Visual search efficiency and functional visual cortical size in children with and without dyslexia

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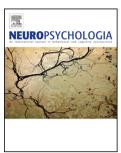
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#### **Abstract**

Dyslexia is characterised by poor reading ability. Its aetiology is probably multifactorial, with abnormal visual processing playing an important role. Among adults with normal reading ability, there is a larger representation of central visual field in the primary visual cortex (V1) in those with more efficient visuospatial attention. In this study, we tested the hypothesis that poor reading ability in school-aged children (17 children with dyslexia, 14 control children with normal reading ability) is associated with deficits in visuospatial attention using a visual search task. We corroborated the psychophysical findings with neuroimaging, by measuring the functional size of V1 in response to a central 12° visual stimulus. Consistent with other literature, visual search was impaired and less efficient in the dyslexic children, particularly with more distractor elements in the search array (p=0.04). We also found atypical interhemispheric asymmetry in functional V1 size in the dyslexia group (p=0.02). Reading impaired children showed poorer visual search efficiency (p=0.01), needing more time per unit distractor (higher ms/item). Reading ability was also correlated with V1 size asymmetry (p=0.03), such that poorer readers showed less left hemisphere bias relative to the right hemisphere. Our findings support the view that dyslexic children have abnormal visuospatial attention and interhemispheric V1 asymmetry, relative to chronological age-matched peers, and that these factors may contribute to inter-individual variation in reading performance in children.

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## **Keywords (max 6 words)**

Dyslexia, visual search, visual cortex, magnetic resonance imaging, reading, attention

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#### 1. Introduction

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Dyslexia is a developmental learning disorder affecting 5-12% of children (Peterson & Pennington, 2012). It is characterised by significant and persistent reading difficulty despite sufficient cognitive abilities and education, such that reading performance (word reading accuracy, reading fluency and reading comprehension) is markedly below that expected for chronological age (WHO, 2018). Albeit one of the most common learning disabilities, the aetiology of dyslexia is not yet fully understood. Altered brain structure and function have been reported to be contributing factors (Galaburda, 2005; Norton, Beach, & Gabrieli, 2015; Ramus, Altarelli, Jednorog, Zhao, & Scotto di Covella, 2018) and familial risks have also been identified (Debska, et al., 2016; Gialluisi, et al., 2020; Hosseini, et al., 2013; Paracchini, Scerri, & Monaco, 2007). There have been decades of evidence in favour of sensory processing deficits, including at early subcortical levels (e.g. (Boets, Vandermosten, Cornelissen, Wouters, & Ghesquiere, 2011; Diaz, Hintz, Kiebel, & von Kriegstein, 2012; Giraldo-Chica, Hegarty, & Schneider, 2015; Giraldo-Chica & Schneider, 2018; Gori, Cecchini, Bigoni, Molteni, & Facoetti, 2014; Gori, Seitz, Ronconi, Franceschini, & Facoetti, 2016; Livingstone, Rosen, Drislane, & Galaburda, 1991; Lovegrove, Bowling, Badcock, & Blackwood, 1980; Muller-Axt, Anwander, & von Kriegstein, 2017). However, most studies, especially neuroimaging and electroencephalographic studies, have focussed on the cerebral cortical networks involved either in phonological or higher language level processes (e.g. Diehl, et al., 2014; Norton, et al., 2015; Power, Colling, Mead, Barnes, & Goswami, 2016; Price, 2012; Sun, Lee, & Kirby, 2010; Vandermosten, Boets, Wouters, & Ghesquiere, 2012)

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Here, we were interested in early visual sensory processing in dyslexia as a potential precursor to higher order brain differences in language and visual word form areas associated with reading (Dehaene & Cohen, 2011). When learning to read, our visual system must be trained to scan the text in a sequential manner to be able to integrate the information into words and sentences. Of the two major afferent streams of visual processing between the retina and primary visual cortex (V1), the

parvocellular-ventral stream possesses the neural architecture for fine spatial resolution and object recognition, whereas the magnocellular-dorsal stream provides temporal and positional information. It has been proposed that during reading, an 'attentional spotlight' is deployed from the magnocellular dominated dorsal cortical areas, sequentially highlighting the letters of the text. This effectively gates the parvocellular information passing through V1 (Vidyasagar, 1999, 2004, 2005), so that only one or two letters of text are processed by ventral stream structures at any one time. A defect in the magnocellular-dorsal pathway, as has been demonstrated previously in dyslexia (Cicchini, Marino, Mascheretti, Perani, & Morrone, 2015; Gori, et al., 2014; Gori, et al., 2016; Kevan & Pammer, 2008; Stein, 2019; Stein & Walsh, 1997), could plausibly contribute to impaired reading by altering visuospatial attention. Indeed, there is growing evidence that from longitudinal studies that suggest a causal link between visuospatial attention deficits and reading difficulties (Bertoni, Franceschini, Ronconi, Gori, & Facoetti, 2019; Carroll, Solity, & Shapiro, 2016; Franceschini, Gori, Ruffino, Pedrolli, & Facoetti, 2012; Valdois, Roulin, & Line Bosse, 2019).

Visuospatial attention can be measured using a visual search task (Treisman & Gelade, 1980), which assesses the ability to find a target hidden amongst a field of distractors. Visual search is slower in dyslexic children (Casco & Prunetti, 1996; Iles, Walsh, & Richardson, 2000; Vidyasagar & Pammer, 1999); however, it is not clear whether slower response times arise from processing delays related not to visual search *per se* but to signal transmission speed. Hence, in this study, we looked for evidence of non-search delays in processing in dyslexic children by modelling visual search performance with a linear regression to quantify slope as the primary indicator of task performance (i.e. search efficiency, ms/item), as well as quantify the intercept to represent non-search processes (Dickinson, Haley, Bowden, & Badcock, 2018).

Furthermore, as the number of distractors in a search array increases (set size = target plus number of distractors), the time taken to find the target increases. People with more 'efficient' visuospatial

attention require less time to successfully execute the task as it becomes more difficult (i.e. lower ms/item slope of the approximately linear function between response time and increasing set size). Since print and text are a commonly encountered instances of a cluttered visual scene, the brain likely uses the same neural circuitry and attentional mechanisms for reading that are used for serially searching for a target amongst visual clutter (Vidyasagar, 2004, 2005; Vidyasagar & Pammer, 2010). Indeed, faster readers show faster response times in visual search tasks among both young (Casco, Tressoldi, & Dellantonio, 1998; Verghese, Kolbe, Anderson, Egan, & Vidyasagar, 2014; Vidyasagar & Pammer, 1999) and adult (Casco, et al., 1998; Verghese, et al., 2014; Vidyasagar & Pammer, 1999) populations. Additionally, in adults with normal reading ability, more efficient visual search performance (i.e. lower ms/item visual search slope) correlates with a larger representation of the central visual field in primary visual cortex, V1 (Verghese, et al., 2014). Thus, the psychophysical evidence for a relationship between visual search and reading ability is supported by neuroimaging findings, at least in adults. Efficient serial visual search is critical for efficient reading, and a better understanding of visual search under-performance and its relationship to functional V1 size may provide insight into atypical visual processing mechanisms in dyslexia.

The focus of our study was to consider the reading ability and visual performance of children of reading-age, as this is the age-group where abilities diverge and problems manifest in school performance. Given that visual search is particularly impaired in dyslexic children when there are more distractor elements in the search array (Vidyasagar & Pammer, 1999), we expected that visual search performance would be impaired in the dyslexic children (i.e. higher ms/item visual search slope) relative to normal-reading children. In addition to grouping the data into 'dyslexic' versus 'non-dyslexic' readers, since reading ability is a continuous variable in the population, we also considered the entire spectrum of visual performance in our participants. We therefore hypothesized, similar to that reported in normal reading adults (Verghese, et al., 2014), that there would be a relationship between visuospatial attention and the size of functional central field

representation on left V1 (measured using retinotopic mapping of V1 by magnetic resonance imaging, MRI) in a cohort of children with varying reading ability.

#### 2. Materials and Methods

### 2.1 Participants

The study was approved by the Monash University Human Research Ethics Committee and complied with the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants and their guardians. We aimed to recruit a minimum of 23 participants based on a power analysis (power of 80% for detecting a moderate correlation at alpha of 0.05) of data from a previous study (Verghese, et al., 2014) that reported a moderate (r = -0.56) correlation between overall visual search performance and functional V1 size in adults with normal reading abilities. Thirty-two children (18 dyslexic, 14 controls) aged 9-11 years were consecutively recruited into the study in response to advertisements circulated at Monash University, The University of Melbourne, local schools, and online community support groups. The narrow age range was chosen to minimize significant developmental variation in brain structural measures such as intracranial, whole brain, grey matter and white matter volume (Mills, et al., 2016).

Participant screening, reading and intellectual aptitude, and visual search tests were conducted at the first visit (no more than 1.5 hours, with regular breaks in between tests). The MRI brain scan (1 hour visit) was conducted within three months of the first visit. Participants were screened by an optometrist to ensure the following inclusion criteria: best corrected visual acuity at least 6/9.5 (logMAR), refractive error within ±5.00 DS, normal ocular health, normal binocular vision on screening tests for accommodation, convergence and stereopsis, no history of attention deficit hyperactivity disorder or Asperger's syndrome. Grouping of children into normal vs dyslexic was determined based on parent/guardian report of a diagnosis of dyslexia or normal reading ability, and confirmed at the first test visit by administration of the Dyslexia Determination Test (Griffin &

Walton, 1981). The Dyslexia Determination Test is a validated screening test (Simmons, 1984) that looks for any dyslexic pattern in relation to reading, writing and spelling, and characterises the dyslexia into dyseidesia, dysphonesia or a combination of both.

To quantify reading ability, the reading subtests ('Word Reading', 'Reading Comprehension', 'Pseudoword decoding') of the WIAT-II (Wechsler Individual Achievement Test, Australian Standardised Edition, 2<sup>nd</sup> Edition) were administered at each participant's current school year level (Year 4, 5, or 6). Raw scores for each subtest were weighted, converted into standard scores and summed to obtain a composite standard score for reading ability, herein referred to as the 'reading ability score'. Intellectual aptitude (intelligence quotient, IQ) was assessed using the Kaufman Brief Intelligence Test (KBIT, 2<sup>nd</sup> edition), which includes both verbal ('Verbal Knowledge' and 'Riddles' subtests, which were read out loud by the investigators) and non-verbal ('Matrices' subtest) IQ measures. The KBIT test of IQ was chosen for its brevity over a full-scale IQ measure in order to remove any confound of reading ability that may impact on a written IQ test, and to minimise possible fatigue effects from the battery of tests. Age-dependent standard scores for verbal IQ, non-verbal IQ and the overall IQ composite score are shown in Table 1.

Given that dyslexia is defined by poor reading ability despite normal cognitive ability, one dyslexic child's data was removed from analysis due to a below average IQ < 78 (i.e. more than 1.5 standard deviations below average IQ composite score of 100), leaving 14 control (mean age 10 years 6 months, 8 females and 6 males) and 17 dyslexic participants (mean age 10 years 9 months, 9 females and 8 males) for which visual search performance was assessed. In addition, one control participant withdrew from the study after the first visit, one dyslexic participant could not complete the brain scan due to claustrophobia, and MRI data from 1 control and 2 dyslexic participants were discarded due to excessive movement artefacts. Thus, the final subset of children (total n=24) with visual

search data and acceptable MRI data included 11 control (mean age 10 years 5 months, 6 females) and 13 dyslexic participants (mean age 10 years 11 months, 6 females).

**Table 1.** Participant demographics (mean  $\pm$  standard deviation, range) and outcomes of the reading and intelligence tests (median  $\pm$  interquartile range, range). Group data were compared (p-values) using t-tests, or Mann-Whitney rank sum tests where data were not normally distributed.

|                       | Controls            | Dyslexic             | <i>p</i> -value               |
|-----------------------|---------------------|----------------------|-------------------------------|
| Ago (months)          | 126 + 0 (110 120)   | 120 ± 12 /100 1/2)   | + -0.79 n=0.44                |
| Age (months)          | 126 ± 9 (110 – 138) | 129 ± 12 (108 – 143) | t <sub>29</sub> =0.78, p=0.44 |
| Reading ability score | 108 ± 26 (92 – 130) | 83 ± 15 (53 – 98)    | Mann Whitney U=5, p<0.0001    |
| IQ composite score    | 114 ± 12 (86 – 122) | 102 ± 20 (84 – 118)  | Mann Whitney U=50.5, p=0.04   |
| IQ verbal score       | 107 ± 13 (93 – 127) | 101 ± 18 (83 – 116)  | Mann Whitney U=64.5, p=0.15   |
| IQ non-verbal score   | 110 ± 19 (82 – 130) | 104 ± 24 (70 – 117)  | Mann Whitney U=64.0, p=0.14   |

#### 2.2 Visual search task

Participants viewed the stimuli binocularly in a darkened room with the appropriate refractive correction for the working distance. Stimuli were generated (Visage VSG2/5, Cambridge Research Systems, Kent, UK) and displayed on a gamma-corrected 21-inch CRT monitor (EIZO Flexscan F980,  $800 \times 600$  pixel resolution, 100 Hz frame rate). The display subtended  $12^{\circ} \times 16^{\circ}$  at a working distance of 137 cm. This distance was chosen so that the visual search display was comparable to the vertical angular subtense of the display for the MRI scans ( $12^{\circ}$ ).

We used the approach of Verghese, et al., (2014) to quantify visuospatial attention based on two visual search tasks: (1) a simple *feature* search that is stimulus-driven (pre-attentive, pop-out target) and shows flat search rates (close to 0 ms/item), and (2) a serial *conjunction* search that requires top-down visuospatial attention and typically shows a linearly increasing search rate (approximately 5-20 ms/item). Examples of the two visual search tasks are shown in Figure 1A. The target was

always a small  $(0.50^{\circ} \times 0.12^{\circ})$ , vertical white bar (CIE chromaticity coordinates: x = 0.3, y = 0.3; luminance:  $25 \text{ cd/m}^2$ ), against a background of uniform grey (luminance:  $18 \text{ cd/m}^2$ ). The distractors were the same colour and luminance (x = 0.3, y = 0.3; luminance:  $25 \text{ cd/m}^2$ ) as the target. For the feature search task, only one type of distractor was present – small horizontal white bars ( $0.12^{\circ} \times 0.50^{\circ}$ ). For the conjunction search task, small horizontal white bars ( $0.12^{\circ} \times 0.50^{\circ}$ ) and large vertical white bars ( $0.98^{\circ} \times 0.24^{\circ}$ ) were presented. Set size included the target (if present) and the number of distractors.

On each trial, 16, 32 or 64 items ('set size') were presented. Set size was randomly interleaved to minimise the effects of fatigue or learning. The target was present in half of the trials. An auditory cue occurred at the onset of each presentation and also when a response was made by button press (CB6 response box, Cambridge Research Systems, Kent, UK). Participants were instructed to indicate as quickly and as accurately as possible whether the target was present or absent in each trial. No feedback was provided. Participants were free to make eye movements and the display remained on the screen until a response was recorded. Trials were separated by 3-second intervals of blank screen, with two extra 6-second rest intervals to allow two short breaks during each test run. After at least one practice run to familiarise participants with the task, participants completed one feature search test (3 runs of 10 trials = 30 trials) and two conjunction search tests (2 × 3 runs of 20 trials = 120 trials) in approximately 30 minutes, with breaks as required.

# 2.3 Visual search data analysis

Visual search response time (in seconds) and accuracy (% correct) data were collected. To address our hypotheses, only correct target-present trials were analysed because target-present trials better represent the visuospatial attentional effect, and because target-present performance has been shown to correlate with functional V1 size (Verghese, et al., 2014). For each individual, a linear model was fit to the median response time data as a function of set size (number of elements in the

visual search array) using Microsoft Excel (Microsoft, Redmond, WA, USA) and a least squares method. From the linear regression, we obtained a measure of slope (i.e. search efficiency) and y-intercept (i.e. non-search visual processing) for the feature and conjunction search tasks. To quantify overall visual search performance, a single measure of slope (ms/item) was calculated as the difference in slope between the feature and conjunction search tasks as per previous work (Verghese, et al., 2014), where a lower ms/item visual search slope indicates better (i.e. more efficient) visual search performance.

### 2.4 Brain imaging

Participants underwent training and familiarisation with the scanning environment in a mock MRI scanner prior to the test session. For the data collection, a Siemens 3T Skyra MRI scanner with a 32-channel receiver head coil was used. For structural imaging, a T1-weighted MPRAGE sequence (repetition time = 2300 ms, echo time = 2.07 ms, inversion time = 900 ms, flip angle = 9, slice thickness = 1 mm, in-plane voxel dimensions =  $1 \times 1 \text{ mm}$ ) was used for anatomical co-registration purposes. Functional brain images were then acquired using a gradient-echo planar imaging sequence (repetition time = 1500 ms, echo time = 30 ms, flip angle = 50 ms, slice thickness =  $2.3 \times 2.32 \times$ 

The conventional stimuli for phase-encoded retinotopic mapping (12° diameter, high-contrast drifting checkerboard expanding ring to map eccentricity and rotating wedge to map polar angle) were presented using PsychToolbox (Brainard, 1997) and Matlab (Version R2011b, Mathworks, Natick, MA, United States), obtained from the VISTA lab retinotopy toolbox online (Stanford Vision and Imaging Group, Stanford University; available from: <a href="http://white.stanford.edu/newlm/index.php/Software">http://white.stanford.edu/newlm/index.php/Software</a>). The stimuli were displayed using an LCD projector (maximum brightness = 1500 lumens, resolution = 1024 x 768 pixels, frame rate = 60 Hz) onto a back-projection screen positioned at 155 cm from the eye plane. To maintain fixation during

scanning, participants were instructed to press a button when the central fixation spot changed colour (red to green and vice-versa). Eye and head movements were continuously monitored in real-time by the investigators via an integrated Eyelink 1000 system (SR Research Ltd., Ottawa, Ontario, Canada).

#### 2.5 Brain imaging data analysis

The anatomical T1-weighted images were averaged and analysed using the FreeSurfer (Fischl, 2012) software package (Version 5.1.0: <a href="https://surfer.nmr.mgh.harvard.edu/">https://surfer.nmr.mgh.harvard.edu/</a>) according to a standard processing pipeline (Dale, Fischl, & Sereno, 1999). In brief, the anatomical images were automatically segmented into grey and white matter using custom software, and any segmentation errors were manually corrected. Grey matter was subsequently grown from the segmented white matter to form a 3-4mm layer covering the white matter surface, and the cortical surface was reconstructed in 3D at the white/grey matter boundary. The data was pre-processed to remove linear trends from the functional MRI time series (without spatial smoothing) and correct for motion (applied between sessions and within individual scans.

Phase-encoded retinotopic mapping (Sereno, et al., 1995) of V1 of the right and left hemispheres was conducted on a flattened representation of the cortical surface in Freesurfer. Pseudo-colour phase maps were used to visualize the retinotopic maps. The V1 region of interest was manually delineated on the inflated cortical surface by two independent graders (authors BNN and SKC), one of whom was blinded to the participants' group (author SKC). In a pilot analysis of half of the MRI data (n=12), the intra-class correlation coefficients for the left and right functional V1 size were 0.92 and 0.95, respectively, indicating excellent internal consistency between graders (Cronbach's  $\alpha$  left V1 = 0.94, right V1 = 0.97). For the final dataset analysis, functional V1 size measurements obtained by grader 1 (author BNN) were taken. A ratio of inter-hemispheric asymmetry (left/right V1 size) was

| calculated, where a ratio of less than 1 indicates a bias towards having a larger representation of |
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| right V1 relative to the left V1.   |

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Last updated: 5 March 2021 Page 14 of 33

#### 2.6 Statistical analysis

Statistical analysis was conducted using SPSS Version 26.0 (IBM Corp., Armonk, NY, USA). A Kolmogorov-Smirnov test was used to assess data normality. To compare group demographic features and functional brain imaging outcomes, t-tests or Mann Whitney rank sum tests were used for normally or non-normally distributed data, respectively. A repeated-measures analysis of variance (RM-ANOVA) was used to assess group differences in visual search performance, where the between-factor was group and the within-factors were set size and search task. Spearman rank correlational analysis was conducted to assess relationships between non-normally distributed measures, otherwise Pearson correlations were calculated. A p < 0.05 was considered statistically significant.

#### 3. Results

### 3.1 Participants

The control and dyslexic groups were not different in age ( $t_{29}$ =0.78, p=0.44) nor in the proportion of females to males (chi square test of proportions: p=0.82). As expected, the dyslexic children had significantly lower reading ability scores on the WIAT-II test (i.e. standardised according to current school year level; Table 1; p<0.001). While we were careful to exclude any participants with below average IQ composite score, our normal-reading control group had higher mean IQ (Table 1; p=0.04) with similar range (controls: 86 - 122, dyslexic: 84 - 118). There was no difference between dyslexia and control participants in group mean non-verbal IQ (Table 1; p=0.14) nor verbal IQ (Table 1; p=0.15). Overall IQ composite score was predictive of reading ability (Spearman r = 0.44, p=0.02). The association between IQ composite score and reading ability appeared to be linked to verbal IQ (Spearman r = 0.35, p = 0.07) rather than non-verbal IQ (Spearman r = 0.28, p = 0.15), but these correlations did not reach conventional statistical significance.

#### 3.2 Visual search

There were no differences in accuracy (% correct) across all target present visual search tasks between control and dyslexic participants (Table 2; p>0.05 for all comparisons); hence, all visual search data was considered reliable and included in the analysis. Figure 1B plots the time taken to correctly detect the target within a field of distractors as a function of set size. While there was no overall group difference in response time (RM-ANOVA main effect of group: F(1,29)=2.91, p=0.10), there was a three-way interaction between group, search task and set size (F(2,58)=3.37, p=0.04). Feature search response times were similar between groups across all set sizes (RM-ANOVA main effect of group: F(1,29)=0.49, p=0.49; set size x group interaction: F(2, 58)=0.23, p=0.80). On the other hand, there was a trend consistent with existing literature that conjunction search response times across all set sizes were slower in the dyslexic children (RM-ANOVA main effect of group: F(1,29)=3.96, p=0.06), with the delay being most prominent with increased number of distractors (set size x group interaction: F(2, 58)=3.48, p=0.04).

When we considered individual performance in terms of slope (search efficiency), the dyslexic group were less efficient than the control group for the conjunction search task only (Figure 1C middle panel; group x search task interaction: F(1,29)=5.43, p=0.03). This translated to poorer overall visual search performance (poorer visuospatial attention) in the dyslexic children, i.e. the difference between feature and conjunction search slopes (Figure 1C, right panel;  $t_{29}=2.33$ , p=0.03). To determine whether the conjunction search delays observed in the dyslexic children might be related to a delay in non-search processing, we tested whether the intercepts of the individual linear fits differed between groups. Both control and dyslexic groups showed similar intercepts for the conjunction search task (control:  $1.4 \pm 0.5$  seconds, dyslexic:  $1.6 \pm 0.5$  seconds;  $t_{29}=0.91$ , p=0.37), suggesting no difference in signal processing or motor activity that might contribute to an overall delay in visual search response times.

**Table 2.** Percent (%) accuracy of target present visual search performance (median, range). Group data were compared (p-values) using Mann-Whitney rank sum tests as data were not normally distributed.

| Search task | Set size | Controls       | Dyslexic       | <i>p</i> -value              |
|-------------|----------|----------------|----------------|------------------------------|
| Feature     | 16       | 100 (80 – 100) | 100 (80 – 100) | Mann Whitney U=100.5, p=0.21 |
| Feature     | 32       | 100 (80 – 100) | 100 (80 – 100) | Mann Whitney U=109, p=0.44   |
| Feature     | 64       | 100 (80 – 100) | 100 (80 – 100) | Mann Whitney U=106.5, p=0.39 |
| Conjunction | 16       | 95 (85 – 100)  | 95 (75 – 100)  | Mann Whitney U=103.5, p=0.51 |
| Conjunction | 32       | 95 (85 – 100)  | 90 (75 – 100)  | Mann Whitney U=85.5, p=0.17  |
| Conjunction | 64       | 90 (70 – 100)  | 90 (65 – 100)  | Mann Whitney U=117.5, p=0.95 |

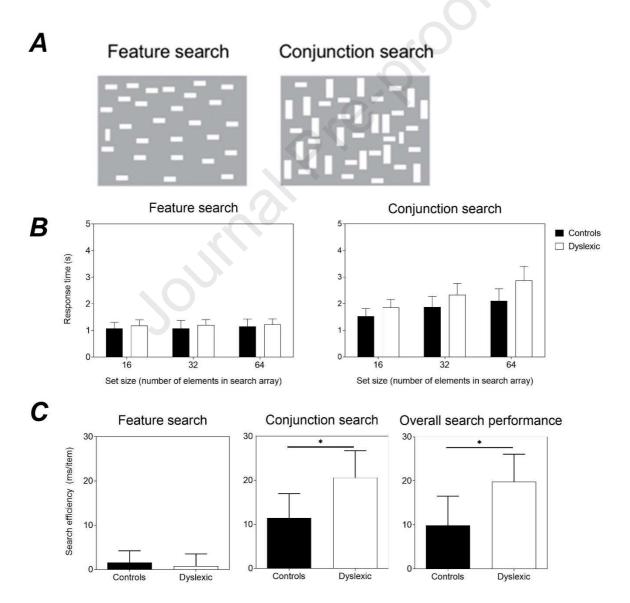
## 3.3 Functional primary visual cortical size

Despite having similar total functional V1 size (Figure 2A; sum of left and right hemispheres;  $t_{22}$ =0.82, p=0.42), dyslexic and control participants showed different right and left hemispheric functional V1 size (group x hemisphere interaction: F(1,22)=6.99, p=0.02). Dyslexic children demonstrated a right hemisphere bias (Figure 2B; ratio <1 indicates larger representation of the visual stimulus in right V1 relative to left V1), whereas normal reading children showed close to 1:1 ratio in functional V1 size between the right and left hemispheres (Figure 2B; group difference in V1 asymmetry:  $t_{22}$ =2.22, p=0.04).

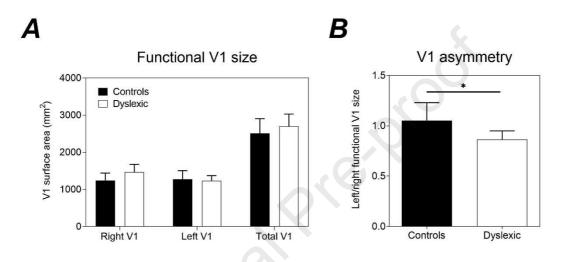
To confirm that any group differences in functional brain measures were not influenced by differences in structural brain size, we determined that the dyslexic and normal-reading children showed similar intracranial volume (mean  $\pm$  standard deviation; control: 1457  $\pm$  160 cm<sup>3</sup>, dyslexic: 1455  $\pm$  151 cm<sup>3</sup>;  $t_{22}$ =0.02, p=0.98), total cortical grey matter volume (control: 588  $\pm$  60 cm<sup>3</sup>, dyslexic: 582  $\pm$  50 cm<sup>3</sup>;  $t_{22}$ =0.25, p=0.81) and total cortical white matter volume (control: 434  $\pm$  62 cm<sup>3</sup>, dyslexic: 435  $\pm$  51 cm<sup>3</sup>;  $t_{22}$ =0.04, p=0.97).



Figure 1. (A) Schematic illustration of the visual stimuli used for the feature search and conjunction search tasks. The target for the visual search task is the smaller vertical bar. (B) Feature and conjunction visual search response time (s) as a function of set size for the control (n=14) and dyslexic (n=17) groups. (C) Visual search efficiency (ms/item slope) for the control (n=14) and dyslexic (n=17) groups for the feature (left panel) and conjunction (middle panel) search tasks. Overall visual search performance (right panel) was the difference between feature and conjunction search slopes. Higher search efficiency slopes imply less efficient visual search performance. For all panels, group means and 95% confidence intervals of the mean are plotted.



**Figure 2. (A)** Functional size of right and left hemispheres of primary visual cortex (V1) from retinotopic mapping in controls (n=11) and dyslexic (n=13) groups. Total V1 size was defined as the sum of the left and right hemispheres. **(B)** Functional V1 size asymmetry, defined as the ratio between left and right hemisphere functional V1 sizes. A ratio less than 1 indicates a larger right V1 size relative to the left V1. For all panels, group means and 95% confidence intervals of the mean are plotted.



3.4 Relationship between measures

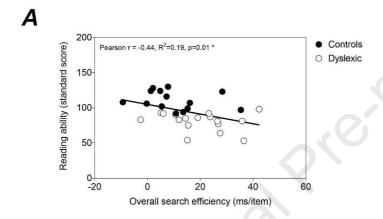
Given the continuum of reading ability (range of standardised scores: 53 to 130) amongst our study participants, we considered the correlation between our visual outcome measures and reading ability across the entire cohort (n=24). Reading impaired children showed poorer overall visual search performance (Figure 3A; Pearson r=-0.44, R²=0.19, p=0.01), needing more time per unit distractor (i.e. higher ms/item search efficiency). Reading ability was also correlated with V1 size asymmetry (Figure 3B; Pearson r=0.45, R²=0.21, p=0.03), such that poorer readers showed less left hemisphere bias relative to the right hemisphere.

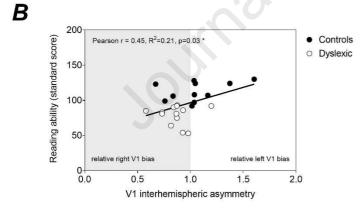
While we hypothesized that better visuospatial attention (i.e. lower ms/item search efficiency) would predict greater central visual field representation in the left V1 hemisphere relative to the right hemisphere (i.e. V1 asymmetry > 1.0), we did not find a statistically significant correlation

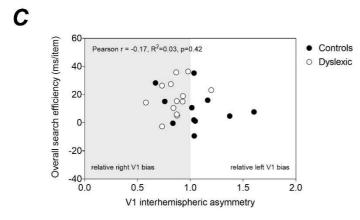
| between these visual outcome measures (Figure 3C; Pearson r=-0.17, R <sup>2</sup> =0.03, p=0.42). Previous |
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| work in a normal-reading adult population (Verghese, et al., 2014) reported right and left V1 size         |
| separately and not as a relative ratio; that study found a correlation between visuospatial attention      |
| (i.e. lower ms/item search efficiency) and left V1 size only. Our analysis did not yield the same results  |
| in children when we considered the left V1 functional size alone (Pearson $r$ =0.21, $R^2$ =0.04, p=0.31)  |
| and the right V1 functional size alone (Pearson $r$ =0.33, $R$ <sup>2</sup> =0.11, p=0.12).                |

Because reading ability was related to IQ, we analysed whether IQ would also be correlated with overall visual search efficiency and V1 functional size asymmetry. Similar in direction to reading ability scores, children with higher overall IQ showed more efficient visual search with lower ms/item slopes (Spearman r=-0.41, p=0.03). We also analysed whether the total activation of V1 would correlate with the measured visual search efficiency or with the non-search related processing time, which is the intercept of the visual search function. We found that total activation of V1 (sum of right and left hemisphere functional V1 size) was not correlated with overall visual search efficiency (Pearson r = 0.30, R<sup>2</sup> = 0.09, p = 0.15), whereas the correlation between total V1 size and non-search related processing time did not reach statistical significance (i.e. intercept of the visual search function for target present trials; Pearson r = 0.37, R<sup>2</sup> = 0.14, p = 0.07).

**Figure 3.** Relationship between visual search performance, reading ability and functional visual cortical size. (B) Reading ability vs overall visual search efficiency, where a lower ms/item slope indicates better (more efficient) visuospatial attention. (B) Reading ability vs V1 functional size interhemispheric asymmetry, where an asymmetry < 1.0 indicates a relative right V1 bias (shaded area) and an asymmetry > 1.0 indicates a relative left V1 bias. (C) V1 functional size interhemispheric asymmetry (ratio) vs overall visual search efficiency (ms/item). Pearson correlational analysis results are shown, with asterisks and solid regression lines denoting statistical significance at p < 0.05.







#### 4. Discussion

This study aimed to investigate overall visual search efficiency in dyslexic and normal-reading children and look for a neurophysiological correlate of impaired visuospatial attention in the functional size of primary visual cortex. First, we confirmed that dyslexic children have poorer visual search efficiency by demonstrating that the dyslexic group showed impaired conjunction search performance in an attention-dependent visuospatial task, but similar feature search performance in a pre-attentive visuospatial task. Thus, regardless of reading ability, children of similar age (9-11 years) have similar visual search response times when the object of interest 'pops out'. Our study builds on previous reports of impaired visual search performance in dyslexia (Casco & Prunetti, 1996; lles, et al., 2000; Vidyasagar & Pammer, 1999) by showing that slower visual search in the dyslexic children, as the task became more complicated with additional distractors (i.e. higher ms/item search slope), was not attributed to an overall increase in non-search related processing time (i.e. intercept of the visual search function). Hence, we consider our findings as supportive of an inherent problem of visuospatial attention in dyslexia (Vidyasagar, 2004; Vidyasagar & Pammer, 2010).

Consistent with other work demonstrating visuospatial attentional deficits in poorer reading children (Facoetti, Paganoni, Turatto, Marzola, & Mascetti, 2000), we show that poorer visual search efficiency measured is correlated with reading ability in children, measured using a standardised academic achievement test (WIAT-II). A previous study in normal-reading adults demonstrated that poorer visual search efficiency was correlated with slower reading speed, i.e. the time required to read standardised comprehension passages at a self-determined pace (Verghese, et al., 2014). Here, we did not report reading speed because there was no single standardised comprehension passage suitable for all our participants at different school levels (ranged from Years 4 to 6). Furthermore, it became apparent in some dyslexic children that reading speed would have been artificially low because they skipped parts of text due to their reading difficulty. Rather, the WIAT-II test was chosen as our primary reading outcome measure as it encompassed a wide range of reading-related

skills (including phonological skills, reading comprehension, and phonetic decoding skills), and not just reading speed alone.

We *a priori* predicted a relationship between overall visual search efficiency and functional V1 size as a neurophysiological correlate of visual behavioural performance in our cohort of children, as previously established in normal-reading adults (Verghese, et al., 2014). If visual search performance and functional V1 size are both measures of primary visual cortical function, then we might expect the two should be correlated. While the prediction was not true in our dataset, reading ability was correlated with both visual search efficiency (poorer readers had higher ms/item search slopes) and functional V1 size asymmetry (poorer readers had lower left/right hemispheric asymmetry, suggesting a relative right V1 bias), suggesting at least one commonality (possibly related to reading and/or cognitive ability) underlying visual search efficiency and functional V1 size. The major difference is that in this study, we studied children, some with 'pathological' poor reading ability (i.e. dyslexia), and not adults with self-reported normal reading ability (i.e. university students) (Verghese, et al., 2014).

We found altered left/right V1 interhemispheric asymmetry (see Figure 2B) in dyslexic children relative to normal reading children, and interpret this as a relative bias towards right hemisphere representation of visual information in dyslexia. A future consideration is to examine how normal childhood development and reading experience, over a longitudinal study, impacts on visuospatial attentional efficiency and functional visual cortical size. Perhaps as children develop from their preschool to school-age years, there is an initial bias towards right hemisphere representation which becomes less apparent as they improve their reading skills, although this could not be explored in this study given the narrow age range of participants (9-11 years). Interestingly, interhemispheric size asymmetry in volume of the lateral geniculate nucleus (LGN) has been reported in young adults with dyslexia (Giraldo-Chica, et al., 2015), suggesting an under-development of the left hemisphere

(akin to the presumed under-development of left functional V1 seen in our dyslexic children) with impaired reading ability. The functional significance of left/right LGN and V1 asymmetry in the dyslexia literature is still unknown, but does suggest a developmental imbalance in the left and right hemispheres that appears to be associated with reading ability. Learning to read is known to alter the connectivity between cortex and thalamus even in adult illiterates (Skeide, et al., 2017) and thus it is possible that the interhemispheric asymmetry seen in normally reading adults (Verghese et al., 2014) and the difference in this measure between adult and paediatric cohorts are the gradual results of decades of literacy.

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From our data, it is not possible to disentangle whether the group differences observed in visual search efficiency and functional V1 size asymmetry reflect the underlying aetiology of dyslexia, or the reduced cumulative reading experience that naturally accompanies a reading difficulty. Normally reading children read, on average, a few hundred times more words in a year than dyslexic children (Anderson, Wilson, & Fielding, 1988), which could underlie some of the structural changes observed in brain connectivity between areas normally involved in reading and language comprehension (Romeo, et al., 2018; Yeatman, Dougherty, Myall, Wandell, & Feldman, 2012). This conflates the traditional dilemma of correlation vs causation that has long bedevilled the pursuit of finding a causal deficit in dyslexia (Goswami, 2015). Nevertheless, there is growing interest in remediation techniques that seek to enhance visuospatial attention, global visual scene perception, and dorsal stream motion discrimination and therefore improve reading such as action video games (Franceschini, et al., 2013), perceptual training (Franceschini, Bertoni, Gianesini, Gori, & Facoetti, 2017; Lawton, 2016) and transcranial current application (Costanzo, et al., 2019). Whether causally related to reading or not, the deficits in dyslexic visual function observed here using psychophysical and neuroimaging methods are likely to be useful in studying the cognitive and neural changes caused by such remediation procedures (see review by (Vidyasagar, 2019).

While we did not formally explore reading habits in this study, we can speculate about the possible role of reading in at least partially shaping visual cortical function in children, given more recent evidence for poorer right/left hemifield visual search performance in bidirectional relative to unidirectional readers (Kermani, Verghese, & Vidyasagar, 2018). Bidirectional adult readers, who have presumably split their cumulative lifetime reading experience between two languages that require left-to-right and right-to-left visuospatial attention (for example, English and Farsi respectively), may have a relative disadvantage when visual search is restricted to the left or right hemifield. In light of this, and the fact that reading in English involves left-to-right attention, it is possible that dyslexia disrupts the typical balanced (or possibly more left-biased) hemispheric symmetry in functional V1 size. Indeed, brain imaging studies find lateralized abnormalities, many of which are left hemispheric, of a range of neural networks in dyslexia (see reviews by Kershner, 2019; Paracchini, Diaz, & Stein, 2016) and that left hemispheric function is disrupted in pre-reading children with a family history of dyslexia, before formal diagnosis of dyslexia is possible (Raschle, Chang, & Gaab, 2011; Raschle, Zuk, & Gaab, 2012). These results, however, do not solve the 'chicken or egg' problem but may shed light on a mechanism of interhemispheric asymmetry underlying the association observed longitudinally between pre-reading visuospatial attention (at a kindergarten level) and future reading acquisition skills later in childhood (Franceschini, et al., 2012). Alternatively, a future approach to dissociate between cause and consequence of dyslexia is to compare groups of children who are not chronologically age-matched, but 'ability-matched' (Goswami, 2015). Because dyslexic children read far fewer words than typical readers of the same age (Anderson, et al., 1988), it is plausible that differences in visual performance and cortical function relate to overall reading experience (Vidyasagar, 2014). Indeed, years of reading experience has been shown to largely account for grey and white matter volume differences between dyslexic and non-dyslexic children (Krafnick, Flowers, Luetje, Napoliello, & Eden, 2014), but is yet to be explored for the left/right asymmetry we observe here.

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While we focused on measuring reading ability as the main outcome of interest, we also encountered inter-individual variation in cognitive ability in our dyslexic and normal-reading children. IQ was predictive of reading ability, as has been reported before (e.g. Kevan & Pammer, 2009; Snowling, Hulme, & Nation, 2020). We also found that poorer IQ was associated with poorer visual search efficiency, which suggests that general task demands may account for differences in visuospatial attention between normal-reading and dyslexic children. It is possible that the differences observed in this study between dyslexic and normal-reading children, and the correlations observed between measures, may be associated with IQ rather than specific to dyslexia. IQ was allowed to vary freely within our consecutively recruited cohort and not matched between the normal-reading and dyslexic groups. We admit the possibility that the higher IQ in our control group may also have been a result of inherent selection bias of our university-based research study, as the normal-reading children were mostly children of university professional and academic staff (with some control participants being siblings or friends/acquaintances of the dyslexic children). Future work could interrogate whether the visual deficits we report in the dyslexic children are an epiphenomenon of cognitive deficit, by controlling for IQ in a multivariate regression analysis with a larger sample population. In particular, while the correlation between verbal IQ and reading ability did not reach statistical significance here, it is known that the vastly reduced amount of reading done by dyslexic children (Anderson, et al., 1988) has a negative effect on verbal and phonemic skills (e.g. see Huettig, Lachmann, Reis, & Petersson, 2018; Snowling, et al., 2020). However, we believe that it is difficult to disentangle the relative contributions of dyslexia and IQ, given that IQ and reading ability are inextricably linked.

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In summary, inter-individual variation in children's reading ability is associated with two visual functional measures, namely visual search efficiency and functional size of V1. We confirm that dyslexia and poorer reading ability is associated with poorer visual search efficiency (higher ms/item search slopes). We also demonstrate, for the first time, functional asymmetry between the left and

| right hemispheres of V1 in dyslexic children relative to normal-reading children, such that there     |
|---|
| appears to be a relative right V1 bias. While reading ability was correlated with visual search       |
| efficiency and functional V1 asymmetry separately, these two measures of visual cortical function     |
| were not correlated with each other. We surmise that, by adulthood, the reduced reading               |
| accumulated by people with dyslexia (or even those at the lower end of the 'normal-reading'           |
| spectrum) is associated with both reduced visuospatial attention as well as a bias away from the left |
| hemisphere in terms of functional V1 size. Our findings highlight the importance of considering the   |
| laterality of functional measures in dyslexia, and the possibility that independent cortical networks |
| responsible for visuospatial attention and functional V1 size both contribute to impaired reading     |
| ability in dyslexic children.   |

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# Highlights

- 1) Visual search efficiency correlates with reading ability in children
- 2) Left/right visual cortical size asymmetry relates to reading ability in children
- 3) Our findings suggest a deficit in visuospatial attention in dyslexia

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