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Introduction

While the use of neural-based measures for predicting response to treatment in post-stroke aphasia (PSA) is of interest for basic science, its utility for clinical purposes is qualified by the relative difficulty and expense of collecting such measures. Thus, neural measures may be worth collecting only if they contribute unique information toward patient diagnosis or prognosis. Resting-state fMRI (rs-fMRI) is attractive because, compared to other neuroimaging approaches, the data are relatively easy to collect. Recent work with rs-fMRI (e.g., Iorga et al., 2021; Demarco & Turkeltaub, 2020; Guo et al., 2019) indicates that *local* rs-fMRI analyses (as opposed to connectivity based approaches) distinguish between healthy and lesioned tissues and index domain-specific language deficits. However, an open question remains as to whether such measures contribute unique information for predicting response to treatment beyond what can be predicted on the basis of demographic, behavioral, or simple structural MRI (lesion volume) measures.

Methods

64 individuals with PSA subsequent to a single left-hemisphere stroke were treated for deficits in naming (n = 28), spelling (n = 22), or syntax (n = 14), and completed rs-fMRI scans prior to beginning treatment. Response to treatment was measured as percentage of maximum gain from pre-to-post assessments on trained items. The rs-fMRI data were used to measures the fractional Amplitude of Low Frequency Fluctuations (fALFF; Zou et al., 2008), which was normalized within participants across the 96 anatomical gray-matter parcels of the Harvard-Oxford Atlas (Desikan et al, 2006).

Response to treatment was first predicted using the best set of demographic and behavioral measures (determined by exhaustive search through all available variables, e.g., pre-treatment accuracy, age, sex, etc.) and prediction accuracy was assessed with cross-validation. The process was repeated including neural measures (fALFF and lesion volume), with the best set of neural measures selected via elastic net regression (Zou &

Hastie, 2005). The difference in the precision and 80% prediction intervals of the two sets of models (demographic/behavioral only versus including neural measures) were statistically assessed using Monte Carlo analysis.

Results

The median absolute error (MAE) and width of the 80% prediction interval were significantly improved when including fALFF measures for all three language domains (see Figure). MAEs for predictions based on behavioral/demographic measures ranged from 11-17% across the language domains, improving to just 1-3% when including neural measures (p's < 0.05). Similarly, 80% prediction intervals around the estimated gains on treated items narrowed from ± 22-32% to ± 4-6% (p's < 0.05), indicating that not only are predictions more precise when including fALFF, they also express more certainty.

Conclusions

These results are the first to statistically assess whether local rs-fMRI measures (fALFF) improve predictions of treatment outcomes in aphasia beyond demographic and behavioral measures. For all three language domains tested (naming, spelling, and syntax), the addition of fALFF measures from anatomical cortical regions significantly improves precision, and provides narrower prediction intervals. Monte Carlo procedures demonstrate that these improvements are not attributable to random chance or "over-fitting" due to including additional predictors.

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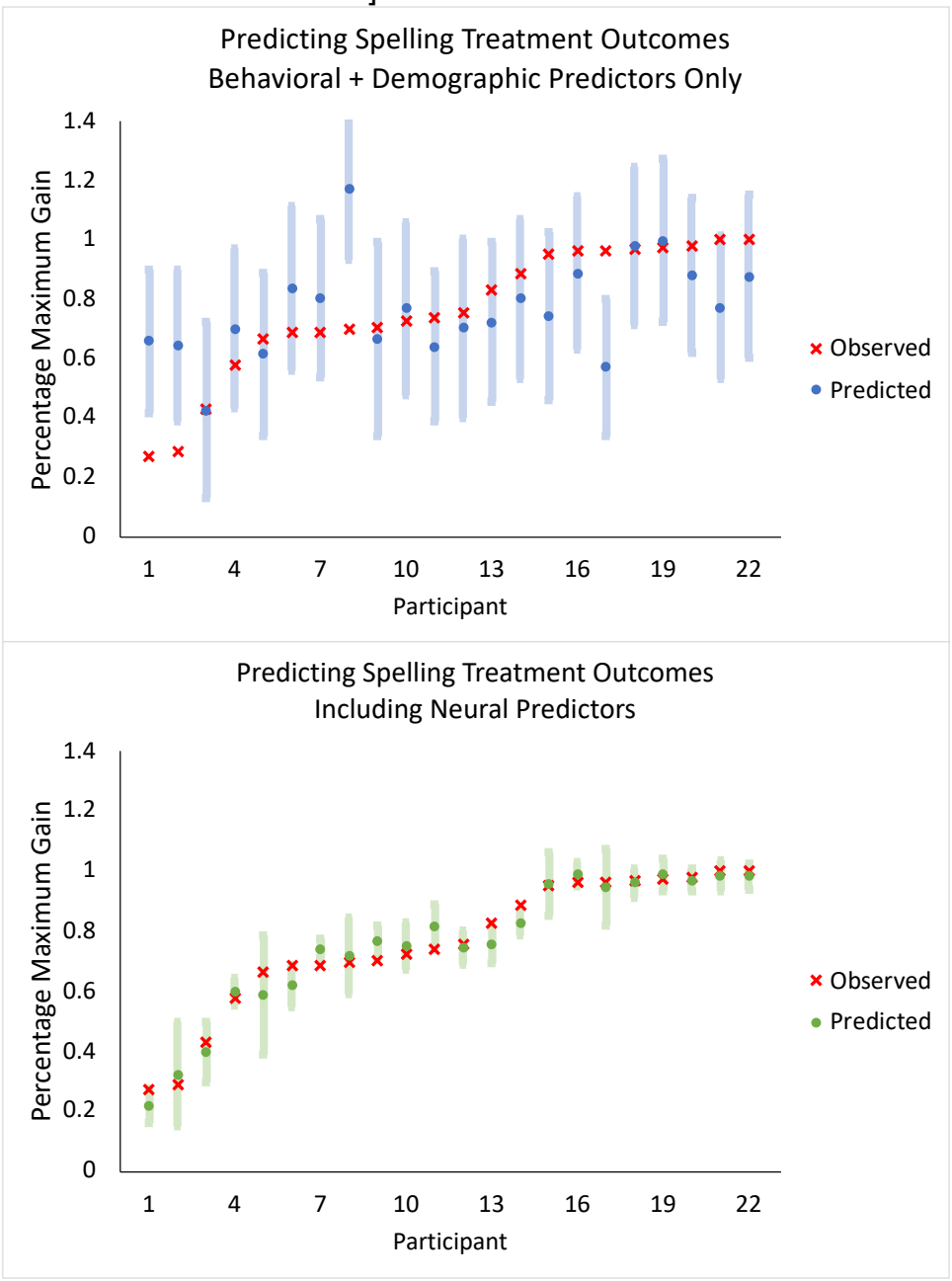

Figure 1. **Top panel:** On the y-axis is the Percentage Maximum Gain achieved on trained items in response to spelling treatment (Observed, red X's) compared to predicted outcomes based only on Behavioral and Demographic predictors. Predictions are depicted by blue circles with 80% prediction intervals. X-axis depicts participants 1-22. **Bottom panel:** The same information (Observed outcomes, red X's) compared to predicted outcomes when including neural measures (green circles with 80% prediction intervals).