Research in Autism Spectrum Disorders 69 (2020) 101456

Contents lists available at ScienceDirect

Research in Autism Spectrum Disorders

journal homepage: www.elsevier.com/locate/rasd

Exploratory study of dorsal visual stream dysfunction in autism; A case series

I Hay[a,*], G N Dutton[b], S Biggar[c], H Ibrahim[b,e], D Assheton[d]

[a] NHS Dumfries and Galloway, UK
[b] Glasgow Caledonian University, UK
[c] Dumfries and Galloway Council, UK
[d] St Helens & Knowsley Teaching Hospitals NHS Trust, UK
[e] Mansoura University, Egypt

ARTICLE INFO

Keywords:
Dorsal visual stream dysfunction
Cerebral visual impairment
motor impairment
Autism

ABSTRACT

Background: Robust neuroscientific evidence supports the existence of an association between autism and a visual motion processing deficit, arising from dysfunction of the dorsal visual stream, a pathway connecting the primary visual and parieto-occipital cortices. The neuro-ophthalmic consequences of dorsal visual stream dysfunction (DVSD) are well-described but seldom reported: simultanagnosia, optic ataxia (OA), and gaze apraxia.

Method: The clinical records of thirteen motor-impaired autistic children, with clinical diagnoses of DVSD, were retrospectively reviewed six years after DVSD diagnosis to determine the frequency and severity of their neuro-visual impairment. Two measures to rate severity of visual perceptual impairment were employed: frequency of parent-reported behaviours denoting impaired visual function, given as mean individual Cerebral Visual Impairment Inventory Scores (CVIS), and severity of age-inappropriate configural disruption of drawings, rated on Beery-VMI Visual Motor Integration standard scores (VMIS). Applying the 90th percentile cut-off CVIS of 0.74 for the typical population as marker of normal visual function a CVIS ≥ 2.5 indicated very severe impairment. Evidence was also sought for a correlation between central OA and severe motor coordination impairment (MCI), rated by the Beery Motor Coordination assessment, using method agreement analysis.

Results: Significant correlation between CVIS and VMIS was determined by linear regression analysis: **r = -0.81** [95% CI -0.94 to -0.47], **p = 0.0008**. Agreement for MCI ≤ 5th percentile with central OA, determined by Cohen's weighted Kappa statistic (K), was significant: K = 1[95% CI: 0.46–1.54], **p = 0.0002**.

Conclusions: We conclude that mechanisms driving OA (which is defined as 'impaired visually guided movement') may underpin severe motor impairment, in autism. CVIS and VMIS may be useful indicators of severity of spatial cognitive impairment.

Lay Summary

Dysfunction of a major vision processing pathway, the dorsal visual stream, can produce movement inaccuracy and may compromise interaction with objects in surrounding space and the spatial relationships between objects and between objects and people in the child's visual environment. We report the profiles of thirteen autistic children with this type of dysfunction and suggest a

* Corresponding author at: NHS Dumfries and Galloway Department of Community Paediatrics, Glencaple Road, Dumfries, DG1 4TG, UK.
E-mail address: isobel.hay@nhs.net (I. Hay).

https://doi.org/10.1016/j.rasd.2019.101456
Received 27 February 2019; Received in revised form 17 August 2019; Accepted 22 September 2019
Available online 19 October 2019

method for identifying those with severe functional disability.

1. Introduction

The dorsal visual stream, which projects from the occipital lobes to the posterior parietal lobes, subserves the immediate, online and continuous visual guidance of movement in three dimensional dynamically mapped space. The ventral visual stream, which projects to the temporal lobe, serves object and face recognition (Milner & Goodale, 2008). Effective co-working of these two streams of processing permits the efficient identification and dynamic spatial location of items and people and our interaction with these.

Autism, or autism spectrum disorder (ASD) is a behaviourally defined neurodevelopmental condition with core deficits of severe impairment in reciprocal social interaction, communication and imagination, together with repetitive and inflexible behaviours (Wing & Gould, 1979; Wing, 1997). ASDs rank as one of the most common causes of neurodevelopmental disability (Baxter et al., 2015). The current estimated prevalence in the developing world is at least 1.5% (Lyall et al., 2017). Concurrent developmental conditions are common (Lai, Lombardo, & Baron-Cohen, 2014), with high prevalence rates for co-occurring motor abnormalities reported in several studies e.g Paquet, Olliac, Bouvard, Golse, & Vaivre-Douret, 2016, 75%; Green et al., 2009, 79%; Green et al., 2002, 100%. Both fine and gross motor delays in early childhood have been proposed as potential markers for the later emergence of autism (Harris, 2017). In infancy, object manipulation and grasping activity has been shown to be impaired in groups at high risk of autism in comparison to low risk groups (Libertus, Sheperd, Ross, & Landa, 2014; Sacrey, Zwaigenbaum, Bryson, Brian, & Smith, 2018), with infants later diagnosed with ASD significantly underperforming in qualitative ratings of reach and grasp compared to children in low risk and high risk non ASD groups (Sacrey et al., 2018).

Kinematic grasp analysis studies lend further support to atypical mechanisms for grasp in ASD in pre-school as well as school-age children: pre-schoolers with ASD, without learning disability, have longer reach to grasp movement duration times (Campione, Piazza, Villa, & Molteni, 2016; Forti et al., 2011) and both age groups show atypical patterns of grasp opening in contrast to typically developing peers (Rodgers, Travers, & Mason, 2019).

Skilled reaching and grasping in an environment which changes from moment to moment deploys the activity of dorsal stream visuomotor zones in the superior parietal lobule (SPL), designated regions V6A, located within the parieto-occipital cortex (Pitzalis, Fattori, & Galletti, 2015), the medial intraparietal sulcus (MIP) and the ventral intraparietal sulcus (VIP), (Galleti & Fattori, 2018). V6A and the anterior intraparietal sulcus (AIP) are actively involved in the grasp process, with AIP serving primarily an object-identification function (Galletti, 2018). V6A may subserve fast prehension and the postural selection of appropriate grasp (Galletti, 2018). Predictably, issues with the visual control of movement are common when there is dorsal visual stream damage or dysfunction (Cooper & O'Sullivan, 2016). The visuomotor deficit may be severe, as reported in term and preterm children with parieto-occipital periventricular **white** matter damage (Saidkasimova, Bennett, Butler, & Dutton, 2007), and reported in children with Williams syndrome, where DVSD has been extensively investigated (Atkinson et al., 1997, 2003; Braddick & Atkinson, 2011).

Support for a "dorsal stream vulnerability" (Atkinson, 2017; Spencer et al., 2000) in autism comes from studies reporting a global motion processing deficiency (Pellicano & Gibson, 2008; Robertson et al., 2014; Spencer et al., 2000) which may ameliorate with maturity (Spencer et al., 2000). In childhood DVSD is variably associated with impairments of simultaneous visual perception, visually guided movement, perception of movement, and saccades (Dutton et al., 2004). In Balint syndrome, where DVSD is severe, a triad of deficits is also variably seen, with impaired visually guided movement (OA), diminished capacity to perceive visual elements surrounding the item of interest (simultanagnosia) (Goodale, 2013), and dysfunction of visual search eye movements (apraxia of gaze) (Barton, 2011; Ptak, 2012). Affected adults may manifest incomplete forms of Balint syndrome e.g. isolated OA (Damasio & Benton, 1979) or simultanagnosia and OA without gaze apraxia (Michel & Henaff, 2004; Vighetto & Krolak-Salmon, 2007). Balint syndrome variants are sporadically reported in the paediatric literature (Yapici, 2006) and few detailed case reports (Drummond & Dutton, 2007; Gillen & Dutton, 2003) exist.

Adults with Balint syndrome have severe visuomotor impairment (Michel & Henaff, 2004) with behaviour suggesting blindness (Vighetto & Krolak-Salmon, 2007) despite unaffected visual acuities. Simultanagnosia produces a variably reduced window of spatial visual attention that results in "piecemeal" perception of objects and scenes (Dalrymple, Barton, & Kingstone, 2013). Impaired visual input to cerebral reach and/or grasp pathways renders the individual dependent on touch/proprioceptive feedback to localize objects and determine their properties (Karl & Whishaw, 2013). The result is OA: a preconfiguration of the reaching hand that is held "too wide, with no or poor preshaping" (Jeannerod, Decety, & Michel, 1994), grasp closure occurring only after hand contact with the object and "tactile search with the palm of the hand and fingers" (Damasio & Benton, 1979). OA and other components of the Balint triad may be identified by neuro-ophthalmic examination (Dutton et al., 2004) which also serves to identify or exclude any co-existing neuromuscular, sensory or visual deficits (Vighetto & Krolak-Salmon, 2007).

Difficulties with the use of cutlery to self-feed, and with handwriting skills are well recognised features of dorsal visual stream impairment (Holmes, 1918; Luria, 1966). In the absence of neuromuscular or visual explanation for dysfunction, children with age inappropriate functional difficulty in either or both of these skill areas merit consideration of DVSD. During a 15 month period we consecutively identified 28 cases of children with ASD who reported such functional difficulty and were found to have evidence of DVSD (see Appendix B for flow chart of this clinical process).To ensure the validity of the DVSD diagnosis in this group the first sixteen children to be identified were referred to a tertiary centre for neuro-ophthalmic assessment.

Of this group, thirteen underwent neuro-ophthalmic, cognitive, and neurodevelopmental assessments that confirmed DVSD. During follow-up the method of diagnosis for OA was progressively refined and is reported here. At 6 years of follow-up, all clinical assessment data that was contemporaneous with the child's age at time of diagnostic examination for OA, was retrospectively analysed. This study reports on those assessment findings, and on their relevance as prognostic indicators of severe functional

impairment in motor-compromised children with autism.

2. Method

2.1. Participants

The thirteen children (9 boys and 4 girls; mean age at DVSD diagnosis 9.1 years; range 5.7–14.0 years; SD 2.31) all attended mainstream primary or secondary schools in Dumfries and Galloway, a mainly rural region of South West Scotland. None had learning disability (see results of cognitive assessments, below and in Table 2). Multidisciplinary assessment for ASD (see Appendix A) met national guidelines (National Institute for Health and Clinical Excellence (NICE), 2011; Scottish Intercollegiate Guidelines Network (SIGN), 2016).

2.2. Data analysis

Paper, computerised, and video records were reviewed for each child, as described. Datasets analysed for all children were derived from neurological and ophthalmological examination, age-standardised visual perceptual and motor skills' assessments, and age-standardised assessments of general ability, undertaken to ensure any difficulties were not simply attributable to cognitive disability. Information was also sought on outcome for each child in respect of whether or not he/she had received specialist visual impairment support and whether the recommendation for support had been derived independently through Education or via Paediatrics. Visual perception, motor skills, and neurological examination datasets used in the final analysis were contemporaneous within a mean time interval of 1.4 years (SD 0.65; range 0.0–2.25 years).

Ophthalmic examination included: visual acuity (Keeler crowded **log** MAR); colour vision (Ishihara); stereo acuity (Frisby stereo test); eye movement assessment and cover test for strabismus; visual field assessment (confrontation testing and static visual field perimetric assessment) and refraction by retinoscopy. Where the eye examination was normal children were discharged to annual follow up by their local optician; otherwise, ophthalmic follow up continued. Vision perception assessments included the VMI, the Beery sub-test of Visual Perception (VP) (Beery, Buktenica, & Beery, 2010) and the Cerebral Visual Impairment (CVI) Inventory (Dutton et al., 2010; Macintyre-Beon et al., 2012), a 51 item standardised questionnaire which seeks information from parents or carers about child behaviours that denote impaired visual perception and function. Responses are rated from zero (never seen) to 4 (always seen). Higher scores 3–4 are rated positive as such behaviours are not seen in the typically developing population. The mean CVI Inventory score (CVIS) is 0.4 for the typically developing population; the 90th percentile cut off is 0.74 (Dutton et al., 2010; Macintyre-Beon et al., 2012). Inventory information was updated at each follow up appointment.

Tests for simultanagnosia in adults look for evidence of 'local capture' (Dalrymple, Bischof, Cameron, Barton, & Kingstone, 2009; Dalrymple, Kingstone, & Barton, 2007; Karnath, Ferber, Rorden, & Driver, 2000) where the items of restricted attentional focus are seen at the expense of the surrounding elements. Methods used include testing the individual's ability to interpret the gist of a pictured scene, briefly presented (Chechlacz et al., 2012; Dalrymple et al., 2009), the ability to locate and identify large letter targets set amongst a background of small-letter distractors (Mesulam, 2018), and/or testing ability to globally reproduce line drawings, looking for evidence of piecemeal reproduction of the elements therein (Luria, 1973, Luria, 1966). In the absence of other age-standardised diagnostic test for simultanagnosia, age-inappropriate configural disruption of elements of drawings (determined using the VMI reference charts) was accepted as evidence of "local capture" and the VMI standard score (VMIS) was used to measure the severity of simultanagnosia. Shape recognition skills up to an 8 year level were assessed by the child's approach to completion of the formboard matching items in the Griffiths Mental Development Scales - Extended Revised (GMDS-ER) (Luiz et al., 2006). Beyond 8 years failure to match wooden forms to their appropriate inserts was accepted as evidence of significant form perception impairment.

Motor skills were assessed by the Beery sub-test of Motor Coordination (MC) (Beery et al., 2010). All Beery assessments were conducted by the first author.

Coexisting neurological disorder was excluded by standard upper and lower limb neurological examination of power, tone, coordination and reflexes (Donaghy, 2009). Tests of cerebellar function comprised examination for nystagmus, finger-nose and heel-shin testing (Donaghy, 2009). Gait assessment was not used because of the confounding effect of impaired visual guidance of movement. Anterior parietal function testing comprised proprioception testing of fingers and toes and testing for astereognosis (Donaghy, 2009) (see Appendix E); posterior parietal function was further assessed by examination for OA. All neurological examinations were carried out by the first author.

Details of the criterion used for diagnosis of OA and the method of examination for OA are given below. The method was originally piloted in a community based study that examined vision perception and hand grasp in randomly selected, typically developing children screening negative for DVSD. This study was approved by the West of Scotland NHS ethics committee (Ref: 14/WS/0056) and funded by NHS Dumfries and Galloway.

2.3. Criterion for diagnosis of OA and rationale

Accurate preshaping of the hand to match the contours of an object grasped appears around 2–2.5 years (Hempel, 1993; Karl & Whishaw, 2013; Touwen, 1995) in typical development, and is present by 4 years (Touwen, 1998). Impaired hand pre-shaping to target is seen in children with cerebral palsy (Jeannerod, 1986) and children at risk of developmental disorders (Hempel, 1993;

Touwen, 1995). In adults, impaired terminal grip size relative to the target grasped (Binkofski et al., 1998; Goodale & Milner, 1992; Jakobson, Archibald, Carey, & Goodale, 1991; Jeannerod et al., 1994; Perenin & Vighetto, 1988) is a feature of OA. We therefore used grasp to target mismatch as the criterion for diagnosis of OA after other visual, sensory or neuromuscular impairments had been excluded. Other performance errors rated as consistent with OA, but not required for diagnosis, were a "double grasp" (Goodale & Milner, 1992; Jakobson et al., 1991) in which the digits close to briefly touch the item, open and then close again to grasp the object (e.g Video, Child I) or other clear evidence of tactile facilitation of grasp (Damasio & Benton, 1979) by touch of the object or its surroundings (e.g Video, Child N).

2.4. Materials and procedure for examination for OA

Methodologies used for adults (Jeannerod, 1986) were adapted for paediatric clinic use. The clinic set-up, and the materials (listed in Appendix D) used in the clinic assessment of the children are illustrated in Fig. 1, below. A parent or carer was also present in the room. As shown, the participant's hand grasp for centrally and peripherally viewed targets was filmed by an assistant using a hand-held video camera (recording speed 25fps).

Each child sat facing the examiner, behind a yellow table of variable height which was adjusted to their waist level. Target distance did not exceed one arm length (measured as axilla-wrist) to optimise conditions for reach-accuracy (Schneiberg, Sveistrup, McFadyen, McKinley, & Levin, 2002).

A clinic assistant using a hand held mobile camera recorded radial views of the child's grasp (this view was used during the last three years of follow-up; earlier films captured a top- down aspect of the grasp movement) with first the left, then the right hand. Prior to grasp the instruction was given to the child to use their corresponding hand to "do all the work" while their other hand rested on the child's knee. No tactile contact was permitted with the table prior to grasp.

2.5. Grasp in central vision task

A single block was positioned by the tester in the centre of a pink laminated sheet (see Fig. 1), so that the tester's hand covered the block completely. As soon as the block was uncovered the tester's hand withdrew 7 cm or so, ready to receive the block.

The child's task was to reach, grasp, and transfer the block to the tester as soon as the item was uncovered. Blocks were presented to each hand in the alphabetical sequence shown in Fig. 2. Each grasp sequence commenced with the left hand. Immediately the item was uncovered the participant was instructed to: "Pick up the block and give it to me". A single trial was permitted for each hand, using a blue 2.5 x 2.5 cm wooden cube as the target object, to ensure understanding of the instruction and adequate camera view of the hand. No further trials were permitted, to reduce the likelihood of memorized spatial information improving performance (Milner et al., 2001; Himmelbach & Karnath, 2007). All targets were removed from the child's view after each grasp sequence. Body to target distance was approximately 20 cm.

2.6. Rationale for use of target objects

Grasp of novel objects of different sizes requires the simultaneous visual perception of their component features (such as colour, texture, and orientation (Friedman-Hill, Robertson, & Treisman, 1995) and the transfer of visual information to the hand configuration so that the in-flight gap between the thumb and fingers is matched to the size of the target for accurate grasp. Normally, the gap increases the bigger the object (Paulignan, Jeannerod, MacKenzie, & Marteniuk, 1991). In simultanagnosia the visual perception of a global object may be challenged by the presence of several visual features such as colours e.g. a coloured star composed of one red and one blue triangle may be seen as one blue triangle (Luria, 1959). Adults with simultanagnostic vision may look at a coloured object and perceive the object but not its colour (Coslett & Lie, 2008). Within-object spatial structure requires an intact dorsal visual stream for determination (Robertson and Triesman, 2000). With severe DVSD, both between-object and within-object spatial coding systems for action control are compromised (Goodale & Milner, 2018; Huberle & Karnath, 2006; Himmelbach & Karnath, 2007). Introducing featural complexity (e.g. colour, spatial axial complexity) to an object may thus render OA more evident (Himmelbach & Karnath, 2007).

2.7. Grasp in peripheral vision task

This task first required an assessment of the extent of the participant's functional field of view (FFOV). When visual fixation is maintained on a central target, simultaneous sight of a peripheral target occurs but the quality of the peripheral image progressively degrades from the point of central visual fixation (Frisen & Glansholm, 1975). We took the limit of sight of a peripheral target, distanced horizontally from a centrally fixated target, as the limit of extent of the participant's FFOV.

Note: all tasks assessing the extent of the peripheral visual field require the child to sustain visual fixation on a centrally viewed target. While accurate visual field testing has been reported for children as young as 4 years (Wilson, Quinn, Dobson, & Breton, 1991), fixation instability for a centrally viewed target becomes progressively less likely (Akar, Yilmaz, & Yucel, 2008) beyond 8 years. We considered that this assessment could be reliably used in the study group reported here, given their ages and cognitive profiles

Schematic representation of the materials used to assess the FFOV is given in Fig. 1(b).The laminated pink sheet was used again for this task and the designated point of central fixation was the nose on the smiley face sticker. The participant was shown the peripheral target, a white plastic fork, with the instruction: "Now we are going to see if you can see this fork at the same time you see

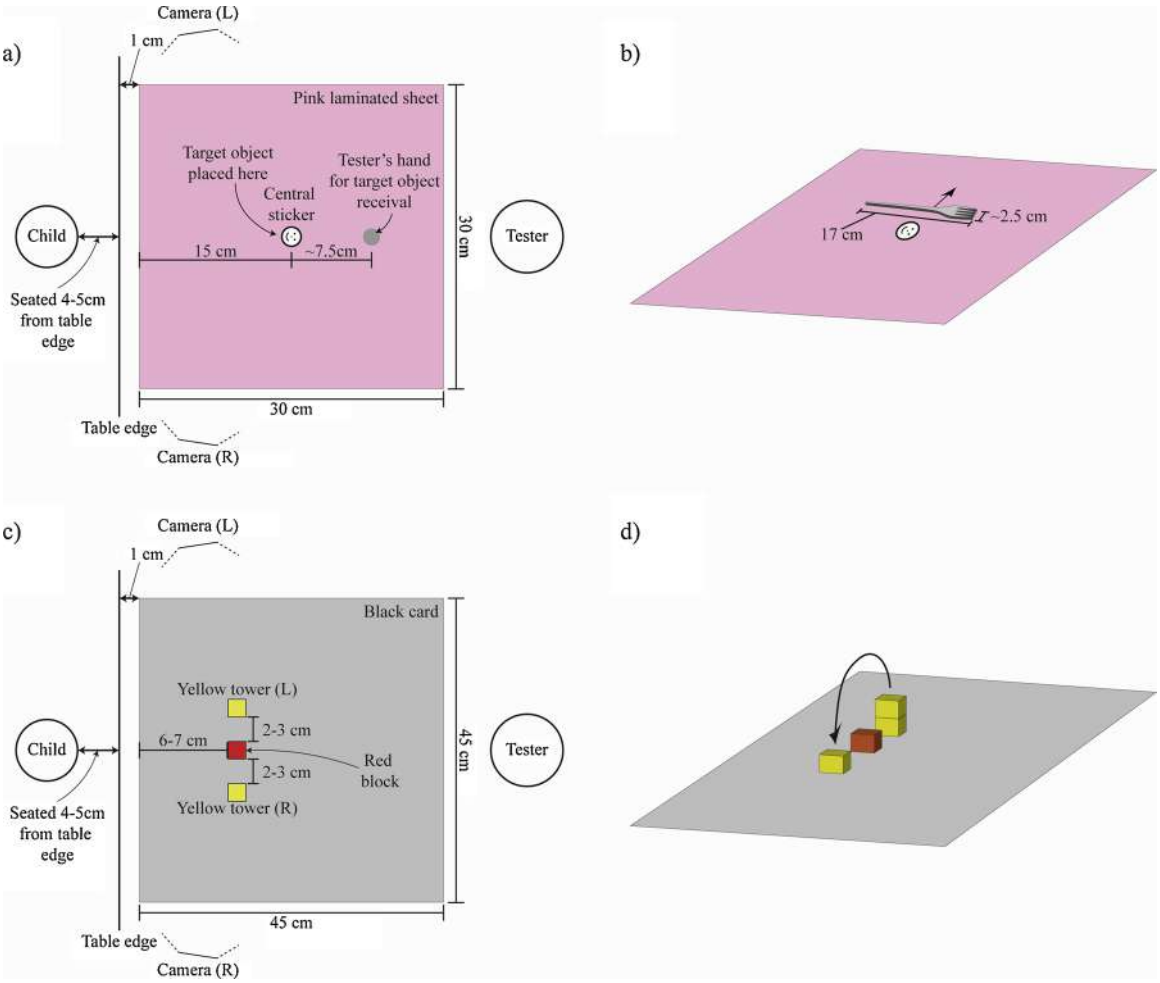


Fig. 1. Schematic representation of clinic set up and materials used in the central and peripheral vision grasp tasks.
(a) Clinic set-up and materials used for the grasp in central vision task.
(b) Materials for estimating the functional field of view (FFOV).
(c) Clinic set-up and materials used for the grasp in peripheral vision task.
(d) Method of transfer of cubes in grasp in peripheral vision task.

the smiley face on the sticker. Now look at the nose on the smiley face. Keep looking at the nose and don't look anywhere else." The fork was placed alongside the sticker in the participant's left hemifield with the instruction to "Keep looking at the nose and tell me if you can see the fork at the same time". If simultaneous sight of the fork and the sticker face was confirmed the examiner slowly (around 1 cm/sec) moved the fork horizontally and centrifugally for incremental distances of 2 cm, stopping after each interval to ask if the participant could see the fork. The last point at which the participant reported seeing the peripheral target before it disappeared was taken as the limit of the extent of the FFOV. If the target disappeared from view at 3 cm or less from the centre, or when persistent head or eye-turn to the fork occurred within this distance limit, grasp in peripheral vision, in the corresponding hemifield, could not be reliably assessed.

Schematic representation of the materials used to assess peripheral grasp is given in 1c) and 1d).Three yellow cubes were constructed by the tester as a tower 1–3 cm to the participant's left of the central target, a red or blue 2.5 cm wooden cube, positioned on a sheet of black card as shown. The task was demonstrated by the tester, transferring one cube at a time, over the central target to reconstruct a tower on the opposite side. Individual cubes were then transferred back to reconstruct a tower on the original side. The process was carried out first with the participant's left hand, then the right. The instruction given to the participant was to "Jump the yellow cubes, one cube at a time, over the blue/red cube and make a tower on the other side. Keep looking at the blue/red cube, if you can". Where the newly constructed tower was placed at more than 3 cm distance from the central target the tester repositioned the tower at 1–3 cm distance prior to transfer. If there was manifest head or eye turn to the peripheral yellow cubes, grasp in peripheral vision could not be assessed.

The original diagnosis of OA was made by slow motion capture of hand movement (see videofile series). For the purpose of this study the original archive video was re-examined for features of OA using still-frame analysis, after Jeannerod (Jeannerod, 1986).

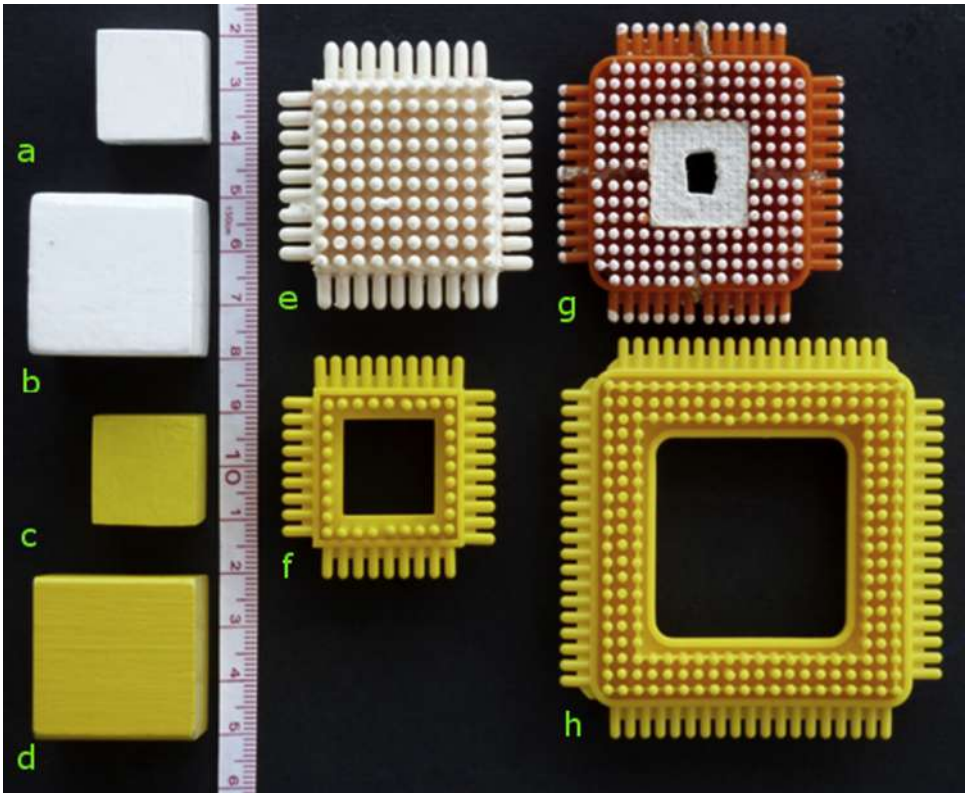


Fig. 2. Target objects used for grasp in central vision.
Items shown are presented alphabetically in increasing order of size, colour combinations and complexity of surface contour. (a),(b): white and yellow cubes, one of each colour, sizes 2 cm and 3 cm ; (f),(h): standard square yellow sticklebricks with a square central cut-out, one of each size, 4 x 4 cm and 7.4 x 7.4 cm; (e): one red or orange 5 x 5 cm sticklebrick painted white; (g): one red or orange sticklebrick 5.4 x 5.4 cm, painted white on the prong tips only and with the central section replaced by a white wooden insert with central cut-out.

Written informed consent to use the anonymised video material for teaching, research and publication had been obtained from all parents and young persons (assent had been obtained from all children) prior to examination; for the purpose of this study this consent was updated.

All statistical tests were carried out using Stats Direct statistical software (Stats Direct Ltd).

3. Results

The developmental histories and co-morbidities of the children are shown in Table 1. Four had clear risk factors for cerebral visual impairment (CVI). One child had been born prematurely at 32/40 and had hypoglycaemia; another had a history of maternal alcohol misuse and a third, birth asphyxia. These three had proven risk factors for acquired brain injury and thus cerebral visual impairment (CVI). In another child, asymptomatic sagittal craniosynostosis (incidentally identified on an otherwise normal MRI), was also considered a risk factor, given the convincing evidence for impaired parietal attentional mechanisms in this type of craniosynostosis (Baranello, Vasco, Ricci, & Mercuri, 2007; Ricci et al., 2007; Vasco et al., 2008). OA in another child who was adopted (with no known history of alcohol or substance misuse) was severe (see supplementary videofile; Child D). MRI was advised to exclude acquired brain injury, but was refused. Two other boys were referred to genetics but by the time of this report no disorder has yet been identified. One of these had a marfanoid habitus and very marked ligamentous laxity; the other had mild facial dysmorphism. A history of antenatal bleeding in two further cases was obtained from mothers who reported vaginal blood spotting throughout pregnancy but no other significant antepartum haemorrhage and both boys had good birth weights. No mothers in this group were smokers. The other participants had unremarkable obstetric and birth histories.

All participants had verbal ability profiles or reading comprehension standard scores within the normal range ([mean 91.2; range 77–104; SD 9.4]; see Table 2). For ten children, Wechsler Intelligence Scale for Children, Third edition (WISC-III) or Fourth edition (WISC-IV) data were available. Reading comprehension age scores offered for one child by the Wechsler Individual Attainment Test, and for another by the Neale Analysis of Reading Ability each gave a reliable index of cognitive ability level for a further two children. School based evidence of academic performance within the 12-22nd percentile of the normal range was obtained from Cognitive Abilities Test assessment results for a third. For two children undergoing Wechsler assessments, high levels of intercurrent anxiety were viewed as producing unreliable results. For others their capacity to deal with attentional demands was assumed to be

evidenced by their performance within the normal range.

3.1. Ophthalmological, functional and visual perceptual data

All children had essentially normal orthoptic reports when first seen (see Table 3).

Three children had evidence of generalized visual field constriction when tested by confrontation; two showed evidence of peripheral visual field disturbance on perimetric examination (see Appendix F, Figs F1 and F2). The third could be pre-cued during confrontation testing to the presence of a peripheral target and had full visual fields on perimetric examination. Normal or corrected normal acuities were recorded for all children during the follow up period. Follow up perimetry was recorded for Child N only, to 14 years (see Appendix F, Figs F2-F4) when a mild peripheral field deficit persisted.

Five children required specialist visual impairment support. Four had been independently referred by their schools to the specialist visual impairment teacher for education; a fifth was referred by the first author to the sensory impairment division of social work on leaving school. The remaining children had mild or moderate impairment needing advisory input only to family and school. The assessment profiles of these two groups differed and are summarized in Tables 3 and 4.

3.2. CVI inventory data

Profiles of functional impairment, yielded by all positive responses to Inventory questions are given in Table 4 and in Fig. 3.

Statistical analysis of Inventory scores excluded questions where parents returned a “not applicable” (n/a) response as the behaviour could neither be excluded nor included.

In order to determine a cut off threshold CVIS for very severe impairment of function we compared CVIS scores for those children receiving specialist VI support with those for whom specialist support was not needed. Fifteen questions: 1, 2, 3, 12, 19, 20, 23, 24, 27, 29, 39, 41, 44, 48 and 50, yielded 75 scores (mean = 3.05) for the five children requiring visual impairment support and 120 scores (mean = 1.91) for the remaining eight children (see Table 2). An unpaired *t*-test (assuming unequal variances) was used to compare the mean scores for the two groups. CVIS values for the group receiving specialist support were significantly higher (two-sided p value for a significant difference between the means: $p < 0.0001$; [95% CI: 0.74–1.55]).

3.3. Vision perception data (see Table 2)

Four children had visual perception standard scores below 80 (i.e below the 10^{th} percentile), indicating visual perceptual impairment (Ortibus et al., 2011). Three of these had required specialist visual impairment support. Analysis of individual VMI tests identified configural disruption, inappropriate for the child’s age and ability, in ten children including the five who required specialist visual impairment support. Evidence of impaired form perception was recorded for performance with the GMDS(ER) shape matching boards in three children in this group.

3.4. Correlation between VMIS, block design scaled scores (BDS), and CVIS

VMIS were plotted against CVIS values for the 15 question items completed for all children (see Appendix G, Fig G1). Linear regression analysis found a strong statistical correlation between these two variables: correlation coefficient r = -0.81; 95% CI: [-0.94 to -0.47]; two-sided p value = 0.0008.

The Block Design sub-test of the Weschler assessment requires the spatial assembly of a global form copy from its constituent parts, thereby challenging both dorsal (Rizzo & Vecera, 2002) and ventral visual stream function. Impairment in Block Design performance has been found in children with dorsal stream dysfunction (Bellugi, Sabo, & Vaid, 1988). We therefore also looked for a correlation between the BDS available for nine children, and their respective CVIS, and VMIS. Linear regression analysis found a significant, correlation between BDS and CVIS: correlation coefficient r = -0.68; 95% CI: [-0.93 to -0.03]; two-sided p value = 0.04. A linear correlation was also present between BDS and VMIS: r = 0.69 ; 95% CI: [0.05 to 0.93]; two-sided p value = 0.04.

3.5. No correlation between VPS and CVIS

No evidence was found for a linear correlation between these two variables:
correlation coefficient r = -0.310; 95% CI: [-0.74 to 0.29]; two-sided p value = 0.302.

3.6. Motor coordination assessments and neurological examinations

These are summarised in Table 3. All motor coordination scores were $\leq 10^{th}$ percentile, meeting current international criteria for significant motor skills impairment (Blank, Smits-Engelsman, Polatajko, & Wilson, 2012). Participants H, *J* and K persistently head turned to the peripheral target in both the FFOV task and the grasp in peripheral vision task so that only grasp in central vision (Prado et al., 2005) could be assessed. While tests of anterior parietal function (proprioception and stereognosis) were normal twelve children had grasp configurations that met the criterion for OAand thus, posterior parietal dysfunction. (see Table 3 and video files for children A, C, D and F–N). Participant E showed grasp accuracy for all targets and was the only participant without evidence of O Ain either central or peripheral vision. The only other significant neurological examination finding was hypotonia, recorded for ten

Table 1
Findings from developmental history, functional impairments and co-existing conditions at time of diagnosis with dorsal visual stream dysfunction.

Child	Sex	Antenatal & Perinatal History	Family history‡	History of extreme passivity in infancy	Handwriting impairment	Issues with independent feeding	Developmental delay and/or co-morbid disorder
A	m	No abnormality	Father had LD as a child	+	+	+	History of G/M delay
C	f	Emergency LSCS; failure to progess, no fetal distress	None		+		History of G/M delay
D	m	No abnormality	Biological father 'possibly dyslexic'		+	+	ADHD
E	f	Possible maternal alcohol misuse; 2.2 kg at term†	Biological mother "low ability"	Unknown	+		Early-neglect-and failure-to-thrive; anxiety; self-harm
F	f	No abnormality.	Father had depression	+	+	+	Anxiety; episode of literacy skills' regression at secondary school
G	m	Maternal gestational diabetes; premature 32wks† hypoglycemic†	None	+	+	+	History of F/M & G/M delay
H	m	Asymptomatic craniosynostosis†	Brother has ASD		+	+	
I	m	Antenatal-vaginal bleeding	None		+	+	
J	m	Elective LSCS; breech presentation.	None	+	+	+	History of F/M and G/M delay; ADHD; anxiety.
K	m	No abnormality	Father and his identical twin have dyslexia	+	+	+	
L	m	Ventouse delivery	None		+	+	Anxiety; low-self-esteem; soiling & enuresis
M	m	Clomiphene-assisted pregnancy; antenatal vaginal bleeding	Autistic traits in father and full sibling		+	+	Low self-esteem; anxiety
N	f	Maternal pre- eclampsia; probable birth asphyxia†	Brother has learning disability		+	+	Anxiety

†Indicates clear risk of CVI.
‡History of ASD or other developmental disorder or of epilepsy, psychiatric disorder, or learning difficulty.
Abbreviations: m: male; f: female; F/M: fine motor; G/M: gross motor; LD: learning difficulty; ADHD: attention deficit hyperactivity disorder;

Table 2
Results of Cognitive Assessments;

Child	Age at test	Wechsler Intelligence Scale for Children – Fourth UK ed. (WISC-IV UK)						Other assessment data and notes.	FSIQ
		VCI	PRI	WMI	PSI	Scaled Scores on Subtests			
						Block Design	Coding		
A	7y4m							**WISC III**:Verbal IQ: 79 Performance IQ: 100	87
	12y01m	71	84	74	80	7	6		72
C	8y00m	89	112	94	121	14	13		104
D	11y1m	104	117	77	68	19	4		92
E	13y08m	85	98	71	91	6	8		84
F	11y00m	77		71				Formal assessments unreliable owing to high intercurrent anxiety; national examination results at 17 yrs permitted higher education entry.	
G	9y05m	96	112	91	100	11	8		101
H	6y01m	96	82	97	106	1	13	Scaled scores on Vocabulary [3] and Block Design [1] lowered VCI, PRI and FSIQ scores. No other scaled scores fell below 9.	92
I	10y03m	104	92	102	62	11	3		89
J	6y11m	81	69	56	70	1	4	Formal assessments unreliable owing to high intercurrent anxiety.	63
K	6y09m							**NARA-II:** Reading comp: 6y04 m.	
L	12y02m							**School based assessment (CAT scores):** Verbal skills : 80; Non verbal skills: 82; Quantitative skills: 90; Mean SAS: 84.	
M	9y03m					7	10	**WISC-III**: Verbal IQ: 99; Performance IQ: 78.	89
N	10y08m							**WIAT-II:** Word Reading: 10y04 m; Reading Comp: 11y00 m.	

Abbreviations.
CAT Cognitive Abilities Test (Education Scotland).
FSIQ Full Scale Intelligence Quotient.
NARA-II Neale Analysis of Reading Abilities, Second edition.
PRI Perceptual Reasoning Index.
PSI Processing Speed Index.
SAS Standardised Attainment Score (Education Scotland).
VCI Verbal Comprehension Index.
WIAT-II Wechsler Individual Attainment Test, Second UK edition, 2008.
WISC-III Wechsler Intelligence Scale for Children, Third UK edition, 1993.
WISC-IV Wechsler Intelligence Scale for Children, Fourth UK edition, 2004.
WMI Working Memory Index.
Note on Wechsler data: in the table, Index scores and IQ scores have a mean in the general population of 100, with a standard deviation of 15. Scaled scores on individual sub-tests have a mean of 10, with scores between 8 and 12 taken to be within the average range of ability.

participants (77%). No clinical markers of cerebellar dysfunction were otherwise detected.

Twelve children had grasp configurations that met the criterion for OA (see Table 3 and video files for Child A, C, D and F–N). The most extreme impairments of terminal grip size were seen as a palmar grasp, where fingers were flat and outstretched (Fig. 4a). Grasps were initiated by tactile contact with the target (Fig. 4b) and/or the surface on which the target rested (Fig. 4a).

Two broad subtypes of OA were identified: one, present across central and peripheral grasp conditions, the other, present in peripheral vision. In adults such sub-types have been designated “foveal OA” and “non-foveal OA” (Buxbaum & Coslett, 1998); the latter proposed as a lesser deficit arising from “partial compensation of the underlying deficit by systems coding different forms of spatial location information”.

We considered that this mechanism offered explanation for the possible evolution, through childhood maturation, of a possibly severe central grasp impairment to a milder, less functionally significant, peripheral grasp impairment. If so, the milder peripheral grasp type should be associated with better motor skills’ development than an OA enduring in central vision (OAc). We therefore examined the relationship between Beery MCI severity and the presence or absence of OAc.

The Beery MC assessment-tests performance in the dominant hand. We predicted an association between OAc for the dominant hand (OAc.dom), or both hands (OAc.bil) and severe motor skills impairment (MCI $\leq$ 5th percentile). In view of the small sample size, correspondence between OAc and MCI was determined by Method Agreement Analysis, using Cohen’s weighted Kappa statistic K. Analysis found very close accordance, in keeping with our hypothesis: [OAc.bil + OAc.dom] and MCI $\leq$ 5th percentile: K = 1.00 [95% CI for K = 0.46–1.54]; P = 0.0002.

Handedness did not appear to influence prognosis: equal numbers (n = 3) of left handers appeared in both ASD groups (severely affected and better compensated).

Table 3
. Neurological and ophthalmological findings in the ASD children examined, correlated with motor coordination scores. Highlights indicate children requiring specialist VI support.

		Ophthalmological examination findings				Neurological examination findings					Beery motor coordination standard scores (MCS) and percentiles(pc) Mean = 100, SD = 15	
Child	Age^{V} Age^{B}	VA^{R}	VA^{L}	SQ	VF	H	S	P	OA	Other	MCS	MC(pc)
A	†14/5 12/4	6/6	6/6	LET	N/A	L	N/A	N/A	OA, $LH^{=}$ & $RH^{=}$, central	Hypotonia	73	3
C	9/0 10/4	6/6	6/7.5	–	F^{P}	R	N	N	OA, ‡LH, LHF	Hypotonia	81	10
D	†12/0 12/6	6/5	6/6	–	F^{P}	R	N	N	OA, LH & ‡RH, central	Hypotonia	< 45	< 0.02
E	14/11 16/2	6/4.8	6/3.8	–	Con^{C} F^{P}	R	N	N	No central or peripheral OA	Hypotonia	78	7
F	16/0 17/7	6/7	6/5	–	Con^{C} Con^{P}	L	N	N	OA, ‡LH, central	–	58	0.6
G	13/8 12/1	6/9.5	6/9.5	–	F^{P}	R	N	N	OA, ‡LH & RH, central	Early hypotonia,	64	1
H	10/11 10/11	6/4	6/4	–	F^{C}	L&R	N	N	OA, ‡LH & RH, central	MRI: sagittal suture stenosis	45	0.02
I	12/0 13/9	6/7.5	6/7.8	–	F^{P}	R	N	N	OA, ‡ LH, central	–	81	10
J	11/6 9/3	6/4	6/4	–	F^{P}	R	N/A	N/A	OA, $LH^{=}$ & $RH^{=}$, central	Hypotonia; MRI: normal.	67	1
K	9/6 11/0	6/4	6/4	–	F^{C}	R	N	N	OA, ‡LH & RH, central	Hypotonia	50	0.07
L	15/6 13/7	6/7	6/6	–	F^{P}	R	N	N	OA, $LH^{=}$ & $RH^{=}$, central	Hypotonia	69	2
M	†13/3 12/3	6/7	6/6	–	F^{P}	L	N	N	OA, ‡LH&RH, central	Hypotonia	46	0.03
N	†14/4 16/5	6/6	6/6	–	Con^{C} Con^{P}	L	N	N	OA, ‡LH & RH, central	Hypotonia; MRI: normal	67	1

† Denotes more than one video sequence available for analysis.
‡ Denotes hand showing greatest magnitude of grasp impairment.
= Denotes equivalent impairment.
Abbreviations.
N/A: not assessed; A^{V}: age (in years/months) at video analysis; Age^{B}: age at Beery assessment; SQ: squint; LET: left esotropia; VF: visual fields; H: hand dominance; S: examination for stereognosis; P: examination for proprioception; F^{P}: full on perimetric testing; F^{C}: full to confrontation; Con^{C}: concentric reduction with confrontation testing; Con^{P}: concentric reduction with perimetric measurement; N: normal; LH: left hand; RH: right hand; LHF: left hemifield in peripheral grasp condition.

4. Discussion

4.1. Evidence for a higher order visual processing deficit in autism

Functional MRI (Haist, 2005; Keehn, Nair, Lincoln, Townsend, & Müller, 2016) and diffusion tractography MRI (Boets et al., 2018; Im et al., 2018., Fitzgerald, 2017) studies provide evidence of impaired higher order visual processing networks in autism. Haist (2005) used functional MRI (FMRI) BOLD activation to investigate networks for automatic and voluntary visual spatial attention in ASD. The task required stimulus (a white letter on black background) orientation discrimination following spatial to target cues of 100 ms (short interstimulus interval [ISI]) or 800 msec (long ISI) respectively. FMRI results showed a reduction across conditions in activity within frontal, parietal, and occipital regions in ASD relative to controls. Results were particularly striking for the short ISI condition: controls showed greater activation over ASD in the left hemisphere inferior parietal lobule (IPL) while right hemisphere IPL activation, present in controls, was absent in ASD participants. Also in contrast to controls, no activation was seen in the ASD group in the posterior cerebellar vermis, for either long or short ISI tasks. Keehn et al. (2016) used FMRI to investigate the neuro-cognitive networks subserving visual attentional capture in 16 high function autism children, relative to controls. Target stimuli were presented in the presence of task- irrelevant distractors. In the ASD group there was failure to activate the ventro-dorsal attentional network (connecting temporo-parietal and inferior frontal cortices [Corbetta & Shulman, 2002]) and cerebellum, compared to controls. Taken together, both these functional studies suggest a dysfunctional fronto-parietal spatial network that has significant connectivity with the cerebellum.

Recent diffusion-MRI tractography studies have reported abnormal fronto-parietal white matter organisation in autism, in the

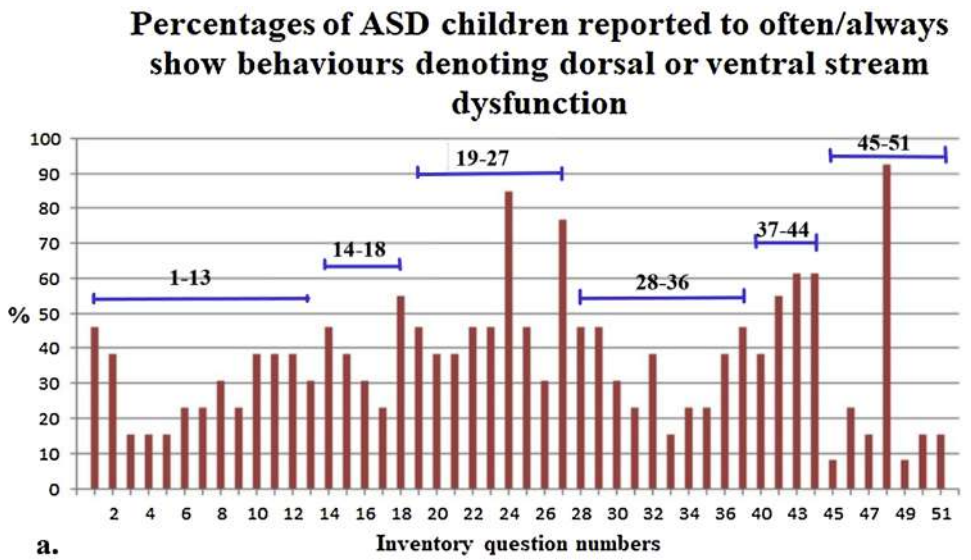
Table 4
CVI Inventory, Beery VP and VMI, and GMDS data. Highlights indicate children requiring specialist visual impairment support.

Child	Visual functional impairments (based on parental CVI Inventory responses)					Mean CVI Inventory score (CVIS) Mean = 0.43,SD = 0.25		Beery VP and VMI total standard scores (VPS,VMIS). Mean = 100,SD = 15		Indicators of"piecemeal" visual perception perception	Indicators of impaired 3d visual form perception
	MP	SP	VAt	OA^R	FEP	All items	Fifteen items (see text)	VPS	VMIS	Configural disruption of BeeryVMI geometric figures (CD) +/-	GMDS formboards: shape recognition impaired to below an 8 year level (+/-)
A	+	+	+CHF	+	+	1.64	2.13	88	72	+	–
C	m	+	mCHF	m	+	0.75	1.00	92	99	+	–
D	+	+	+LHF mRHF	+	+	1.64	2.20	88	80	+	–
E	+	+	+CHF	+	+	1.7	2.47	89	88	–	–
F	+	+	+LHF	m	+	1.95	2.40	73	91	+	–
G	+	+	N/A	+	+	1.95	2.13	110	90	+	–
H	+	+	+CHF	+	+	3.03	3.40	79	60	+	+ (10y/11 m)
I	+	+	mCHF	–	+	1.19	1.27	101	93	–	–
J	+	+	+LHF	+	+	2.58	2.80	91	55	+	+ (11y/6 m)
K	+	+	+CHF	+	+	2.15	2.53	77	72	+	–
L	m	+	mCHF	–	+	1.58	1.67	92	89	–	–
M	+	+	+CHF	+	+	2.04	2.73	73	62	+	–
N	+	+	+CHF	+	+	3.66	3.80	97	62	+	+ (10y/2 m)

Abbreviations.
VAt: lower field or hemifield perceptual impairment for right (R), left (L),or combined fields (CHF); MP: movement perception impairment; SP: impaired simultaneous visual perception; OA^R: optic ataxia reported; FEP: poor ability to correctly interpret facial expressions. Pluses denote the presence of impairment; minuses, the absence; m:denotes milder impairment; seen sometimes rather than often.

superior longitudinal fasiculus (SLF) (Fitzgerald, 2017), neuroanatomical correlate of the dorsal visual stream (Merabet et al., 2018), and the inferior longitudinal fasiculus (ILF) (Boets et al., 2018; Im et al., 2018), neuroanatomical correlate of the ventral visual stream (Merabet et al., 2018; Ortibus et al., 2012; Woloszyn & Sheinberg, 2009). Impaired connectivity has been reported by Im et al. (2018) in the SLF, ILF and inferior fronto-occipital fasiculus (IFOF) in high-function autism. Given that a combined role for the ILF and the IFOF in face-processing has also been proposed (Avidan et al., 2014), these diffusion MRI tractography studies are consistent with severe impairment in the largescale networks subserving spatial attention, object and face recognition, in autism.

The evidence we present in our study for the co-occurrence of visual functional impairment in autism concurs with much earlier reports of behaviours in children with the disorder. In 1969 Lorna Wing (1969) reported remarkable similarities in the parent-reported, visually dependent behaviours seen in children with autism as well as non-autistic children with partial sight. These included difficulties walking downstairs and seeing items at distance, difficulties predicted of DVSD. In addition, both groups showed similar tendencies to examine people and objects by employing non-visual aids to recognition: touch, taste and smell. Frith and Hermelin (1969), and, later, Masterton and Biederman (1983), subsequently published experimental data suggesting a superior performance in children with autism (in comparison to typically developing controls) for tasks reliant on tactile-proprioceptive rather than visual perceptual feedback. Masterton and Biederman (1983) further proposed a link between abnormal visual function and movement in ASD, positing that impaired processing of "sequential visual information" might compromise the visual control of movement and increase "reliance on proprioceptive input". Marko et al. (2015) more recently undertook a motor learning analysis in children with ASD which again found reliance on proprioceptive over visual feedback, in contrast to controls, in association with smaller sensorimotor regions of the cerebellum on volumetric MRI analysis. The authors propose that in ASD, indirect cortical visual input to the cerebellum may be compromised, resulting in compensatory proprioceptive feedback through uncompromised spino-cerebellar tracts. Visual neural data from primate studies supports such hypothesis: the source of cortical visual input to the pontine nuclei is derived from cells in the dorsal stream, while there is little if any ventral stream input to the pons (Glickstein, Sultan, & Voogd, 2011). Depleted dorsal visual stream input, from the posterior parietal cortex to the posterior cerebellum via the pons (Schmahmann, 1991), appears consistent with an increased dependence on proprioceptive, over visual, feedback in ASD and, indeed, consistent with the neuroimaging data (see above) reported by Haist (2005) and Keehn et al. (2016). Such reduced neurovisual input to the cerebellum in ASD may also account for the hypotonia reported in several studies (Akshoomoff, Farid, Courchesne, & Haas, 2007; Haas et al., 1996; Rapin, 1996). The rate we report for coexisting hypotonia is high (77%) in contrast to that reported in other larger scale studies e.g Rapin (1996), 25%, but not dissimilar to that reported by Akshoomoff et al. (2007), of 69%.



a.

Inventory questions	Function measured	Neuroanatomical pathway
1-13	Hemifield/ lower field attention	Predominant Dorsal
14-18	Movement perception	
† 19-27	Simultaneous visual perception	
28-36	Visual guidance of body movement	
37-44	Ability to split visual attention	
45-51	Face/ object recognition	Predominant Ventral

b.

Fig. 3. Frequency of visual functional impairments reported for the group, according to inventory question items.
3a. Percentages of ASD children in the group showing impairment, according to Inventory item.
3b. Impairment types and their corresponding neuroanatomical correlates, according to question range.
*Question 23 relates to navigational landmark memory, predominantly within the ventral stream domain.

4.2. Dorsal and ventral visual stream impairments

Across our group the frequency of parent-reported behaviours denoting DVSD varied considerably, but those indicating compromise to visual movement perception, simultaneous visual perception (including compromise to visual search of complex visual environments) and face expression processing, were universally reported.

Impaired visual search of complex visual environments is consistent with simultanagnostic vision and with an atypical visual processing biased towards focal elements of the global scene. This in turn is consistent with the concept of weak central coherence proposed by Frith (1989) as an underlying processing bias towards local information, with relative failure to integrate elements into global wholes or to “see the wood for the trees”. The piecemeal visual processing that accompanies simultanagnosia has previously been reported in autism (Booth, Charlton, Hughes, & Happé, 2003) as well as in Williams syndrome, where the coexistence of a dorsal stream visual deficit has been extensively proven (Atkinson et al., 1997; Atkinson, 2017; Cowie, Braddick, & Atkinson, 2012).

Constriction of the peripheral visual field, present in three children in this study, is consistent with DVSD (Milne, Scope, Griffiths, Codina, & Buckley, 2013): the cortical visual projections of central and peripheral vision markedly differ, with heavy dorsal stream bias evident in the peripheral visual field (Milne et al., 2013). While compromise to peripheral visual field function in ASD is consistent with reports of reduced peripheral visual field sensitivity (Milne et al., 2013) and a reduced functional field of view (Song,

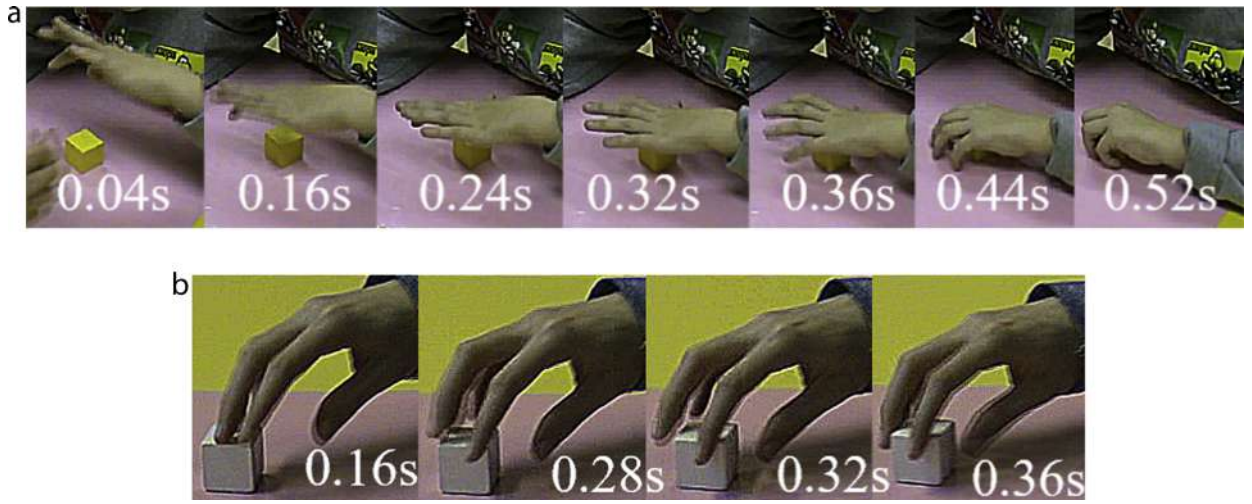


Fig. 4. Examples of still frame sequences ofOA.
(a) Grasp sequence for Child K, 9y6m: left hand grasp of a 2 cm yellow wooden cube placed in central vision, showing major impairment, palmar approach, fingers outstretched. The fingertips touch the table surface and "slide" towards the target.
(b) Grasp sequence for Child A, 14y5m: right hand grasp for a 3 cm white cube, seen in central vision. Initial grasp is facilitated by early target contact by the second and third digits, followed by positional adjustment of these as the thumb closes in.

Hakoda, Sanefuji, & Cheng, 2015) in ASD, severe constriction of the peripheral visual field (as seen in Child N) is not, however, commonly reported in simultanagnosia. Visual fields are usually full or near-normal (Vighetto & Krolak-Salmon, 2007) in simultanagnosia, even for one reported adult who "essentially saw the world with the ventral system" (Michel & Henaff, 2004). One possible explanation for this is that the spatial attentional visual field fluctuates (Dalrymple et al., 2013; Tyler, 1968): while attentional resources are allocated to central vision at the expense of peripheral information, spatial attentional dimensions may not be fixed. Expansion of the visual attentional field is possible, though at the expense of detail (Dalrymple et al., 2013).

We found objective evidence for DVSD, in respect of grasp impairments that met the criterion for OA, in twelve of the thirteen children in this study. In nine, a bilateral OA was consistent with a bilateral posterior parietal deficit. In five of these OA was most severe in the left hand, indicating a greater deficit in the right hemisphere. Three children had a unilateral OA affecting the left hand, consistent with either a unilateral right posterior parietal deficit, or possibly a bilateral deficit that was most marked in the right hemisphere (participant D was the only child with a bilateral OA that was most severe in the right hand and interestingly the only child to have ADHD as a coexisting diagnosis).

In adults, lesional studies of neglect and fMRI studies of attention lend support to a model of spatial attention where the right hemisphere subserves attention for both contra- and ipsilateral hemispace while the left hemisphere primarily subserves a degree of attention for contralateral hemispace (Mapstone et al., 2003; Ting et al., 2011). Competent manipulation of items requires the continuous transfer of updated visual data from the cortex to the hand, and the right hemisphere may play a more significant part in such processing (Pisella et al., 2011). In childhood, DVSD (particularly in the critically important right hemisphere) might be expected to trigger alternative visual perceptual development. OA may be the outcome of more ventral-stream mediated, visually guided movement, replacing or supporting the "depleted automatic control" (Milner & Goodale, 2008) arising from impaired dorsal visual stream function.

We consider that the significant correlation between OAc.dom and severe MCI lends weight to the hypothesis that mechanisms generating central OA and simultanagnosia, potentially arising in the parieto-occipital cortex, may underpin the motor skills impairment seen in autism. The linear relationship we found for VMIS and CVIS evidences a direct link between the severity of piecemeal visual perception and the severity of global functional impairment that we suggest is caused by DVSD, in this group of motor impaired children. The evidence found for a linear relationship between BDS, CVIS and VMIS suggests that performance in Block Design, like the Beery VMI, is heavily dorsal visual stream dependent.

The five most functionally impaired children in this study all had CVIS $\geq$ 2.5 and had parent-reported behaviours consistent with global dorsal visual dysfunction. Impaired recognition of faces, objects, or familiar environments was also reported for these children, consistent with impaired global ventral visual stream processing, and correlating, for three, with the impaired perception of three dimensional shape recorded on Griffiths' assessment. Three children in this group also had visual perception standard scores (VPS) that indicated visual perceptual impairment of global form perceived within a very narrow field of two-dimensional view (test items are presented on paper in 1.2 x 1.2 cm boxes). We found no evidence, however, for a linear correlation between VPS and CVIS, and therefore no evidence to suggest that a low VPS score may be a reliable indicator of functional impairment. Indeed, a similar order of VPS was recorded for participant F, a less significantly functionally compromised child.

Ventral as well as dorsal visual stream impairment has been reported in both Williams syndrome and autism. In Williams syndrome, ventral visual stream dysfunction (in respect of impaired object recognition (O'Hearn et al., 2011) and impaired navigation of

familiar environments (Broadbent, Farran, & Tolmie, 2014) may coexist with dorsal stream visual impairment. In autism, there is substantial evidence for ventral visual stream efficiency (in respect of superior visual perception of detail and form: see detailed reviews in Dakin and Frith (2005) and Happe and Frith (2006), but impaired global processing within the ventral visual stream (in respect of dysfunctional face-processing (Dalrymple, Corrow, Yonas, & Duchaine, 2012) and impaired form perception (Grinter, Maybery, Pellicano, Badcock, & Badcock, 2010) has also been reported. We found evidence for impaired global ventral stream processing only in those children with exceptionally severe DVSD and suggest that the link between DVSD and global ventral stream impairment may usefully be considered a subject for future research.

5. Conclusions

We propose that the presence of age-inappropriate configural disruption in patterns or line drawings copied by the motor-impaired autistic child should alert the tester to the presence of simultanagnosia in the same way such performance already does in children with Williams syndrome.

We suggest that assessment to determine the pattern and severity of global DVSD should be considered when motor impairment is identified in autism, in order to provide families and schools with effective interventional strategies (McKillop et al., 2006) for visual perceptual impairment (Macintyre-Beon et al., 2010) and to ascertain the need for specialist visual impairment support.

Larger scale studies to explore the prevalence and the severity of DVSD across the spectrum of autism in childhood, are needed. There is a pressing requirement in particular to investigate how targeted visual impairment support may positively influence the academic, social and emotional development of autistic children with severe DVSD.

6. Study limitations

We acknowledge that the greatest limitation of this study is the mixed aetiology of the group with only a minority of participants conclusively having no evidence of risk of injury to the developing brain as a causal link to DVSD.

We followed the thirteen children reported here because of the lack of long term data for outcomes in children with normal ocular examination and DVSD. Lack of clinic capacity precluded follow up for those children receiving local assessment.

Ideally all children would have been assessed using the same standardised cognitive assessment tool but this was not always possible. Our aim was to find evidence of cognition that was within the normal range and we therefore accepted a range of standardised assessments (see Table 2).

A structural brain abnormality has also not been excluded in the majority of children. Given the lack of developmental skills' arrest or regression the likelihood of abnormality on MRI was considered low and imaging only deemed justifiable if the neurological presentation deviated from a purely Balint-type. Participants H and N had evidence of possible unilateral neglect and underwent MRI (with normal outcome) on these grounds. Participant G was offered imaging because of prematurity and neonatal hypoglycaemia, but declined.

None of the children underwent visual electrodiagnostic studies, as no signs of visual or visual perceptual deterioration and no fundus abnormalities were identified during follow up. Given convincing evidence (Milne et al., 2013; Song et al., 2015) of abnormal full-field electroretinographic findings in a subgroup of normally sighted individuals with ASD, such future study in children with severe DVSD merits consideration.

Analysis of many of the archive video grasp sequences was impossible owing to blur or poor grasp aperture views. Quality film that was recorded contemporaneously with the other assessments (eye examination, CVI Inventory, Beery and Griffiths' assessments) was not often available and we had to accept a chronological difference of over 2 years in the datasets compared for some children (see Table 3).

Finally, we accept that a major limitation of this work is the lack of any comparison with a dataset from motor- impaired children, without autism. To identify a valid group of age and ability- matched controls for such study would have been difficult given the variability in age at time of the assessments reported here. Of note, however, validation of the method of examination for OA included an earlier study, approved by the West of Scotland NHS ethics committee (https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/assessment-of-vision-processing-and-hand-movement-in-children/) funded by Research and Development, NHS Dumfries and Galloway, Scotland, UK. This study sought to examine the characteristics of vision processing and hand grasp in a group of twelve randomly selected, typically developing children screening negative for DVSD. Despite strict exclusion criteria for developmental disorder the study identified (on Beery assessment) three children with unrecognised motor skills' impairment. Within the total group, 225 grasp conditions were examined. The proportions of abnormal grasps (meeting the criterion for OA) in the two groups (typicals versus motor-impaired) significantly differed: 0.5:0.01; $p < 0.0001$. We considered that these results both lent further support to proposals for a spectrum of DVSD in the developmental disorders (Atkinson, 2017; Braddick & Atkinson, 2011) and cautioned against the assumption of reliability of the CVI Inventory as a single tool for the assessment of DVSD.

Acknowledgements

We are particularly grateful to the late Lorna Wing, without whose enthusiasm, support and encouragement, this project would not have proceeded.

Individual licence to modify sticklebricks, as described, by kind permission of Hasbro Inc. 2013. The modifications were carried

out with the kind assistance of Remap.

Thanks to the Research and Re-standardisation subcommittee of ARICD in 2011 for their kind permission to use certain items from the Griffiths Mental Development Scales - Extended Revised (GMDS-ER) for the purpose of observational analysis of approach to task by children with CVI; and to the same for releasing the original GMDS-ER dataset for the purpose of an earlier control study.

The authors wish to thank Professor Anne O'Hare for her invaluable guidance on revision to text, and Drs Paul Eunson and Gwen Baxter for their encouragement, support and advice. We also extend thanks to Helen Cameron and Julie McDougall for their invaluable help in assessing the children, to Heather Barrington for the statistical analysis, and to Hamish Hay for the schematic illustrations.

The service for children with CVI would not exist without the combined support of our many colleagues from NHS Dumfries and Galloway, in particular orthoptics and ophthalmology, and from Dumfries and Galloway regional council. We extend our very particular thanks to the children and their parents for their enthusiastic support for the service for children with cerebral visual impairment.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.rasd.2019.101456.

References

Akar, Y., Yilmaz, A., & Yucel, I. (2008). Assessment of an effective visual field testing strategy for a normal pediatric population. *International Journal of Ophthalmology, 222*(5), 329–333. https://doi.org/10.1159/000144101.

Avidan, G., Tanzer, M., Hadj-Bouziane, F., Liu, N., Ungerleider, L., & Behrmann, M. (2014). Selective dissociation between core and extended regions of the face processing network in congenital prosopagnosia. *Cerebral Cortex, 24*(6), 1565–1578. https://doi.org/10.1093/cercor/bht007.

Atkinson, J., King, J., Braddick, O., Nokes, L., Anker, S., & Braddick, F. (1997). A specific deficit of dorsal stream function in Williams' syndrome. *Neuroreport, 8*(8), 1919–1922.

Atkinson, J., Braddick, O., Anker, S., Curran, W., Andrew, R., Wattam-Bell, J., et al. (2003). Neurobiological models of visuospatial cognition in children with Williams syndrome: Measures of dorsal-stream and frontal function. *Developmental Neuropsychology, 23*(1-2), 139–172. https://doi.org/10.1080/87565641.2003.9651890.

Atkinson, J. (2017). The Davida Teller award lecture, 2016: Visual brain development: A review of "dorsal stream vulnerability" motion, mathematics, amblyopia, actions, and attention. *Journal of Vision, 17*(3), 26. https://doi.org/10.1167/17.3.26.

Akshoomoff, N., Farid, N., Courchesne, E., & Haas, R. (2007). Abnormalities on the neurological examination and EEG in young children with pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 37*(5), 887–893.

Baranello, G., Vasco, G., Ricci, D., & Mercuri, E. (2007). Visual function in nonsyndromic craniosynostosis: Past, present, and future. *Child's Nervous System : ChNS : Official Journal of the International Society for Pediatric Neurosurgery, 23*(12), 1461–1465.

Barton, J. J. S. (2011). In C. Kennard, & R. J. Leigh (Eds.). *Chapter 9 - Disorders of higher visual processing*Elsevierhttps://doi.org/10.1016/B978-0-444-52903-9.00015-7.

Baxter, A. J., Brugha, T. S., Erskine, H. E., Scheurer, R. W., Vos, T., & Scott, J. G. (2015). The epidemiology and global burden of autism spectrum disorders. *Psychological Medicine, 45*(3), 601–613.

Beery, K. E., Buktenica, N. A., & Beery, N. A. (2010). *Beery-Buktenica developmental test of visual-motor integration, 6th edition (BEERY™ VMI* (6th ed.). Minneapolis, MN: NCS Pearson, Inc.

Bellugi, U., Sabo, H., & Vaid, J. (1988). Spatial deficits in children with Williams syndrome. In J. Stiles-Davis, M. Kritchevsky, & U. Bellugi (Eds.). *Spatial cognition brain bases and development* (pp. 273–298). USA: Lawrence Ehrlbaum Associates.

Binkofski, F., Dohle, C., Posse, S., Stephan, K. M., Hefter, H., Seitz, R. J., et al. (1998). Human anterior intraparietal area subserves prehension: A combined lesion and functional MRI activation study. *Neurology, 50*(5), 1253–1259.

Blank, R., Smits-Engelsman, B., Polatajko, H., & Wilson, P. (2012). European academy for childhood disability (EACD): Recommendations on the definition, diagnosis and intervention of developmental coordination disorder (long version)*. *Developmental Medicine and Child Neurology, 54*(1), 54–93.

Booth, R., Charlton, R., Hughes, C., & Happé, F. (2003). Disentangling weak coherence and executive dysfunction: Planning drawing in autism and attention–deficit/hyperactivity disorder. *Philosophical Transactions of the Royal Society of London Series B, Biological Sciences, 358*(1430), 387–392.

Braddick, & Atkinson (2011). Development of human visual function. *Vision Research, 51*(13), 1588–1609. https://doi.org/10.1016/j.visres.2011.02.018.

Broadbent, H. J., Farran, E. K., & Tolmie, A. (2014). Egocentric and allocentric navigation strategies in Williams syndrome and typical development. *Developmental Science, 17*(6), 920–934.

Buxbaum, L. J., & Coslett, H. B. (1998). Spatio-motor representations in reaching: Evidence for subtypes of optic ataxia. *Cognitive Neuropsychology, 15*(3), 279–312.

Campione, G. C., Piazza, C., Villa, L., & Molteni, M. (2016). Three-dimensional kinematic analysis of prehension movements in young children with autism spectrum disorder: New insights on motor impairment. *Journal of Autism and Developmental Disorders, 46*(6), 1985–1999.

Chechlacz, M., Rotshtein, P., Hansen, P. C., Riddoch, J. M., Deb, S., & Humphreys, G. W. (2012). The neural underpinings of simultanagnosia: Disconnecting the visuospatial attention network. *Journal of Cognitive Neuroscience, 24*(3), 718–735. https://doi.org/10.1162/jocn_a_00159.

Cooper, S. A., & O'Sullivan, M. (2016). Here, there and everywhere: Higher visual function and the dorsal visual stream. *Practical Neurology, 16*(3), 176–183. https://doi.org/10.1136/practneurol-2015-001168.

Cowie, D., Braddick, O., & Atkinson, J. (2012). Visually guided step descent in children with Williams syndrome. *Developmental Science, 15*(1), 74–86.

Dakin, S., & Frith, U. (2005). Vagaries of visual perception in autism. *Neuron, 48*(3), 497–507.

Dalrymple, K. A., Kingstone, A., & Barton, J. J. (2007). Seeing trees OR seeing forests in simultanagnosia: Attentional capture can be local or global. *Neuropsychologia, 45*(4), 871–875. https://doi.org/10.1016/j.neuropsychologia.2006.07.013.

Dalrymple, K., Bischof, W., Cameron, D., Barton, J., & Kingstone, A. (2009). Global perception in simultanagnosia is not as simple as a game of connect-the-dots. *Vision Research, 49*(14), 1901–1908. https://doi.org/10.1016/j.visres.2009.05.002.

Dalrymple, K. A., Corrow, S., Yonas, A., & Duchaine, B. (2012). Developmental prosopagnosia in childhood. *Cognitive Neuropsychology, 29*(0), 402.

Dalrymple, K. A., Barton, J. J., & Kingstone, A. (2013). A world unglued: Simultanagnosia as a spatial restriction of attention. *Frontiers in Human Neuroscience, 7*, 145.

Damasio, A. R., & Benton, A. L. (1979). Impairment of hand movements under visual guidance. *Neurology, 29*(2), 170–174.

Donaghy, M. (2009). The clinical approach. In M. Donaghy (Ed.). *Brain's diseases of the nervous system* (pp. 17–63). (12th ed.). USA: Oxford University Press.

Drummond, S. R., & Dutton, G. N. (2007). Simultanagnosia following perinatal hypoxia: A possible pediatric variant of Balint syndrome. *Journal of Aapos: American Association for Pediatric Ophthalmology & Strabismus, 11*(5), 497–498.

Dutton, G. N., Saaed, A., Fahad, B., Fraser, R., McDaid, G., McDade, J., et al. (2004). Association of binocular lower visual field impairment, impaired simultaneous perception, disordered visually guided motion and inaccurate saccades in children with cerebral visual dysfunction-a retrospective observational study. *Eye, 18*(1), 27–34.

Dutton, G. N., Calvert, J., Ibrahim, H., Macdonald, E., McCulloch, D. L., Macintyre-Beon, C., et al. (2010). Structured clinical history taking for cognitive and perceptual visual dysfunction and for profound visual disabilities due to damage to the brain in children. In G. N. Dutton, & M. Bax (Eds.). *Visual impairment in children due to damage to the brain* (pp. 117–128). London: Mac Keith Press.
Forti, S., Valli, A., Perego, P., Nobile, M., Crippa, A., & Molteni, M. (2011). Motor planning and control in autism. A kinematic analysis of preschool children. *Research in Autism Spectrum Disorders, 5*(2), 834–842. https://doi.org/10.1016/j.rasd.2010.09.013.
Friedman-Hill, S. R., Robertson, L. C., & Treisman, A. (1995). Parietal contributions to visual feature binding: Evidence from a patient with bilateral lesions. *Science, 269*(5225), 853–855.
Frith, U. (1989). *Autism: Explaining the enigma* (1st ed.). London: Blackwell.
Frisen, L., & Glansholm, A. (1975). Optical and neural resolution in peripheral vision. *Investigative Ophthalmology, 14*(7), 528–536.
Frith, U., & Hermelin, B. (1969). *The role of visual and motor cues for normal, subnormal and autistic children.* ENGLAND: Blackwell Publishers.
Galletti, C. (2018). The dorsal visual stream revisited: Stable circuits or dynamic pathways? *Cortex : A Journal Devoted to the Study of the Nervous System and Behavior. 98*, 203–217. https://doi.org/10.1016/j.cortex.2017.01.009.
Gillen, J. A., & Dutton, G. N. (2003). Balint's syndrome in a 10-year-old male. *Developmental Medicine and Child Neurology, 45*(5), 349–352.
Glickstein, M., Sultan, F., & Voogd, J. (2011). Functional localization in the cerebellum. *Cortex; A Journal Devoted to the Study of the Nervous System and Behavior, 47*(1), 59–80.
Goodale, M. A., & Milner, A. D. (2018). Two visual pathways - where have they taken us and where will they lead in future? *Cortex; A Journal Devoted to the Study of the Nervous System and Behavior, 98*, 283–292.
Goodale, M. A. (2013). *Sight unseen: An exploration of conscious and unconscious vision* (2nd ed.). Oxford UK: Oxford University Press.
Goodale, M. A., & Milner, A. D. (1992). Separate visual pathways for perception and action. *Trends in Neurosciences, 15*(1), 20–25.
Green, D., Baird, G., Barnett, A. L., Henderson, L., Huber, J., & Henderson, S. E. (2002). The severity and nature of motor impairment in Asperger's syndrome: A comparison with specific developmental disorder of motor function. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 43*(5), 655–668.
Green, D., Charman, T., Pickles, A., Chandler, S., Loucas, T., Simonoff, E., et al. (2009). Impairment in movement skills of children with autistic spectrum disorders. *Developmental Medicine and Child Neurology, 51*(4), 311–316.
Grinter, E., Maybery, M., Pellicano, E., Badcock, J., & Badcock, D. (2010). Perception of shapes targeting local and global processes in autism spectrum disorders. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 51*(6), 717–724. https://doi.org/10.1111/j.1469-7610.2009.02203.x.
Haas, R. H., Townsend, J., Courchesne, E., Lincoln, A. J., Schreibman, L., & Yeung-Courchesne, R. (1996). Neurologic abnormalities in infantile autism. *Journal of Child Neurology, 11*(2), 84–92. https://doi.org/10.1177/088307389601100204.
Haist, F. (2005). The functional neuroanatomy of spatial attention in autism spectrum disorder. *Developmental Neuropsychology, 27*(3), 425–458. https://doi.org/10.1207/s15326942dn2703_7.
Happe, F., & Frith, U. (2006). The weak coherence account: Detail-focused cognitive style in autism spectrum disorders. *Journal of Autism and Developmental Disorders, 36*(1), 5–25.
Harris, S. R. (2017). Early motor delays as diagnostic clues in autism spectrum disorder. *European Journal of Pediatrics, 176*(9), 1259–1262. https://doi.org/10.1007/s00431-017-2951-7.
Hempel, M. S. (1993). *The neurological examination technique for toddler-age.* University of Groningen.
Himmelbach, M., & Karnath, H. (2007). Optic ataxia: A gateway to the human visual action system. In F. Mast, & L. Jäncke (Eds.). *Spatial processing in navigation, imagery and perception* (pp. 85–105). US: Springer. https://doi.org/10.1007/978-0-387-71978-8_6.
Holmes, G. (1918). Disturbances of visual orientation. *The British Journal of Ophthalmology, 2*(10), 506–516. https://doi.org/10.1136/bjo.2.10.506.
Huberle, E., & Karnath, H. O. (2006). Global shape recognition is modulated by the spatial distance of local elements-evidence from simultanagnosia. *Neuropsychologia, 44*(6), 905–911 doi:S0028-3932(05)00294-0.
Im, W., Ha, J., Kim, E., Cheon, K., Cho, J., & Song, D. (2018). Impaired white matter integrity and social cognition in high-function autism: Diffusion tensor imaging study. *Psychiatry Investigation, 15*(3), 292–299. https://doi.org/10.30773%2Fpi.2017.08.15.
Jakobson, L. S., Archibald, Y. M., Carey, D. P., & Goodale, M. A. (1991). A kinematic analysis of reaching and grasping movements in a patient recovering from optic ataxia. *Neuropsychologia, 29*(8), 803–809.
Jeannerod, M. (1986). The formation of finger grip during prehension. A cortically mediated visuomotor pattern. *Behavioural Brain Research, 19*(2), 99–116.
Jeannerod, M., Decety, J., & Michel, F. (1994). Impairment of grasping movements following a bilateral posterior parietal lesion. *Neuropsychologia, 32*(4), 369–380.
Karl, J. M., & Whishaw, I. Q. (2013). Different evolutionary origins for the reach and the grasp: An explanation for dual visuomotor channels in primate parietofrontal cortex. *Frontiers in Neurology, 4*, 208. https://doi.org/10.3389/fneur.2013.00208.
Karnath, H., Ferber, S., Rorden, C., & Driver, J. (2000). The fate of global information in dorsal simultanagnosia. *Neurocase, 6*(4), 295–306. https://doi.org/10.1080/13554790008402778.
Keehn, B., Nair, A., Lincoln, A., Townsend, J., & Müller, R.-A. (2016). Under-reactive but easily distracted: An fMRI investigation of attentional capture in autism spectrum disorder. *Developmental Cognitive Neuroscience, 17*(C), 46–56. https://doi.org/10.1016/j.dcn.2015.12.002.
Lai, M., Lombardo, M. V., & Baron-Cohen, S. (2014). Autism. *Lancet, 383*(9920), 896–910. https://doi.org/10.1016/S0140-6736(13)61539-1.
Libertus, K., Sheperd, K. A., Ross, S. W., & Landa, R. J. (2014). Limited fine motor and grasping skills in 6-month-old infants at high risk for autism. *Child Development, 85*(6), 2218–2231. https://doi.org/10.1111/cdev.12262.
Luiz, D., Barnard, A., Knosen, N., Kotras, N., Horrocks, S., McAlinden, P., et al. (2006). *Administration manual. Griffiths mental development scales - extended revised: 2 to 8 years (GMDS-ER 2-8).* Oxford: Hogrefe.
Luria, A. R. (1959). Disorders of "simultaneous perception" in a case of bilateral occipito-parietal brain injury. *Brain, 82*, 437–449.
Luria, A. R. (1966). Disturbances of higher cortical functions with lesions of the occipital and occipitoparietal regions. In B. Haigh (Ed.). *Higher cortical functions in man* (pp. 123–164). London: Tavistock Publications Ltd.
Luria, A. R. (1973). The parietal regions and the organisation of simultaneous syntheses. In K. H. Pribram (Ed.). *The working brain (B. Haigh trans.)* (pp. 147–168). Great Britain: Penguin Books Ltd.
Lyall, K., Croen, L., Daniels, J., Fallin, D., Ladd-Acosta, C., Lee, B., et al. (2017). The changing epidemiology of autism spectrum disorders. *Annual Review of Public Health, 38*, 81–102.
Macintyre-Beon, C., Young, D., Calvert, J., Ibrahim, H., Dutton, G. N., & Bowman, R. (2012). Reliability of a question inventory for structured history taking in children with cerebral visual impairment. *Eye (London, England), 26*(10) 1393-1393.
Mapstone, M., Weintraub, S., Nowinski, C., Kaptanoglu, G., Gitelman, D. R., & Mesulam, M. M. (2003). Cerebral hemispheric specialization for spatial attention: Spatial distribution of search-related eye fixations in the absence of neglect. *Neuropsychologia, 41*(10), 1396–1409.
Masterton, B. A., & Biederman, G. B. (1983). Proprioceptive versus visual control in autistic children. *Journal of Autism and Developmental Disorders, 13*(2), 141–152.
McKillop, E., Bennett, D., McDaid, G., Holland, B., Smith, G., Spowart, K., et al. (2006). Problems experienced by children with cognitive visual dysfunction due to cerebral visual impairment – And the approaches which parents have adopted to deal with these problems. *The British Journal of Visual Impairment, 24*(3), 121–127.
Mesulam, M. M., et al. (2018). Aphasia, memory loss, hemispatial neglect, frontal syndromes, and other cerebral disorders. In D. L. Longo, A. S. Anthony, E. Fauci, D. Braunwald, S. L. Kasper, & D. Hauser (Eds.). *Harrison's textbook of internal medicine*(20th ed). New York: McGraw-Hill Education.
Michel, F., & Henaff, M. A. (2004). Seeing without the occipito-parietal cortex: Simultagnosia as a shrinkage of the attentional visual field. *Behavioural Neurology, 15*(1-2), 3–13.
Milne, E., Scope, A., Griffiths, H., Codina, C., & Buckley, D. (2013). Brief report: Preliminary evidence of reduced sensitivity in the peripheral visual field of adolescents with autistic spectrum disorder. *Journal of Autism and Developmental Disorders, 43*(8), 1976–1982.
Milner, A. D., & Goodale, M. A. (2008). Two visual systems re-viewed. *Neuropsychologia, 46*(3), 774–785.
National Institute for Health and Clinical Excellence (NICE) (2011). *Autism diagnosis in children and young people: Recognition, referral and diagnosis of children and young people on the autism spectrum* (pp. 173-174-176)London: National Institute for Health and Clinical Excellence.

O'Hearn, K., Roth, J. K., Courtney, S. M., Luna, B., Street, W., Terwillinger, R., et al. (2011). Object recognition in Williams syndrome: Uneven ventral stream activation. *Developmental Science, 14*(3), 549–565.
Ortibus, E., Laenen, A., Verhoeven, J., De Cock, P., Casteels, I., Schoolmeesters, B., et al. (2011). Screening for cerebral visual impairment: Value of a CVI questionnaire. *Neuropediatrics, 42*(4), 138–147.
Ortibus, E., Verhoeven, J., Sunaert, S., Casteels, I., De Cock, P., & Lagae, L. (2012). Integrity of the inferior longitudinal fasciculus and impaired object recognition in children: A diffusion tensor imaging study. *Developmental Medicine and Child Neurology, 54*(1), 38–43.
Paulignan, Y., Jeannerod, M., MacKenzie, C., & Marteniuk, R. (1991). Selective perturbation of visual input during prehension movements. The effects of changing object size. *Experimental Brain Research, 87*(2), 407–420.
Paquet, A., Olliac, B., Bouvard, M. P., Golse, B., & Vaivre-Douret, L. (2016). The Semiology of Motor Disorders in Autism Spectrum Disorders as Highlighted from a Standardized Neuro-Psychomotor Assessment. *Frontiers in Psychology, 7*, 1292. https://doi.org/10.3389/fpsyg.2016.01292.
Pellicano, E., & Gibson, L. Y. (2008). Investigating the functional integrity of the dorsal visual pathway in autism and dyslexia. *Neuropsychologia, 46*(10), 2593–2596. https://doi.org/10.1016/j.neuropsychologia.2008.04.008.
Perenin, M. T., & Vighetto, A. (1988). Optic ataxia: A specific disruption in visuomotor mechanisms. I. Different aspects of the deficit in reaching for objects. *Brain, 111*(Pt 3), 643–674.
Pisella, L., Alahyane, N., Blangero, A., Thery, F., Blanc, S., & Pelisson, D. (2011). Right-hemispheric dominance for visual remapping in humans. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 366*(1564), 572–585.
Pitzalis, S., Fattori, P., & Galletti, C. (2015). The human cortical areas V6 and V6A. *Visual Neuroscience, 32*, E007. https://doi.org/10.1017/S0952523815000048.
Prado, J., Clavagnier, S., Otzenberger, H., Scheiber, C., Kennedy, H., & Perenin, M. T. (2005). Two cortical systems for reaching in central and peripheral vision. *Neuron, 48*(5), 849–858.
Ptak, R. (2012). The frontoparietal attention network of the human brain: Action, saliency, and a priority map of the environment. *The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology and Psychiatry, 18*(5), 502–515 doi:1073858411409051.
Rapin, I. (1996). Neurological examination. In P. Davis (Ed.). *Preschool children with inadequate communication: Developmental language disorder, autism, low IQ (Clinics in developmental medicine; Vol 139)* (pp. 98–122). London: MacKeith Press.
Ricci, D., Vasco, G., Baranello, G., Salerni, A., Amante, R., Tamburrini, G., et al. (2007). Visual function in infants with non-syndromic craniosynostosis. *Developmental Medicine and Child Neurology, 49*(8), 574–576.
Rizzo, M., & Vecera, S. (2002). Psychoanatomical substrates of Bálint's syndrome. *Journal of Neurology, Neurosurgery, and Psychiatry, 72*(2), 162–16278.
Robertson, C. E., Thomas, C., Kravitz, D. J., Wallace, G. L., Baron-Cohen, S., Martin, A., et al. (2014). Global motion perception deficits in autism are reflected as early as primary visual cortex. *Brain: A Journal of Neurology, 137*(Pt 9), 2588–2599.
Rodgers, R. A., Travers, B. G., & Mason, A. H. (2019). Bimanual Reach to Grasp Movements in Youth With and Without Autism Spectrum Disorder. *Frontiers in Psychology, 9*, 2720. https://doi.org/10.3389/fpsyg.2018.02720.
Sacrey, L. R., Zwaigenbaum, L., Bryson, S., Brian, J., & Smith, I. M. (2018). The reach-to-grasp movement in infants later diagnosed with autism spectrum disorder: A high-risk sibling cohort study. *Journal of Neurodevelopmental Disorders, 10*(1), 41. https://doi.org/10.1186/s11689-018-9259-4.
Saidkasimova, S., Bennett, D. M., Butler, S., & Dutton, G. N. (2007). Cognitive visual impairment with good visual acuity in children with posterior periventricular white matter injury: A series of 7 cases. *Journal of AAPOS : the Official Publication of the American Association for Pediatric Ophthalmology and Strabismus, 11*(5), 426–430.
Schmahmann, J. D. (1991). An emerging concept: The cerebellar contribution to higher function. *Archives of Neurology, 48*(11), 1178–1187.
Vasco, G., Baranello, G., Ricci, D., Salerni, A., Tamburrini, G., Amante, R., et al. (2008). Longitudinal assessment of visual development in non-syndromic craniosynostosis: A 1-year pre- and post-surgical study. *Archives of Disease in Childhood, 93*(11), 932–935. https://doi.org/10.1136/adc.2007.128421.
Schneiberg, S., Sveistrup, H., McFadyen, B., McKinley, P., & Levin, M. F. (2002). The development of coordination for reach-to-grasp movements in children. *Experimental Brain Research, 146*(2), 142–154.
Scottish Intercollegiate Guidelines Network (SIGN) (2016). *Assessment, diagnosis and interventions for autism spectrum disorders. No. 145).* Edinburgh: Healthcare Improvement Scotland.
Song, Y., Hakoda, Y., Sanefuji, W., & Cheng, C. (2015). Can they see it? The functional field of view is narrower in individuals with autism spectrum disorder. *PloS One, 10*(7), e0133237. https://doi.org/10.1371/journal.pone.0133237.
Spencer, J., O'Brien, J., Riggs, K., Braddick, O., Atkinson, J., & Wattam-Bell, J. (2000). Motion processing in autism: Evidence for a dorsal stream deficiency. *Neuroreport, 11*(12), 2765–2767.
Ting, D. S., Pollock, A., Dutton, G. N., Doubal, F. N., Ting, D. S., Thompson, M., et al. (2011). Visual neglect following stroke: Current concepts and future focus. *Survey of Ophthalmology, 56*(2), 114–134. https://doi.org/10.1016/j.survophthal.2010.08.001.
Touwen, B. C. L. (1995). The neurological development of prehension: A developmental neurologist's view. *International Journal of Psychophysiology, 19*(2), 115–127.
Touwen, B. C. L. (1998). The brain and development of function. *Developmental Review, 18*(4), 504–526.
Tyler, H. R. (1968). Abnormalities of perception with defective eye movements (Balint's syndrome). *Cortex; A Journal Devoted to the Study of the Nervous System and Behavior, 4*(2), 154–171. https://doi.org/10.1016/S0010-9452(68)80028-0.
Vighetto, A., & Krolak-Salmon, P. (2007). Balint's syndrome. In O. Godefroy, & J. Bogousslavsky (Eds.). *The behavioural and cognitive neurology of stroke* (pp. 294–314). USA: Cambridge University press.
Wilson, M., Quinn, G., Dobson, V., & Breton, M. (1991). Normative values for visual fields in 4- to 12-year-old children using kinetic perimetry. *Journal of Pediatric Ophthalmology and Strabismus, 28*(3), 151–153.
Wing, L. (1969). *The handicaps of autistic children- a comparative study*.
Wing, L. (1997). The autistic spectrum. *Lancet, 350*(9093), 1761–1766.
Wing, L., & Gould, J. (1979). Severe impairments of social interaction and associated abnormalities in children: Epidemiology and classification. *Journal of Autism and Developmental Disorders, 9*(1), 11–29.
Yapici, Z. (2006). Subacute sclerosing panencephalitis presenting with Balint's syndrome. *Brain & Development, 28*(6), 398–400.