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# Developmental trajectories of grey and white matter in dyscalculia

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ABSTRACT

Developmental dyscalculia is a significant neural deficit with broad social impact. A number of techniques have been used to identify the brain basis of dyscalculia, and many of these have highlighted the role of the intraparietal sulci and a left fronto-parietal network in the representation of core number skills. These studies offer conflicting explanations of the neurobiological deficits associated with dyscalculia, and to date few studies have elucidated the timeline of cortical changes involved.

Here we report a volumetric study comparing well-characterized dyscalculic learners aged from 8 to 14 years with tightly matched controls. Using automated cortical parcellation of anatomical MRI, we show that the posterior parietal and fronto-parietal systems in dyscalculia may undergo abnormal development during the pre-teenage and teenage years. As a result, the present study more clearly characterizes the underlying neural basis of dyscalculia than previous studies have hitherto achieved.



## 1. Introduction

Developmental dyscalculia (DD) is a congenital disability in learning about numbers and arithmetic. A recent review of prevalence studies across many countries suggests that it affects between 3% and 6% of the population [1], a prevalence comparable with dyslexia [2]. Like dyslexia, DD is a serious handicap for individual sufferers, affecting their employment and health [3,4], and therefore constitutes a significant burden on national economies [5,6].

The core deficit in DD is now generally agreed to be a disability in processing numerosities – the number of objects in a set [7,8] ([9] for slightly different methodology). It is possible to identify this deficit in kindergarten simply by the speed and accuracy of naming the number of dots in a visual array (up to nine dots). Moreover, a longitudinal study using this method, was able to predict age-appropriate arithmetical attainment up to the age of 11 years [10].

Just as specialized teaching is required for dyslexics that focuses on their core deficit in phonology [11], it is now recognized that DDs also need specialized teaching that focuses on their core deficit in numerosity processing and which the teaching schedule carefully adapts to the learner's current level of competence [7,12,13].

Several studies have shown that learners identified as DD have abnormalities in brain regions known to be critical for number processing [14–16]. Many of these highlight the intraparietal sulci, either unilaterally or bilaterally, as well as a larger fronto-parietal arithmetic network, typically in the left hemisphere (see [17] for a recent review).

Despite this progress in describing the dyscalculic brain, the current body of literature fails to distinguish brain changes occurring over time from brain changes occurring over space. It is now quite clear that cortical grey and white matter development varies both temporally and regionally during childhood and the early teenage years [18], and this changing cortical landscape presents a unique problem to the study of cognitive development in children: baseline regional changes will vary by group (DD vs. controls) and by age. Such regional shifts in developmental trajectories may reflect longer-term influences on cortical maturation than are typically examined in functional activation studies.

A morphometric analysis of such shifting trajectories requires careful phenotypic characterization of DD learners. While a variety of criteria for classifying learners as DD can be found in the literature [19], the first study comparing brain structure in DDs and matched controls, performed by our group, used a discrepancy between measured and predicted performance on the Numerical Operations subtest of the WOND [20]. The subjects in this study were drawn from a population of low-birthweight adolescents who had normal or superior IQs when tested [21]. The study found reduced grey-matter density in the left intraparietal sulcus (IPS). However, one study of 9 year olds, using an unspecified clinical

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diagnosis, found reduced grey-matter density in the *right* IPS [22]. Another study of 7–9 year olds, identified as DD if they scored at or below 95 on one of two subscales of the WIAT-II (Numerical Operations Score or Math Composite Score), found reduced grey matter bilaterally in superior parietal lobule, intra-parietal sulcus, as well as the fusiform gyrus, parahippocampal gyrus and the right anterior temporal cortex in children with DD as compared with controls [23].

Another potentially useful way of identifying grey matter regions that may be implicated in DD is to consider those areas that are active in the development of arithmetical abilities. An recent meta-analysis [24] suggests that the network active in arithmetical development comprised: bilaterally the inferior and superior parietal cortex (BA40), including the precuneus (BA7) the inferior frontal gyrus (BA9), premotor cortex (BA6), the insula (BA47, BA13); also, the right angular gyrus (BA39), and the left inferior temporal gyrus (BA20), along with striate and extrastriate cortex bilaterally (BA18, BA19). (p776-777)

This meta-analysis also confirmed that DDs showed lower activations in left precuneus (BA 7), right inferior parietal lobe (BA 40), left frontal paracentral lobe (BA 6), left fusiform gyrus (BA 37), left superior frontal gyrus (BA 10) and right middle frontal gyrus (BA 9).

In addition to grey matter (GM) differences, more recent work has also reported differences in white matter (WM) [23]. White matter differences may be even more critical in the description of dyscalculia, since white matter changes are known to be associated with learning. For example, structural changes in white matter are correlated with learning a motor skill in both humans [25] and monkeys [26], and in learning to read [27] (see [28] for a recent review). Furthermore, voxel-based morphometric techniques have been used to demonstrate reduced white matter (WM) volume in right temporo-parietal cortex of DD learners, while diffusion-tensor imaging revealed reduced fractional anisotropy (FA) in this WM region. This reduction in white matter integrity in DD learners correlated in turn with their performance on a standardized test of simple arithmetic [23].

In order to describe the brain basis of dyscalculia with validity, both the morphometric and functional aspects of the dyscalculic brain must be characterized by age. The present study examines regional variation in cortical grey and white matter morphology in dyscalculics and carefully matched controls over a range of ages between 8 and 14 years. See Table 1.

The aim of this study was to describe in detail the differences in regional cortical anatomy that characterize the dyscalculic brain, and to establish how those regional differences might vary during cortical development. We used, Freesurfer, a method of automatic parcellation of brain regions that provides measures of the area, thickness and volume of GM and the volume of WM [29–32].

We argue that both temporal and regional changes in cortical surface parameters might account for the phenotype of developmental dyscalculia.

## 2. Results

Using data processed using Freesurfer 5.1.0, we were able to compare grey-matter (GM) volume, area and thickness, and white-matter (WM) volume between the DDs and matched controls.

### 2.1. Main effects

#### 2.1.1. Grey-matter

There was a main effect of group on a number of cortical structures; these are illustrated graphically in Fig. 1 and summarized in Table 2. The largest group differences in cortical surface area were seen in the bilateral subcentral gyri (BA43); dyscalculics had significantly reduced cortical surface area in these regions compared to matched controls. Cortical thickness was also reduced in the dyscalculic group, most prominently in the left temporal (BA22) and right inferior frontal lobes (BA44). Finally, dyscalculics had large reductions in grey matter volume in the right parahippocampal gyrus (BA36) and the right inferior and posterior parietal lobe (BA39, BA40).

#### 2.1.2. White matter

In addition to these grey matter deficits, dyscalculics had reduced white matter volume in the right inferior parietal lobe, the right temporal pole and transverse temporal lobe, and the right pars orbitalis. See Table 3.

### 2.2. Age effects

To describe the effect of age on cortical morphology, we performed a regional ANCOVA in dyscalculics and matched controls.

#### 2.2.1. Grey matter

We found significant age-related increases in GM area in left frontal cortex in controls only, depicted anatomically in Fig. 2, the trends are depicted graphically in Fig. 4; see also Table 3. The largest effect on cortical surface area was in the left supramarginal gyrus (BA40), where dyscalculics gained area more slowly over the age range than controls. Relative to controls, grey matter volume in dyscalculics increased as they grew older in the left lateral frontal cortex (dorso-lateral prefrontal cortex, essentially BA 46) and the right superior occipital lobe (BA19), but decreased slightly in the left primary motor cortex. Cortical thickness was minimally decreased around the right cingulate cortex.

### 2.3. White matter

Dyscalculics had notable delays in white matter development relative to controls, with changes seen broadly in the left frontal and parietal cortices, with additional effects seen in right superior and medial frontal cortex. These effects were typically characterized by an age-related increase in WM in the control subjects, while in DDs WM volume remained stable or even decreased. Significant differences were observed in the left precuneus, left supramarginal gyrus, and bilaterally in the superior frontal lobes. These results are depicted anatomically in Fig. 3 and the trends are depicted graphically in Fig. 5, and tabulated in Table 4.

By contrast, in the posterior corpus callosum there was a *decrease* in volume in controls, compared to a relatively unchanged volume over time in DDs (see Fig. 5)(Table 5).

**Table 1**
DD and Control Demographics.

| | *N* | Age at test (years) | Gestational age | FSIQ | VIQ | WOND NOp |
|---|---|---|---|---|---|---|
| Dyscalculics | 11 | 8–14 | 36.4 weeks (15 days) | 111 (16) | 110 (16) | 91 (18) |
| Matched controls | 11 | 8–14 | 36.5 weeks (15 days) | 111 (16) | 114 (14) | 113 (14) |

DDs were paired with controls matched for chronological age, gestational age, Full Scale IQ, and Verbal IQ. Independent *t*-tests of each of these variables confirmed that there were no group differences (all $p$-values > 0.05). SDs given in parentheses.