MEG Resting State Functional Connectivity and Network Topology in Dyslexia related genotype

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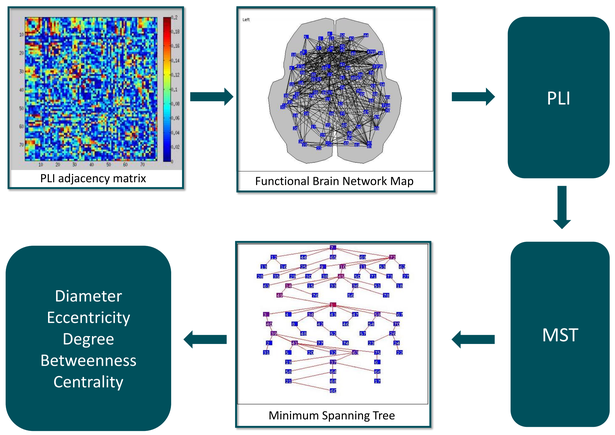
Introduction

- One dyslexia candidate gene-PCSK6- has recently been proposed to provide a molecular link between brain asymmetry, handedness and reading impairment. [1]
- Studying resting state neuro-functional interactions and their network distribution may tell us more about differences in typical and atypical brain development.
- Combining neuroimaging techniques and genetic information may provide a powerful means to investigate the biological basis of reading delay.
- Here, we used a MEG source-space method and Minimum Spanning Tree sub-graph to investigate resting state functional connectivity and topology in children with diagnoses of dyslexia with and without PCSK6 genetic risk. [2]

Methods

- We used an atlas-based (AAL) beamformer to reconstruct alpha, beta, theta and delta time series in source space. [2]
- **PLI** provides an index of asymmetry of the distribution of phase differences between 2 signals and it is insensitive to volume conduction. We used PLI to measure functional connectivity and MST to describe network topology. [2 & 4]
- **MST** is a sub-graph that connects all the nodes of the network in a loopless way and its topology has variety of parameters (degree, eccentricity, betweenness centrality). [4]

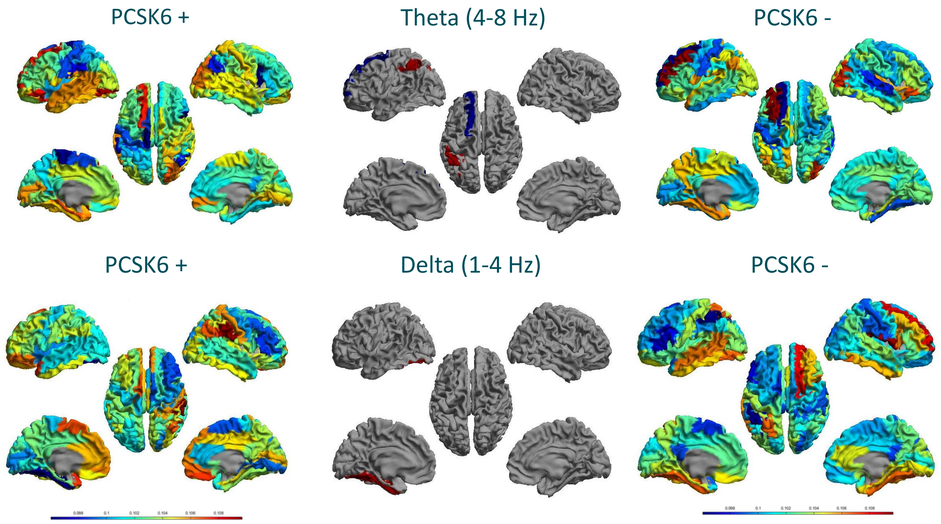


Participants

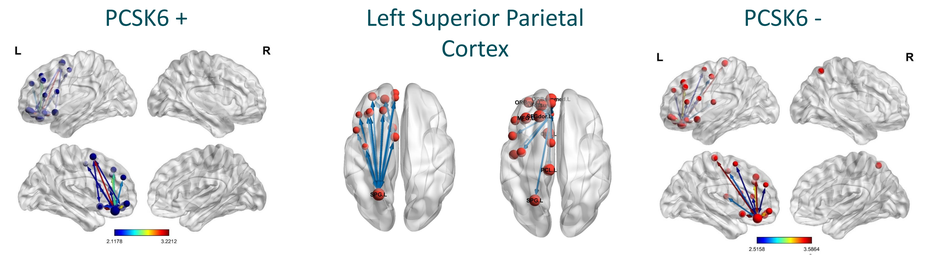
- 14 dyslexic participants (7-17 years old, mean age 12.5 y)
- Sub-divided, based on genotypic mapping information, in PCSK6 carriers (PCSK6 +) and (PCSK6 -) free group , matched by age and handedness
- 6 mins of eyes-open/eyes-closed MEG, resting state recording
- T-1 weighted MRI for each subject
- No difference between the two groups in the psychometric measures, except parental ratings for ADHD Oppositional Defiant Disorder. [3]

Phase Lag Index Results

The mean relative power, PLI and MST measures of Degree, Betweenness Centrality and Eccentricity were compared between groups for each of the 78 ROIs. Estimates of statistical significance for t-tests were stringently corrected for multiple comparisons, by using 1000 permutations at each ROI and deriving the threshold for significance from the distribution of maximum t-values across ROIs. [5]

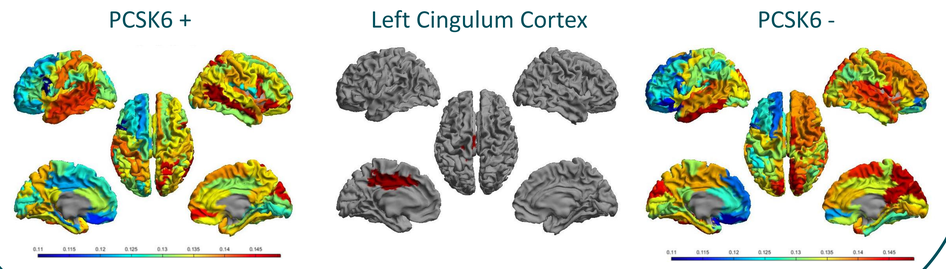


MST network – Degree (1-4 Hz)



Degree of a node: number of edges connected to it, average path length between all pairs of nodes. [4]

MST network – Eccentricity (1-4 Hz)



Eccentricity : Longest shortest path from reference node to any other node in the MST. [4]

Conclusions

- Functional connectivity estimated by PLI estimates appears to be different in PCSK6 + and PCSK6- genotypes in dyslexic participants, particularly in specific regions of the reading network (Left Fusiform Gyrus and Inferior Parietal cortex). [6]
- MST Degree and Eccentricity descriptives suggests differences in topology of large-scale networks in lower frequency band (1-4 Hz), in the left Parietal Superior cortex and left Cingulum cortex, across groups.
- The preliminary results from this first MEG-genetics study of dyslexia indicate differences in RSFC and MST network topology (Degree) related to PCSK6 expression *within* the dyslexic population.

Future Directions

Although the preliminary results look promising the sample size is not big enough to draw strong conclusions. Currently, we are analysing a new batch of data and with a larger pool of participants (~30) we will be able to define the effects of PCSK6 on developmental dyslexia.

Furthermore, the overall aim is to define dyslexic traits or based not only on genetic information but also on the behavioural profile (fluency, phonology and possible comorbidities)

References

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Acknowledgments

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