Relationship of atrophy to task-related activity in the language network for different PPA clinical phenotypes

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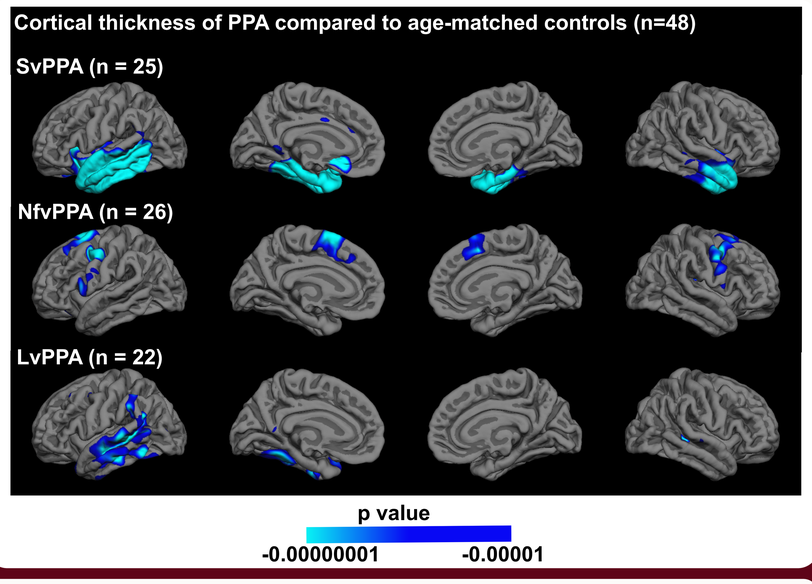
Background

Primary Progressive Aphasia (PPA) is a neurodegerative condition that is characterized by progressive language impairment. There are three subtypes, which generally have distinct clinical phenotypes. Semantic variant PPA (SvPPA) patients have most severe deficits in picture/object naming and single word comprehension. Nonfluent variant PPA (NfvPPA) patients have dysfluent/effortful speech with errors in grammar comprehension. Logopenic variant PPA (LvPPA) patients are characterized by impairment in the auditory-verbal short-term memory known as the "phonological loop" [123].

Numerous studies have identified a network of brain regions that are selectively engaged during linguistic processing in the healthy brain. The subcomponents of this language network are differentially vulnerable to neurodegeneration in each of the distinct clinical phenotypes of PPA. The goal of this study was to investigate the effects of PPA on the functional integrity of the language network during linguistic processing.

Atrophy signatures



fMRI task design

Sentences Condition

THE	BUTLER	STARTED	A	RUMOR	BUT	THE	COOK	DID	NOT	BELIEVE	HIM

Non-words Condition

GOR	SCAVED	CRE	MISPRINE	TICAITING	UL	IM	LAS	TROMER	CRE	CLUD	CRE

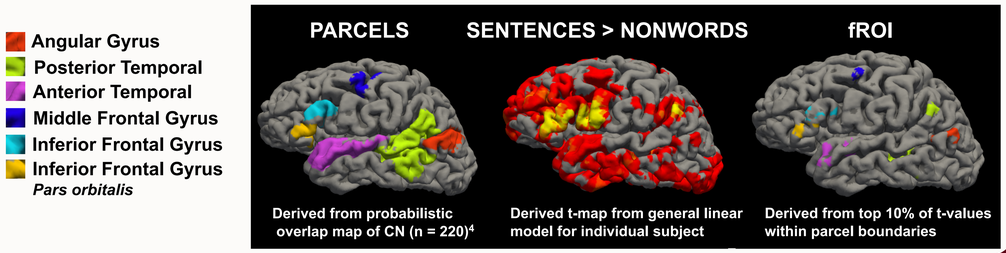
Fedorenko Language Localizer[4]
Passive reading task
6 seconds per trial

Functional Analysis: methods & sample

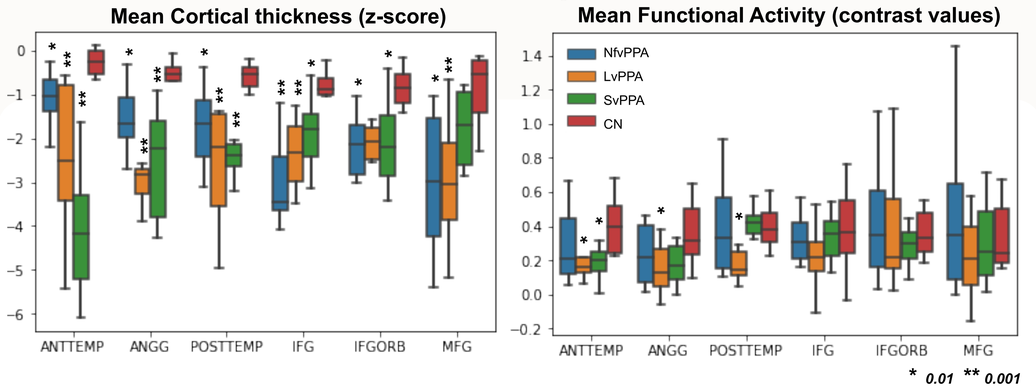
- Functional ROIs defined for 6 language parcels per individual by selecting top 10% of voxels based on t-value
- fROIs used as a mask to determine mean Sentence > Nonwords contrast and mean cortical thickness z-score
- Interregional correlations computed by correlation matrix of spatially averaged BOLD signal per ROI

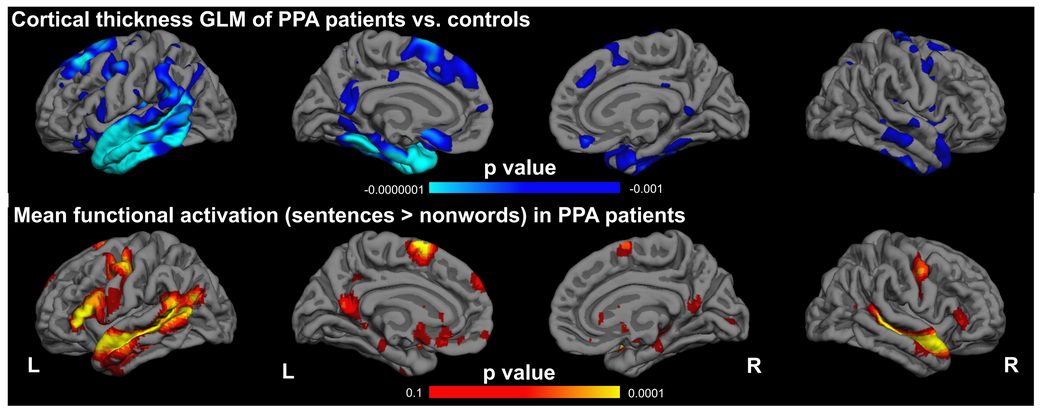
DIAGNOSIS	n	MEDIAN CDR (lang)	AGE RANGE	MEAN AGE	% MALE
SVPPA	8	1.0	63-70	66.7 yrs	38%
NfvPPA	8	0.5	62-86	73.8 yrs	87%
LvPPA	11	0.75	60-79	69.5 yrs	64%
CN	8	n/a	32-61	48.7 yrs	13%

Defining functional regions-of-interest (fROIs)



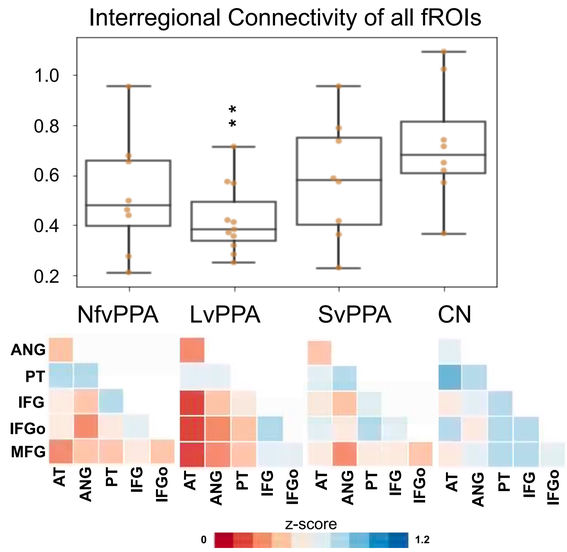
Cortical thickness and functional activity in PPA





Whole brain GLM of sentences > non-words. The functional localizer activates the language network in the whole PPA sample. As expected, the activity is left lateralized and includes lateral temporal cortex, angular gyrus, inferior frontal gyrus, and caudal middle frontal gyrus.

Task-based functional connectivity



BOLD signal is significantly less correlated across regions in the LvPPA group compared to controls, with the language network fractionation being impacted most by the fractionation of the anterior temporal area.

Key Findings and Conclusions

Linguistic task-related activity is altered in PPA which is evident in the magnitude of functional activity compared to controls.

Our data demonstrates that the fedorenko localizer targets regions in the language network for the PPA sample, which warrants comparison to control group.

LvPPA patients, who have most prominent atrophy in the posterior temporal cortex and angular gyrus, have the most compromised functional connectivity across regions. This is consistent with the notion of this region serving as a hub for the language network.

References

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