

Regional Cortical Thinning Patterns Distinguish TDP-C and Pick's Disease in Primary Progressive Aphasia

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INTRODUCTION

- **Anterior temporal lobe (ATL)** degeneration is a hallmark of several primary progressive aphasia syndromes
- In particular, ATL atrophy is characteristics of frontotemporal lobar degeneration due to TDP-43, type C (FTLD-TDP type C, or **TDP-C**)
- However, Pick's disease (**PiD**), a subtype of FTLD-tau, can also affect the ATL early, along with the **inferior frontal gyrus (IFG)**.
- We examined differences in ATL atrophy between TDP-C and PiD and tested whether combined ATL and IFG thinning could distinguish TDP-C from PiD pathology.

METHODS

- 28 right-handed PPA cases (PiD, N = 11; TDP-C, N = 17) and 35 age-matched controls underwent structural MRI at their initial visit to the Northwestern PPA Program (see table).
- T1-weighted images were acquired on a Siemens 3T scanner and processed with FreeSurfer to extract cortical thickness.
- Two global regions of interest (ROIs) were defined using the HCP atlas: the left anterior temporal lobe (ATL; 9 parcels) and inferior frontal gyrus (IFG; 6 parcels) (**Figure 1**).
- Cortical thickness values were converted to z-scores relative to the control mean for each ROI.
- Logistic regression models evaluated whether mean ATL and IFG thickness predicted pathology, first at the global ROI level and then at the sub-ROI (parcel) level.
- We then tested whether a composite measure of ATL and IFG thinning better predicted postmortem pathology than models including each ROI separately, with models compared using AIC.

	N	Sex, M/F	Mean Education (yrs)	Mean Age at Scan (yrs)	Mean Disease Duration at Scan (yrs)
TDP-C	17	8:9	14.71	62.76	3.87
PiD	11	6:5	15.36	62.72	4.11
Control	35	17:18	15.91	60.58	NA

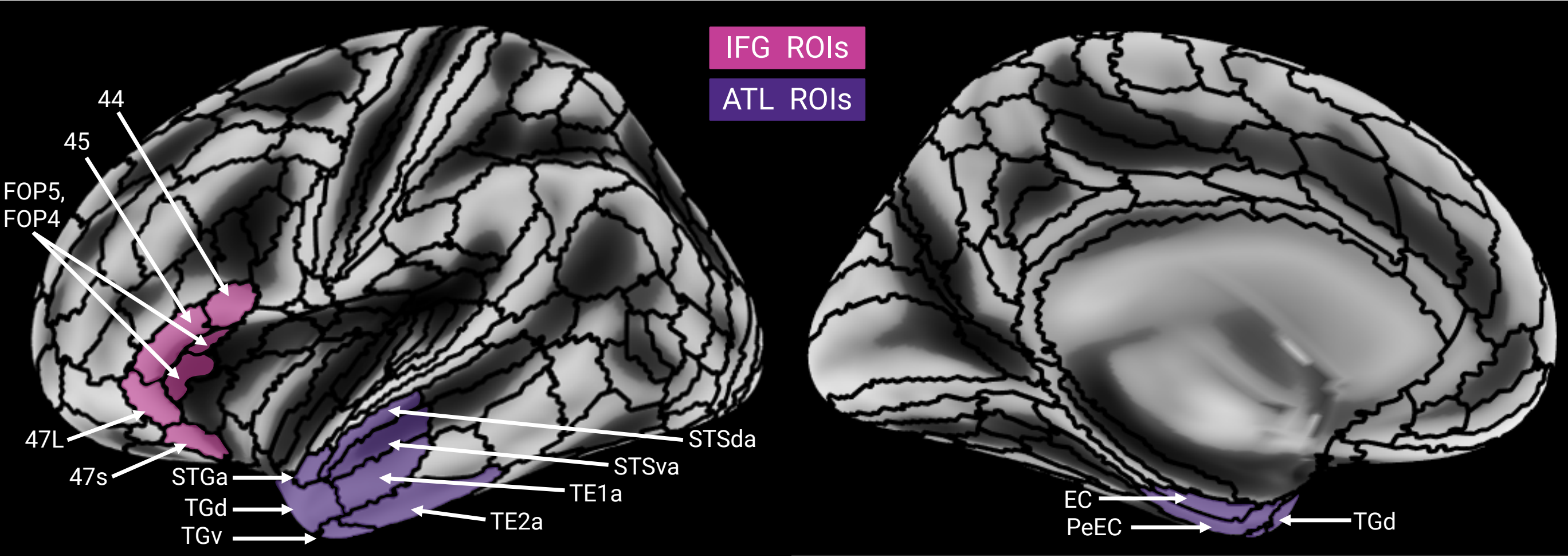


Figure 1. Global ROIs and their parcellations. **ATL:** TGd=dorsal temporopolar region; TGv=ventral temporopolar region; TE1a=anterior middle temporal gyrus; TE2a=anterior inferior temporal gyrus; STSda=anterior superior bank of superior temporal sulcus; STSva= anterior inferior bank of superior temporal sulcus; STGa=anterior superior temporal gyrus; PeEC=perirhinal cortex; EC=entorhinal cortex. **IFG:** 47s=posterior pars orbitalis; 45=pars triangularis; 47L=inferolateral pars orbitalis; anterior pars opercularis; FOP4=frontal operculum, inner pars opercularis; FOP5=frontal operculum, inner pars triangularis.

RESULTS

- ROI-wise analyses revealed a dissociation in regional vulnerability (**Figure 2**).
- ATL cortical thickness patterns were similar between TDP-C and PiD, with TGd and TGv as the most atrophied regions.
- IFG cortical thickness patterns differed between TDP-C and PiD, with mean values for TDP-C regions were almost all above -1.5 SD except for Area 47s.
- Logistic regressions showed ATL thinning predicted TDP-C ($\beta = -1.95$, $p = 0.006$), and IFG thinning predicted PiD ($\beta = 1.59$, $p = 0.018$).
- When examining individual ROIs, thinning in several ATL parcels specifically predicted TDP-C (TGd, STSda, STGa, TGv, PeEC, TE2a, STSva, and TE1a), whereas thinning in IFG parcels FOP4, FOP5, and area 44 significantly predicted PiD (FDR-corrected $p < 0.05$) (**Figure 3**).
- A model including ATL and IFG as independent predictors provided the best fit and resulted in near-complete separation of the pathology groups (**Figure 4**).

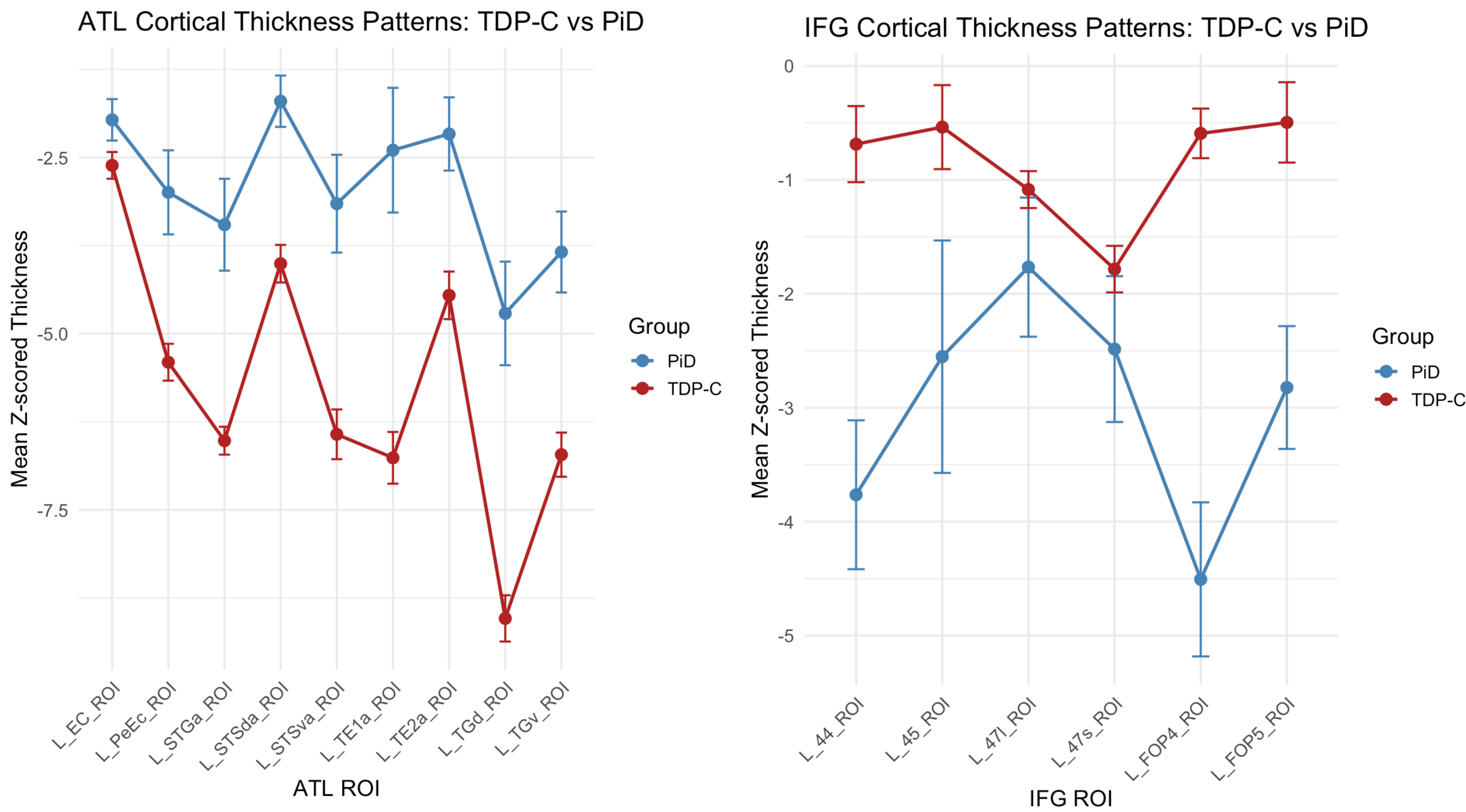


Figure 2. Mean Z-Scored Cortical Thickness Values for Anterior Temporal Lobe (ATL; left) and Inferior Frontal Gyrus (IFG; right) for PiD and TDP-C groups. Y-axis values are mean standard deviations, and X-axis shows ROI parcels per Human Connectome Project Atlas. All values are from the left hemisphere.

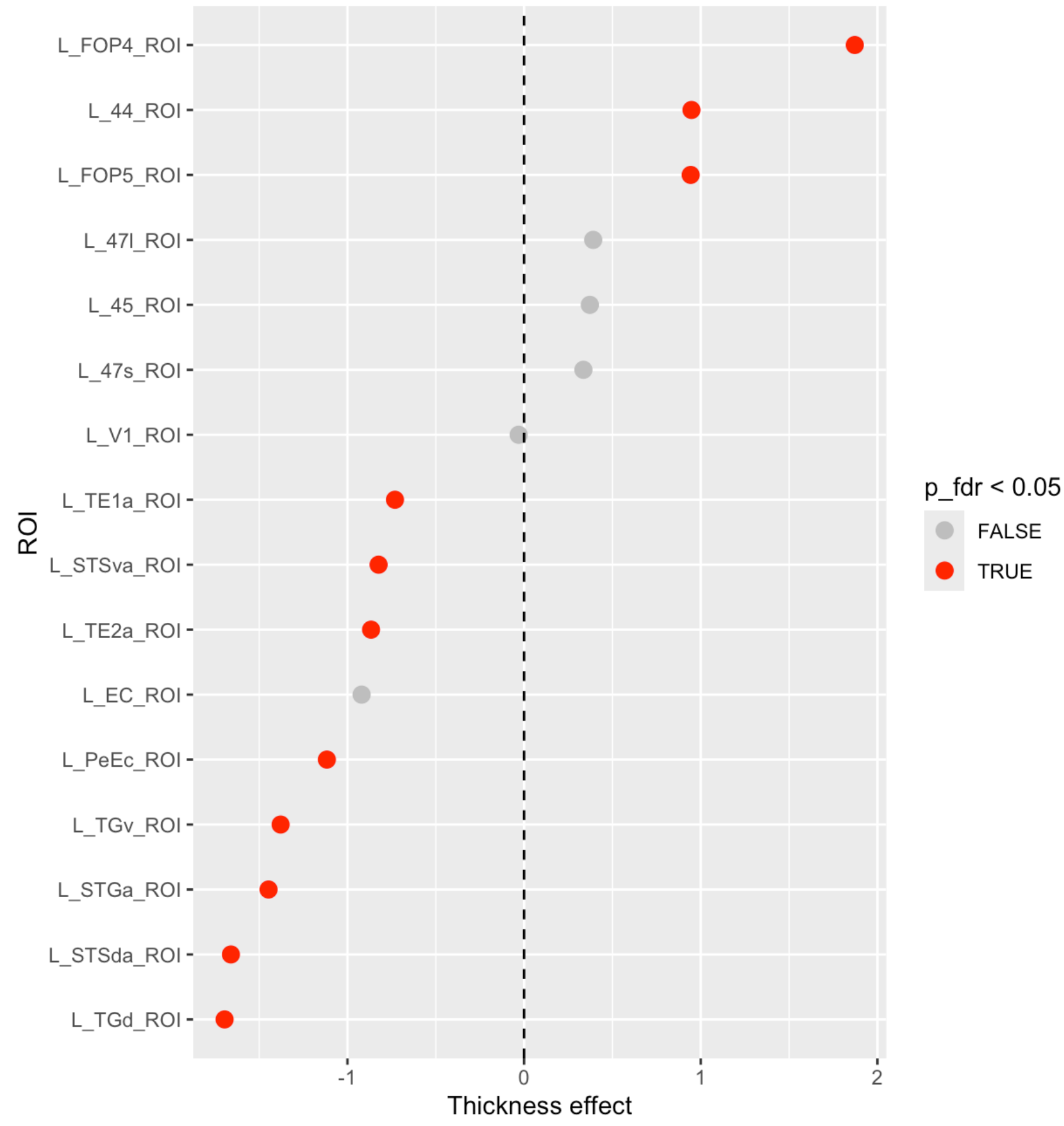


Figure 3. Individual ROIs predicting pathology groups. Data points on the left of the dotted line predict TDP-C as final pathology, and those on the right predict Pick's Disease (PiD).

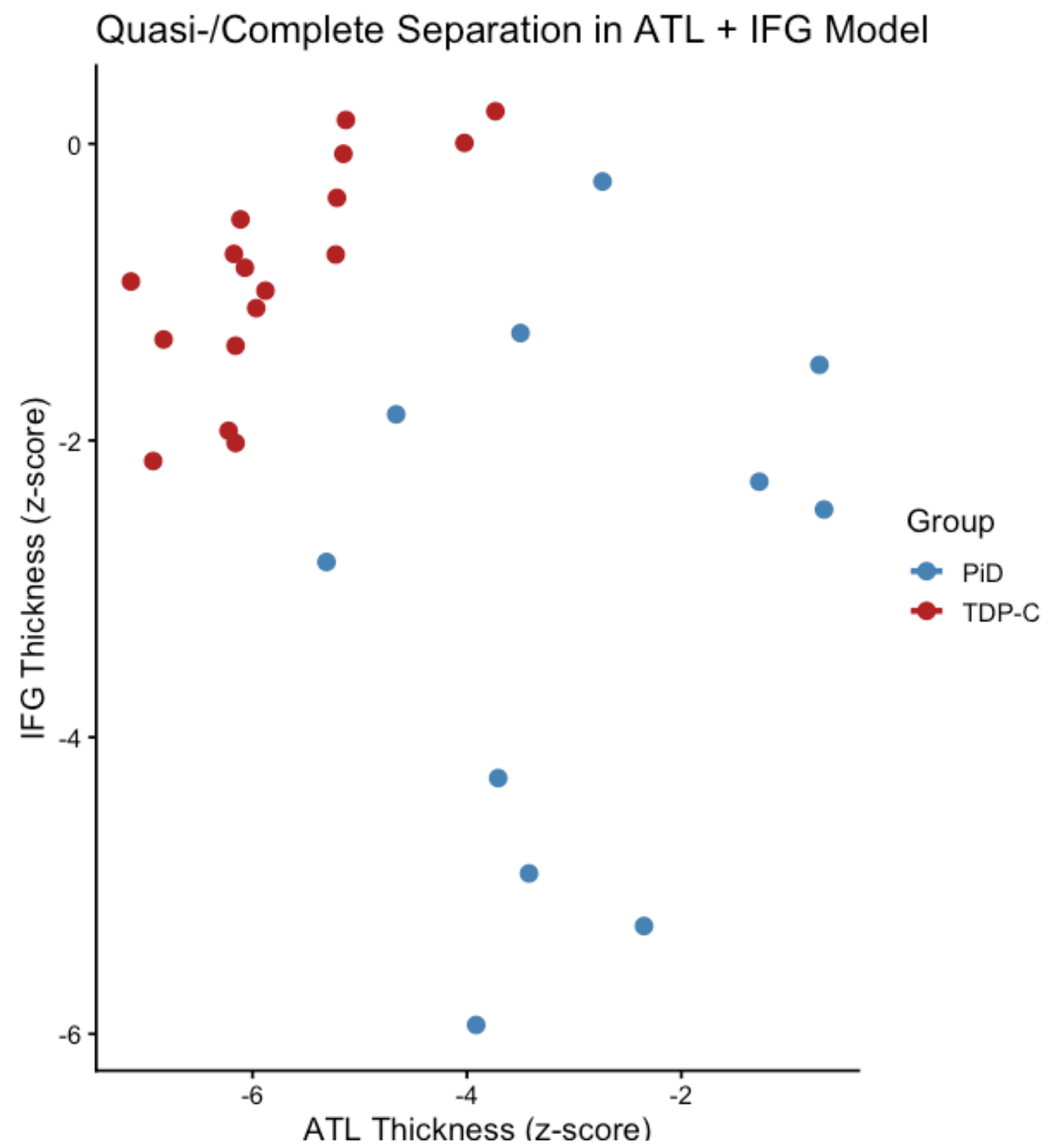


Figure 4. Regional Z-Score Cortical Thickness Values for ATL and IFG shows clear separation between PiD and TDP-C groups.

CONCLUSION

- TDP-C and PiD exhibit distinct regional atrophy patterns, with TDP-C showing predominant ATL thinning and PiD greater IFG involvement.
- Despite early ATL degeneration, IFG atrophy alone remained the best predictor of underlying PiD.
- Future studies will assess other imaging modalities (e.g., white matter tracts) to further characterize ATL vulnerability across these pathologies.

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