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Introduction

Despite numerous studies investigating the right hemisphere's (RH) language processing capacity[1-3], this question is still vigorously debated. The current study aims to provide additional evidence from analyzing white matter (WM) tract integrity in Primary Progressive Aphasia (PPA). Previous PPA research has highlighted differences in WM tract integrity between PPA and healthy individuals and associations of tract integrity with language processing, primarily in the LH[4-6]. This study examines these issues in both hemispheres, and also investigates the effects of disease progression on each hemisphere's role in language processing.

Methods

Participants were 33 PPA individuals (22 early-PPA & 11 late-PPA) and 20 healthy controls (HC). Language scores on naming, syntax and spelling were collected from the PPA group. DTI data were collected from both groups, and mean diffusivity (MD) – a measure of WM integrity - was calculated in both hemispheres for: anterior and posterior inferior fronto-occipital fasciculus (IFOF), inferior longitudinal fasciculus (ILF), uncinate fasciculus (UF) and the long, anterior and posterior arcuate fasciculus (AF). (Note: anterior-AF is also known as SLF-III).

(1) Tract integrity differences between early/late PPA and HC were investigated in each hemisphere, using linear mixed-effects models (LMEMs). (2) Associations of language domains with tract integrity in the two hemispheres were investigated by model comparisons of LMEMs with and without language scores. (3) To assess the effects of disease progression on the language-tract integrity relationship, model comparisons of LMEMs with and without an interaction term of language scores by disease progression (i.e., early vs late) were performed. For both (2) and (3), comparisons were performed for models including the three language domains together, and for each language domain separately.

Results

Early and Late PPA vs HC: In the LH, MD values were higher in the PPA group compared to the HCs for both early-PPA ($p=0.018$) and late-PPA ($p=0.001$). In the RH, no statistically significant differences between HC and PPA groups were found.

Language domains in the two hemispheres: Analyses including the three language domains showed highly significant effects in both hemispheres (LH: $p<0.001$; RH: $p<0.001$). When language domains were

examined separately, significant or marginal effects were found for all three language domains in the LH and for Naming and Syntax in the RH (Table 1A).

Effects of disease progression on hemisphere-language relationships: Analyses including the three language domains revealed a marginal effect for the LH (p=0.089). When language domains were examined separately, a significant effect for Syntax in the LH was found (Table 1B and Figure 1).

Conclusions

We found, in PPA, a strong relationship in the left hemisphere between language performance and the integrity of WM tracts across multiple language domains. Further, this relationship was significantly affected by disease progression. Importantly, we also found language processing performance was also strongly associated with WM integrity in the right hemisphere. These results provide novel evidence of the right hemisphere's capacity for language and point to the effects of disease progression on the relationships between white matter integrity and language.

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Table 1. Language domains and the effects of disease progression in PPA (p values). (A) The results of model comparisons evaluating the relationship between language performance and white matter integrity. (B) The results of model comparisons evaluating the effect of disease progression on the relationship between language performance and white matter integrity. (LH=left hemisphere, RH=right hemisphere)

A. Relationship between language and white matter integrity		
	LH	***RH***
Syntax	**0.015**	**0.004**
Naming	**<.001**	**0.069**
Spelling	0.553	**0.022**
B. Effects of disease progression on the relationship between language and white matter integrity		
	LH	***RH***
Syntax	**0.035**	0.240
Naming	0.292	0.538
Spelling	0.751	0.335

Figure 1. Interaction effect between Syntax and Disease Progression in the LH