Research Report

Visual magnocellular and structure from motion perceptual deficits in a neurodevelopmental model of dorsal stream function

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Abstract

Williams syndrome (WS) is a neurodevelopmental disorder of genetic origin that has been used as a model to understand visual cognition. We have investigated early deficits in the afferent magnocellular pathway and their relation to abnormal visual dorsal processing in WS. A spatiotemporal contrast sensitivity task that is known to selectively activate that pathway was used in six WS subjects. Additionally, we have compared visual performance in 2D and 3D motion integration tasks. A novel 3D motion coherence task (using spheres with unpredictable axis of rotation) was used in order to investigate possible impairment of occipitoparietal areas that are known to be involved in 3D structure from motion (SFM) perception. We have found a significant involvement of low-level magnocellular maps in WS as assessed by the contrast sensitivity task. On the contrary, no significant differences were observed between WS and the control groups in the 2D motion integration tasks. However, all WS subjects were significantly impaired in the 3D SFM task. Our findings suggest that magnocellular damage may occur in addition to dorsal stream deficits in these patients. They are also consistent with recently described genetic and neuroanatomic abnormalities in retinotopic visual areas. Finally, selective SFM coherence deficits support the proposal that there is a specific pathway in the dorsal stream that is involved in motion processing of 3D surfaces, which seems to be impaired in this disorder.

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1. Introduction

Williams syndrome (WS) is a genetic neurodevelopmental disorder characterized by predominant visuospatial impairment and relatively preserved auditory and verbal processing [3]. Little is known about the neural mechanisms underlying this disability, although most reported deficits have been related to high-order cognitive processes [30]. Visual dorsal processing seems to be specifically affected in WS, while the ventral pathway is relatively spared. As a result, this condition has been taken as a model to study parallel ventral/dorsal visual processing [3,30,31,48].

Motion coherence paradigms have classically been used to address dorsal stream function, as validated by single unit studies in monkeys as well as functional imaging in humans [5,7,8,33,35]. These studies indicate that detection of motion coherence relies, at least partially, on a dedicated brain area in the dorsal stream (MT in monkeys, area V5 in humans). Indeed, some evidence has accumulated that WS children
show poor performance in motion integration tasks [1,2]. Dorsal stream impairment in WS has also been suggested by visuospatial tasks that require manipulation of elements in spatial arrays (e.g. object assembly, block copying, and drawing) [3,29]. However, the presence of general high-level motion coherence deficits is still controversial [20,32,41]. It is possible that impairment is also present concerning low level visual functions, as suggested by deficits in illusory contour processing in WS [17].

One should also take into account that although V5/MT lies along the dorsal stream, it has extensive connections with the ventral stream, which is consistent with the notion that motion processing involves multiple distributed pathways [9,41]. The fact that motion processing is not a unitary function is corroborated by the recently demonstrated deficit in perception of form–from-motion stimuli in WS, even when motion coherence thresholds are preserved [41]. Furthermore, biological motion perception is preserved in WS [20]. These findings do not contradict the results of Atkinson and colleagues [1,2] who required their subjects to detect a rectangular area in which coherently moving signal dots moved in a direction opposite to the background signal dots. This task may therefore contain a form–from-motion component [41].

We have hypothesized that the origin of dorsal stream deficits might also involve early levels of visual processing within the magnocellular pathway. The contribution of a low level mechanism may help explain previously reported contradictory results from studies that have analyzed the genetic basis of cognitive deficits in WS. As an example, it has been postulated that the hemizygous deletion of LIMK1 on chromosome 7 could explain the classically described visuospatial impairment in WS [28]. However, Tassabehji et al. [44] have found that three subjects with small deletions did not fit the criteria for such deficits, despite their LIMK1 deletions. This suggests that quantitative phenotyping at different processing levels may be important in clarifying genotype–phenotype relationships. Furthermore, our working hypothesis of early level magnocellular impairment is also consistent with recently described genetic and neuroanatomic abnormalities in retinotopic visual areas [13,14,40].

To probe the magnocellular M/Y pathway at early retinotopic levels, we have chosen a contrast sensitivity task that uses a sinusoidal grating stimulus at high temporal (25 Hz) and low spatial frequencies (0.25 cycles per degree). These stimulus parameters are such that an illusory duplication of the number of grating stripes is perceived [22]. This Frequency-Doubling (FD) illusion reflects a nonlinearity that resembles the response properties of the M/Y system [42]. Between 5% and 20% of M cells in the lateral geniculate nucleus of the thalamus (LGN) respond with this nonlinear Y-type response [11]. Given the low percentage of M/Y neurons [21,37,38], testing this pathway in isolation ensures the likelihood of detecting specific early level impairment.

The value of FD stimuli to assess retinotopic magnocellular damage as early as the retina or retinotopic cortex has already been applied in glaucoma [10,19,24,25,36,46] and patients with focal lesions in visual cortex [9]. Based on all these findings, we have used a FD paradigm to study early magnocellular function in WS.

We have also explored whether known topographical asymmetries in retinotopic processing [39,43] are magnified in WS when compared to controls and looked for asymmetries in performance between eyes within the same subject. These would indicate an early level source of damage. Anisotropies of contrast sensitivity across the visual field are, per se, an important indicator of localized retinotopic impairment [12,51]. In any case, it is known that human brain regions subserving contrast sensitivity tasks are very much centered in retinotopic areas V1 and V2, with barely any modulation beyond these areas [4,45].

Additionally, we aimed to compare visual performance in 2D and 3D motion integration tasks. A novel 3D motion coherence task (using spheres defined by moving dots with unpredictable axis of rotation) was used in order to investigate possible impairment of occipitoparietal areas that are known to be involved in structure from motion (SFM) perception. This type of task seems to recruit a recently described pathway within the dorsal stream that extends into the human motion complex and parietal regions, and also ventrally into object-related areas [23,34,35,47,49]. Specific deficits in this task support the proposal that dorsal pathways involved in SFM perception are damaged in WS.

2. Materials and methods

2.1. Clinical and Standard neuropsychological assessment

2.1.1. Participants

The patient group comprehended 6 WS subjects, 4 females, 2 males, chronological mean age 16 ± 3.52, ranging from 11 to 20 years; mental mean age 8.67 ± 1.44, ranging from 6.5 to 10 years. The mental age-matched control group comprehended 11 subjects, 7 males and 4 females with ages ranging from 5 to 14 years averaging at 9.09 ± 3.08 years. Chronological age-matched control groups are described below (see Results section for specific group size for each test).

All control and WS subjects were naive to the tests performed and had normal or corrected-to-normal visual acuity. A complete ophthalmological examination was performed in all WS individuals. This exam consisted of best-corrected visual acuity (VA-Snellen chart), stereopsis evaluation using RANDOT, IOP measurement (Goldman applanation tonometer), slit lamp examination of anterior chamber, angle and fundus examination and photography under pupil dilation. Controls were only recruited provided they had a recent normal ophthalmological examination.
The diagnosis of WS was confirmed by fluorescence in situ hybridization (FISH) analysis following suspicion of the diagnosis by clinical criteria. All participants had hemizygous deletions for Elastin (ELN). Further genetic analysis revealed that deletion size (~1.55 Mb) was the same in all WS subjects.

2.1.2. All 6 WS subjects underwent comprehensive neuropsychological assessment

Psychological evaluation was carried out using standard methods adapted for the Portuguese population (Menezes Rocha et al. Escala de Inteligência de Wechsler para Crianças, 3ª ed CEGOC-Lisbon, 2003; Barbosa P., Escala de Inteligência de Wechsler para Adultos, ed IPAF-Lisbon, 2001) [26,27]. Average verbal (VIQ) and performance (PIQ) IQs were 52 and, 44.3, respectively. Individual IQs are presented in Table 1. Three of the adolescents were following the standard school program with special support (JAS, ASA and MPO) with moderate success, one was following a special educational program (RPB), and two had temporarily attended primary school (one being relatively autonomous in daily routines such as shopping). WS subjects also performed Benton’s Facial Recognition Test and Benton’s Judgment of Line Orientation (Form H). We found the classical dissociation pattern reported in the literature [3]: borderline performance was observed in the Facial Recognition test (average raw score: 38.8), in contrast to the severe deficits observed in the Judgment of Line Orientation test (average raw score: 5.7). Individual % scores for these tests are shown in Table 2.

This research followed our local institutional guidelines, and both parental and the subjects’ informed consent were obtained before participation.

2.2. Data analysis

Distribution-free nonparametric statistics (Mann–Whitney U test) were carried out in all tasks, to avoid biases due to deviations from normality and given the lack of data homoscedasticity. This method is also very robust when sample sizes are very unequal [16,50]. Heterogeneity in performance between the two groups (normal and WS) was analyzed by the F test for homogeneity of variance. All statistical analyses were performed with STATVIEW software package (SAS, Cary, NC).

2.3. Psychophysical techniques to address the function of the M-y pathway

Frequency-doubling (FD) inducing stimuli (see Introduction) were generated by means of a video board (Cambridge Visual Stimulus Generator, VSG2/5) and were displayed on a gamma-corrected 21-inch color Trinitron GDM-F520 monitor (frame rate 100 Hz). Each stimulus was a $10^\circ \times 10^\circ$ patch of 0.25 cycle/degree sinusoidal grating, vertically oriented, undergoing 25 Hz counter phase flicker. Stimuli were presented within 17 locations that were organized into two zones (Fig. 4): zone 1, with a central circular $5^\circ$ radius stimulus and 4 paracentral square stimuli and zone 2, with 12 peripheral square stimuli. Zone 1 extended over $10^\circ$ eccentricity and zone 2 between $10^\circ$ and $20^\circ$. During the test procedure, stimuli were presented pseudo-randomly at each zone. Stimulus duration was 400 ms and the interstimulus interval was at a minimum of 250 ms and up to 3 s.

Subjects were instructed to report the presence of “flickering striped” targets. Responses were recorded by the experimenter, to avoid motor confounds, using a button box.

Both eyes of all WS subjects were tested in zone 1 and 2, under monocular conditions, and were compared with a group of 11 mental age-matched (mean age = 9.09 ± 3.08 years, range 5–14 years) and 16 chronological age-matched control subjects (mean age = 14.50 ± 5.21 years; range 9–24). Subjects wore, when necessary, a correction appropriate for the 36 cm viewing distance.

Threshold calculation used an adaptive logarithmic staircase method with a total of four reversals, two practice and two experimental ones (the value to be used for a given trial is calculated using the previous trial value, plus or minus the step size in dB and the final two reversals are averaged to obtain the final threshold). The initial step size was 3 dB. Luminance contrast or modulation was expressed according to the Michelson formula: luminance contrast (%) = 100 * ($L_{max} - L_{min}$)/
(L_{\text{max}} + L_{\text{min}}). To compute logarithmic staircase steps, we have first converted luminance contrast threshold in % units to dB units according to the following formula:

\[ -20 \times \log(c), \quad c = \text{threshold}(\%) / 100. \]

Mean background luminance was 61.7 cd/m².

Participants’ reliability was evaluated by intermittently including false positive and negative “catch trials”, shown in Table 3, and exclusions were made according to standard criteria [6]. As a further control for task compliance, we had checked, in all subjects, eye movement patterns using a videomonitor device and 61 flickering central and peripheral light targets.

Test design attempted to mimic as closely as possible the standard clinical C-20 perimetric strategy (Fig. 4). Results obtained with our custom method were further validated by comparison with results obtained from a commercial FDT perimeter, using a sample of 97 eyes (mean age 14 ± 2.36 years) [Silva et al., unpublished results].

2.4. Psychophysical techniques to address motion integration deficits

2.4.1. General stimulus description (see Figs. 1 and 2 for stimulus schemes)

The stimuli used were random dots kinetograms (RDKs) presented within a circular spatial window of 6° of visual angle diameter generated using VisionWorksTM for Windows (Vision Research Graphics, Wisconsin, USA) and were displayed in a Trinitron GDM-F520 monitor. The refresh rate was 75 Hz. Viewing distance was 56 cm. Pixel size was 0.056 degree² and dot size was 3 × 2 pixels. Dot density was 3 dots/degree². For all tests, the background luminance was ~0 cd/m² and one pixel had approximately 18 cd/m². Dot coherence was 100% (except in tasks where the dependent variable was coherence). The fixation point was a 0.4° cross-hair with 0.05° arm thickness.

In all experiments, a two-alternative forced-choice staircase method was used (with 12 reversals, 6 practice and 6 experimental). Steps were 0.01 log units in size, unless otherwise stated. Step size was 1 down and 4 up. Audio feedback was always provided and consisted of 1 bip for correct and 5 bips for incorrect responses, each time a motor response was executed.

In the motion coherence of both planar and spherical surfaces and direction discrimination tasks, a single window centered in the middle of the monitor was used. In these cases, the fixation point was centered inside the window (the direction discrimination task had no fixation point to avoid reference landmarks). In the speed discrimination of planar RDK surfaces task, two windows were positioned with 6° horizontal separation, with the fixation point located halfway between them. Depending on the task, the stimulus was either always present until the subjects responded or had a fixed presentation time. Fixed presentations were of 85 frames (1.133 s) or 15 frames (200 ms, in the case of motion coherence of spherical surfaces task), after which a gray background appeared, and was present until the subject responded and the next trial commenced. Since no reaction time parameters were being measured, subjects responded verbally and the experimenter introduced the response.

2.4.2. Specific stimuli and task description

2.4.2.1. Motion coherence of planar surfaces. 100% noise dots alternated randomly within one aperture with coherent motion in a particular direction that varied pseudo-randomly from trial to trial. At the start of the experiment, planar surfaces moved 100% coherently. Dots moved at 3°/s. Subjects had to report the presence or absence of coherent motion. Average luminance was 1.13 cd/m².

2.4.2.2. Direction discrimination. The stimulus was presented within a single circular aperture in the middle of the screen and consisted of dots moving coherently in a horizontal manner to the right (0°) or vertically downwards (270°) at 2.5°/s. Subjects had to indicate whether dots were moving horizontally (0°). Correct answers caused the vertical stimulus to change its direction of motion to approximate the horizontally moving stimulus (from 270 towards 0°). Average luminance was 0.82 cd/m². Step size was 0.02 log units.

2.4.2.3. Surface speed discrimination. Dots moved horizontally, rightwards with 100% coherence. The initial speed of the test stimulus was 50°/s and the standard stimulus was moving at 15°/s. Subjects had to indicate which aperture contained the fastest moving dots. Average luminance was 1.88 cd/m².

2.4.2.4. Motion coherence of spherical surfaces. The stimulus consisted of dots placed on the surface of a rotating sphere 3° in diameter revolving around an imaginary axis, whose angle varied in a pseudo-random way. Speed of revolution was purposefully slow (20 rpm). The sphere alternated within one aperture with a stimulus consisting of 100% noise dots that moved at 2°/s. Subjects had to report the presence or absence of a rotating sphere.

<table>
<thead>
<tr>
<th>Patient</th>
<th>FP (%)</th>
<th>FN (%)</th>
</tr>
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<tbody>
<tr>
<td>MOP</td>
<td>16.5</td>
<td>19.5</td>
</tr>
<tr>
<td>RPB</td>
<td>14.3</td>
<td>6.5</td>
</tr>
<tr>
<td>JAS</td>
<td>12.8</td>
<td>19.0</td>
</tr>
<tr>
<td>JMG</td>
<td>14.8</td>
<td>10.5</td>
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<tr>
<td>ASA</td>
<td>1.8</td>
<td>16.0</td>
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<tr>
<td>SLT</td>
<td>13.3</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Table 3: “False positive” (FP) and “false negative” (FN) scores on standard catch trials, depicted as percentages.
3. Results

3.1. Standard motion integration tasks

3.1.1. Analysis of mental age-matched groups

We have first examined whether we could confirm in our WS subjects a similar pattern of deficits in classical motion integration tasks as the one described in the literature. Fig. 1 shows that average performance is slightly worse in the patient group for the following tasks: motion coherence for planar surfaces (controls, $n=8$, WS, $n=6$), direction discrimination (controls, $n=8$, WS, $n=5$) and speed discrimination for planar surfaces (controls, $n=9$, WS, $n=5$). However, these differences were not significant, which is consistent with some patients having normal or near normal performance (Mann–Whitney, ns for all tests). Indeed, threshold variance was significantly different between controls and WS subjects, except for the motion coherence of planar surfaces task, suggesting heterogeneity in level of impairment regarding these particular tasks ($F$ test: motion coherence for planar surfaces, $P=0.0611$; direction discrimination, $P=0.0189$; speed discrimination for planar surfaces, $P=0.0018$).

It is worth pointing out that normal performance cannot simply be explained by low level task difficulty. Indeed, our motion coherence task was particularly difficult since it required detection of global coherent motion whose direction varied pseudo-randomly.

![Fig. 1. WS pattern of deficits in classical motion integration tasks. Left insets—basic sketch of stimuli and tasks (note that for motion coherence many surface directions are possible; for details see Materials and methods and text). Relative performance in WS and control subjects for motion tests: (1) speed discrimination for planar surfaces (mental age-matched controls, $n=9$, WS, $n=5$), (2) motion coherence for planar surfaces (mental age-matched controls, $n=8$, WS, $n=6$) and (3) direction discrimination (mental age-matched controls, $n=8$, WS, $n=5$). In all tests, stimuli were presented for 1 s. Mann–Whitney statistical test found no significant differences between WS and control subjects for all tests. Variance in performance was significantly different for WS subjects vs. controls (see text) which is consistent with some subjects being impaired and others not. Error bars correspond to 1 SE.](image-url)
3.1.2. Analysis of chronological age-matched groups

We have also analyzed our results using a chronological age-matched group. The sample sizes for each task were as follows: motion coherence for planar surfaces (controls, \(n = 22\), WS, \(n = 6\)), direction discrimination (controls, \(n = 12\), WS, \(n = 5\)) and speed discrimination for planar surfaces (controls, \(n = 22\), WS, \(n = 5\)). As in mental age-matched analysis, differences between groups remained nonsignificant.

3.2. 3D structure from motion coherence task

3.2.1. Analysis of mental age-matched groups

In order to investigate whether the nature of the motion integration task could influence phenotypic assessment and, in particular, whether high-level dorsal stream impairment could be consistently documented or not, we have analyzed WS subjects performance in a novel high-level 3D motion coherence task. The axis of rotation of spherical surfaces varied randomly, which increased difficulty and introduced a spatial component to the task. Motion coherence thresholds were measured with and without temporal constraints (200 ms and stimulus presentations that were only interrupted upon a response—"on until response" scheme (UR)—Fig. 2). We found significant differences between WS and control subjects for both temporal schemes (Mann–Whitney test; UR presentation, \(P = 0.0032\), 200 ms presentation \(P = 0.0192\); mental age-matched controls, \(n = 9\); WS, \(n = 6\) and mental age-matched controls \(n = 8\), WS, \(n = 5\), respectively). Remarkably, control and WS subjects showed a proportionate deterioration of performance when the UR scheme was switched to brief (200 ms) presentations, suggesting that time was not the most critical variable in this task. Temporal integration deficits were only evident in subject JMG, whose thresholds changed when stimulus presentation was constrained. For this subject, there was a significant deterioration of performance when the UR scheme was switched to brief (200 ms) presentations. Significant differences were observed between WS and control subjects (Mann–Whitney; stimulus presentation "until response" \(P = 0.0032\), 200 ms stimulus presentation \(P = 0.0192\)). Error bars correspond to 1 SE.

Fig. 2. WS subjects are all impaired in a difficult high-level 3D motion integration task, even when no time constraints are imposed. (a) axes of rotation of target spheres change randomly. Gray levels are present just to highlight 3D perception of spherical surfaces and are not present in the actual stimulus. (b) Motion coherence thresholds for the “on until response” (see text) paradigm (mental age-matched controls, \(n = 9\); WS, \(n = 6\)); (c) motion coherence thresholds for brief (200 ms) stimulus presentations (mental age-matched controls, \(n = 8\), WS, \(n = 5\)). Significant differences were observed between WS and control subjects (Mann–Whitney; stimulus presentation “until response” \(P = 0.0032\), 200 ms stimulus presentation \(P = 0.0192\)). Error bars correspond to 1 SE.
when the 3D task had to be performed at 200 ms stimulus presentations (data not shown). Regarding the other tasks, he was the only subject whose performance clearly benefited from unlimited stimulus presentations.

The value of our new 3D task is further emphasized by comparing the performance of all WS subjects in all motion tasks (Fig. 3). Subject ASA and JAS had similar performance to control subjects at all standard motion tasks and by this criterion, they would have been labeled as having a “negative perceptual phenotype”. However, they were clearly impaired in our novel motion coherence for spherical surfaces task (Fig. 3d), the only one where all WS subjects showed impaired performance. It is interesting to compare the individual performance pattern of WS patients as compared to controls (Figs. 3a–d). It is also worth pointing out that only two of our six WS subjects were impaired in all motion tasks (JMG and MPO). MOP was excluded from the analysis in tasks where her performance never improved below 90% during the test procedure.

3.2.2. Analysis of chronological age-matched groups

This analysis revealed the same pattern of deficits seen using the mental age-matched control group. Significant differences between the groups were found (motion coherence for spherical surfaces, UR: controls, n = 12, WS, n = 6; P = 0.015. motion coherence for spherical surfaces, 200 ms: controls, n = 16, WS, n = 5; P = 0.003).

3.3. Perimetric assessment of magnocellular function

3.3.1. Analysis of mental age-matched groups

We have also measured monocular contrast sensitivity detection thresholds (CDT) across the visual field, using FD

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Fig. 3. Relative performance of all WS subjects (ASA, JAS, JMG, RPB, SLT and MOP) as compared to control group (CTRS). Black bars correspond to the control group (error bars correspond to 1 SE). It is worth noting that the performance of some WS subjects does not differ from the control group, except for the 3D motion coherence task. UR—“on until response”, (d), only thresholds below 90%.

Fig. 4. Basic scheme of the frequency-doubling (FD) stimulus (for details on the 17 test regions see Materials and methods).
stimuli (Fig. 4, see Introduction and Materials and methods). Threshold comparisons between WS and control subjects (controls, $n = 11$; WS, $n = 6$) were computed for each perimetric quadrant, zone 1, zone 2 and the central visual field (C) (see Figs. 5 and 6). CDTs were all significantly higher in the WS group, except for region C (Mann–Whitney tests for each quadrant: supero-temporal (ST), $P < 0.0001$; infero-temporal (IT), $P = 0.0004$; C, $P = 0.70$; zone 1, $P = 0.0003$ and zone 2, $P < 0.0001$).

When analysis was performed separately for each eye, results remained significant for most parameters of both eyes (data not shown). We have also observed that WS eyes could have some normal locations with similar thresholds to the control group, which also shows that lack of task compliance was not confounding the results. The asymmetric pattern of abnormal locations did not necessarily match across eyes within the same subject, which suggests a retinal origin without necessarily excluding damage in cortical retinotopic maps (Fig. 5).

Although all but one WS subject had abnormal thresholds in at least three locations, their performance was less homogeneous as compared to control participants, which is consistent with the pattern of visual field asymmetry found ($F$ test: ST, IN, SN and IT, $P < 0.0001$). This is corroborated by analysis of individual subject data. Fig. 5 shows clear intra- and intersubject heterogeneity of performance across the visual field. WS participants showed substantial impairment in multiple regions, with strong asymmetries between eyes, in particular of the supero-temporal type for the right eye (Fig. 5). These asymmetries are quite evident in the plots of JMG, SLT and ASA. Heterogeneity per se is an indicator of localized retinotopic damage (darker regions in plots depict higher contrast thresholds). The fact that, in some subjects, damage was predominant in the supero-temporal fields (corresponding to the inferior nasal retina)

Fig. 5. Perimetric FD threshold detection plots of all WS subjects and mental age-matched controls. Columns depict performance of the right (OD) and left (OS) eyes, respectively, of each WS subjects. Control eyes plots are shown on the two bottom plots (median of the respective population distribution). Darker gray regions correspond to higher contrast thresholds (%)—see bar on right hand side of picture. It is worth noting that thresholds are above normal in many regions, and asymmetric between eyes within the same subject. Crosses depict non-measured regions.

Fig. 6. Achromatic contrast sensitivity detection thresholds compared across visual field regions for each group of subjects (mental age-matched controls). C—Central visual field; ST—Supero-temporal; SN—Supero-nasal; IN—Infero-nasal; IT—Infero-temporal quadrant (a); zone 1 and zone 2 (b). Error bars correspond to 1 SE.
seems to represent an accentuation of subtle physiological asymmetries that may be found in normal subjects. In any case, 5 out of 6 WS subjects show significant retinotopic damage of early magnocellular contrast sensitivity maps.

3.3.2. Analysis of chronological age-matched groups

Impairments in CDTs remained significant for all analyzed locations when our WS group was compared to the chronological age-matched group (controls, n = 16; WS, n = 6). CDTs were all significantly higher in the WS group, except for region C (Mann–Whitney tests for each quadrant: supero-temporal (ST), infero-nasal (IN), supero-nasal (SN) and infero-temporal (IT), \( P < 0.0001; C, P = 0.1784; \text{zone 1 and zone 2, } P < 0.0001\).

4. Discussion

Our study provides two important results. First, we have found a new form of high-level 3D structure from motion coherence deficit. In this case, subjects were required to use motion information to infer 3D shape, which was rendered particularly difficult given the object’s unpredictable axis of rotation. This deficit was observed in all WS individuals in our sample, in contrast with the heterogeneity of impairment found in the other motion integration tasks (Figs. 1–3). The pattern of heterogeneity in classical tasks has been documented before [1,2,20,32] which renders the homogeneity of the SFM impairment quite intriguing.

The presence of such 3D motion integration deficit fits well with recent neuroimaging studies, which imply an important role for dorsal extrastriate and parietal regions in SFM processing [18,23,34,35,47,49]. This network includes the human motion complex and parietal regions and is connected with object-related ventral cortex. Interestingly, Kriegeskorte et al. have found a region in the intraparietal sulcus that reflects the motion state of the SFM object. Evidence for a separate functional role of this pathway is now accumulating [9,15,23]. We speculate that deficits in our SFM task become apparent because this pathway is more specifically involved in WS. We hypothesize that the key difference between our 3D motion coherence task and other tasks is that the subjects had to segment transparent surfaces moving in different depth planes (the anterior and posterior walls of the sphere). A similar hypothesis was raised by Reiss et al. [41] in relation to form–from-motion tasks: it was argued that the deficits could be explained by the difficulty of segmenting the coherently moving object from its background. A failure to segment anterior and posterior coherent areas in our 3D SFM task would produce poor thresholds.

Normal performance in the 2D motion coherence task cannot simply be explained by low level task difficulty, because it required detection of global motion whose direction varied pseudo-randomly.

In any case, this raises important questions on how to classify the presence or absence of perceptual impairment. This question is critical given recent controversies on the genes that contribute to the cognitive phenotype in WS [44]. It is likely that quantitative phenotyping strategies that isolate different pathways at different levels in a sensitive manner will help improve genotype–phenotype relationships in WS.

Second, we have found that a significant involvement of early magnocellular retinotopic maps occurs in WS. Contrast sensitivity deficits relate to early level retinotopic damage (e.g. as early as the retina or retinotopic cortex). Functional damage of the magnocellular pathway, which serves as the primary input to cortical motion area MT/V5, may contribute to impairment in local motion processing, and thereby to deficits in motion tasks. However, this is likely to be true only in tasks in which dot density is quite sparse, under which conditions motion integration tasks become more difficult. In other words, cortical integration mechanisms may compensate for peripheral retinotopic deficits under nonsparse conditions [9].

The work of Tootell and Heeger has clearly shown that human brain regions subserving contrast sensitivity processing are essentially centered in V1 and V2, with barely any modulation beyond retinotopic areas [4,45]. Our results are consistent with current morphometric and genetic expression studies suggesting abnormal patterns of development in the primary visual cortex [13,14,40].

Future studies should, when possible, investigate the expression of genes involved in WS in the retina and LGN. If the source of impairment actually occurs earlier in visual processing, then it is possible that some subjects can compensate for low level magnocellular deficits through cortical integration mechanisms. Such cortical compensatory mechanisms may lead to negative results, as measured by classical tasks, and to incorrect phenotyping of visuo-spatial deficits. Moreover, they might help explain why previous reports have found contradictory results regarding specific dorsal stream damage in WS. In our study, some of our subjects would have been classified as having a “negative” dorsal stream phenotype if only the standard methods (classical motion integration tasks) had been used. However, they had the same profile of sensory deficits, which implies that they would have been classified as a “positive” phenotype in terms of early, magnocellular, dorsal stream function.

In summary, our study demonstrates for the first time the presence of a retinotopic magnocellular deficit in WS that could provide a contributory mechanism for the origin of high-level dorsal stream deficits. Future studies should correlate these findings with the recently described genetic and neuroanatomic abnormalities in early visual areas [13,14,40].

This new framework suggests that the model of gene-dorsal stream relationships in this disorder has to be refined, both in what concerns degree of involvement of different
visual pathways and their relevance to cognitive phenotypical classification. Finally, selective deficits in the SFM task support the proposal that there is a separate pathway in the dorsal stream that is involved in structure from motion processing, which seems to be more specifically impaired in this disorder.

The present study extends previous work suggesting the notion of differentially affected motion classes and dorsal stream processing in WS [32,41]. Future studies should dissect how the magnocellular pathway relates to different functional streams within the dorsal pathway, both in the normal and WS brain.

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