Examining the cingulum in vivo subjects with ADHD using Multi Shell Data.

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Trinity College Dublin 2020

Introduction

- Attention deficit hyperactivity disorder is a neurodevelopmental disorder characterised by inattention, hyperactivity and impulsivity that causes significant functional impairment.
- The pathophysiology of ADHD is not well understood, but it is widely accepted that it is a disorder characterised by disrupted neural connectivity and it is thought that there is a delay in maturation of white matter.
- Diffusion Magnetic Resonance Imaging allows in vivo examination of brain white matter. There are different ways to acquire diffusion data; single-shell and multi-shell acquisition are considered in this pilot study. Essentially multi-shell data is an amalgamation of diffusion MRI scans that have different diffusion weighting (b-values).
- Multi-shell diffusion data offers better anatomical accuracy and sensitivity when compared with single-shell data, but there is a much greater computational demand during analysis so it is important to quantify the benefits of using this approach.
- The limbic system is a collection of subcortical structures and associated white matter fibre pathways within the brain that are involved with memory and emotional responses. It is implicated in many psychiatric disorders including ADHD.
- The cingulum is a major white matter tract that allows communication between components of the limbic system. It is a large and robust tract that is relatively easy to delineate using diffusion tractography (Fig 1 shows in vivo diffusion tractography and ex vivo sample of the cingulum).

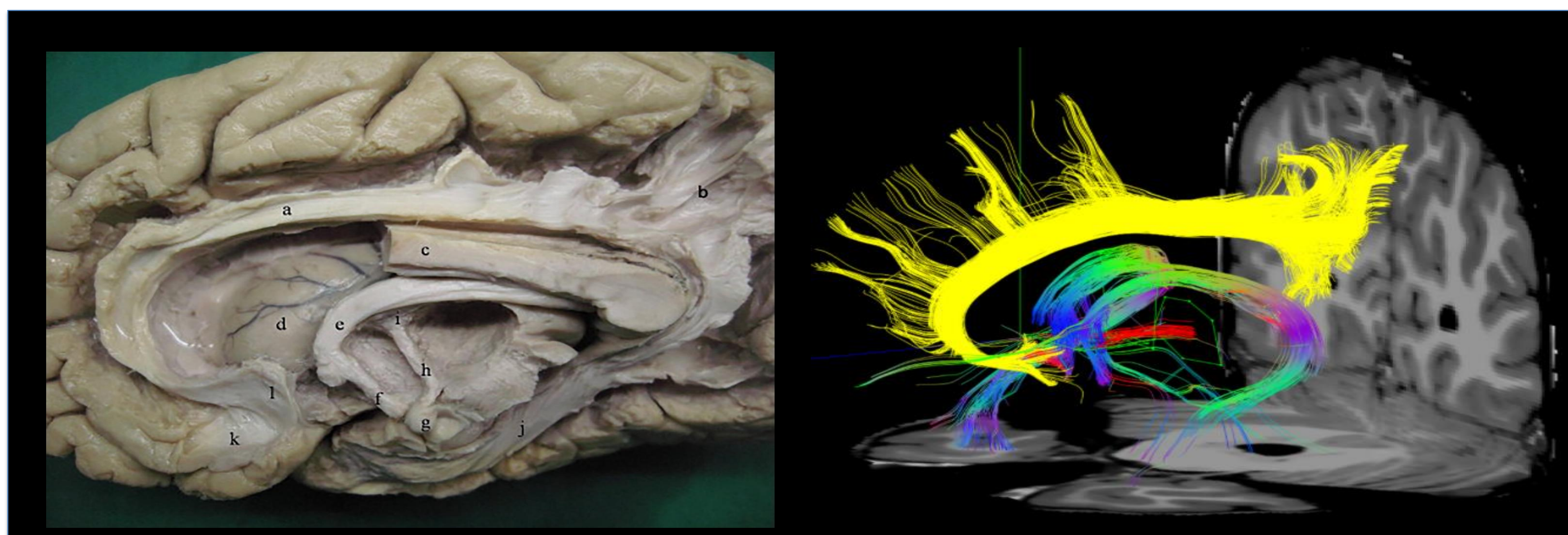

Fig1a. Dissected brain exposing cingulum and fornix (Bubb et al 2018)

Fig 1b. Tract delineations from multi-shell data showing cingulum(yellow), Stria medullaris (red), and fornix (mixed).

Aims

- To isolate the cingulum from single-shell and multi-shell diffusion datasets
- To perform a qualitative assessment of images obtained using multi-shell data and single-shell data.
- To perform a quantitative assessment of diffusion metrics
- To compare time taken to process and delineate tracts obtained using both techniques.

Methods

- The NICAP (Neuroimaging of the Children's Attention Project) dataset comprises >600 diffusion MRI scans that were collected longitudinally at three time-points from children with ADHD and neurotypical controls at age 10, 11.5 and 13 years. In total there are scans from 194 subjects in this study (ADHD n= 103, controls n=91).
- The scans were pre-processed and analysed using the software programmes ExploreDTI and Matlab.
- Subjects were scanned at three timepoints with three data sets at each time point. High quality multi-shell (b-values of 1000, 2000 and 2800) diffusion data was acquired on a 3T MRI scanner using the Human Connectome Protocol.
- Processing consisted of signal drift, Gibbs artefact, motion, eddy current and echo planar distortion correction. Finally all possible tracts in the brain were calculated to yield a whole brain tract representation (WBT). From these WBTs, the tracts of interest were extracted and examined.
- For this study, a pilot data set of n=12 scans, delineating the cingulum tract for comparisons was selected.
- To create the multi-shell image, the three scans obtained using the three b-values are concatenated and generate a single '.mat' file. This is also then corrected for motion and EPI distortion.

Analysis

- The cingulum was isolated in all 12 scans using diffusion tractography with ExploreDTI software.
- Diffusion measures were extracted from the cingulum tracts that had been isolated from both the single-shell and multi-shell data.
- Diffusion metrics included fractional anisotropy (FA), mean diffusivity(MD), approximate tract volume(AV) and mean tract length(ML).
- The time it took to perform both data processing techniques was also noted.

Results

Figure 2

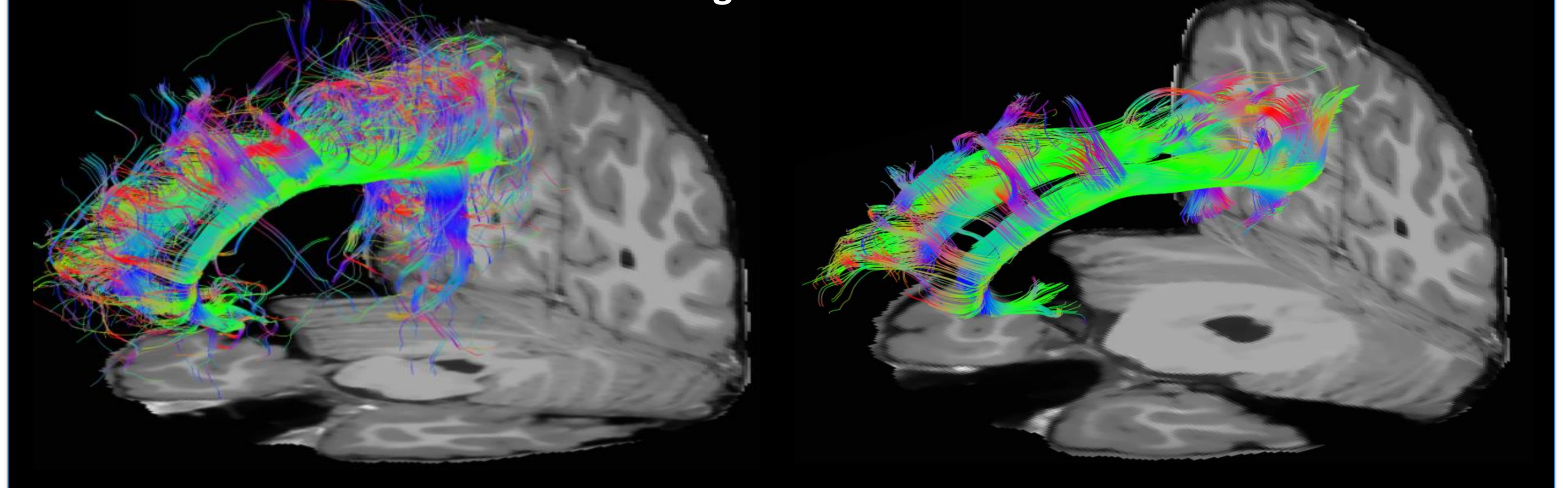

Fig 2a. Single-shell bilateral cingulum

Fig 2b. Multi-shell bilateral cingulum

	Multi-shell data	Single-shell data	p-value
Mean Fractional Anisotropy(FA)	0.415531032	0.376484776	0.0000963217648
Mean Diffusivity(MD)	0.000989896	0.000634613	6.12628E-18
Mean Tract Length(ML)	98.96261597	108.7213325	0.0006151236293
Approximate tract volume(AV)	12664.1262435	23025.4631700	0.0000000189866

Table1: Diffusion metrics measured and compared between multi-shell and single-shell acquisition of cingulum

- Figure 2a. and 2b. show the cingulum delineated using single-shell and multi-shell processing respectively. Visually it is evident that the multi-shell image is less noisy (contains less stray fibres) and more anatomically realistic.
- Approximate preprocessing analysis times were 5 hours and 8 hours per subject for the single and multi-shell approaches respectively.
- Tract delineations however were much longer for single shell data (3 hours versus 1.5 hours)
- Table1 shows diffusion metrics collected from the delineations of the cingulum. In every measure, the multi-shell was more compact than single-shell.
- This equates to less interference from stray fibres and miscalculated tracts. The p-values are significant at $p < 0.05$.

Conclusions and Subsequent Goals

- Multi-shell data collected as part of the NICAP study results in higher quality data than the traditional single-shell data. It was more time consuming, but it is possible to develop an automated processing pipeline for the full dataset (n=194 over three timepoints).
- There were no marked differences between cases and controls in this small pilot dataset. An analysis focusing on the major tracts and structures of the limbic system in the full dataset is ongoing.
- Correlation analyses between white matter microstructure and behaviour in ADHD will be investigated in future analyses.

Declarations

- Ethics approval was granted by the Royal Children's Hospital Human Research Ethics Committee, Melbourne (#34071).
- Financial Sponsorship was gained through the Health Research Board (HRB) Summer Studentship grant.

References:

1. The cingulum bundle: Anatomy, function, and dysfunction **E Bubb, C Metzler-Baddeley, J Aggleton, 2018**