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SHORT REPORT

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# Hemispheric asymmetries in the orientation and location of the lateral geniculate nucleus in dyslexia

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Human brain asymmetry reflects normal specialization of functional roles and may derive from evolutionary, hereditary, developmental, experiential, and pathological factors (Toga & Thompson, 2003). Geschwind and Galaburda (1985) suggested that processing difficulties in dyslexia are due to structural differences between hemispheres. Because of its potential significance to the controversial magnocellular theory of dyslexia, we investigated hemispheric differences in the human lateral geniculate nucleus (LGN), the primary visual relay and control nucleus in the thalamus, in subjects with dyslexia compared to normal readers. We acquired and averaged multiple high-resolution proton density (PD) weighted structural magnetic resonance imaging (MRI) volumes to measure in detail the anatomical boundaries of the LGN in each hemisphere. We observed hemispheric asymmetries in the orientation of the nucleus in subjects with dyslexia that were absent in controls. We also found differences in the location of the LGN between hemispheres in controls but not in subjects with dyslexia. Neither the precise anatomical differences in the LGN nor their functional consequences are known, nor is it clear whether the differences might be causes or effects of dyslexia.

**KEYWORDS**

dyslexia, hemispheric asymmetry, lateral geniculate nucleus

## 1 | INTRODUCTION

Neurological asymmetries are believed to reflect an evolutionary adaptive variation and specialization, and disease processes might interact with existing brain asymmetries to reduce or exacerbate them (Toga & Thompson, 2003). Several asymmetries have been reported in dyslexia, including absence of the normal asymmetry of the planum temporale (Geschwind & Galaburda, 1985; also see Altarelli et al., 2014), absence of the normally larger neuronal size of the left versus right primary visual cortex (Jenner, Rosen, & Galaburda, 1999), and a greater number of Heschl's gyrus full duplications in the right hemisphere (Altarelli et al., 2014).

  

The lateral geniculate nucleus (LGN) is the primarily visual relay nuclei from the retina to the cortex and is an important control structure in visual processing and attention (O'Connor, Fukui, Pinsk, & Kastner, 2002; Schneider, 2011; Schneider & Kastner, 2009; Sherman & Guillery, 2002). It is the only location in the brain where the magnocellular and parvocellular visual streams are spatially disjoint, and therefore in a previous study (Giraldo-Chica, Hegarty, & Schneider, 2015), we examined the LGN in subjects with dyslexia compared to controls. In that study, we found reductions in the volume of the LGN in dyslexia that were consistent with the controversial magnocellular theory of dyslexia (Livingstone, Rosen, Drislane, & Galaburda, 1991; Stein, 2001; Stein & Walsh, 1997). Stein (1994) suggested that normal magnocellular development promotes normal hemispheric asymmetry and that impaired magnocellular development is responsible for some of the problems associated with impaired hemispheric specialization and dyslexia.

In this study, we analyse asymmetries in morphology, orientation, and location of the LGN in a group of subjects with dyslexia and normal readers. We conducted detailed morphological analyses comparing the left and right LGN between the two groups using two different methods. First, we registered each LGN by its centre of mass to compare the LGN morphology in the native space of each subject. Second, to test for differences in the location of the nuclei, we computed a probabilistic atlas of the LGN location in a standard space.

## 2 | MATERIALS AND METHODS

### 2.1 | Subjects and behavioural measurements

This study included 13 subjects with dyslexia (five female) and 13 IQ-matched controls (three female), 22–26 years old. None had other neurological disorders, their native language was English, and all were right-handed. The subjects with dyslexia were recruited from the University of Missouri Learning Center, where they had been registered as having reading disorders on the basis of professional assessments. All subjects provided informed written consent, and the university ethics committee approved the research protocol. Behavioural assessments were administered to all subjects to verify their classifications. The results have been previously reported (Giraldo-Chica et al., 2015) and are summarized in Table 1.

### 2.2 | Identification of the LGN

Details of the methodology to image and segment the LGN have been reported previously (Giraldo-Chica et al., 2015). Briefly, for each subject, 40 proton density (PD) images were acquired with a 3T magnetic resonance imaging scanner, registered, and averaged to create a high signal-to-noise ratio (SNR) image in which the extent of the LGN was clearly discernible (Devlin et al., 2006). Each LGN in each subject was manually segmented by six independent experimenters blind to the subject's group membership, and the six binary segmentations were combined into a median mask.

### 2.3 | LGN orientation

The brain was extracted from the PD images (Smith, 2002) and rigidly (no scaling) oriented (Jenkinson & Smith, 2001) in native space to the anterior commissure-posterior commissure (AC-PC) line and interhemispheric plane. This reorientation was then applied to the LGN masks using nearest neighbour interpolation. To measure the orientation of each LGN, we used principal components analysis to fit a plane to the median mask, projected the normal vector of this fitted plane into the coronal plane, and measured its angle with the axial plane (Figure 1). We subjected these angles to a repeated measures analysis of covariance (ANCOVA, SPSS v20 for Mac, IBM, Inc.). The repeated measure was the angle with two levels (left and right). The between-subjects factors were group membership and gender. Brain volumes (sum of the grey and white matter) were covariates.

**TABLE 1** Behavioural measures: Full scale (4) IQ, performance IQ, verbal IQ, and digit span (scaled) from the Wechsler adult intelligence scale (WAIS-III) test (Wechsler, 1997); word attack, letter-word identification, spelling, and the composite basic reading skills (percentile) from the Woodcock–Johnson tests of achievement (Woodcock, McGrew, & Mather, 2001); and phonological awareness, rapid naming (digits and letters), and alternate rapid naming (colors and objects) from the comprehensive test of phonological processing (CTOPP) (Wagner, Torgesen, & Rashotte, 1999)

| | Dyslexia | | Controls | | Statistics | | |
|---|---|---|---|---|---|---|---|
| Variable | *n* = 13 | | *n* = 13 | | $t/x^2$ | *df* | *p* |
| Sex (M/F) | 10:3 | | 8:5 | | .83 | 24 | .42 |
| | Mean | *SD* | Mean | *SD* | | | |
| Age | 24.08 | 1.9 | 23.5 | 1.3 | −.945 | 24 | .35 |
| Full scale (4) IQ | 110.2 | 8.0 | 114.2 | 9.4 | 1.2 | 24 | .25 |
| Performance IQ | 107 | 11 | 110.3 | 8.5 | .78 | 24 | .44 |
| Verbal IQ | 110.9 | 8.4 | 114 | 10 | .98 | 24 | .34 |
| Digit span | 9.0 | 2.8 | 11.0 | 2.4 | 2.0 | 24 | .063 |
| Word attack | 23.7 | 5.1 | 29.3 | 2.3 | 3.6 | 24 | .001 |
| Letter-word identification | 65.0 | 3.6 | 71.5 | 3.0 | 5.0 | 24 | <.001 |
| Spelling | 41.4 | 6.3 | 52.6 | 2.1 | 6.1 | 24 | <.001 |
| Basic reading skills | 28 | 17 | 64 | 15 | 5.6 | 24 | <.001 |
| Phonological awareness | 91 | 13 | 98.4 | 8.0 | 1.8 | 24 | .093 |
| Rapid naming | 82 | 14 | 100 | 14 | 3.4 | 24 | .002 |
| Alternative rapid naming | 88 | 13 | 102 | 18 | 2.3 | 24 | .032 |

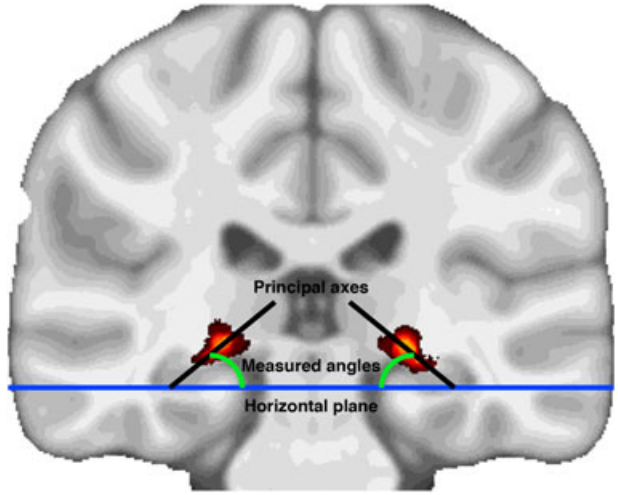


**FIGURE 1** Illustration of the measurement of the inclination of the lateral geniculate nucleus relative to the axial plane [Colour figure can be viewed at wileyonlinelibrary.com]

## 2.4 | LGN morphology

To compare the morphology of the LGN between hemispheres, the left and right masks (in reoriented native space) of all subjects were registered according to their centres of mass. We then reflected the left LGN about its midline, subtracted it from the right LGN, and averaged this difference map across subjects in each group. To test the significance of the differences, we carried out a repeated measures analysis of variance using Randomise v2.9 (Winkler, Ridgway, Webster, Smith, & Nichols, 2014). We applied voxel-wise general linear model for each group

(corresponding to a single-group paired *t* test), using permutation-based non-parametric testing, and correcting for multiple comparisons across space and for family-wise error.

### 2.5 | LGN location

To measure the position of both LGN within the brain, we transformed the PD images and the LGN masks into standard space via nonlinear transformation using Advanced Normalization Tools (Avants et al., 2011). To examine the effect of the transformation into common space on the relative position of the LGN within the brain, we measured the lateral distance from the centre of mass of the LGN to the midline of the brain before and after transformation. We reflected the left LGN about the midsagittal plane, and subtracted it from the right LGN, and averaged the difference maps across subjects in each group. A second analysis of covariance was performed using the lateral distance between the centres of mass of each LGN to the midline of the brain as the repeated measures factor with the same between-subjects factors and covariate as above. All variables were normally distributed for the groups as assessed by the Shapiro–Wilk test and passed the Levene's Test of Equality of Error Variances.

## 3 | RESULTS

### 3.1 | Differences in the orientation of the left and right LGN

In subjects with dyslexia, the right LGN was inclined 36.8 ± 4.8° relative to the axial plane compared to the left LGN, 27.0 ± 2.5°. In controls, the right LGN was inclined 31.0 ± 2.8° compared to the left, 29.5 ± 1.4°.

The main effect of angle was significant ($F_{1,24}$ = 5.75, $p$ = .025). But the main effect of group was not ($F_{1,24}$ = 0.21, $p$ > .1) nor was the angle by group interaction ($F_{1,24}$ = 3.11, $p$ = .091). Looking at the simple effects, we see that in controls, there is no effect of hemisphere on angle ($F_{1,24}$ = .20, $p$ > .1). However, there is a significant effect in subjects with dyslexia ($F_{1,24}$ = 8.65, $p$ = .007).

### 3.2 | Morphological differences between the left and right LGN in native space

Figure 2 shows the mean difference maps for subjects with dyslexia and controls; voxels with negative values have a higher probability of belonging to the right hemisphere than the left. The morphological changes observed here are consistent with the orientation difference reported above; however, only 14 (of 2,846) voxels in subjects with dyslexia had significantly different probabilities of belonging to the left versus right LGN ($p$ < .05), with an additional 22 voxels showing a trend ($p$ < .1). No significantly different voxels between hemispheres where found in controls.

### 3.3 | Differences in the lateral position of the LGN between hemispheres

In Figure 3, the probability maps of the left LGN were reflected across the brain midline and compared to the right. In control subjects, the centre of mass of the right LGN was located 28.38 ± 0.46 mm from the midline, which was significantly closer ($F_{1,24}$ = 7.62, $p$ = .011) than the left, 30.00 ± 0.58. There was no significant difference between hemispheres in subjects with dyslexia ($F_{1,24}$ = 2.70, $p$ = .11) nor a significant interaction between group and location ($F_{1,24}$ = .62, $p$ > .1).

### 3.4 | LGN volume

As reported in our previous study (Giraldo-Chica et al., 2015), we found that the volume of the left LGN was significantly reduced in dyslexia compared to controls, 98.9 ± 8.0 $mm^3$, versus 120.7 ± 6.2 $mm^3$ ($F_{1,23}$ = 6.12, $p$ = .021). This difference was not significant in the right hemisphere, 103.8 ± 7.0 versus 112.3 ± 7.0 $mm^3$ ($F_{1,23}$ = 2.89, $p$ = .10). There

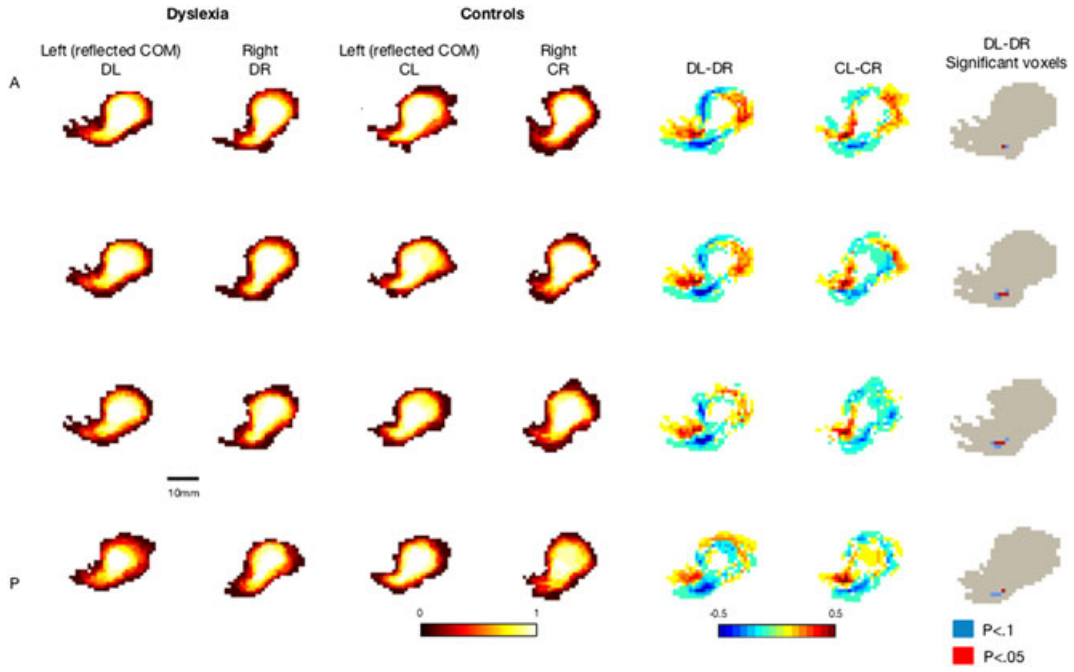


**FIGURE 2** Left columns: Probability maps of the lateral geniculate nucleus (LGN) in native space for dyslexia and control groups registered across subjects by the centres of mass. Left LGN masks have been reflected about their centres of mass. The colour, as shown on the colour bar below, indicates the probability of the voxel to belong to each LGN. Right columns: Difference maps of the probability of belonging to the left LGN minus its probability of belonging to the right. Blue voxels have high probability of belonging to the right LGN as opposed to the left; red voxels have high probability of belong to the left LGN as opposed to the right. Significantly and marginally different ($p < .05$ and $p < .1$) voxels are shown for the dyslexia group; no voxels had significantly different probabilities for the control group [Colour figure can be viewed at wileyonlinelibrary.com]

were no significant volume differences between hemispheres in controls ($F_{1,23} = 0.65$, $p = .43$) nor in subjects with dyslexia ($F_{1,23} = 0.14$, $p = .71$).

## 4 | DISCUSSION

After analysing the hemispheric differences in the LGN, we conclude that the structure has a significantly different morphology and orientation in each hemisphere in the population with dyslexia. The LGN of subjects with dyslexia is oriented more parallel to the axial plane in the left hemisphere in comparison to the right one. In addition, we have found that in the group of controls, the LGN is located further from the midline in the left hemisphere. The precise anatomical differences in the LGN that have led to these observed differences is not known nor are their functional consequences. Alterations in the volume or location of other brain structures could alter the orientation and location of the LGN.

Asymmetries in the position and morphology of the LGN are important to report because of the potential significance of the LGN in the magnocellular theory of dyslexia. Reversed hemispheric asymmetry and abnormal hemispheric lateralization have been previously associated to several brain disorders that have deficits in the magnocellular pathway, including dyslexia, autism, or schizophrenia (Stein, 1994). Stein suggested that normal magnocellular development promotes normal hemispheric asymmetry. On the other hand, he suggested that impaired magnocellular development is responsible for a spectrum of problems associated with impaired hemispheric specialization, including dyslexia. It was not possible with these data to test the relationship between these asymmetries and

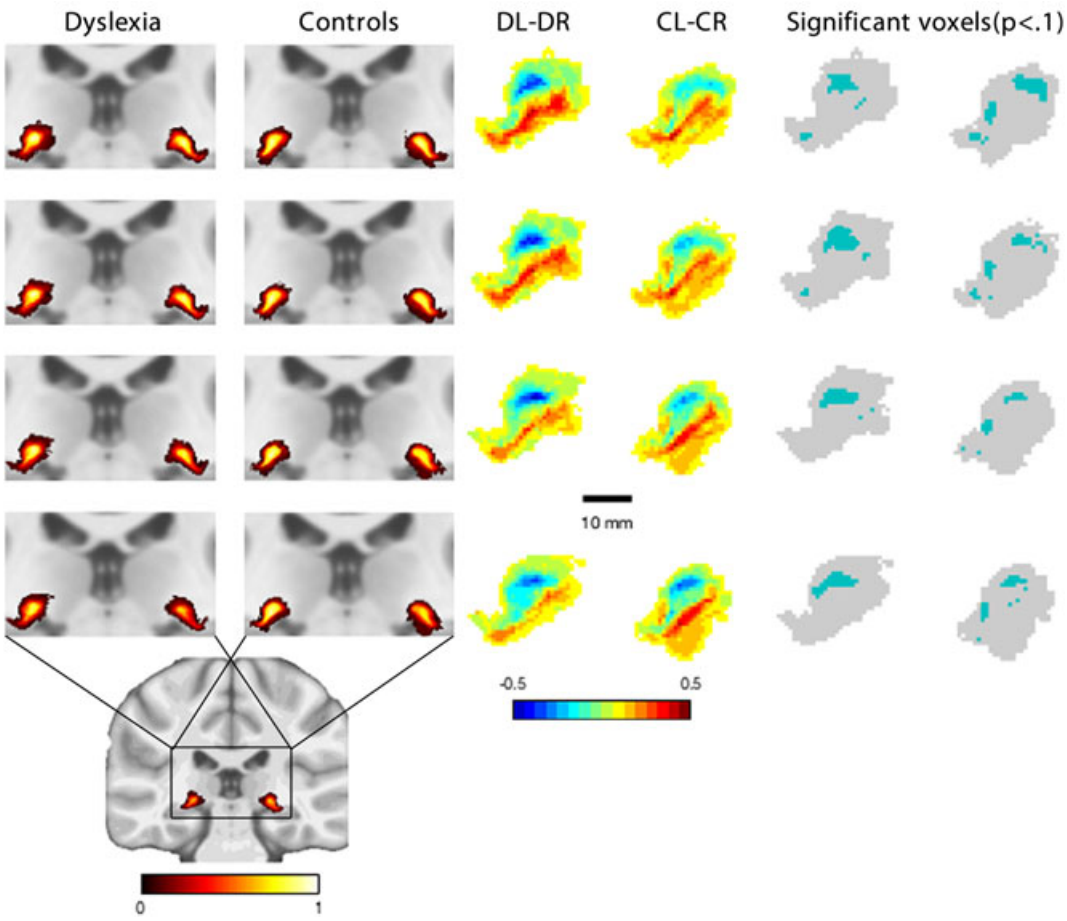


**FIGURE 3** Probability maps of the location of the LGN in standard space. Left columns: Central slices, arranged anterior (A) to posterior (P) of the mean LGN for subjects with dyslexia and controls overlaid on a PD slice. Right columns: Difference maps (left−right) for dyslexia (DL − DR) and control (CL − CR) groups. Voxels that were marginally different ($p < .1$) between hemispheres are indicated in the rightmost columns. Conventions as in Figure 2.
LGN = lateral geniculate nucleus; PD = proton density [Colour figure can be viewed at wileyonlinelibrary.com]

magnocellular deficits, which should be the focus of future studies. Further measurements with higher resolution need to be conducted to be able to quantify differences in the individual layers of the LGN.

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