

Fibre dispersion in the corpus callosum relates to interhemispheric functional connectivity

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Authors:

[Jeroen Mollink](#)^{1,2}, Saad Jbabdi², Stephen Smith², Fidel Alfaro-Almagro², Michiel Kleinnijenhuis², Anne-Marie van Cappellen van Walsum¹, Karla Miller²

Institutions:

¹Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, Netherlands, ²FMRI centre, University of Oxford, Oxford, United Kingdom

First Author:

[Jeroen Mollink](#) - [Lecture Information](#) | [Contact Me](#)

Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center | FMRI centre, University of Oxford
Nijmegen, Netherlands | Oxford, United Kingdom

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Introduction:

The corpus callosum (CC) plays a key role in cross-hemispheric information transfer. Although the CC is generally thought of as a well-organized bundle of parallel axons connecting homotopic areas, recent studies have demonstrated complex fibre architecture within the CC¹⁻³. In particular, fibre orientation dispersion at the midline is greater than in nearby lateral areas of the CC⁴. This might reflect interhemispheric connections of non-homotopic (heterotopic) areas. Here we hypothesize that dispersion in the CC is a signature of heterotopic connectivity. We evaluated this by looking for associations between diffusion MRI (dMRI) estimates of dispersion and resting-state functional MRI (rfMRI) estimates of interhemispheric connectivity.

Methods:

We analyzed dMRI and rfMRI data from 4903 subjects in the UK Biobank project (acquisition parameters and pre-processing detailed elsewhere)⁵.

Group-ICA yielded 55 resting-state networks. These were then split for each hemisphere and further split if a component contained non-contiguous brain areas. To estimate connectivity between the resulting brain areas (network 'nodes'), average time-series were generated for every node and correlated with each other using partial correlation. These connectivity values then form a node-by-node matrix of network connectivity. To quantify the balance of homo- to heterotopic interhemispheric connections for a given node, a functional asymmetry index (AI) was defined as the homotopic connection strength minus the mean of the 10% strongest heterotopic connections.

To calculate orientation dispersion (OD), the NODDI model⁶ was fit to dMRI data. OD values were extracted from the CC after transforming all subjects to the same space and mapping ODs onto a skeleton using TBSS⁷. To estimate which CC area connects

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homotopic areas, structural connectivity probability maps for each node were obtained in the CC using a tractography template. Dispersion was calculated as the mean OD at the center minus the mean OD at the lateral aspects of the CC, referred to as OD hereafter (Figure 1.C).

Associations between OD and AI were calculated, with statistical significance assessed using permutation testing. Reproducibility was demonstrated by dividing the subjects into two equally sized groups. For each AI vs OD comparison, the OD values were taken from a region of the CC that connects to the cortical node of interest. A negative control analysis was done by correlating AIs with OD derived from the CC region that is least likely to interconnect a node.

Results:

As reported previously⁴, high dispersion was found in the center of the CC (Figure 1.C). Figure 1.A illustrates the group-average functional network matrix. Significant associations between AI and OD were primarily found in medial nodes, with correlation coefficients ranging between $r=0.05$ - 0.11 (Figure 3). Of 16 significant associations in the "discovery" group of subjects (that survive FDR multiple comparison correction), seven were found in the replication group. The highest regression coefficients (β) were found closer to the CC, and lower regression coefficients distal to the CC (Figure 3.D). Finally, the negative control analysis yielded one significant association between AI and OD in an implausible CC region (Figure 4), with a lower regression coefficient ($\beta=1.55$) than the anatomically plausible CC area ($\beta=1.82$).

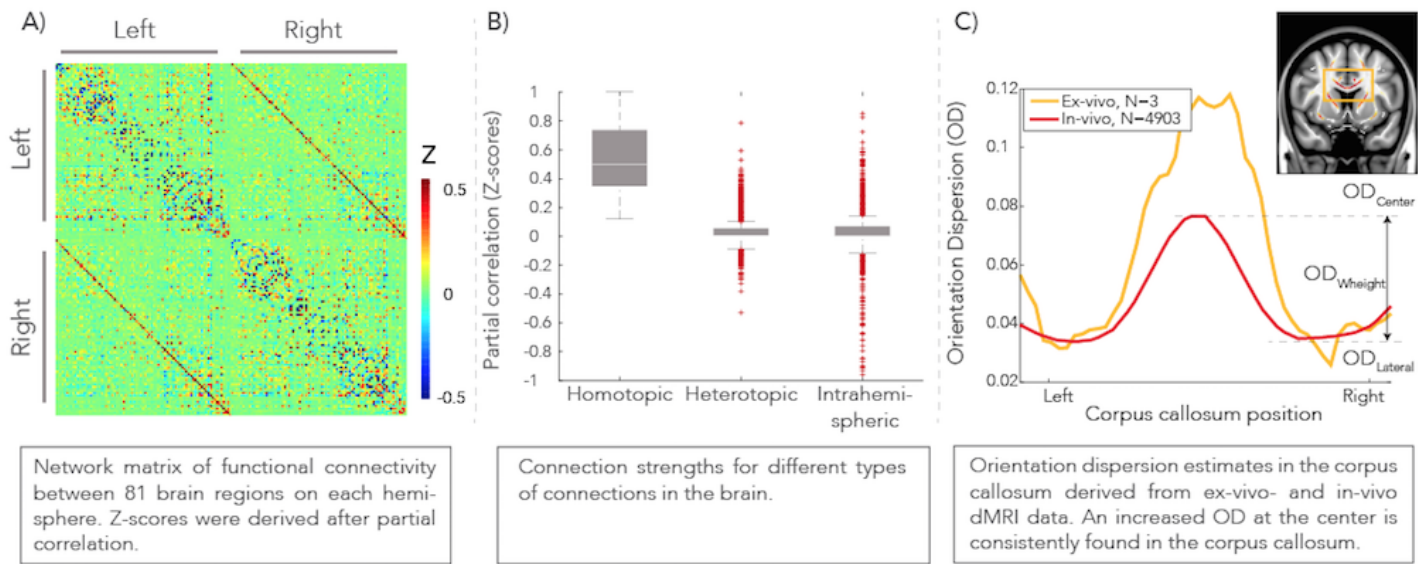
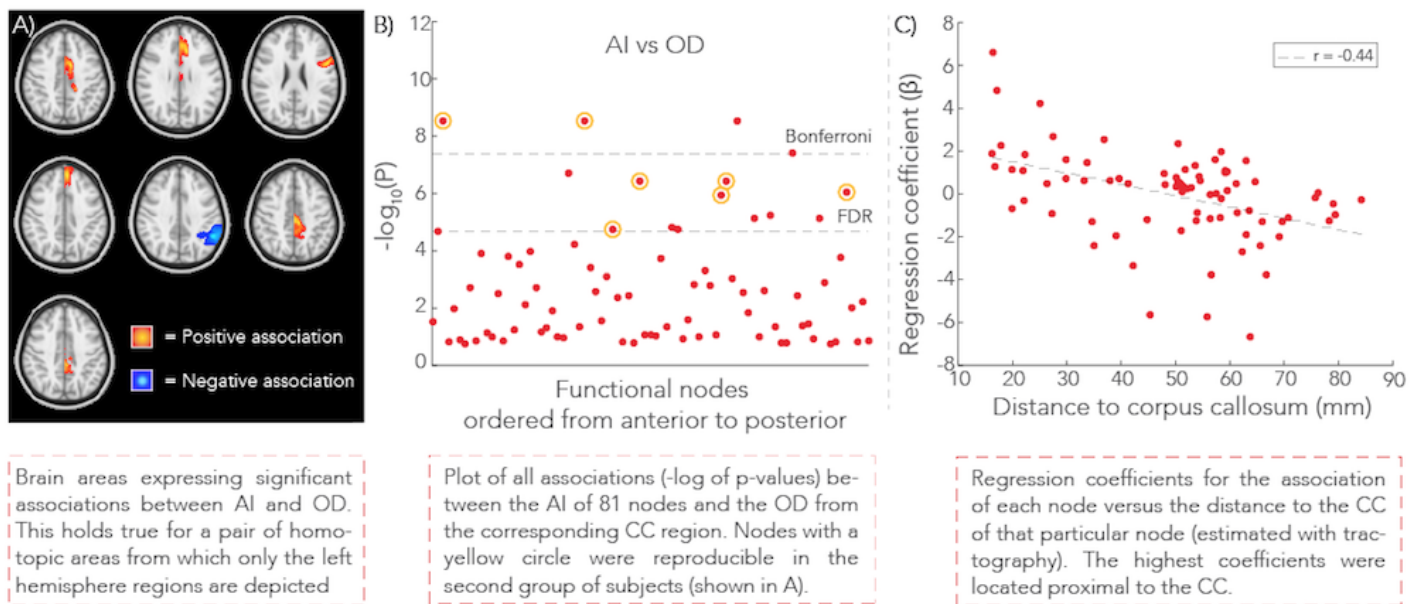


Figure 1



Negative control analysis: Correlate AI with OD from implausible corpus callosum area

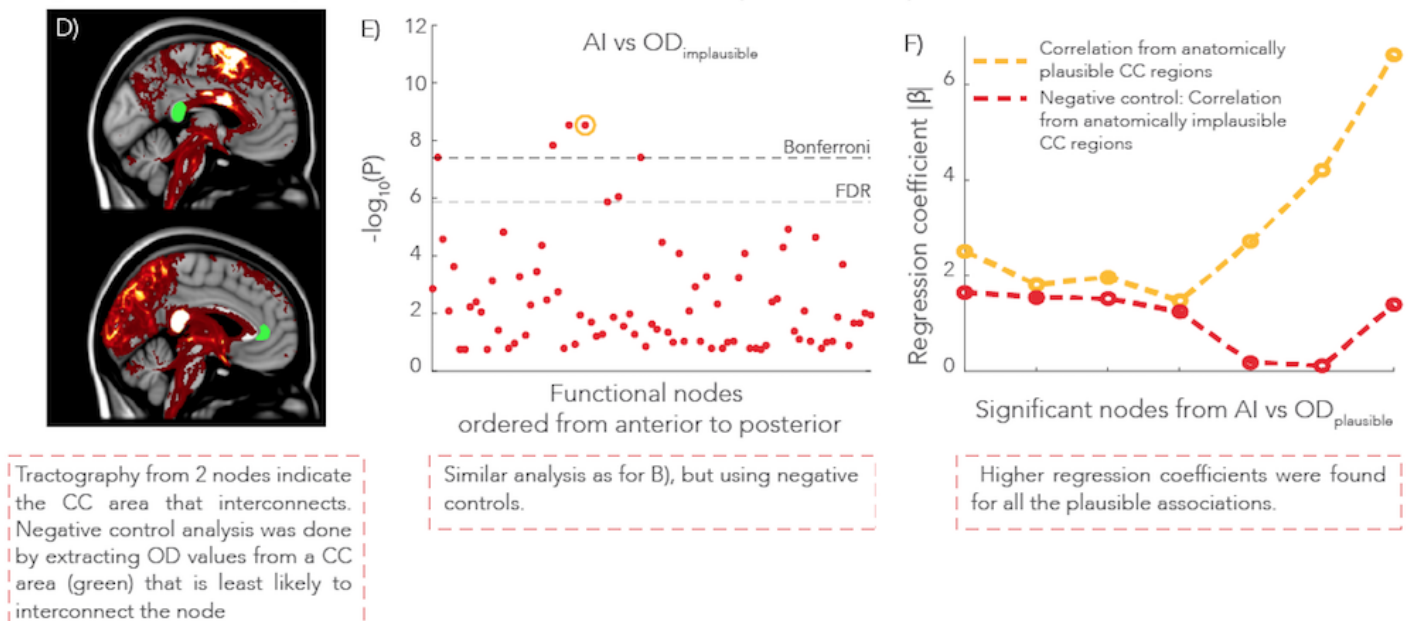


Figure 2

Conclusions:

Significant associations were found between AI vs OD in regions close the CC, such as the cingulate cortex. In addition, the AI of a node appeared to be less associated with OD if the node was more laterally located. We hypothesize that dispersion in the CC is more crucial for midline nodes to project to nearby heterotopic regions, while more distant nodes can form a path to heterotopic areas in other tracts. The negative control analysis yielded one significant node that may be explained by correlation of ODs among different areas of the CC.

Modeling and Analysis Methods:

Diffusion MRI Modeling and Analysis ²
fMRI Connectivity and Network Modeling ¹

Poster Session:

Poster Session - Thursday

Keywords:

FUNCTIONAL MRI
Tractography
White Matter

WHITE MATTER IMAGING - DTI, HARDI, DSI, ETC

Other - Dispersion

^{1|2}Indicates the priority used for review

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