Cortical language network functional neuroanatomy in dyslexia

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Summary

- **Developmental dyslexia** is characterized by a specific reading impairment, the underlying cause of which remains uncertain.
- Neural circuits for **reading** have been extensively studied in neuroimaging studies of dyslexia, but the function of **core language-comprehension regions** independent from the task of reading remains largely unexplored.
- Here, we used an **auditory language localizer**[2] to identify cortical regions selectively responsive to higher-level linguistic processing in adults with dyslexia and in typically reading controls.
- Comparing the language activation maps between the two groups using group- and individual-level analyses revealed similar activation patterns and parcellation of the language network, as well as no group difference in the selectivity of the functional regions-of-interest (**fROIs**) for language vs. spatial working memory ("multiple-demand") tasks.
- Using **probabilistic diffusion tractography**, we also found no difference between groups in the structural connectivity among individually-defined language fROIs.
- **For these measures, we found that functional neuroanatomy within the core language network is fundamentally similar in dyslexia.**

Methods

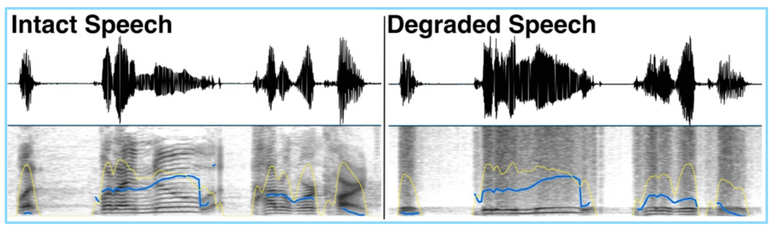
Participants: N = 23 fluent English-speaking adults with dyslexia (18 female; age 19-28, mean = 22.4 years) and N = 24 control adults (13 female; age 19-32 years, mean = 23.1 years)

fMRI data acquisition: Continuous-sampling block design, using simultaneous multi-slice imaging. TR = 750 ms, TE = 30 ms, flip angle = 90º, 3.0 mm isotropic voxels, FOV = 72×72, 45 axial slices, 5 simultaneous slices

DWI data acquisition: 6 non-diffusion-weighted reference volumes (b = 0) and 66 diffusion-weighted volumes per b = 1000 s/mm^2 with acquisition parameters: TR = 4400 ms, TE = 88 ms, flip angle = 90º, voxel resolution = 2.0 mm^3, FOV = 240 × 240, 66 transverse slices, 2 simultaneous slices

Task design: Participants listened passively to audio recordings of speech and unintelligible degraded speech. Two runs per session, each consisted of sixteen 18-second blocks of intact and degraded speech conditions.

Conditions

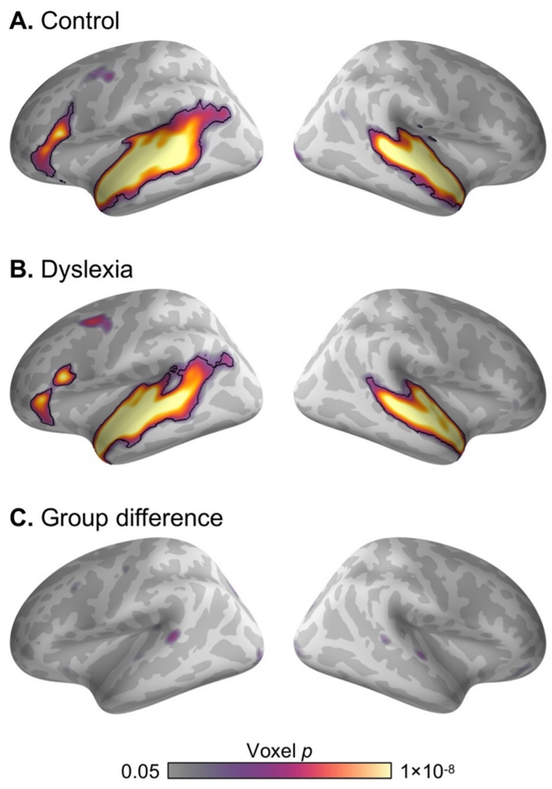


Analyses: **(1)** Whole-brain univariate analysis for intact > degraded language contrast[2] between dyslexics and controls. **(2)** Group-constrained Subject Specific (GCSS) analysis to define regions of interest[1,3], creating parcels from group probability maps and subject-specific functional regions-of-interest (fROIs). **(3)** DWI *probtrackx* to identify probabilistic tracts from each control fROI seed to the rest of the fROI seeds in language network.

Univariate Group Activation

Ordinary least squares (OLS) group mean of the intact > degraded contrast by group. Voxel threshold $p < 0.01$, cluster FWE $p < 0.05$. The color scale indicates the uncorrected voxelwise significance.

Figure 1. Whole-brain, group-average activation did not differ between the control and dyslexia. In both **(A)** control and **(B)** dyslexia groups, the intact > degraded contrast was significant in bilateral STG and left IFG. PreCG activation found in both groups did not reach the univariate cluster threshold for significance. **(C)** Despite some small and local differences (only control > dyslexia), such as left PT, no region showed a significant group difference in the intact > degraded contrast after correction for multiple comparisons.



Subject-specific fROIs

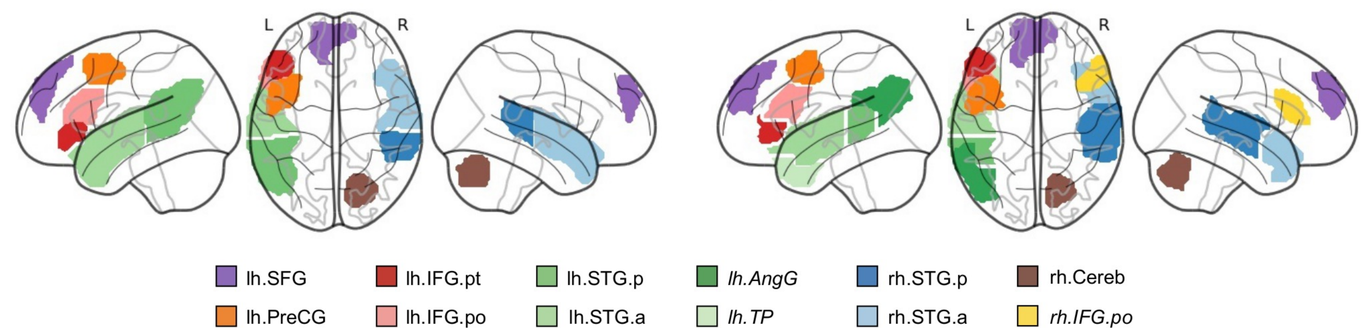


Figure 2. Group-constrained Subject Specific (GCSS) parcellation of the cortical language network. Glass brains show parcels with significant intact > degraded voxels in >80% of the participants in either group. **(A)** The control group parcellation identified canonical language areas, including some not found in the univariate group analysis (lh.SFG, lh.PreCG, rh.Cereb). **(B)** The dyslexia group parcellation was very similar, but with more granular parcellation of left temporal lobe, including separate parcellation of lh.TP (from lh. STG.a) and lh.Ang.G (from lh.STG.p). A parcel for rh.IFG.po was also found in dyslexia.

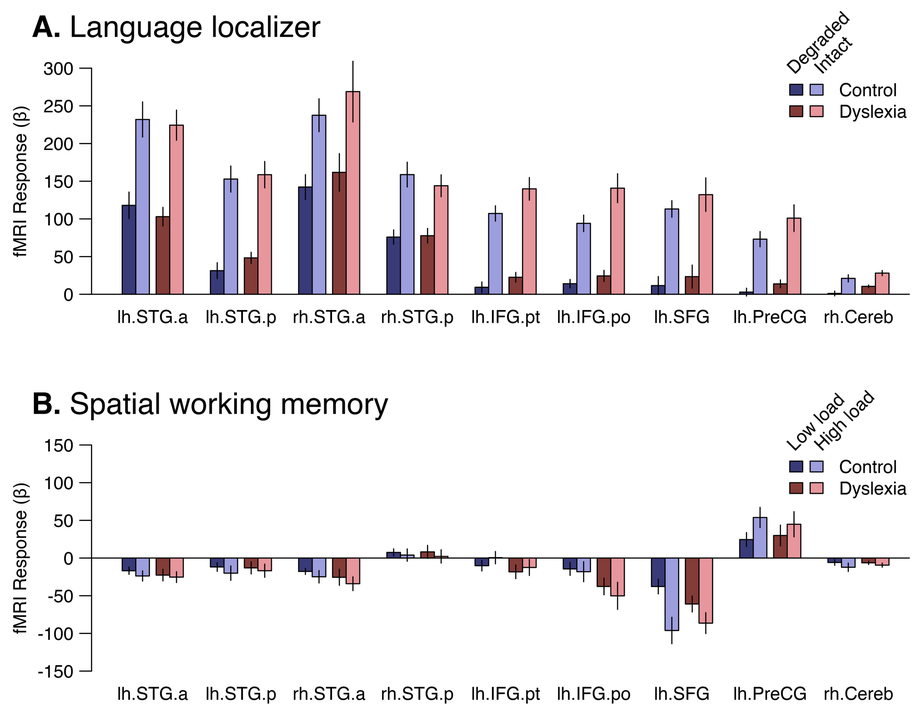
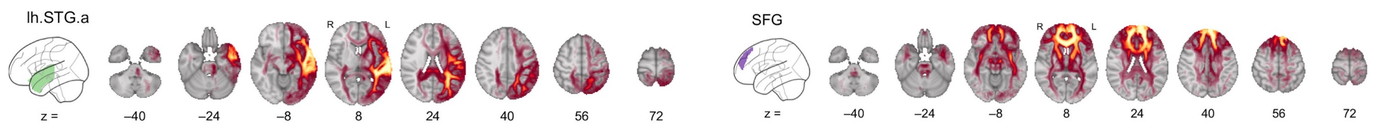


Figure 3. Functional selectivity of cortical language regions in control and dyslexia. Bar plots show mean fMRI response magnitude across subjects for each level of the tasks obtained from the subject-specific fROIs within each language parcel. Error bars show ±1 s.e.m. across subjects. **(A)** Both the control (blue) and dyslexia (red) groups showed a high degree of selectivity for intact vs. degraded speech in each language fROI, with no difference in between groups. **(B)** Likewise, both the control and dyslexia groups showed no difference in the (lack of) selectivity of these regions for the hard vs. easy spatial working memory task manipulation.

Diffusion: Probabilistic Tractography



Using individual subjects' language-selective fROIs as seeds, we generated an fROIxfROI connectivity matrix for each subject, quantifying the number of streamlines seeded in one fROI that terminated in another fROI.

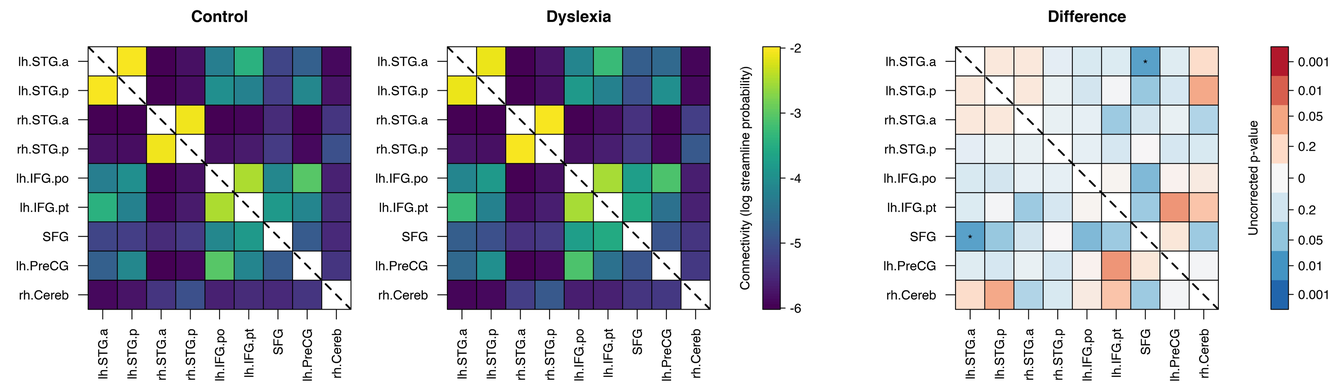


Figure 4. Structural connectivity within the language network does not differ in dyslexia. (A) fROI-fROI probabilistic connectivity matrices for each group. Each cell depicts the mean of the probabilistic connectivity values (log proportion of streamlines seeded in each fROI that terminated in each other fROI) across participants in that group. **(B)** Group differences (independent-sample *t*-tests) for each node in the network. Warm colors show greater connectivity in the control group, cool colors show greater connectivity in dyslexia.

Discussion

- Coactivation of the functional network and the selectivity of functional response profiles within the language-selective regions of interest did not differ for individuals with dyslexia.
- Anatomical connectivity between these regions were also essentially the same between typical readers and individuals with dyslexia. No atypical patterns of connectivity were detected.
- These findings suggest that the functionality of the core language comprehension network in dyslexia is intact and that the dysfunction in reading development may therefore lie outside this facet of the brain's support for fundamental linguistic processing.

[1] Fedorenko, Hsieh, Nieto-Castañón, Whitfield-Gabrieli & Kanwisher (2010). *Journal of Neurophysiology*, 104(2): 1177-1194.
[2] Scott, Gallée, & Fedorenko (2017). *Cognitive Neuroscience*, 8(3): 167-176. [3] Nieto-Castañón & Fedorenko (2012). *NeuroImage*, 63(3): 1646-1669.

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