Combined Volumetric MRI and MR Spectroscopic Analyses of the Cerebellum in Developmental Dyslexia

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Introduction

Developmental dyslexia is associated with problems in a range of linguistic and non-linguistic skills. There are a number of hypotheses for the underlying causes for dyslexia, however, the cerebellar deficit hypothesis proposes that the difficulties experienced by dyslexics are attributable to abnormal cerebellar development and subsequent dysfunction[1].

Method

This pilot study was conducted in 5 dyslexic and 7 control adult, male participants. The dyslexics were formally diagnosed by having an IQ greater than 90 and demonstrating the dyslexic profile in nonsense passage reading, spelling and reading[2]. The control participants showed no evidence for dyslexia. All subjects were right-handed and were matched for age (dyslexics 21.3±0.8yrs, controls 21.4±1.9yrs) and IQ (dyslexics 121±9, controls 125±3). All imaging was conducted at 3T scanner (Philips Achieva 3.0T, Philips Medical Systems, Best, Holland). Whole-brain volumetric MRI (T1-weighted 3D-MPRAGE) datasets with a spatial resolution of 0.8x0.8x0.8mm^3 were obtained. The vermis, the grey matter and white matter volumes of both cerebellar hemispheres were measured using a stereological technique[3]. MR spectra were obtained using a single-voxel PRESS technique (TE=144ms, TR=1600ms). Three spectra were obtained per participant, one in both the left and right cerebellar hemispheres (1.5x1.5x1.5cm^3 voxels), and one from the vermis (2x2x1cm^3 voxel). Spectral post processing was performed offline (jMRUI[4]) using the AMARES algorithm[5]. The 3 usual fitted peak areas corresponding to choline (Cho at 3.2ppm), creatine (Cr at 3.0ppm) and N-acetyl aspartate (NAA at 2.02ppm) were determined. Comparative analyses were performed on the NAA/Cho, NAA/Cr and Cho/Cr metabolite ratios. Between-group differences were tested using a two-tailed Mann-Whitney U test. Within-group differences were assessed with Wilcoxon Signed Ranks Tests. Effect sizes (ES) were calculated with the following formula: [(Participant value – control group mean)/ control group s.d.], were a $|ES|$ >0.5 is medium and a large $|ES|$ >0.8. Effect sizes provide a magnitude of difference, independent of group sizes.

Left Cerebellar Hemisphere Effect sizes

	MRS: NAA/Cho	MRS: Cho/Cr	White matter volume	White /Grey matter ratio
Dyslexic Participant				
D1	-1.20	1.05	0.83	0.56
D2	-1.00	1.55	3.18	3.35
D3	-2.02	1.38	0.59	1.75
D4	-0.09	2.33	0.59	1.00
D5	-1.44	0.28	1.08	1.74
Mean Dyslexic 'Direction' of Effect Size Difference				
	(-)	(+)	(+)	(+)
Control Participant				
C1	-0.72	1.83	-0.15	-0.04
C2	0.77	-1.11	1.47	0.82
C3	1.47	-0.77	-1.08	-0.53
C4	0.85	0.06	0.69	0.79
C5	-0.97	0.22	-1.37	-1.63
C6	-0.54	0.44	-0.10	-0.59
C7	-0.86	-0.72	0.54	1.18

Results

The volumetric data demonstrated no between-groups differences for any cerebellar region, however, the dyslexic participants tended to have a larger volume of white matter in both cerebellar hemispheres (p=0.07, for both). The Dyslexics possessed a significantly larger ratio of white matter to grey matter within both cerebellar hemispheres (p=0.02). MR spectroscopy showed that the dyslexic group's left cerebellar hemisphere had a lower mean NAA/Cho ratio and a higher mean Cho/Cr ratio than the control group. No between-group differences for the metabolite ratios occurred for the right cerebellar hemisphere or vermis. The effect sizes for the volumetric and spectroscopic left hemisphere differences (see table) demonstrate that the dyslexic participants all had medium or greater ES for *both* the volume and spectra in the dyslexic direction of magnitude (i.e. a greater volume of white matter, large ratio of Cho/Cr, small ratio of NAA/Cho, etc). However, only one control subject (C7) possessed the dyslexic-like profile for the effect sizes of the volume and spectroscopy data.

Discussion

The results demonstrate that our dyslexic adults have different cerebellar neuroanatomy and spectroscopy compared with the non-dyslexic individuals. We speculate that the white matter to grey matter ratio in the cerebellar hemispheres reflects the dyslexic participants tendency to have a larger volume of white matter. We propose that the spectroscopy differences in the left cerebellar hemisphere NAA/Cho and Cho/Cr ratios implies higher choline signal, which may reflect a higher concentration of choline or T2 components may be involved as the data were acquired at long TE. The combined volume and spectroscopy data for the left cerebellar hemisphere suggest our dyslexic subjects have some common 'profile', and that the volume and spectra changes are related to one another. We tentatively propose that they may reflect developmental delay in the myelination pathways from cerebral cortical areas.

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