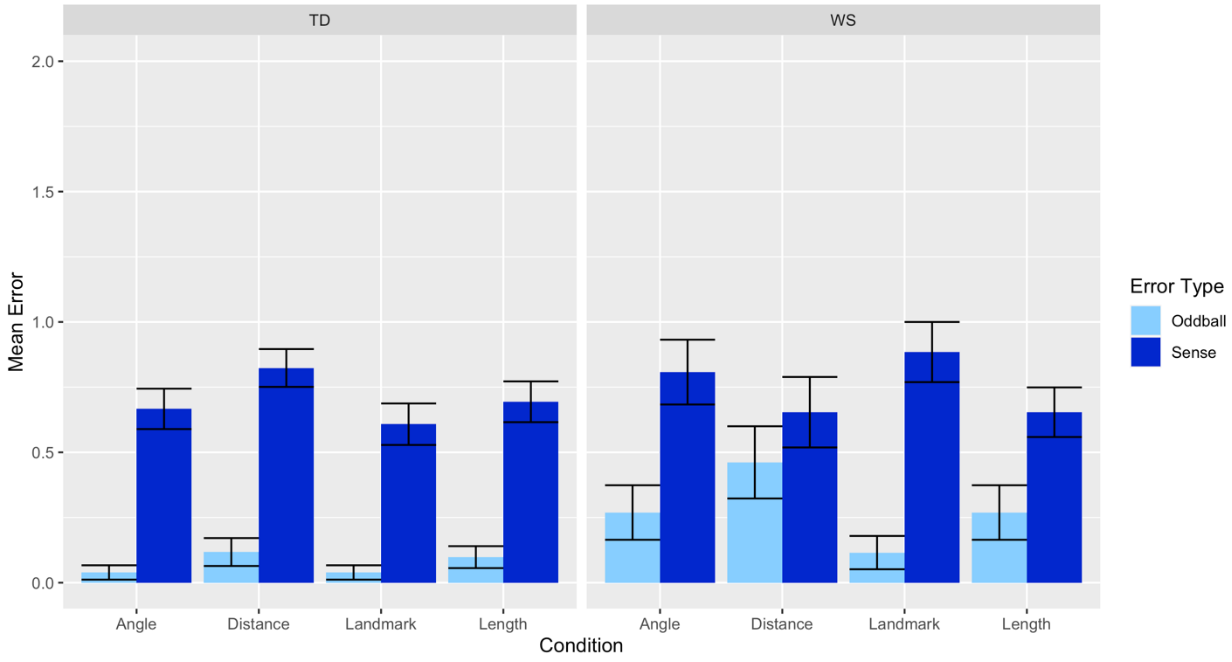


Figure 9. Mean error at Target B split by population and error type. The TD cohort (left) predominantly makes sense errors. The WS cohort makes a similar number of

sense errors, but they also make substantially more oddball errors. TD = typically developing; WS = Williams syndrome.

Table 3

Coefficient estimates from the linear mixed effects model predicting error type (sense or oddball) at Target B.

	Coefficient	*SE*	*p(|z|)*
WS	1.47	0.55	**0.0076**
Angle	0.62	0.62	0.32
Distance	1.32	0.57	**0.022**
Length	1.13	0.60	0.06
Chronological Age	-0.0068	0.028	0.80
Sex M	-0.56	0.41	0.17
Left/Right	0.059	0.10	0.57

Note. For the condition variable, landmark is the reference category. Comparisons that were significant at the *p*<.05 level are in bold.

Discussion

The WS profile is known for substantial deficits in the domain of visuospatial cognition. The results of this study support a more nuanced cognitive profile, highlighting areas of sparing and vulnerability that have not been previously identified in WS patients.

We first asked whether individuals with WS could use maps with symbolic geometry to navigate. We found that they could do so, with results above chance in all conditions. We then asked if WS participants would perform worse than TD participants, given the documented deficits in spatial processing (Atkinson et al., 2001; Meyer-Lindenberg et al., 2004). We found that they did indeed perform worse than the mental-age-matched controls. We finally asked whether the WS performance profile would be similar to or different from TD individuals. WS participants did not show a different pattern of performance than TD participants. In both groups, participants performed worse at locations that required relational spatial reasoning, namely Target B and the Distance condition.

Most importantly, our results show that individuals with WS have the ability to use maps to navigate in real-world arrays. Previous work documents spontaneous map use among young children, highlighting an early-rising ability to use 2D symbols to represent environments, including their geometric properties (Shusterman, Ah Lee, & Spelke, 2008). The parallel success between this WS cohort, which included children and adults, and typically developing young children underscores the hypothesis that foundational elements of spatial cognition, such as sensitivity to geometric representations and the intuitive ability to translate spatial information from maps to the real world, are spared in this disorder.

While researchers studying WS patients have overwhelmingly focused on spatial deficits, our findings show significant sparing in one of the primary facets of spatial thought: core knowledge of geometry. In addition to successful map use, we show that individuals with WS are sensitive to the geometric properties of distance, angle and directionality: the properties that constitute the foundation of symbolic spatial representations (Lee, Sovrano, & Spelke, 2012; Spelke et al., 2010).

Strikingly, WS participants were able to successfully navigate to Target A of the landmark condition, showing sensitivity to the symbolic information presented in the map. Object recognition is known to be spared in WS which might explain why these individuals are able to recognize the landmark object on the map and perform well when asked to directly match the object in the map to the object in the array.

While WS participants performed near-ceiling at Landmark A, they performed well above chance at Target A in the other conditions as well, showing an impressive baseline understanding of Euclidean geometry, since Target A was distinguished by Euclidean properties of length, distance, or angle. Target A assessed direct use of the geometric feature (i.e., the feature’s uniqueness), while Target B assessed the indirect use of the feature (i.e., positions to the left or right of the geometrically unique container).

Intact object recognition could explain why WS individuals would be able to identify and navigate to the landmark feature; however, object recognition does not explain the WS cohort's success in the geometric conditions. The hiding container in the geometric conditions was identical at Target A to the containers at B and C, so the only difference between Target A and the other two targets was the spatial property in use. Considering the WS performance profile in each condition, we argue for the sparing of two distinct systems that are foundational to spatial cognition: object recognition and geometric intuitions.

WS Performance Profile: Sparing of Core Spatial Knowledge

WS participants show sensitivity to angle, distance, and surface length both as symbolic representations in the map, and as geometric properties within the array, as seen through their above-chance overall performance in each condition. While the landmark condition draws on object-recognition skills, the other three conditions, Angle, Distance, and Length, draw on a core understanding of geometry. Given the documented deficits in spatial thought within this population, we hypothesized that WS participants would perform worse in the geometric conditions. Interestingly, this was not the case. While WS participants generally performed worse than TD participants overall, they did not show a greater deficit relative to TD participants in the geometric conditions as seen through the lack of interaction between condition and population. Herein lies the pattern of vulnerability and sparing. There is a deficit in the WS cohort's overall performance, showing vulnerability in spatial perception and navigation, but the pattern of performance mirrors that of the TD cohort. Overall, participants in both cohorts performed the worst in the Distance condition, and predominantly made sense errors at Target B, which indicates that they were able to discriminate between the unique Target A and the nonunique Target B. Because the broad pattern of results, including both correct trials and errors, between WS and TD participants is similar, we argue that the foundational elements of spatial knowledge are spared in WS.

Core knowledge of geometry seems to be a highly conserved cognitive ability, as geometric relationships provide a central framework to how humans understand space and navigate through it (Hermer & Spelke, 1994; Spelke et al., 2010). In contrast with well-documented deficits in visuospatial cognition in people with WS (Farran & Jarrold, 2003), these results support the hypothesis that individuals with WS have the ability to understand basic Euclidean properties. The preserved abilities seen here, specifically the sensitivity to symbolic Euclidean spatial relations, mirror those of typically developing children (Shusterman et al., 2008) and older populations that have not been exposed to traditional teaching of geometry (Dehaene et al., 2006). Because geometric intuitions appear to emerge spontaneously both in the WS population and these typically developing populations, we not only posit that such fundamental cognitive skills are intact in WS, we ask where the deficit occurs if the foundation of spatial thought is present.

Sparing and Vulnerability in Relational Knowledge

While humans exhibit an intuitive ability to understand and represent distance and angle relationships (Dillon et al., 2013), relational knowledge appears to be harder to conceptualize at an early age, and seems to improve over the course of development (Dillon & Spelke, 2018; Lee et al., 2006). Understanding of sense is, by definition, relational, as left and right have to be defined relative to another axis. WS participants particularly struggled with higher-level relational knowledge, as seen through their performance at Target B, paralleling the performance of very young children (Lourenco & Huttenlocher, 2008; Winkler-Rhoades et al., 2013). While the foundational elements of spatial thought may be preserved in WS, the more challenging components of spatial tasks (i.e., those that draw on more than spatial intuition) show a more intricate pattern of sparing and vulnerability.

Critically, WS participants demonstrate the ability to use the spatial information that is presented as a relational cue, as seen through their performance at Target B, albeit significantly lower than performance at Target A. WS participants perform significantly above chance at Target B in all of the conditions except for distance. Taken together, these findings lead us to believe that WS participants are capable of, if not entirely proficient in, a rather sophisticated line of spatial reasoning: WS participants not only could perceive geometric cues in a map, they were able to identify the corresponding geometry in a real-world array and use it as an indirect, relational cue by which to navigate to a goal location.

Relational knowledge, however, may extend beyond Target B. In the Landmark, Length and Angle conditions, the spatial feature in each condition is defined by an object. For example, the object in the Landmark condition is the distinct container; the objects in the Length condition are the walls with varying lengths; and the object in the Angle condition is the corner between the two walls. The Distance condition, however, breaks the pattern as it is purely relational: the distinguishing feature is the relative distance one target is away from the other two. As such, *both* Target A and B in the Distance condition draw on a relational processing. This could potentially explain why Distance proved to be the most challenging condition for both cohorts. TD children also performed worse in the conditions that drew on relational knowledge: the Distance condition, and trials at Target B. The parallel results between the WS and TD participants suggest that relational understanding is, universally, a more difficult process that develops later, in contrast with the foundational understandings of core geometric representations.

Relatedly, the Angle condition also may draw on higher-level spatial cognition because the acuteness of the angle is denoted by the relationship the two walls have to one another. In other words, the relative orientation of the two sides comprises the angle. Consequently, relational knowledge is needed to differentiate the two angles from one another. We intuited that because of the relational knowledge needed, Distance and Angle would be more difficult. While both populations struggled more in the Distance condition, neither population was particularly challenged by the Angle condition. This could be because the Angle condition is not *purely* relational as it includes objects (i.e., the walls making the angles). The conjunction of the walls could be seen as a physical object and thus could provide a visual cue, potentially drawing on object recognition skills that would enable the participant to use an element of directness (e.g., "at") even when the task was designed to elicit relational knowledge (Lee et al., 2012; Lever et al., 2009; Solstad et al., 2008).

Why might the performance profiles of WS participants be similar to that of TD participants? While individuals with WS appear to have abnormalities in hippocampal activation, our results indicate that some key neurons underlying spatial representation, such as boundary cells, vector trace cells, and place cells, may be preserved in WS. Intact boundary cells could be the reason why WS participants performed well in the Length condition, as the walls suggested an environmental boundary. Vector trace cells could explain sensitivity to angular relationships within the task, such as target differentiate in the Angle condition. Place cells could underscore the participant's understanding of their own location in relation to the spatial features. These data raise the possibility that aspects of the hippocampal network for representing space are relatively spared in WS; further research examining patterns of neural activation would be needed to better understand the connection between such neural networks and resulting behavior in WS. The question that begs further research is: if there is a preservation of the core understanding of geometry in WS but a deficit in overall performance on the map-reading task, what is the nature of this interruption, and what are the neural and genetic underpinnings?

Performance as a Function of Age

WS participants' performance improved with chronological age (Supplementary Figure 1), mirroring the delayed developmental trajectory of other skills such as visuospatial construction (Bertrand & Mervis, 1996; Porter & Dodd, 2011). The sensitivity to geometric forms and map-reading abilities seen in both the WS population and young typically developing population indicate that humans have an instinctual understanding of Euclidean geometry and symbolic representations, which come together to create the foundational skills of spatial cognition. Because these cognitive abilities are so highly conserved, humans do not necessarily have to learn them and thus exhibit these intuitions at a very young age (Dillon et al., 2013; Winkler-Rhoades et al., 2013). Individuals with WS appear to have the same foundational skill set, although they make more errors than TD participants. This suggests that, perhaps, the foundational skills of spatial cognition are paramount to evolutionary success and therefore are protected against the WS deletion. More sophisticated skills, however, such as relational knowledge, appear to be more fragile in WS.

Analysis of Errors

Because both populations made significantly more errors at Target B than at Target A, we conducted an error analysis to better understand which elements of the task they were struggling with. For each cohort, sense errors were by far the most common, indicating that sense is a less robust aspect of spatial understanding that develops later in typically developing individuals (Izard & Spelke, 2009). Notably, the overall pattern of errors differed significantly by population, with WS participants making the same number of sense errors as TD participants, but more oddball errors.

The oddball errors show vulnerability in the understanding of the spatial element present: if the participant goes to the unique container instead of one of the nonunique containers, their understanding of the spatial property that makes Target A unique is fragile. The fact that WS participants made more oddball errors than TD participants shows that even though their core knowledge of geometry appears to be preserved, it is not identical to that of typically developing individuals.

Sex Differences in WS

Our results also bring to light a startling sex difference in the WS population. To our knowledge, sex differences in spatial cognition or other cognitive domains have not been previously documented in the WS population. WS appears to affect males and females equally (Gito et al., 2015). Sex differences in WS have only been found in physiological domains, such as cardiovascular health, as opposed to cognitive domains (Sadler et al., 2001). Among typically developing individuals, some researchers argue in favor of sex differences within the broad field of spatial cognition (Geary et al., 2000); however, such subtle differences are not seen in children (Wynn et al., 1996). Mental rotation is the only spatial task in which males consistently outperform females (Collins & Kimura, 1997). That said, the findings are inconsistent and could be explained by gendered expectations within society (such as video game use, see (Feng et al., 2007)) instead of inherent ability, or biological predisposition (Schug et al., 2022; Wynn et al., 1996). While mental rotation abilities are needed to rotate the map at a 90-degree angle in the present study, the task was designed to test sensitivity to geometry rather than mental rotation. That said, the mental rotation element could have drawn out more pronounced sex differences in a population that appears to have a vulnerable set of spatial skills.

Apart from mental rotation, some researchers argue in favor of sex differences in the perception of Euclidean geometry (Cashdan et al., 2012). Interestingly, we found no difference in sensitivity to geometric information between TD males and females. We did, however, find a striking difference between WS males and females. The WS males performed at a comparable level to the TD participants, while the WS females performed at chance. The WS females drove the effect of WS, bringing the average score for WS males and females down substantially. Interestingly, WS females performed well at Target A of the Landmark condition, showing they are capable of performing the map-reading task, but they perform poorly at both Target A and B in the geometric conditions, indicating that they struggled with either perceiving the Euclidean geometry or applying it to the array. This difference cannot be explained by age: analyses of mental and chronological age show no difference between males and females within the WS cohort. The lack of a statistically significant difference in chronological or mental age between the males and females in the WS cohort could be due to a lack of statistical power. The variability in the WS females' chronological and mental age appeared to be greater than their male counterparts, which could begin to explain the performance deficit (Supplementary Figure 2). Alternatively, the effect could be the result of selection bias. For example, perhaps the men and women who attend (or skip) the WS conference are motivated by different reasons. If, for example, the women who attend experience more grave deficits and therefore are motivated to seek help, then the female participants in this study may not be representative of WS patients as a whole.

Limitations

A logistical limitation is that mental rotation data was not collected for the WS cohort. If there had been a sex difference on the mental rotation task among WS participants, that would indicate a potential area of weakness that might account for the WS females' deficit on the map-reading task. A conceptual limitation is that the Angle and Length conditions are constructed with walls that inherently have object properties in addition to geometric properties. This makes it more difficult to differentiate which element success can be attributed to.

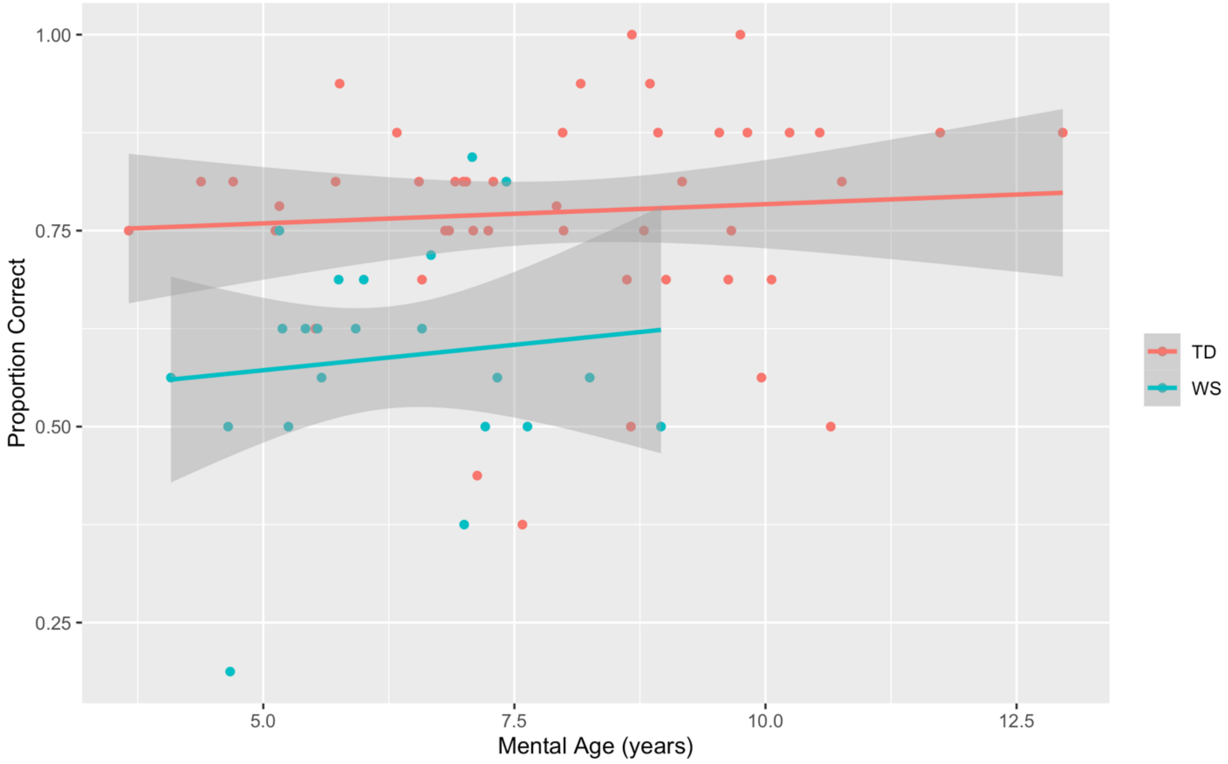
Future Directions

Further research is needed to corroborate the finding that core knowledge of geometry is preserved in WS. To separate perception of core geometry in a map from applying it to the array, one could measure WS participants' ability to judge distance between objects, angles, and lengths of lines in a comparison task (e.g., same or different). This would allow researchers to understand where along the pathway of map-based navigation the disruption is in WS. Future work should examine spatial-relational reasoning is possible that WS causes a delay in development instead of a distinct inability to complete certain tasks. The most notable area that warrants further research is the sex difference observed in this study. Because WS males perform at a comparable level to TD males on the map-reading task, the WS deletion is not solely responsible for impaired navigation. Instead, there is an interaction between WS and sex that places females at a disadvantage. Further research is needed to see if there are neurological differences between males and females with WS that could underly the difference in spatial abilities.

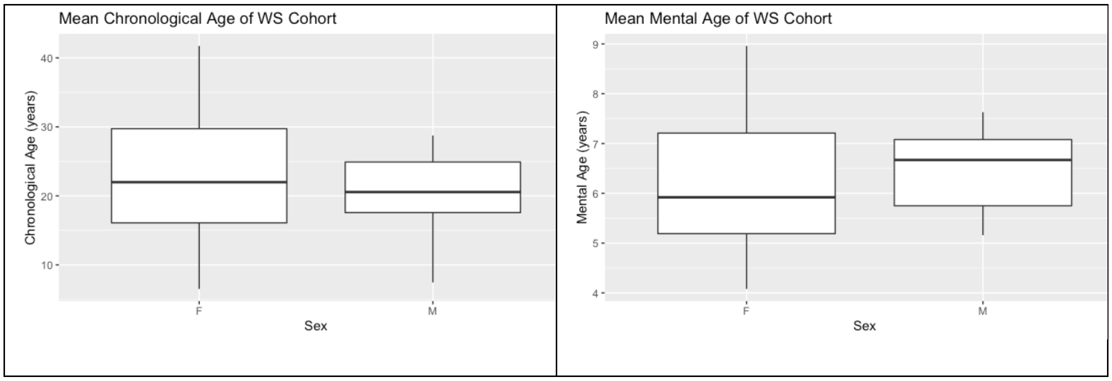
Conclusion

The cognitive profile of WS shows strength in verbal communication, which is indicative of symbolic understanding, and weakness in spatial cognition. The present study used a map-based navigation task to assess whether individuals with WS are able to use the spatial symbols to navigate the array, and are sensitive to the core geometric properties of angle, distance, and surface length. Strikingly, WS participants performed significantly above chance in each condition, which shows successful map use and perception of fundamental geometric relationships. While the WS cohort scored lower than the TD cohort, the WS performance profile generally reflected that of the TD group. The parallel performance between individuals with WS and typically developing children suggests that sensitivity to core principles of Euclidean geometry, one of the most foundational aspects of spatial thought, are present in the WS population. While WS participants exhibited strong foundational spatial abilities, their performance on tasks that drew on relational knowledge was substantially lower. Performance improved with chronological age, indicating that, perhaps, the spatial deficits noted in the WS population are more similar to a developmental delay, given that their intuitive spatial skills (e.g., understanding geometric representations) are similar to typically developing children. Notably, the effect of WS was driven by the WS females who perform substantially worse than the males across conditions. While there are numerous reasons as to why this finding occurred, further research is needed to substantiate a sex difference in spatial cognition, specifically map use and sensitivity to Euclidean geometry, in the WS population. While I argue that core geometry is preserved in WS, further research is needed to better understand the nuanced pattern of sparing and vulnerability.

Supplementary Figures: Chronological and Mental Age of WS and TD Participants



Supplementary Figure 1. Performance as a Function of Mental Age



Supplementary Figure 2. Mean Chronological and Mental age of WS participants.

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