

Alterations of hemispheric segregation and integration in clinical schizophrenia



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Introduction

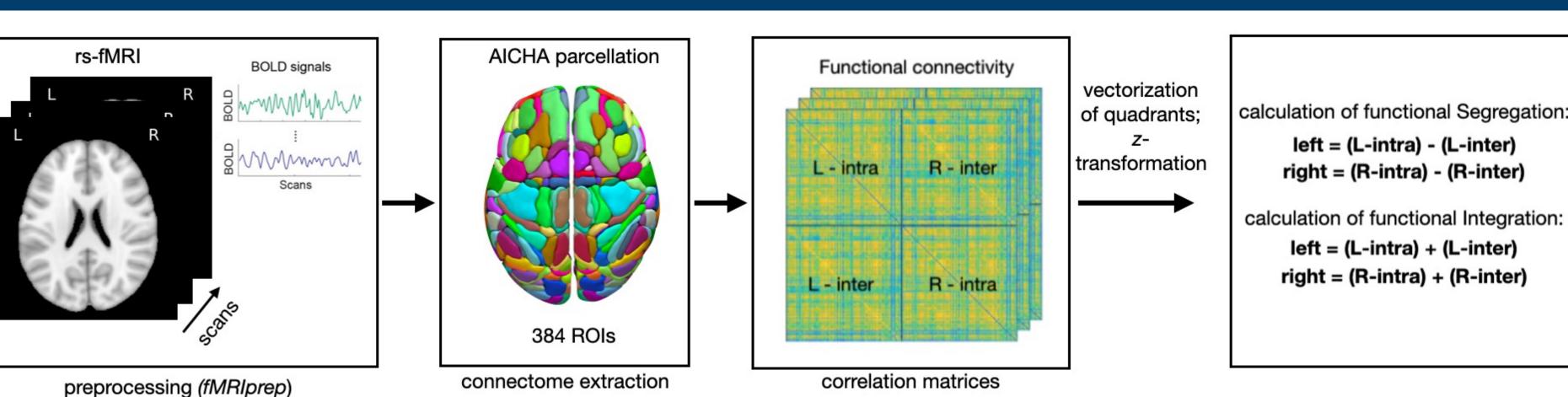
Functional Brain Lateralisation

- Is a fundamental principle of human brain organization that is often affected in clinical neuropsychiatric populations
- In particular, schizophrenia is often associated with an atypical hemispheric organization, commonly investigated by comparing the activation magnitude in left and right hemispheric regions
- Alternative [1]:
 - Functional integration: integrative interaction with both hemispheres
 - Functional segregation: preferential interaction with one hemisphere with itself
- We further investigated the strength of asymmetries in functional integration and segregation in schizophrenic and healthy subjects

Aim:

 To examine how regional functional integration/ segregation as well as functional asymmetry differs between schizophrenic patients and healthy controls

Methods



- Open source dataset COBRE (The Center for Biomedical Research Excellence) [2], including 60 schizophrenic patients (48 male); 69 healthy control (49 male), age: 18-65y, right-handed
- Resting state fMRI data: 150 volumes (TR 2000ms, TE: 29ms, 64x64, 32 slices, voxel size: 3x3x4mm³), Siemens Trio Tim 3T and standard pre-processing using fMRIPrep (https://fmriprep.org/en/stable/)
- Extraction of the mean time course from each parcel of the AICHA atlas [3] and computation of whole brain parcel wise connectome using Pearson's linear correlation coefficients
- Functional integration and functional segregation of each parcel were then computed as [1]:

Integration left = L-intra + L-inter; Integration right = R-intra + R-inter Segregation left = L-intra – L-inter; Segregation right = R-intra – R-inter

 A Laterality Index (measure of functional asymmetry strength) was calculated for schizophrenic and healthy subjects and statistically compared for significant differences

LI Integration = (R-intra + R-inter) – (L-intra + L-inter)
LI Segregation = (R-intra – R-inter) – (L-intra – L-inter)

Functional Decoding (https://www.brainmap.org [4])

Results: within-group comparisons

Integration

- Both controls and patients display more pronounced rightward (mainly medial) than leftward (mainly lateral) integration
- Both leftward and rightward integration is more pronounced in controls vs. patients, particularly in lateral temporal cortex (leftward) and temporal pole (rightward)

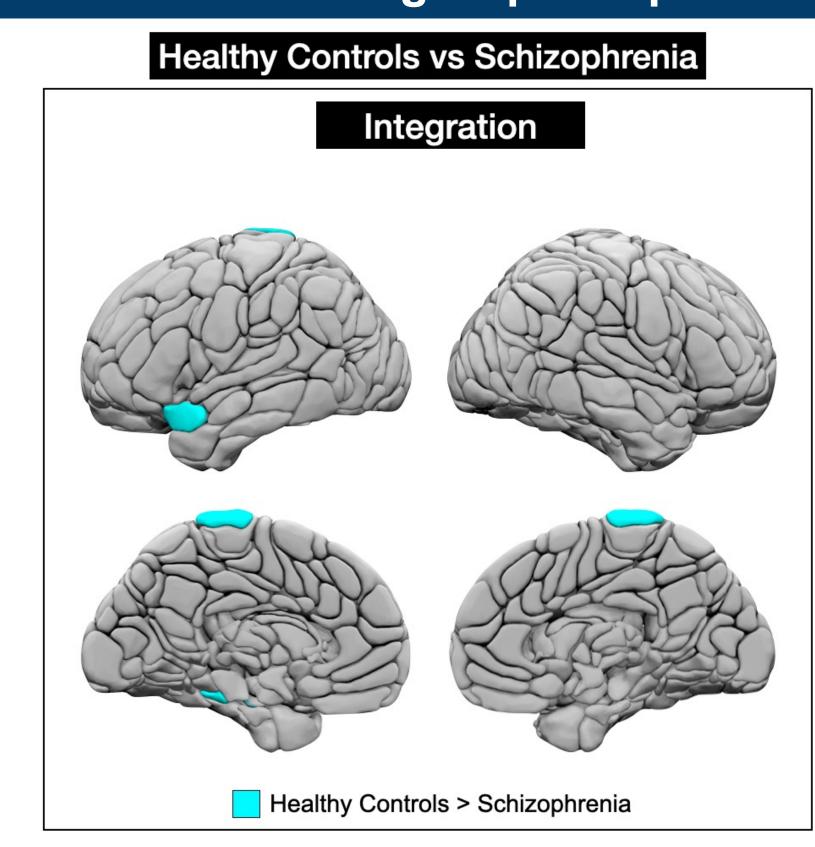
Segregation

■ Both controls and patients display more pronounced rightward than leftward segregation, with patients displaying stronger segregation in superior temporal and temporo-parietal cortex as compared to controls

Discussion

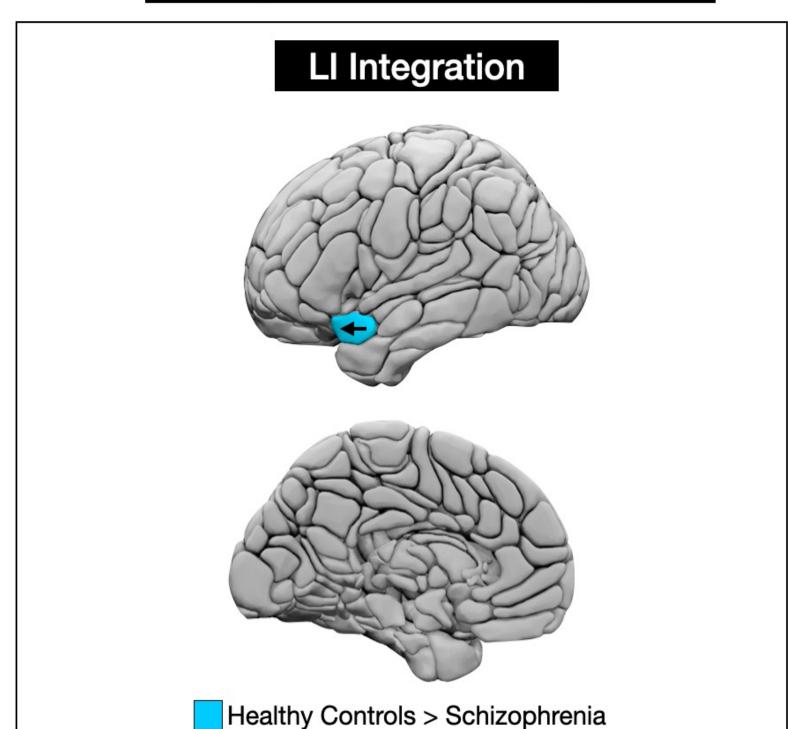
- Results from within-group comparisons show stronger leftward integration in healthy controls and stronger rightward segregation in patients in regions of the lateral temporal cortex, which might reflect often reported aberrant functional connectivity in schizophrenic patients [5,6]
- Functional decoding [4] shows that group differences are most pronounced in brain areas related to emotion, memory, and language, reflecting core symptoms in schizophrenia
- Comparing asymmetries in functional integration and segregation only revealed reduced leftward functional integration in schizophrenic subjects in one parcel (frontal STS)

Results: between-group comparisons



Controls show significantly higher functional integration as compared to schizophrenic subjects in parcels covering the anatomical regions of the left superior temporal sulcus, left and right paracentral gyrus and left parahippocampal gyrus after Bonferroni correction

Healthy Controls vs Schizophrenia



 Controls show significantly stronger leftward asymmetry as compared to schizophrenic subjects in the parcel covering the anatomical region of the frontal superior temporal sulcus after Bonferroni correction

References: [1] Gotts SJ, Jo HJ, Wallace GL, Saad ZS, Cox RW, Martin A. (2013) Two distinct forms of functional lateralization in the human brain. Proc Natl Acad Sci USA 110(36):3435-3444. [2] COBRE (2013), retrieved from http://fcon_1000.projects.nitrc.org/indi/retro/cobre.html. [3] Joliot M, Jobard G, Naveau M, Delcroix N, Petit L, Zago L, Crivello F, Mellet E, Mazoyer B, Tzourio-Mazoyer N.(2015) AICHA: An atlas of intrinsic connectivity of homotopic areas. J Neurosci Methods. 254:46-59. [4] Fox PT, Lancaster JL, Laird AR, Eickhoff SB. (2014) Meta-analysis in human neuroimaging: computational modeling of largescale databases. Annu Rev Neurosci. 37:409–434. [5] Berken JA, Chai X, Chen JK, Gracco VL, Klein D. (2016). Effects of Early and Late Bilingualism on Resting-State Functional Connectivity. J Neurosci. 36(4):1165-72. [6] Hull R, Vaid J. Bilingual language lateralization: a meta-analytic tale of two hemispheres. (2007) Neuropsychologia. 45(9):1987-2008.