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Note

Dorsal-stream motion processing deficits persist into adulthood in Williams syndrome

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Abstract

Previous studies of children with Williams syndrome (WS) have found a specific deficit in dorsal cortical stream function, indicated by poor performance in coherence thresholds for motion compared to form. Here we investigated whether this is a transient developmental feature or a persisting aspect of cerebral organization in WS. Motion and form coherence thresholds were tested in a group of 45 WS individuals aged 16–42 years, and 19 normal adult controls.

Although there was considerable variation in the coherence thresholds across individuals with WS, the WS group showed overall worse performance than controls. A significant group × threshold condition interaction showed a substantially greater performance deficit for motion than for form coherence in the WS group relative to controls. This result suggests that the motion deficit is an enduring feature in WS and is a marker for one aspect of dorsal-stream vulnerability.

Keywords: Williams syndrome; Brain development; Motion coherence; Form coherence; Dorsal stream

1. Introduction

Individuals with Williams syndrome (WS) show a characteristic and unique cognitive and behavioural profile. Although there are wide variations across individuals with WS, they generally have IQ's between 50 and 90, with a relative sparing of expressive language, good visual object recognition (especially of faces), 'hypersocial' behaviour with generally 'friendly' personality traits, but poor performance on most visuo-spatial and constructional tasks (Atkinson et al., 2001; Bellugi, Bihrle, Trauner, Jernigan, & Doherty, 1990; Bellugi, Lichtenberger, Jones, Lai, & St George, 2000; Jones et al., 2000; Mervis et al., 2000). The syndrome is associated with a specific deletion on chromosome 7, and therefore provides a way to explore links between specific gene expression, brain development, and cognitive function (e.g., Bellugi et al., 1990; Bellugi, Lichtenberger, Mills, Galaburda, & Korenberg, 1999). However, while structural differences between WS and typically developing brains have been identified (Eckert et al., 2005; Mercuri et al., 1997; Meyer-Lindenberg et al., 2004; Reiss et al., 2004; Schmitt, Eliez, Bellugi, & Reiss, 2001), the brain basis of the cognitive profile is still far from fully understood.

It is now widely accepted that visual information in the primate cortex is processed through two distinct, yet interacting, processing streams (Milner & Goodale, 1995; Mishkin, Ungerleider, & Macko, 1983). From studies of non-human primates the *ventral* stream, projecting from primary visual cortex to the temporal lobe, performs the visual computations needed for the recognition of objects and faces (i.e., 'what' and 'who' tasks) and its intermediate stages (e.g.,

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area V4) show specific sensitivity to shape and colour information. The *dorsal* stream, projecting from primary visual cortex to the parietal lobe, performs computations needed to register spatial relationships relative to the observer and to provide the visual information needed for the control of spatially directed actions (i.e., 'where' and 'how' information). Its intermediate stages (e.g., area V5/MT) show sensitivity to motion and stereo information. Measures of global form and motion processing have therefore been taken as indicators of the function within extrastriate visual areas in the two streams (Atkinson et al., 1997; Braddick, Atkinson, & Wattam-Bell, 2003; Gunn et al., 2002); functional imaging results have supported this separation by demonstrating that global coherence of form and motion activate largely non-overlapping systems in posterior cortex (Braddick, O'Brien, Wattam-Bell, Atkinson, & Turner, 2000). However, these imaging studies suggest that the independent networks for form and motion both involve areas in occipital, parietal and temporal lobes, a rather different picture to the division, suggested by work with non-human primates with the ventral stream being primarily directed to the temporal lobes and the dorsal stream to the parietal lobes.

The profile of abilities in WS suggests that visual abilities subserved by the ventral stream, such as face recognition, are relatively well developed, whereas those subserved by the dorsal stream, such as visuospatial manipulation, are markedly impaired. Experimental identification of a specific dorsal stream deficit in WS was first provided by Atkinson et al., who showed that children with WS showed deficits in a visuomotor task (the 'mailbox' task) compared to a corresponding visual matching task (Atkinson et al., 1997), and in motion compared to form coherence thresholds (Atkinson et al., 1997, 2003). Since these initial results this 'dorsal-stream vulnerability' has also been found to characterise a number of other developmental disorders, including hemiplegia, autism, developmental dyslexia, and fragile X (e.g., Braddick et al., 2003; Gunn et al., 2002; Kogan et al., 2004; Spencer et al., 2000).

However, the identification of dorsal-stream dysfunction in WS children leaves open the question of the developmental course and ultimate outcome of perceptual and visuospatial skills in the disorder. Is the development of functions normally served by the dorsal stream merely delayed in WS, either because the mechanisms mature slowly or because, given time, WS individuals develop alternative neural routes for such performance? Alternatively, are dorsal-stream functions permanently impaired by an enduring difference between WS and typically developing brains in the absence of successful neural reorganization? Although the answers to these questions have yet to be found, studies have shown quite diverse levels of performance in the young WS groups (Atkinson et al., 1997, 2003), suggesting that the WS phenotype does not lead to a fixed outcome for 'dorsal' processing, but rather that alternative strategies or pathways can be developed.

Williams syndrome has aroused wide interest as an example of genetically determined anomalous cognition. However, its neurocognitive phenotype has to be understood as the result of a developmental cascade, not as a simple expression of a genetic anomaly (Karmiloff-Smith & Thomas, 2003). It is important, therefore, to examine processes of developmental change and stability in the disorder, not simply snapshots at a given stage of development.

In the present study we use global motion and form sensitivity tests with adult WS individuals to assess the developmental course of these abilities. The group tested have shown the ability to participate in wide-ranging cognitive testing, alongside similar testing of controls. They therefore provide a good and well-characterised group to examine whether a stable difference in basic dorsal-stream visual processing persists into adulthood.

2. Participants

Forty-five adults with Williams syndrome were recruited for studies at the Laboratory of Cognitive Neuroscience, Salk Institute, in co-operation with the Williams Syndrome Association. All WS participants met clinical criteria for a diagnosis of WS and obtained a score of at least three points on the WS Diagnostic Score Sheet (DSS), indicating the presence of a minimum threshold for common medical and physical characteristics associated with WS in clinical studies (Korenberg et al., 2000). Furthermore, all WS participants tested positive on a fluorescence in situ hybridization (FISH) test for the absence of one copy of the gene for elastin on chromosome 7 (AAP, 2001). Also recruited was a group of 19 typically developing age-matched controls, generally naïve concerning psychophysical testing. Control participants were screened for the existence of any developmental neurological or psychiatric conditions. Characteristics of the two groups are summarized in Table 1.

The WS participants took part in a wide range of investigations of cognitive performance in the Salk Institute's Laboratory for Cognitive Neuroscience, including administration of the Wechsler intelligence tests (WAIS-R or WISC-R), which yield both verbal and performance component scores. Control participants were assessed on the same test.

Table 1
Characteristics of WS and control groups

	N	Mean age (year)	Age range (year)	Verbal IQ score (S.D.)	Performance IQ score (S.D.)	Full scale IQ score (S.D.)
WS	45	28.3	16–47	69.2 (10.1)	63.8 (9.6)	64.8 (10.5)
Controls	19	27.5	18–41	101.7 (10.4)	98.6 (10.5)	99.8 (9.9)

3. Methods

Form and motion coherence thresholds were tested by procedures that have been established in work with WS children (Atkinson et al., 1997, 2003) and others with neurodevelopmental disorders (Gunn et al., 2002; Spencer et al., 2000).

3.1. Stimuli

Coherence stimuli were displayed on a 85 Hz VGA computer monitor viewed at a distance of 50 cm (visual angle 30° × 24°). For measurement of form coherence thresholds, the stimulus was a static array of randomly oriented short line segments (white lines on a black background, density 1.9 segments/degree^2) containing a 'target' area on one side of the display (diameter 12°, centred 7.5° from midline) where segments were oriented tangentially to concentric circles. The proportion of tangentially oriented ('coherent') line segments amongst the randomly oriented 'noise' segments in the target area defined the coherence value for a given trial. An example of the stimuli is given in Fig. 1.

For motion coherence threshold estimates, the stimulus comprised two random dot kinematograms (white dots on a black background, density 5.9 dots/degree^2, individual dots subtended 0.29°), one each side of a central vertical strip. The pattern on one side was divided into three horizontal strips, each 13° × 6°, such that the direction of the coherent motion of the middle 'target' strip was opposite to that of the two outer strips. The dot array on the opposite side of the screen displayed a uniform direction of motion consistent with the direction of the two outer strips. During each trial a variable proportion of the dots oscillated horizontally across each array forming these coherent motions (velocity 6.9 °/s), while the remaining dots moved in random directions (incoherent motion) (updates occurred every 12 ms). The direction of coherent motion reversed every 240 ms. To limit subjects' use of tracking strategies, the trajectory of each 'signal' dot had a limited lifetime of seven video frames (82 ms). The additional 'noise' created by the disappearance of signal dots at the end of their lifetime was taken into account when calculating coherence levels on this task.

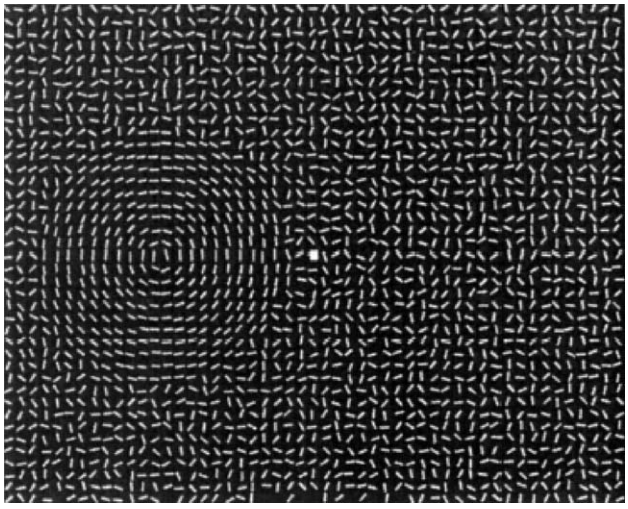

Fig. 1. Illustration of the test stimulus for form coherence thresholds. In this example, coherence is 100%.

Table 2
Form and motion coherence thresholds for WS and control groups

Group	Mean coherence threshold (S.D.)		Mean standardized coherence threshold scores (S.D.)	
	Form	Motion	Form	Motion
Williams syndrome	19.8 (5.9)	22.5 (10.8)	1.07 (1.10)	3.37 (2.71)
Controls	14.1 (5.4)	9.0 (4.0)	0.0 (1.0)	0.0 (1.0)

Data in right-hand columns are standardized based on the control group distribution for the particular threshold.

3.2. Procedure

Thresholds were obtained by a two-alternative forced-choice procedure. Participants were required to locate the target regions, which were presented randomly either in the left or the right half of the display. WS participants reported verbally or by pointing at the screen to the target, control participants by means of a computer key, indicating that the target was either on the left or the right. Stimuli remained on screen until participants responded. Between trials participants' attention was drawn to the midline of the display with a flashing or oscillating spot.

In each task, the initial coherence level was set to 100% and two to six practice trials were conducted to ensure that participants understood the task and gave correct responses. In the following test phase the coherence level of the target regions was varied according to a staircase rule. Starting at 100%, coherence was decreased stepwise on each trial by a factor of 0.84 until an error was made; following this the coherence was increased by 1/0.84 whenever an error was made and decreased by a factor 0.84 following two successive correct responses. After every fourth trial, there was a trial at 100% coherence so that the participant was motivated by a task which they could readily perform; these 100% coherence trials were not included in the procedure for estimating threshold. The two-up/one-down staircase rule was followed until six reversals had occurred, and the threshold was taken as the mean coherence level of the last four reversal points. Each participant performed the staircase procedure once for each task. The motion and form coherence tasks were run successively for each subject, with the motion threshold determined first.

4. Results

Fig. 2 shows a scattergram of thresholds on the two tasks for each group; Table 2 presents the means and standard errors of the two thresholds by group.

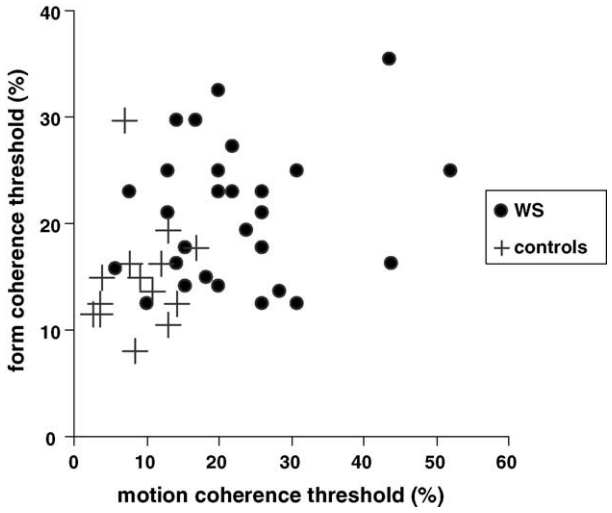

Fig. 2. Scattergram of form coherence thresholds plotted against motion coherence thresholds, for each individual participant. Crosses: control participants. Open circles: Williams syndrome participants.

Data were analysed using a two factor mixed-effects ANOVA (group × threshold type). There was a significant main effect of group, $F(1, 62) = 38.1$; $p < 0.001$, with the WS group showing overall higher coherence thresholds than controls. Follow-up analysis of the differences between group thresholds on each task was conducted using independent samples t-tests. As expected, the coherence thresholds for the WS group were significantly higher on both the motion ($t(61.39) = 7.279, p < 0.001$, correcting for unequal variances) and the form ($t(62) = 3.649$, $p = 0.001$) tasks.

There was also a significant group × threshold type interaction, $F(1, 62) = 7.17$; $p = 0.009$. The difference between the coherence thresholds of the WS and control groups was substantially greater on the motion than the form task. This difference is apparent from Fig. 1: the WS results (filled circles) lie somewhat higher than those for controls (crosses), indicating poorer form performance. The much more striking effect is that they lie further to the right, indicating a relatively greater difference in motion performance. The relation between the two thresholds within each group was analyzed by standardizing all scores based on the control group distribution. The mean and standard deviation of these standardized scores for each group are included in Table 2. For the control group, both form and motion thresholds necessarily had a mean of 0 and a standard deviation of 1. In contrast, the WS group showed a significant difference between standardized motion and form thresholds, $t(44) = 5.513$, $p < 0.001$, demonstrating that their motion thresholds showed a significantly greater deviation from typically developing individuals than they did for form. The values in Table 2 illustrate that as well as being elevated, the motion thresholds for the WS group show greater variability than for controls, while the variability of the form thresholds for each group are very similar.

To assess whether the measured thresholds did indeed represent an asymptotic developmental state, we examined the correlations of form and motion coherence threshold with age for the two groups separately. None of these relationships were significant (controls, motion thresholds versus age: $r = -0.36$, $p = 0.113$; controls, form thresholds versus age: $r = 0.22$, $p = 0.358$; WS, motion thresholds versus age: $r = -0.02$, $p = 0.881$; WS, form thresholds versus age: $r = 0.252$, $p = 0.094$)

5. Discussion

Adults with WS show, on average, a deficit in the detection of global motion compared to global form. We do not believe that this can be attributed to a difficulty in these individuals finding the general cognitive demands of the motion task too difficult. First, the general demands of the form and motion tasks were very similar; both required the detection of a spatially extended signal in noise, and both had the same format of two-alternative forced choice between locations either side of the display midline. Second, WS participants responded readily and accurately to the high-coherence motion patterns that were presented at the beginning of the staircase and interspersed among later trials to maintain motivation. Thus, WS participants appear to have a specific difficulty with the visual processing demands of the motion task above and beyond any difficulty with the broader cognitive demands posed by global judgments in a psychophysical task.

These results extend into adulthood the findings that WS children show a problem in global motion processing. The absence of any relationship of motion thresholds with age, within the 16–49 year age range of the WS group, argues against any suggestion that this group is showing a very slow maturation of motion performance beyond the age at which typical development reaches adult values.

Performance outside the normal range is not a feature of every WS individual: variability of motion thresholds within the WS group is quite striking (Table 2 and Fig. 2), as was also observed in WS children (Atkinson et al., 2003) with some individuals showing very good performance on both the form and motion tasks We do not know whether this finding reflects variability in the efficiency of the underlying mechanism, or differential strategies in exploiting the information that this mechanism provides. Whichever is correct, the source of the deficit and its diversity is not completely overcome in development, but is an enduring feature of WS behaviour and brain development.

The tasks of visuospatial manipulation that generally show the most striking deficits in WS are likely to depend on dorsal stream processing, but at higher levels in that stream than the structures (e.g., MT/V5) believed to be critical for determining motion coherence thresholds (Britten, Shadlen, Newsome, & Movshon, 1992; Newsome & Paré, 1988). Indeed, visuospatial deficits can be marked in WS individuals whose motion performance is in the normal range (e.g., the individual studied by Nakamura, Kaneoke, Watanabe, and Kakigi (2002), also Atkinson et al. (2003)). From

our fMRI studies in normal adults, using very similar form and motion coherence stimuli to the present study, we have shown that coherence activates two separate and independent brain networks, running from extrastriate visual areas to parietal areas (Braddick et al., 2000). If the same networks are critical in WS then two hypotheses (not necessarily exclusive) can be suggested: either the basic pathology of the WS brain extends through a large part of the dorsal-stream network, or the limitations in processing in low- and mid-level dorsal-stream structures impairs the information delivered for parietal/frontal visuo-spatial processing during development, with long-lasting effects on visuo-spatial abilities throughout life. In any case, the specific motion processing deficit appears to be a stable signature of the cortical characteristics of Williams syndrome, rather than a developmental stage on the route to the mature state.

Recent studies using quantitative neuroimaging methods, such as voxel-based morphometry, have endeavoured to identify structural differences between typically developing and WS brains. It has been reported that areas related to spatial vision show lower grey-matter densities in the WS brain (Eckert et al., 2005; Meyer-Lindenberg et al., 2004; Reiss et al., 2004). It should be pointed out, however, that the networks activated by form and motion coherence, respectively, although independent, are not separated by large distances in the brain (Braddick et al., 2000). This may mean that it will be difficult to differentiate these two networks even by sophisticated methods of measuring cerebral structures in imaging. It should also be noted that similar deficits in global motion are to be found in a range of neurodevelopmental disorders [see Braddick et al. (2003) for review], although the possibility of common structural characteristics in these disorders remains to be investigated.

Finally, the finding of an enduring functional (and possibly structural) deficit related to visuo-spatial problems in many individuals with WS should not be taken to imply that these problems are not open to remediation. Rather, such findings as these should help to focus attention on the strategies that WS individuals might be encouraged to acquire, and that some individuals have acquired, to work around the limitations placed on their development by early difficulties in visual processing.

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