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Cerebellar morphology in developmental dyslexia

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Abstract

Recent evidence has suggested cerebellar anomalies in developmental dyslexia. Therefore, we investigated cerebellar morphology in subjects with documented reading disabilities. We obtained T1-weighted magnetic resonance images in the coronal and sagittal planes from 11 males with prior histories of developmental dyslexia, and nine similarly-aged male controls. Proton magnetic resonance spectra (TE = 136 ms, TR = 2.4 s) were obtained bilaterally in the cerebellum. Phonological decoding skill was measured using non-word reading. Handedness was assessed using both the Annett questionnaire of hand preference and Annett's peg moving task.

Cerebellar symmetry was observed in the dyslexics but there was significant asymmetry (right grey matter > left grey matter) in controls. The interpretation of these results depended whether a motor- or questionnaire-based method was used to determine handedness. The degree of cerebellar symmetry was correlated with the severity of dyslexics' phonological decoding deficit. Those with more symmetric cerebella made more errors on a nonsense word reading measure of phonological decoding ability. Left cerebellar metabolite ratios were shown to correlate significantly with the degree of cerebellar asymmetry ($P < 0.05$) in controls. This relationship was absent in developmental dyslexics.

Cerebellar morphology reflects the higher degree of symmetry found previously in the temporal and parietal cortex of dyslexics. The relationship of cerebellar asymmetry to phonological decoding ability and handedness, together with our previous finding of altered metabolite ratios in the cerebellum of dyslexics, lead us to suggest that there are alterations in the neurological organisation of the cerebellum which relate to phonological decoding skills, in addition to motor skills and handedness.

Keywords: Magnetic resonance imaging; Phonological processing; Magnetic resonance spectroscopy; Volumetric morphometry; Handedness

1. Introduction

Developmental dyslexia is now well established as a disorder of neurobiological origin. Documented abnormalitites include visual [8,34,53] and auditory processing deficits [35,54,59], probable altered lateral cerebral asymmetry [29,32,47] histological and biochemical cerebral abnormalities [20,42,45] and altered patterns of cerebral activation on particular visual, auditory and verbal tasks [9,13,40,44,46,49].

Evidence has emerged to implicate the cerebellum in some aspects of dyslexic dysfunction. Indirect evidence includes the presence of "soft cerebellar signs", delayed motor milestones such as crawling, walking and learning to ride a bicycle and a characteristic clumsiness [14–16,38]. Evidence directly indicating cerebellar involvement has also emerged. We have previously shown biochemical abnormalities in the right cerebellum of people with developmental dyslexia compared to control subjects and also differences in the right side of dyslexic cerebellum compared to the left side [42]. The right cerebellum has also been shown to display a functional deficit, exhibiting decreased blood flow in response to both learned and novel motor tasks [37]. Blamire et al. [5] have shown biochemical abnormalities similar to those seen in humans with dyslexia [42] in the cerebella of mice injected with sera from mothers who have two or more dyslexic offspring, and have shown that the degree of

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severity of the biochemical abnormality correlates significantly with motor performance in these mice.

Morphological examination of the brains of those with dyslexia has typically been confined to the cerebral cortex, mostly focussing on the planum temporale [36]. These studies have yielded contradictory findings (e.g. [20,26,27, 32,52]) and may have been confounded by the method employed and how handedness was assessed (reviewed in [3,28]). Galaburda et al. [20] analysed brains from persons with dyslexia post-mortem. These brains showed symmetry in the planum temporale (a temporal lobe language area), an effect that was argued to result from enlarged right hemisphere areas rather than a relative decrease on the left side. The cortical symmetry was later interpreted as a difference (increase) in the numbers of right hemisphere neurons [17], a potential consequence of altered neuronal migration patterns and/or a decreased rate of neuronal "pruning" in development. Patterns of neuronal migration may be abnormal in dyslexics [20] and our own magnetic resonance spectroscopy (MRS) studies have provided data consistent with different patterns of relative cell distribution in the right temporo-parietal lobe compared with the left, a histological/biochemical asymmetry which is not present in control subjects [42].

Little is known about the morphology/asymmetry of the cerebellum in developmental dyslexia so, given our findings of anomalous cerebellar biochemistry in dyslexia, it was of interest to determine whether cerebellar morphology in dyslexia reflects anomalous patterns already reported in the cortex. Therefore, we quantified cerebellar asymmetry by the comparison of relative amounts of tissue on the left and right sides of the cerebellum as well as relative amounts of grey and white matter on each side using subjects from our recent MRS study.

2. Subjects and methods

2.1. Subjects

Twenty adult male volunteers, aged 20–41 years, participated with informed consent. Nine were normal readers and 11 had prior histories of developmental dyslexia. These men were recruited for an investigation into possible alterations in brain biochemistry in developmental dyslexia as detailed previously [42]. The study was approved by the Central Oxford Research Ethics Committee.

All the individuals with dyslexia had been formally diagnosed by educational psychologists as reading disabled, either as adults or as children, most within the previous 2 years. Diagnosis was based upon an unexpected and large discrepancy between literacy achievement and expected achievement based upon age- and intelligence-defined norms (APA, 1994). Developmental dyslexia is ubiquitously associated with poor phonological skills [57]. We measured all subjects' phonological skills with non-word reading tests, a measure of phonological decoding sensitive to differences between dyslexics and controls [55]. As a group, the dyslexic subjects named significantly fewer items correctly and took significantly longer to name the non-word items on the Castles and Coltheart [6] ($P = 0.0006$ and 0.0027, respectively, Mann–Whitney) and Snowling [50] test batteries ($P = 0.0025$ and 0.0027, respectively, Mann–Whitney). There was no significant difference (Mann–Whitney U) in non-verbal intelligence between the dyslexic and control groups as measured by the Wechsler Adult Intelligence Scales (WAIS-R) [58]. Handedness was assessed using both the Annett questionnaire of handedness [1] and Annett's peg moving task [2]. The Annett questionnaire ascertains hand *preference* for 12 common manual tasks by subject's self report, whereas the peg moving task measures hand *skill* by assessing subject's time to move a series of 10 pegs from one row to another with each hand.

2.2. Magnetic resonance imaging

All magnetic resonance imaging and spectroscopy was obtained at 85.2 MHz using a Bruker AVANCE DBX spectrometer. Images were acquired in two orientations using a quadrature head birdcage coil [25]. T1-weighted sagittal images were acquired as two "packs" of eight slices with each pack centred laterally through the temporal lobes. T1-weighted coronal images were acquired as a single contiguous set of 16 slices across the cerebellum. Imaging parameters for both orientations were repetition time (TR), 803 ms; echo time (TE), 13 ms; matrix, 256×192; field of view, 25.6 cm; slice thickness, 5 mm; slice separation, 5 mm.

Images were reconstructed with one degree of zero filling. Quantitative volumetric analysis was obtained on the left and right cerebellum from the coronal slices. Coronal slices have been shown to be especially useful for the identification of morphologic differences between the cerebellar hemispheres [41]. The anterior and posterior extent of the cerebellum was guided by published atlases and literature with the cerebellar hemispheres grey and white matter, the cerebellar tonsils, the vellum (included in hemisphere grey matter), and the corpus medullare (included as hemisphere white matter) included in the separate measurement of each cerebellar hemisphere. The cerebellar peduncles and the fourth ventricle were excluded [12,41,43,56].

The proportion of the left grey and right grey matter as well as the proportion of the left and right white matter of the total cerebellum was determined. The proportion of the left and the right hemisphere of the entire cerebellum was also analysed. Asymmetry indices were determined using proportional measures from the left grey compared to the right grey indices. Each region of interest or cerebellum hemisphere was point counted on the relevant reconstructed cortical slices against a grid of 37×54 points with the grey and white matter analysed separately. All regions of individual coronal slices were able to be delineated with this method. The proportional volume fraction of each