Introduction. Primary progressive aphasia (PPA) is characterized by distinct patterns of left-lateralized neural degeneration and declining language functioning. Although deficits in grammatical processing (e.g., complex sentence production and comprehension, production of grammatical morphology) are primarily seen in the agrammatic variant (PPA-G), subtle impairments also may be observed in the logopenic (PPA-L) and semantic (PPA-S) variants (see Wilson, et al., 2012; Thompson & Mack, in press, for a review). In cognitively healthy individuals, production and comprehension of syntactically complex structures involves both the left middle temporal cortex (Ben-Shalom & Poeppel, 2008; Indefrey & Levelt, 2004) and the left inferior frontal and motor cortices (Friederici, 2002; Kielar et al., 2011; Shapiro, et al., 2012; Tyler et al., 2005), with similar regions engaged for production of grammatical morphology. However, impaired complex sentence production and comprehension in PPA has been linked primarily to atrophy in the left inferior frontal gyrus (IFG) (Amici et al., 2007; Rogalski et al., 2011; Wilson et al., 2011) and atrophy patterns associated with deficits in grammatical morphology have not been previously studied. The present study aimed to identify the cortical areas of atrophy associated with deficits in complex sentence production, complex sentence comprehension, and production of grammatical morphology in PPA. Identification of these patterns has relevance for understanding the neural mechanisms of grammatical processing and as well as for clinical management of individuals with PPA.

Methods. Fifty-four participants with a root diagnosis of PPA were included in the study (25 males, mean age = 64.6 yrs, mean symptom duration = 3.9 yrs, mean education = 15.8 yrs, all right-handed), which included 21 with PPA-G, 11 with PPA-L, 14 with PPA-S, 2 with a mixed subtype diagnosis, and 6 with unclassifiable PPA. The *Northwestern Assessment of Verbs and Sentences* (Thompson, 2011) was used to assess noncanonical sentence production in 45 participants using the Sentence Production Priming Test, and noncanonical sentence comprehension in 49 participants using the Sentence Comprehension Test. Finite verb production (i.e., grammatical morphology) was measured in 35 participants using the *Northwestern Assessment of Verb Inflection* (Lee & Thompson, experimental version). For each linguistic measure, backward elimination step-wise regression was performed with age, education, symptom duration, and performance on a related control condition (e.g., canonical sentence production or comprehension, and non-finite verb production) as initial covariates to determine the best linear model. This method controlled for variables of no interest as well as overall task performance. Residuals were extracted from each model, scaled, and then correlated with the cortical thickness of 12 left perisylvian regions-of-interest in Freesurfer (i.e., Desikan atlas; Desikan et al., 2006), using false discovery rate (FDR) correction for multiple comparisons. The left postcentral gyrus was considered a control region, as there is no evidence that grammatical processing is supported by this cortical region.

Results. The model for noncanonical production ($F(41)=18.06$, $p<0.001$) included age ($T(41)=-1.429$, ns), education ($T(41)=-2.121$, $p<0.05$) and canonical sentence production ($T(41)=7.235$, $p<0.001$) as covariates. There was a positive correlation between the model's residuals and cortical thickness in left pars opercularis ($r=0.408$, $p=0.05$) and pars orbitalis ($r=0.372$, $p=0.05$). The model for noncanonical sentence comprehension ($F(47)=28.89$, $p<0.001$) included canonical sentence comprehension as the only covariate ($T(47)=5.375$, $p<0.001$), and the residuals were marginally correlated with cortical thickness in the left supramarginal cortex ($r=0.395$, $p=0.065$). The model for finite verb production ($F(33)=7.994$, $p<0.001$) included non-finite verb production

as the only covariate ($T(33)=2.827$, $p<0.01$), but the residuals did not correlate with any regions after multiple comparison correction. Before correction, the residuals correlated with cortical thickness in the left middle temporal area ($r=0.375$, $p<0.05$, uncorrected).

Discussion. Grammatical impairments are predominant in PPA-G, but may also be observed in PPA-S and PPA-L. Results from the present study suggest an association between complex sentence production deficits and cortical atrophy in the left IFG. Such findings are consistent with previous studies showing atrophy in left anterior and posterior IFG correlated with impaired production of simple and complex sentences in PPA (Rogalski et al., 2011), and the left rolandic operculum associated with syntactic construction and phrase-structure building in healthy individuals (Indefrey et al., 2001). Our investigation also showed a relationship between deficits in comprehending noncanonical sentences and atrophy in the left supramarginal gyrus. Though deficits in complex sentence comprehension in PPA have previously been linked to atrophy in left inferior frontal regions (Wilson, 2010, 2011), in the stroke aphasia literature sentence comprehension deficits have also been associated with lesions in posterior perisylvian regions (e.g., Thothathiri et al., 2012). Further research is needed to identify the contributions of left anterior and posterior perisylvian regions to sentence comprehension deficits. In addition, this is the first study to examine the neural correlates of grammatical morphology production in PPA. Our results show that grammatical morphology deficits may be linked, though weakly, to the left middle temporal cortex. Studies with healthy individuals suggest that the left middle temporal gyrus is important for accessing lexically-encoded syntactic information (Ben-Shalom & Poeppel, 2008; Indefrey & Levelt, 2004), and the left inferior frontal, motor and premotor regions for processing inflectional morphology (Kielar et al., 2011; Shapiro, et al., 2012; Tyler et al., 2005). Therefore, deficits in grammatical morphology in PPA may stem from impaired access to lexically-encoded syntactic information rather than faulty syntactic combinatorial processes.

Conclusion. The present study identified regions of atrophy that are related to grammatical deficits in complex sentence production, complex sentence comprehension, and producing grammatical morphology across PPA subtypes. These findings contribute to what we know about the neural networks of grammatical sentence processing and are useful for clinical management of patients with PPA.

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