

BOLD Resting State Networks in Adults with Complete Callosal Agenesis

J. M. Tyszka¹, L. K. Paul², and R. Adolphs^{1,2}

¹Biology, California Institute of Technology, Pasadena, CA, United States, ²Humanities and Social Sciences, California Institute of Technology, Pasadena, CA, United States

Introduction Agenesis of the corpus callosum (AgCC), a failure to develop the large bundle of fibres that connect the cerebral hemispheres, occurs in 1:4000 individuals (1). The morphological differences between neurotypical and acausal brains are pronounced in some areas and subtle in others. The absence of the corpus callosum, the presence of the Probst bundles, mesial cortical reorganization and enlarged posterior lateral ventricles (colpocephaly) must be accounted for in any voxel-wise analysis. The impact of agenesis of the corpus callosum on resting state connectivity in the human brain is largely unknown. In this study, we apply well-established probabilistic independent component analysis (PICA) methods (2) to BOLD fMRI time course data in a minimum deformation space to identify those resting-state networks preserved and altered by callosal agenesis.

Methods Adult subjects with complete isolated AgCC (n=8) and neurotypical controls (n=8) were recruited under a protocol approved by the institutional Human Subjects Protection Committee. All subjects were right-handed as assessed by the short-form Edinburgh handedness questionnaire. All MRI data were acquired using a 3 Tesla Magnetom Trio (Siemens Medical Solutions, NJ) equipped with an 8-channel phased array head coil. Subjects were asked to lie still within the magnet with eyes closed, think of nothing specifically and to stay awake. The resting-state image acquisition consisted of approximately 5 minutes of T2*-weighted single-shot EPI with the following parameters: TR/TE = 2000/30ms, 3 mm isotropic voxels, fat suppression, 30 degrees axial-coronal slice angle. A minimum deformation mid-space template was constructed by iterative non-linear registration of individual T1-weighted structural images to a reference template, initially the MNI152 template, replaced by the mean image of the previous pass in subsequent iterations. Functional data analysis was performed using a combination of FMRIB's Software Library (FSL – www.fmrib.ox.ac.uk/fsl) and custom-written Matlab functions. Preprocessing included slice timing and rigid-body motion correction, grand mean normalization and Gaussian spatial smoothing (5mm FWHM). Independent components (ICs) associated with respiration or cardiac cycles with more than 33% of spectral power above 0.1Hz were removed at the single subject level. Group level PICA was performed on AgCC and control groups independently using temporal concatenation (3). An additional 5mm Gaussian smoothing was applied and group-level ICs associated with motion x field effects, CSF pulsatility, venous sinuses and white matter excluded from final analysis. The spatial patterns of the remaining ICs were compared between AgCC and control groups using spatial cross correlation analysis.

Results and Discussion A total of 33 ICs were identified in each group of which 22 and 17 were classified as non-artifactual in the AgCC and control groups respectively. AgCC spatial IC modes were matched to control modes using the maximum correlation coefficient as a metric. Invertible pairings were defined as reliable (ie A is the best match for B and B is the best match for A). Using these criteria, 18/22 AgCC ICs could be matched reliably to control ICs and 17/19 control ICs could be matched reliably to AgCC ICs. The four ICs unique to AgCC were all bilateral and nominally classified as premotor, posterior cingulate and prefrontal (Fig. 1a). The two ICs unique to neurotypical controls were right unilateral and bilateral parietal-frontal networks respectively (Fig. 1b).

Conclusions Over 80% of neurotypical BOLD resting state networks identified by group PICA are preserved in adult AgCC subjects suggesting that compensatory networks established during brain development play a major role in this condition. Further work is required to identify the role of the remaining RSNs both unique to and absent in AgCC.

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References (1) Paul et al. Nat Rev Neurosci (2007) vol. 8 (4) pp. 287-99 (2) Beckmann and Smith. IEEE Trans Med Imaging (2004) vol. 23 (2) pp. 137-52 (3) Schöpf et al. MAGMA pp. 1-9.

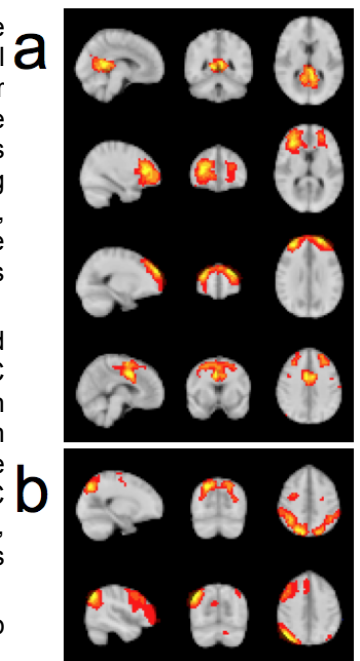


Figure 1: Independent components identified as unique to (a) AgCC and (b) of neurotypical subjects