DTI Investigation of the cerebellar peduncles in youths at high risk of psychosis

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Introduction

The cerebellar peduncles have long been associated with motor function however, recent studies describe the important function of the cerebellum in emotional regulation, decision making, attention, and working memory1,2,3. The cerebellum is attached to the brainstem via three groups of nerve fibres – the superior (SCP), middle (MCP), and inferior (ICP) cerebellar peduncles which efferent and afferent fibres pass through4. The impairment of excitatory or inhibitory function in the cerebellum has been implicated in conditions including schizophrenia, attention disorders, bipolar and depressive disorders, and cognitive function deficits2,5,6.

Diffusion tensor imaging (DTI) can be used to assess brain network connectivity and allows for the investigation of neuronal integrity and architecture especially in the context of behaviour7,8. For example, DTI has been used extensively in the assessment of white matter abnormalities and schizophrenia9. The potential etiological relationship between cerebellar degeneration or abnormality and psychosis is both a compelling and vital pursuit in the understanding of disease mechanisms and potential therapeutic opportunities for mental illness10. The use of DTI and tract reconstruction allows for further investigation into white matter pathology and the development of psychosis11.

Aims

Our study posited that young adults with psychotic experiences have different cerebellar diffusion metrics compared to those without at both baseline and time point 2 and furthermore, any differences in metric will change with time.

Method

Participants

16 participants who had had psychotic experiences (14 female, 2 male), determined using a 7-item Adolescent Psychotic-Like Symptom Screener (APSS) and the Schedule for Affective Disorders and Schizophrenia for School-aged Children, Present and Lifetime Versions (K-SADS), and 17 controls (7 female, 10 male) were included. Participants were recruited as part of the Adolescent Brain Development Study. Mean age at time point 1 (TP1) was 15, mean age at time point 2 (TP2) was 20. Ethical approval was granted by the Beaumont Hospital Research Ethics Committee.

Diffusion weighted imaging & Pre-processing

Participants underwent High Angular Resolution Diffusion Imaging (HARDI) in a 3 Tesla scanner 61 directions at two time points. ExploreDTI, a diffusion magnetic imaging toolbox, was used for complete pre-processing, modelling and computation of diffusion data.

Tractography:

The peduncles were isolated individually using AND and NOT gates in ExploreDTI around anatomically determined landmarks. Isolated tracts are cleaned and segmented for statistical analysis as shown in figures 1 to 3.

Results

There were no significant differences between Controls and PE for any peduncle under any metric at either time point. (*Table 1)*

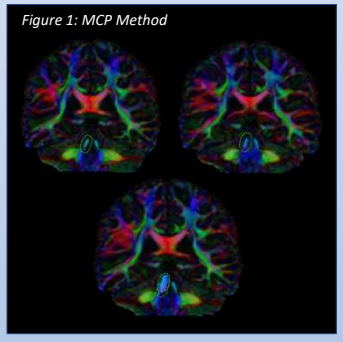

Figure 1: MCP Method

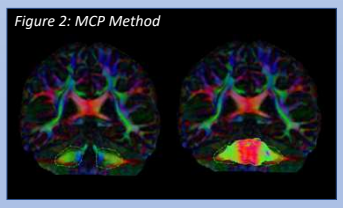

Figure 2: MCP Method

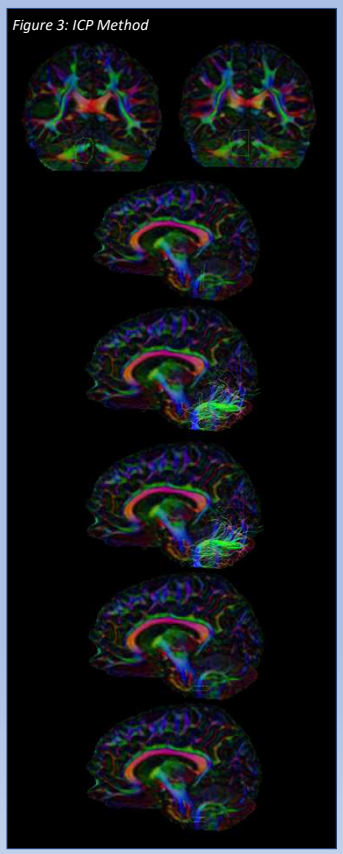

Figure 3: ICP Method

	Time Point	Cohort	No. Tracts	Tract volume	FA	ADC (mm2)	λ1 (mm2)	(λ2*λ3)/2 (mm2)
ICP_L	TP1	PE	355.50	165.385	0.512	0.000774	0.00123	0.000541
		Con	466.29	184.179	0.549	0.000735	0.00123	0.000484
	TP2	PE	322.50	162.293	0.587	0.000701	0.00122	0.000440
		Con	382.82	169.127	0.585	0.000719	0.00124	0.000451
ICP_R	TP1	PE	393.88	177.146	0.542	0.000730	0.00121	0.000486
		Con	385.00	167.498	0.568	0.000722	0.00124	0.000462
	TP2	PE	273.45	163.538	0.573	0.000694	0.00122	0.000452
		Con	329.82	155.459	0.579	0.000719	0.00124	0.000455
SCP_L	TP1	PE	1652.88	368.372	0.552	0.00110	0.00184	0.000733
		Con	1559.47	343.573	0.514	0.00100	0.00175	0.000751
	TP2	PE	1356.62	302.529	0.590	0.00106	0.00185	0.000669
		Con	1423.24	304.550	0.542	0.00108	0.00179	0.000724
SCP_R	TP1	PE	1739.00	350.876	0.534	0.00105	0.00176	0.000694
		Con	1603.59	324.404	0.513	0.00110	0.00178	0.000768
	TP2	PE	1424.38	317.980	0.564	0.00110	0.00185	0.000723
		Con	1308.00	304.679	0.548	0.00106	0.00177	0.000705
MCP	TP1	PE	2503.13	9887.972	0.528	0.000834	0.00137	0.000566
		Con	2554.41	10087.386	0.518	0.000863	0.00139	0.000595
	TP2	PE	2197.87	9914.672	0.536	0.000826	0.00136	0.000556
		Con	2372.29	9697.543	0.527	0.000825	0.00139	0.000581

Table 1: Diffusion metrics

Discussion

Our study found no significant differences in the neuronal integrity of the cerebellar peduncles between adolescents who had had psychotic experiences compared to controls at either of two time points approximately 5 years apart. This suggests that the cerebellar peduncles are not involved in the progression of psychotic experiences in adolescents, and that alternative structures may be the cause of these symptoms. Rather than the input/output tracts to the cerebellum, the cerebellar matter itself may have a role in psychosis. For example, the integrity of the cerebellar vermis has been implicated in early psychosis thus suggesting another alternative structure deserving of investigation[12].

Limitations

Interpretation of tractography maps has its limitations thus, having a possible contributory effect to our results. Tractography mapping makes the assumption of homogenous unidirectional populations within voxels, and may lead to incorrect estimations of fibre direction and tract termination[7]. Further misinterpretation may arise from the misconception that changes in FA values indicate damaged or impaired fibres however, depending on location and disease processes this may not be the case[7]. Confounding errors due to overlapping fibre regions, misinterpretation of collected values, and the subjective nature of our methodology all present clear limitations to the use of DTI tractography[8]. Further, the sample used for this study was small (16 PE, 17 Control) so the results may not be accurate.

Future Directions

Rescanning these individuals at a later date may reveal any cerebellar peduncle changes which may not be present or detectable after 5 years. Our group also has structural cerebellar data (lobe sizes etc) that may show differences betweeen groups. In future investigations we would hope to broaden our sample size and scan our participants at more time intervals to assess for trends in fibre changes. Investigating the impact of early childhood adversity and the development of psychotic symptoms would also provide a compelling trajectory for further research.

Conclusion:

We explored the link between the neuronal integrity of the cerebellar peduncles and adolescent psychotic experiences to enhance our understanding of psychosis and its pathogenesis, concluding no significant differences between control and affected groups.

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