Neural network underlying abnormal sentence production in primary progressive aphasia: physiologic evidence from resting state functional MRI

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Background: Primary progressive aphasia (PPA) is a syndrome of progressive decline of language function due to neurodegeneration. Individuals with PPA may make grammatical errors when producing sentences (agrammatism). Cortical volume loss within dorsal perisylvian regions (dorsal language stream) has been shown to be related to degree of agrammatism. However, the relationship between physiologic network changes and agrammatism has not been well investigated. In this study, we examined the relationship between resting state functional connectivity of the dorsal language stream nodes and sentence production in PPA using resting state functional MRI, asking the question of whether decline in production of grammatical sentences in PPA would correlate with strength of dorsal stream connectivity.

Methods: Forty-eight individuals with PPA underwent resting state fMRI scanning. They scored 14.65 ± 6.64 (/30) on a composite score of grammatical sentence production. Based on previous studies, we chose two 10 mm spherical nodes from the dorsal perisylvian language stream: supramarginal gyrus (SMG), and Broca’s area pars opercularis (PO) nodes. Using Pearson test, we investigated whether grammar scores and strength of connectivity of the PO-SMG node pair measured by REST toolbox were correlated. Additionally, we probed whether grammar scores and connectivity of the three control non-language node pairs (contralateral PO-SMG, left SMG-SM [sensorimotor] and PO-SM) were correlated.

Results: There was a significant correlation between connectivity of the left PO-SMG and grammar scores (r = 0.409, p = 0.0088). In contrast, the contralateral connectivity between right PO-SMG did not correlate with grammar scores. Similarly none of the SM connections correlated with grammar scores.

Conclusions: In individuals with PPA, grammar scores correlated with the strength of connectivity of a left lateralized parieto-frontal connection (PO-SMG), but not with the control non-language connections, confirming specificity of our finding. Historically processing of grammar was attributed to Broca’s area. However, by providing physiologic evidence, our finding adds to a growing literature that supports involvement of a network (containing both PO and SMG) in sentence production. By providing targets for intervention, this study may be useful in future for guiding therapeutic neuromodulation of the language network (e.g. repetitive transcranial magnetic stimulation).