Clusters of seed-based voxel-wise functional connectivity predict local glutamate in pregenual anterior cingulate cortex

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Introduction

- Magnetic resonance spectroscopy (MRS) measurements of excitatory neurotransmission may provide valuable insights into underlying neurobiology of altered functional connectivity (FC) in psychiatric disorders
- Local measures of glutamate (Glu) are often reported to moderate resting-state FC1,2
- Inherently low signal-to-noise ratio (SNR) of conventional single-voxel MRS necessitates voxel sizes far exceeding those of functional magnetic resonance imaging (fMRI)
- This leads to crude measurements of local neurometabolism
- Hypothesis: decomposing the pregenual anterior cingulate (pgACC) functional connectome using hierarchical clustering provides incremental information on the neurotransmitters governing its function

Methods

- 89 healthy subjects underwent structural, resting-state (TR/TE: 2800/22 ms, FA = 80°, 62 slices, number of volumes = 270, voxel size 2 mm isotropic) and MRS (STEAM, TE/TM/TR = 20/10/3000 ms, voxel-size 20 x 15 x 10 mm3) measurements at 7 Tesla.
- fMRI: preprocessed using default CONN pipeline, then denoised in Matlab
- MRS: fitted with LCMoDe6, expressed as ratio to total Creatine (tCr)
- Seed voxels: only those fMRI voxels in composite MRS mask
- FC with CONN atlas nodes
- Hierarchical clustering of pgACC seed-voxels (3 clusters)
- Prediction of Glu/tCr and GABA/tCr from cluster FC to atlas regions: partial-least-squares regression (PLSR) and Elastic Net (EN)

Results

- PLSR for Glu/tCr, trained on FC matrix for each pgACC cluster
- Elastic net results are congruent with PLSR
- EN: Non-zero ROIs cluster 1
- Hierarchical clustering results (Insert: Palomero-Gallagher et al.)
- Identical analyses for GABA/tCr yielded no significant results.

Conclusion

- A pgACC MRS voxel can be parcellated into functionally distinct clusters that differentially predict local Glutamate.
- Prediction of Glu using the best performing cluster (corresponding to p32) is partially driven by connectivity between pgACC and subcortical regions.
- Take-home: capitalize on higher spatial resolution of fMRI to get more fine-grained insight into local neurometabolism (e.g. in psychiatric disorders)

References


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