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Working memory impairment in people with Williams syndrome: Effects of delay, task and stimuli

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ABSTRACT

Williams syndrome (WS) is a neurodevelopmental disorder associated with impaired visuospatial representations subserved by the dorsal stream and relatively strong object recognition abilities subserved by the ventral stream. There is conflicting evidence on whether this uneven pattern in WS extends to working memory (WM). The present studies provide a new perspective, testing WM for a single stimulus using a delayed recognition paradigm in individuals with WS and typically developing children matched for mental age (MA matches). In three experiments, participants judged whether a second stimulus 'matched' an initial sample, either in location or identity. We first examined memory for faces, houses and locations using a 5 s delay (Experiment 1) and a 2 s delay (Experiment 2). We then tested memory for human faces, houses, cat faces, and shoes with a 2 s delay using a new set of stimuli that were better controlled for expression, hairline and orientation (Experiment 3). With the 5 s delay (Experiment 1), the WS group was impaired overall compared to MA matches. While participants with WS tended to perform more poorly than MA matches with the 2 s delay, they also exhibited an uneven profile compared to MA matches. Face recognition was relatively preserved in WS with friendly faces (Experiment 2) but not when the faces had a neutral expression and were less natural looking (Experiment 3). Experiment 3 indicated that memory for object identity was relatively stronger than memory for location in WS. These findings reveal an overall WM impairment in WS that can be overcome under some conditions. Abnormalities in the parietal lobe/dorsal stream in WS may damage not only the representation of spatial location but may also impact WM for visual stimuli more generally.

1. Introduction

Williams syndrome (WS) is a rare genetic disorder characterized by physical anomalies, a friendly personality, and an uneven cognitive profile (Bellugi, Lichtenberger, Jones, & Lai, 2000; Mervis et al., 2000; Meyer-Lindenberg, Mervis, & Berman, 2006). This uneven profile consists of relatively strong skills on tasks related to social interaction, including visual tasks such as face recognition and the perception of biological motion, and severe deficits on other types of visuospatial processing, most often in block construction and drawing tasks (Atkinson et al., 1997; Bellugi, Lichtenberger, Jones, Lai, & George, 2001; Hoffman, Landau, & Pagani, 2003; Jordan, Reiss, Hoffman, & Landau, 2002; Landau et al., 2005; Reiss, Hoffman, & Landau, 2005; Tager-Flusberg, Plesa-Skwerer, Faja, & Joseph, 2003; Wang, Doherty, Rourke, & Bellugi, 1995). Previous evidence has indicated that the pattern of performance on visual tasks in WS may reflect selective damage to dorsal stream areas that subserve visual processing of 'where' or 'how' information (i.e., spatial location) with relative sparing of ventral stream areas in the temporal lobe that subserve visual processing of 'what' information (i.e., object recognition: Atkinson et al., 1997; Dilks, Hoffman, & Landau, 2008; Meyer-Lindenberg et al., 2004).

The present paper explores whether the uneven deficit in visuospatial tasks evident in WS extends to working memory (WM), with memory for location more impaired than memory for object identity, including face identity/recognition. We tested individuals with WS and typically developing children matched for mental age in three experiments using a delayed match to sample paradigm. Participants remembered either the location or the identity of the stimulus, similar to tasks used previously to examine perceptual processing in WS (Paul, Stiles, Passarotti, Bavar, & Bellugi, 2002). We tested memory for a single stimulus to simplify task demands for younger and lower functioning participants. To examine whether the uneven pattern was evident across memory demands, we used both a 5 s (Experiment 1) and a 2 s (Experiments 2 and 3) delay. To test the generality and specificity of the previously proposed expertise for faces in WS, we changed the

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set of stimuli used between Experiments 1/2 and Experiment 3. The new stimuli used in Experiment 3 included a wider range of stimulus types and face stimuli that were better controlled for hairline, orientation, and expression.

Paul and colleagues (2002) did a behavioral study using the well-established 'face/place' paradigm to examine the perception of human faces compared to locations in children, adults, and a group of individuals with WS. Since this paradigm is known to differentially activate dorsal and ventral streams in typical adults and children (Haxby et al., 1994; Passarotti et al., 2003), Paul and colleagues hypothesized that, if dorsal stream function was more affected by WS than ventral stream function, perception of location would be relatively more impaired in WS than the perception of human faces. Participants saw two stimuli and then, after a 0.5 s delay, judged whether the identity or the location of the third stimulus matched either of the previous ones. Their results suggested that the representation of location was more impaired than face recognition in WS, consistent with their hypothesis. While suggestive, there were several limitations to this experiment: the faces included hair which could be used for recognizing the faces without processing the internal features; it tested only face recognition not other kinds of objects; and the comparison to the control group was difficult to interpret, as the controls were not individually matched to the WS group on intellectual ability and were older (*M* age of 9-years-old) than controls in other studies (generally mental age matches are around 6 years of age—Jarrold, Phillips, & Baddeley, 2007; O'Hearn, Landau, & Hoffman, 2005; Vicari, Bellucci, & Carlesimo, 2006).

Evidence on the structure and function of the brain in WS supports the proposal of dorsal stream dysfunction (Eckert et al., 2005; Meyer-Lindenberg et al., 2004, 2006; Reiss et al., 2000). Studies of WS have reported decreased gray matter volume (Eckert et al., 2005; Meyer-Lindenberg et al., 2004; Reiss et al., 2000), sulcal depth (Kippenhan et al., 2005; Van Essen et al., 2006), and functional activation (Meyer-Lindenberg et al., 2004; Mobbs et al., 2004) in the parietal and dorsal occipital regions. For instance, a neuroimaging study of WS (Meyer-Lindenberg et al., 2004) used a face/place task to compare functional activation in the dorsal and ventral streams in adults with WS, who had IQs in the normal range, and controls matched on both age and IQ. This study used stimuli similar to that of Paul and colleagues, but with minimal hair included (same stimuli as those used in the present Experiments 1 and 2, from Haxby et al., 1994). Participants reported whether two sequential stimuli were at the same vertical position (i.e., location task) or were the same object (i.e., identity task) while in the scanner. No behavioral differences were found on either task. However, there were differences in the level of functional activation during the location task. The group with WS displayed decreased activation in bilateral parietal lobe when compared to controls during the location > identity contrast. While, controls exhibited significant activation in the parietal lobe during the location task relative to the identity task, individuals with WS did not. In contrast to these effects for the location task, the level of activation in ventral stream areas during the identity > location contrast did not differ between groups. Specifically, there were similar patterns of activation across groups in the temporal lobe for both face recognition (e.g., in fusiform face area, FFA) and house recognition (e.g., parahippocampal place area, PPA). A path analysis associated the differences in functional activation in the parietal lobe found in WS with decreased gray matter volume in the intraparietal sulcus (IPS), a dorsal stream area posterior to where significant functional activation was evident in controls.

Meyer-Lindenberg and colleagues' (2004) results suggest intact ventral stream function in people with WS for faces *and* houses, raising the possibility that the strength for faces in WS extends to houses and possibly other objects. A recent study using passive viewing with the same set of stimuli (Sarpal et al., 2008) also found that the pattern of activation in the ventral stream areas was comparable for individuals with WS and matched controls. However, Sarpal and colleagues also found differences between the two groups. People with WS showed decreased activation in dorsal stream areas (IPS) when they viewed houses, relative to viewing scrambled pictures (house > scrambled contrast), compared to controls. In addition, there were group differences in the functional connectivity between ventral stream and other regions, with the WS group exhibiting increased connectivity among temporal lobe regions and decreased connectivity between temporal regions and parietal and prefrontal cortex, compared to controls. While the group differences in functional connectivity was evident for both house and face stimuli, differences between the WS group and controls in the magnitude of activation in IPS was specific to the house stimuli, since face stimuli did not activate this area in either group. This result suggests that individuals with WS might show uneven ability across object types, with specific deficits evident with object types that activate the parietal lobe such as houses.

Vicari and colleagues propose that uneven performance is also evident across working memory (WM) tasks in individuals with WS, with WM for location more impaired than WM for identity (Vicari, Bellucci, & Carlesimo, 2003; Vicari et al., 2006). However, this claim is controversial (Jarrold, Phillips et al., 2007). WM provides short-term maintenance of immediately pertinent information, and is thought to be subserved by limited capacity storage buffers that are specialized for different types of information (Baddeley, 1993), including distinct visual WM stores for spatial location and object identity (Carlesimo, Perri, Turriziani, Tomaiuolo, & Caltagirone, 2001; Humphreys & Riddoch, 2001; Riddoch, Humphreys, Blott, Hardy, & Smith, 2003; Wilson, Clare, Young, & Hodges, 1997). One possibility is that uneven WM performance reflects uneven perceptual processes rather than WM per se, which may help account for the inconsistent evidence as perceptual demands differ across the studies. For instance, parietal lobe dysfunction in WS could impair the encoding of location information used for subsequent memory maintenance more than it affects the encoding of other types of information (Picchioni et al., 2007; Smith et al., 1995; Ungerleider & Haxby, 1994). Alternatively, the uneven impairment could extend to WM, possibly reflecting particular damage to dorsal frontal regions representing spatial WM and/or to frontoparietal circuitry (Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998; Courtney, Ungerleider, Keil, & Haxby, 1996; Haxby, Petit, Ungerleider, & Courtney, 2000; Munk et al., 2002; Sala, Rama, & Courtney, 2003; van Leijenhorst, Crone, & van der Molen, 2007). Impaired frontoparietal circuitry in WS could lead to decreased communication from parietal lobe to dorsal frontal regions required for spatial WM. This possibility is consistent with previous proposals that frontoparietal connectivity subserving visuospatial WM is impaired (Atkinson et al., 2003).

In the current study we tested whether, in a face/place task, WM for location was relatively poorer than WM for object identity in individuals with WS, as previously indicated by the work of Vicari and colleagues. To examine whether this profile was different across memory demands, indicating a WM impairment rather than perceptual encoding impairments affecting WM task performance, we varied the delay between Experiments 1 (5 s) and 2 (2 s). Also, on the basis of relatively normal performance with houses in Meyer-Lindenberg et al. (2004), we hypothesized that the relatively strong performance in WS on face recognition would extend to nonface objects. We first used faces and houses to examine this proposal because houses seemed the strongest test of our hypothesis: Houses are more likely to be impaired in WS than other objects because they are particularly spatial objects (Sala et al., 2003) and they engage hippocampal or parietal areas that are abnormal in WS