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Supplemental information

Temporal lobe perceptual predictions for speech are instantiated in motor cortex and reconciled by inferior frontal cortex

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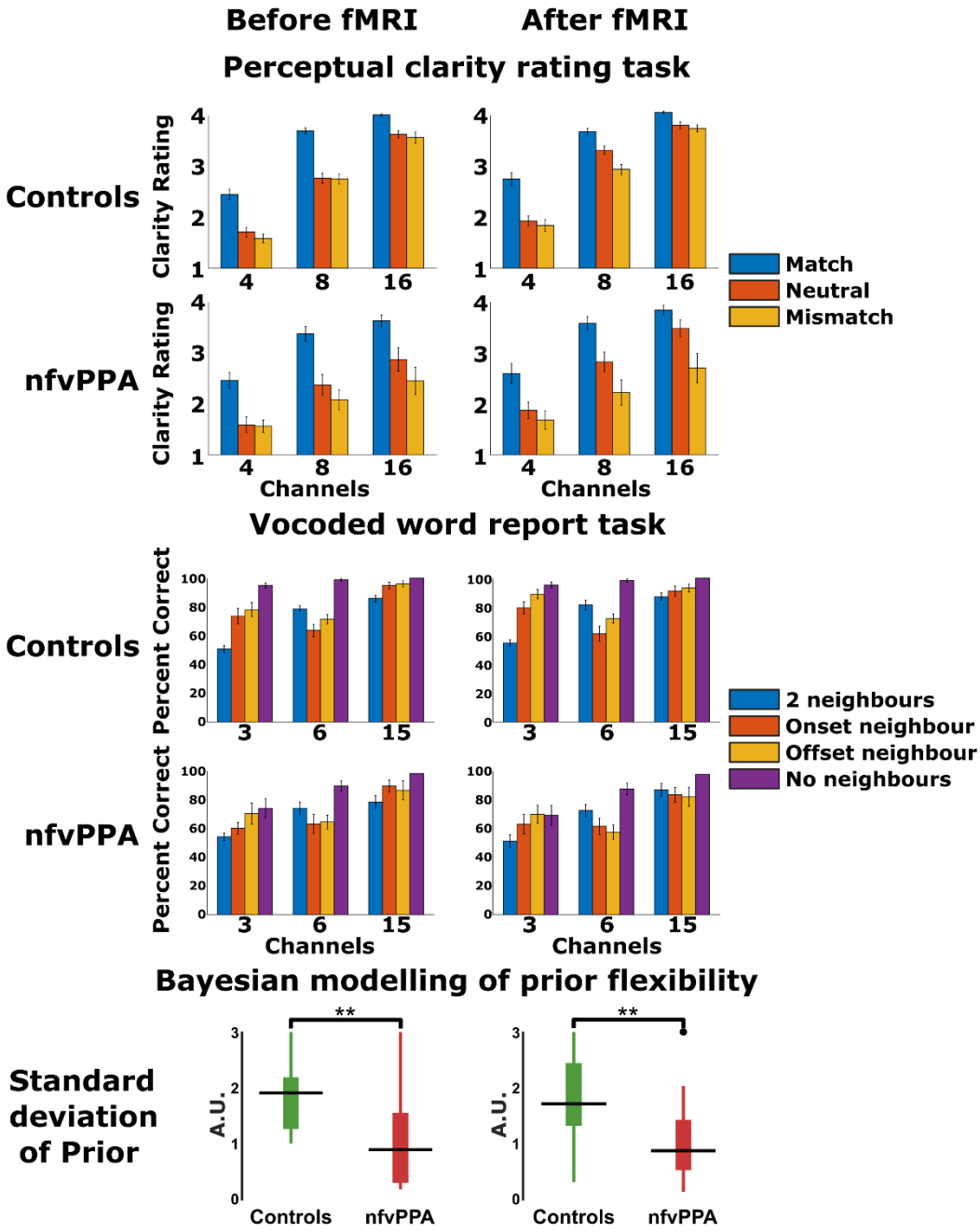
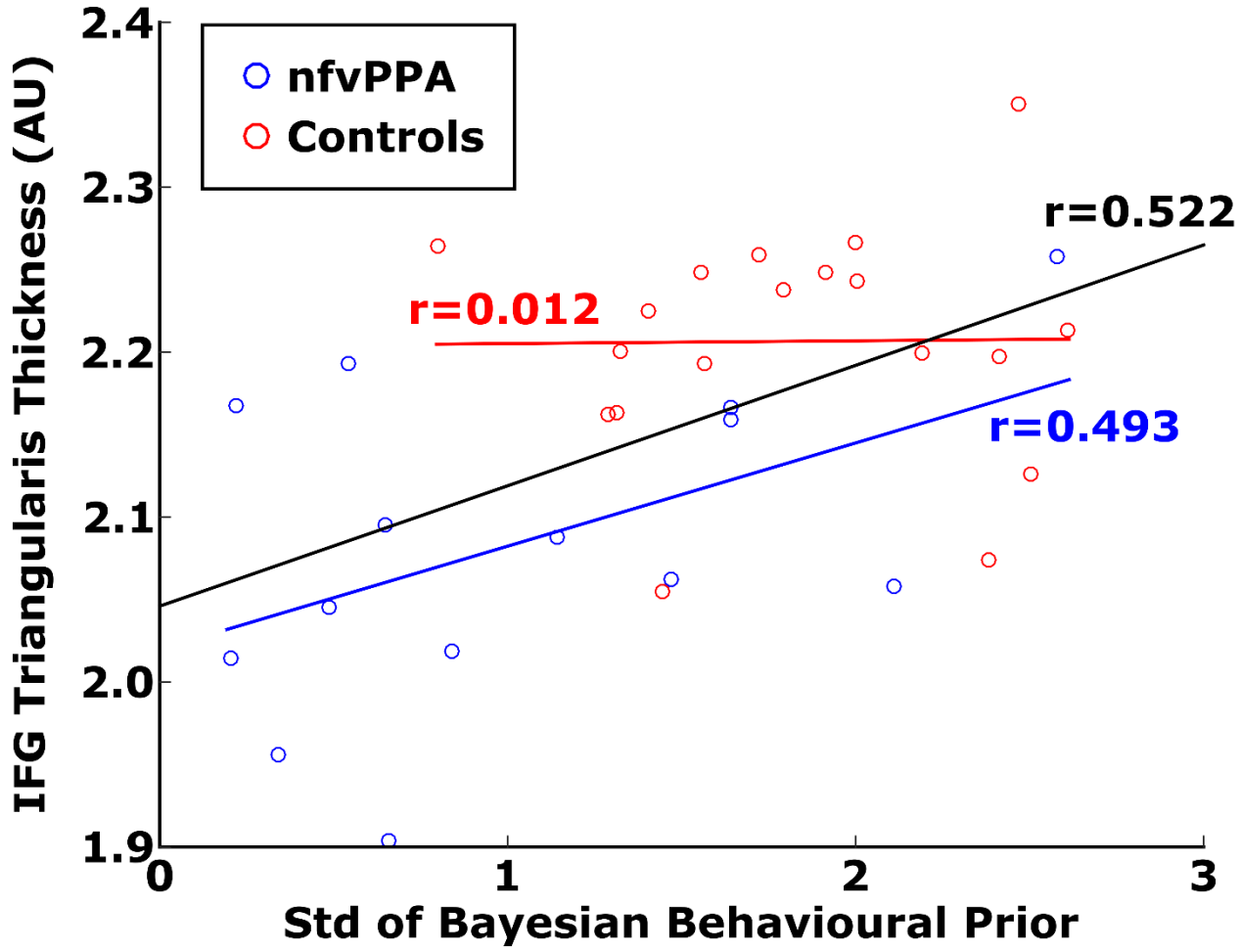
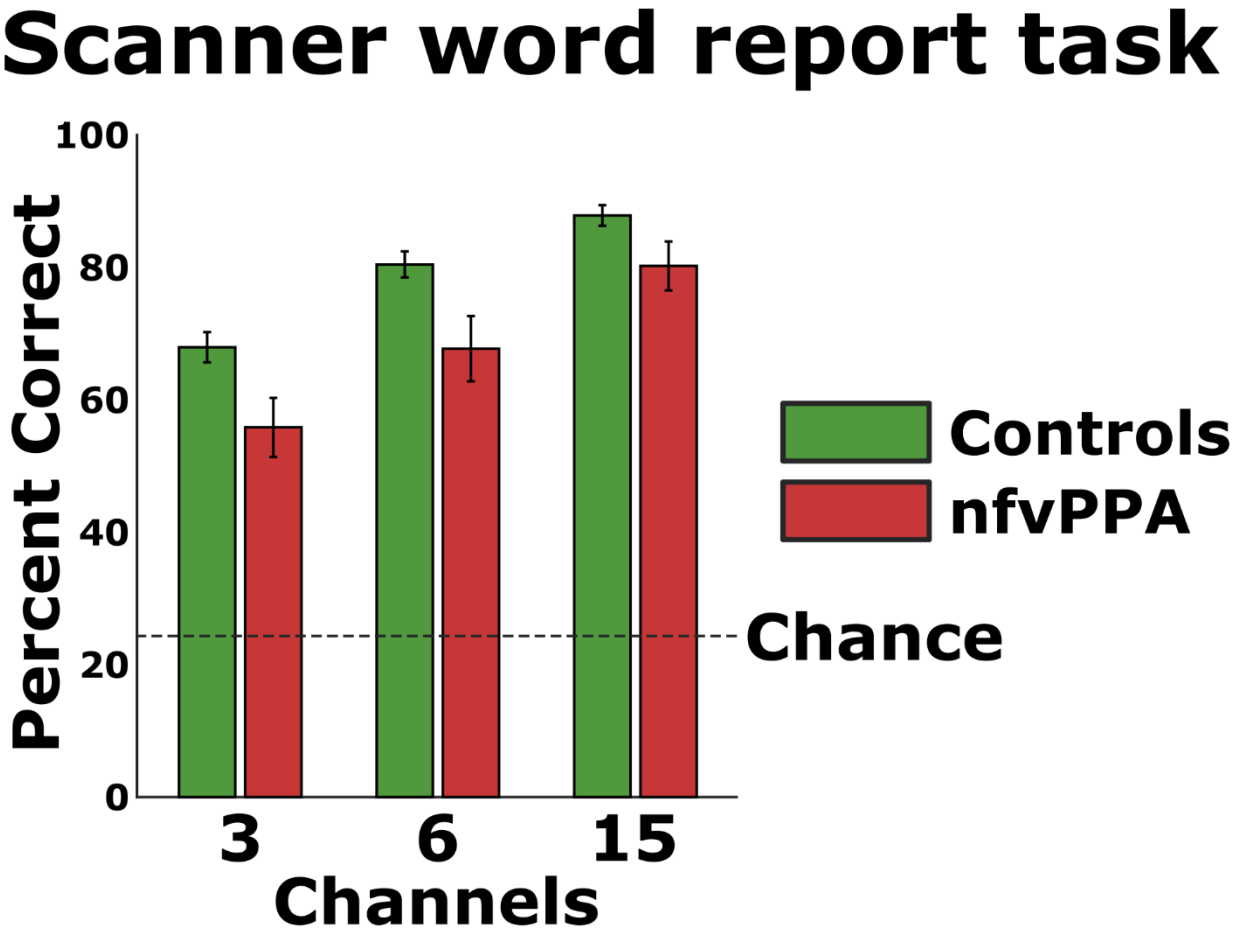
Supplementary figures:



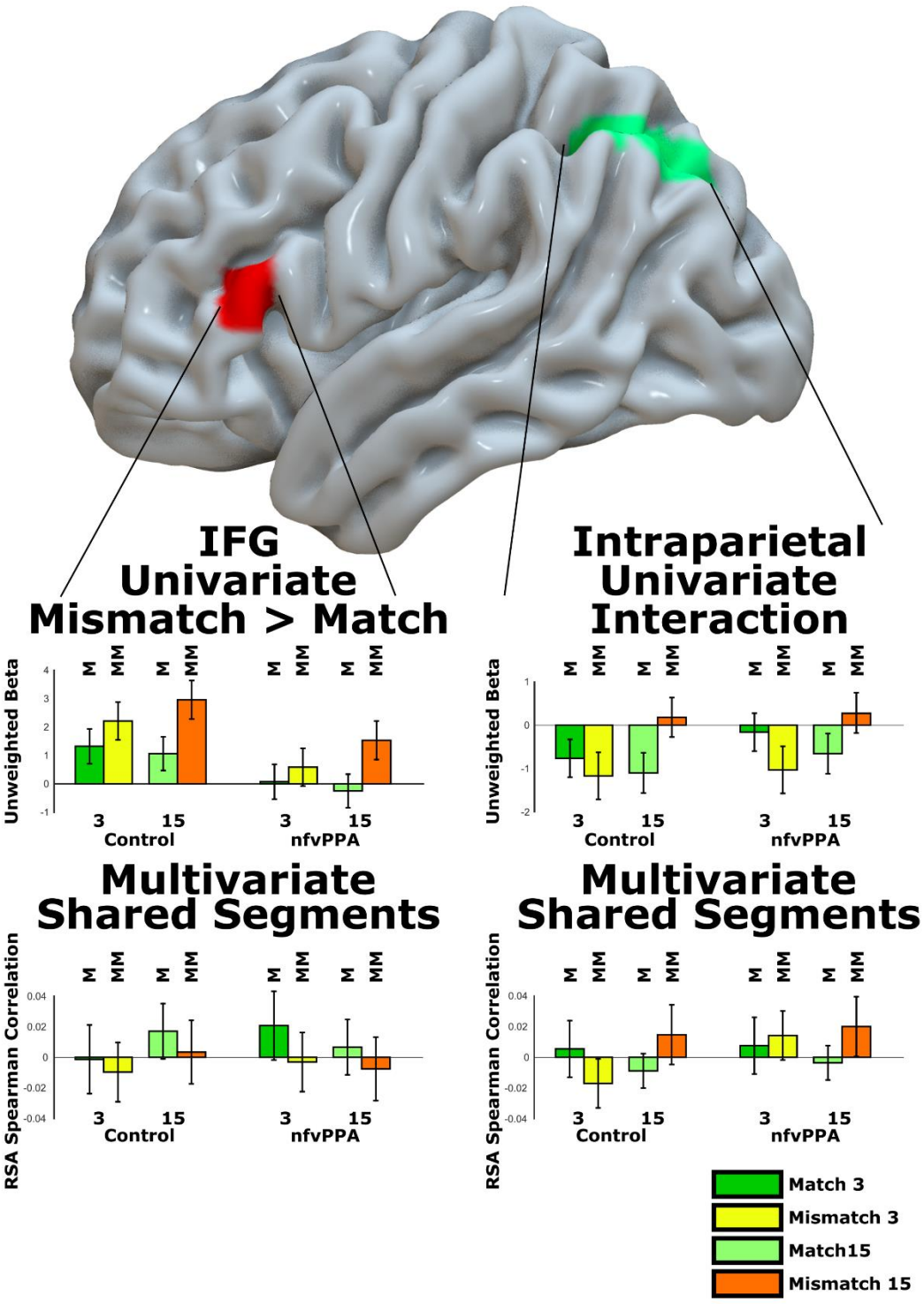
Supplementary Figure 1: Replication of out-of-scanner behaviour from Cope et al. [13], related to Results, Behaviour. Upper: Perceptual clarity rating task, with manipulations of prior congruency and sensory detail. Bar heights represent group-averages for each condition and error bars represent standard error across individuals within each group. Middle: Four alternative forced choice vocoded word identification task. Bar heights represent group-averages for each condition and error bars represent standard error across individuals within each group. Chance performance at 25%. Bottom: Derived parameters from the Bayesian data modelling. A.U., arbitrary units. In all replications, patients with nfvPPA displayed significantly more precise prior expectations than controls (all Wilcoxon U $p < 0.01$).



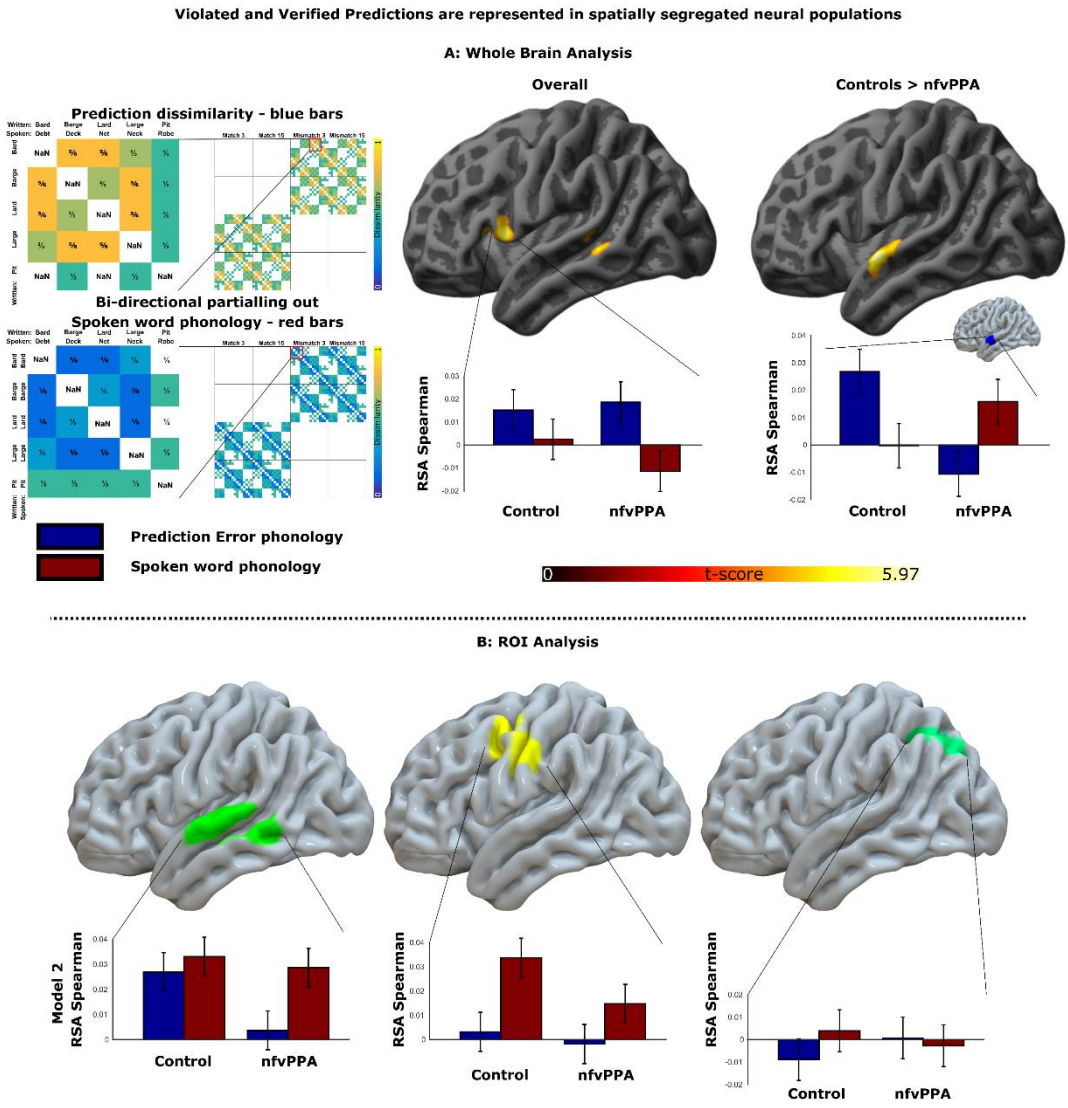
Supplementary Figure 2: As in Cope et al. [13], frontal atrophy resulted in inflexible perceptual predictions, related to Results, Behaviour. This was measured as a reduction in the standard deviation of the behavioural prior from Bayesian modelling. Black trend line is for all participants; blue trend line for only patients with nfvPPA; red trend line for only controls.



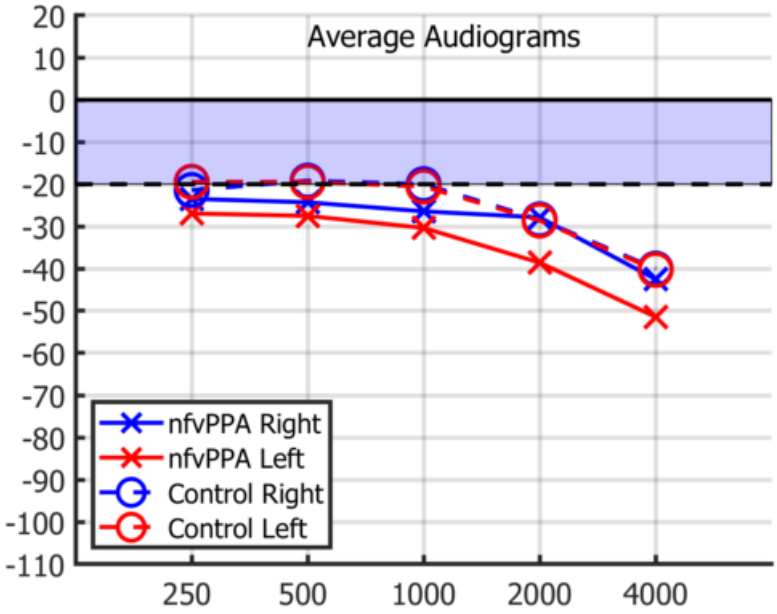
Supplementary Figure 3: Four alternative forced choice vocoded word identification task of the fMRI paradigm words, related to Results, Behaviour. Conducted after the scan session. Bar heights represent group-averages for each vocoder channel number, and error bars represent standard error across individuals within each group. Note that every trial had two close neighbour and one shared vowel distractor items, i.e. the target 'pit' had distractor items 'pick', 'kit' and 'kick'. Chance performance at 25%.



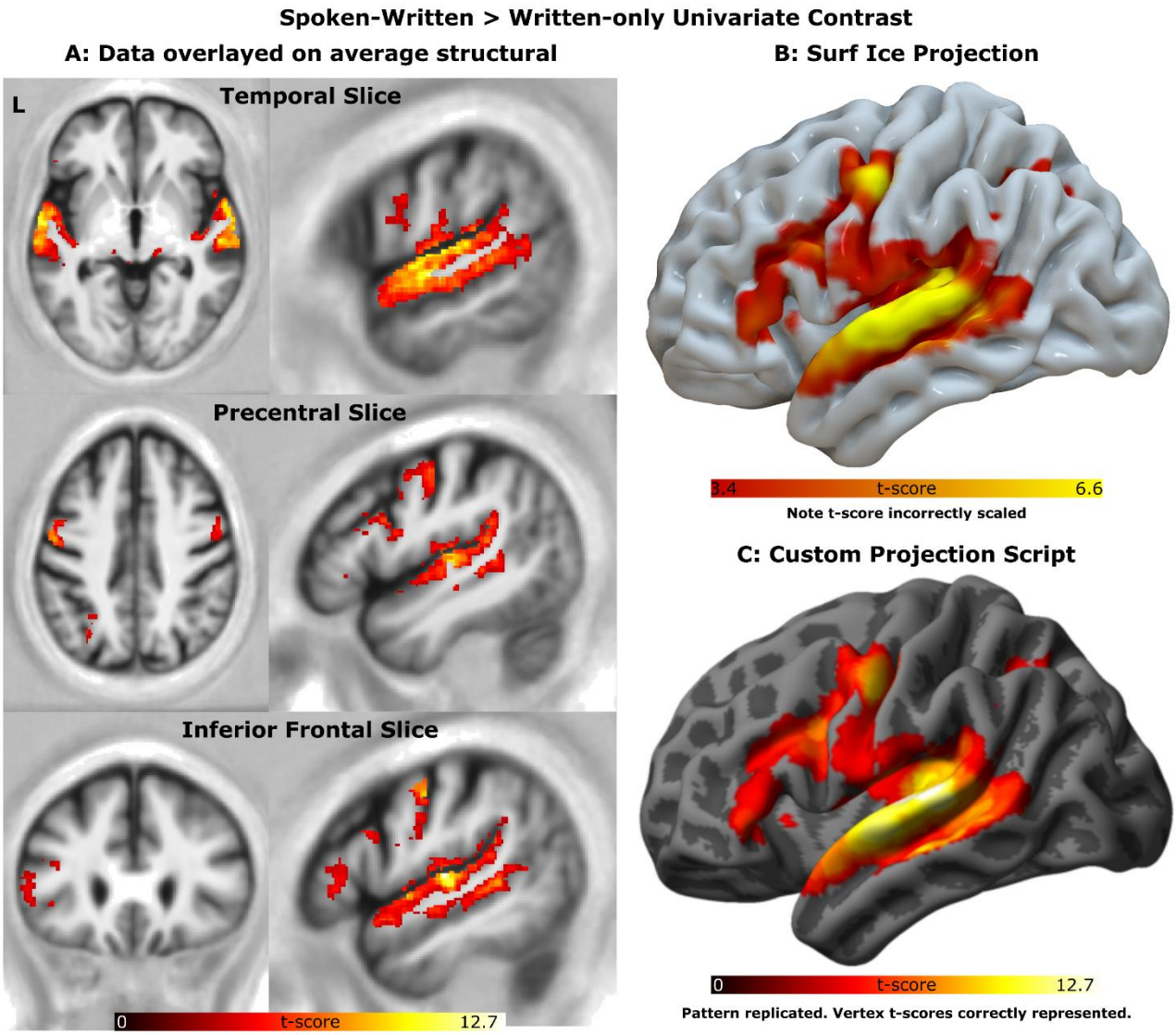
Supplementary Figure 4: <u>Intraparietal and IFG region of interest analysis broken down by condition and group for the shared segments model of phonological similarity</u>, related to Figure 3. ROIs were defined from the univariate Mismatch > Match main effect of congruency (for IFG) and the interaction between sensory detail and cue congruency (for intraparietal sulcus). For univariate bar charts, where statistics were done on the whole brain and these figures are illustrative of the effects, error bars represent between-subject standard error to show variability in response magnitude. For multivariate bar charts, where the ROI was independently determined so the results are not double-dipped, error bars represent the standard error of the mean after removing between-subject variance, suitable for repeated-measures comparisons [2]. There was no significant multivariate representation of word phonology in any condition for either group in either region.



Supplementary Figure 5: Multivariate assessment of consistent relationships between verified and violated predictions, related to Figure 4. All observed sparse correlations were such that verified and violated predictions were more dissimilar than would be observed by chance – we have inverted the prediction RSA matrix such that these correlations are displayed as positive dark blue bars. ***A:*** *Whole brain analysis, cluster corrected at FDR p<0.05. Bar charts show separate ROI analyses of the model of prediction dissimilarity and its matching model of spoken word phonology. The IFG ROI is as shown, defined from all subjects. However, using the anterior STG cluster from the whole brain Controls> nfvPPA contrast would be double dipping. We therefore assessed the anterior STG ROI defined from our univariate Mismatch > Match contrast, displayed in blue on the inset illustrative brain. There was a group by condition interaction in this region (F(1,32)=5.95, Greenhouse Geisser p=0.020) that matched that shown in Figure 5 using partial correlations (F(1,32)=5.51, Greenhouse Geisser p=0.025).* ***B:*** *Analysis within regions of interest not implicated in the whole brain analysis of prediction dissimilarity, showing shared representations of consistent prediction error and sensory input phonology in STG in controls, but no consistent prediction dissimilarity representations in patients in STG, or either group in PrG. STG ROI defined from the 15>3 vocoder channel univariate contrast. PrG ROI defined from the multivariate between-condition shared segment analysis. IPS ROI defined from the univariate interaction between cue congruency and sensory detail*



Supplementary Figure 6: Average pure tone audiograms for study participants, by group and ear, Related to STAR Methods. No statistically significant group differences were observed at any frequency in either ear. One nfvPPA participant had a left tympanic membrane perforation, accounting for the threshold asymmetry in that group, but they had excellent right-sided hearing and reported being able to clearly perceive the auditory stimuli in the scanner environment.



Supplementary Figure 7: Different methods for presenting 7T functional imaging data, Related to STAR Methods. Using the Written+Spoken > Written-only contrast as an illustrative example. A: Overlaying data on the average structural brain represents it precisely and accurately, but it is difficult to visualise multiple brain regions simultaneously. Multiple slices must be user specified to highlight each activated region, making it a poor choice for network-level activations presented here. B: Projecting volumetric data onto a partially inflated cortical surface using the open source software Surf Ice gives an immediate impression of regional activations, including those deep in sulci that would be obscured in anatomically faithful renderings. However, these projections are not quantitative, as they work on the basis of inflation and averaging, including white matter voxels without activation. For the data presented here, open source software Surf Ice represents a peak t-score of 6.6, while the original data extend to 12.7. C: Custom projection, as described in the methods text and available at https://github.com/thomascope/7T_pilot_analysis/blob/master/atlas_Neuromorphometrics/jp_spm8_surfacerender2_version_tc.m. This replicates the visual impression of spatial extent generated by Surf Ice, while correctly representing the range of t-scores in the data.

Supplementary tables:

Desikan-Killiany region average thickness	nfvPPA Mean	Patient SE	Control Mean	Control SE	t_stat	df	p_value	BF10 for group difference	BF_null for no atrophy
lh_bankssts	2.144	0.056	2.087	0.032	0.924	32	0.362	0.459	**6.012**
lh_caudalanteriorcingulate	2.182	0.075	2.195	0.039	-0.160	32	0.874	0.334	2.661
lh_caudalmiddlefrontal	**2.007**	**0.044**	**2.324**	**0.025**	**-6.609**	**32**	**0.000**	**54773.821**	0.000
lh_cuneus	1.805	0.032	1.851	0.028	-1.112	32	0.274	0.531	1.091
lh_entorhinal	2.299	0.066	2.413	0.069	-1.181	32	0.246	0.564	1.011
lh_fusiform	2.212	0.031	2.149	0.026	1.552	32	0.131	0.825	9.287
lh_inferiorparietal	2.130	0.028	2.171	0.022	-1.169	32	0.251	0.558	1.025
lh_inferiortemporal	2.167	0.032	2.139	0.016	0.832	32	0.411	0.432	5.632
lh_isthmuscingulate	1.984	0.038	2.003	0.027	-0.424	32	0.674	0.354	2.130
lh_lateraloccipital	1.941	0.021	1.949	0.022	-0.252	32	0.803	0.339	2.467
lh_lateralorbitofrontal	2.230	0.030	2.258	0.017	-0.859	32	0.397	0.439	1.420
lh_lingual	1.885	0.024	1.882	0.025	0.075	32	0.941	0.331	3.210
lh_medialorbitofrontal	2.167	0.022	2.148	0.025	0.566	32	0.576	0.374	4.646
lh_middletemporal	2.267	0.040	2.298	0.018	-0.755	32	0.456	0.412	1.572
lh_parahippocampal	2.201	0.047	2.217	0.044	-0.243	32	0.810	0.338	2.486
lh_paracentral	**2.139**	**0.039**	**2.241**	**0.029**	**-2.142**	**32**	**0.040**	**1.826**	0.279
lh_parsopercularis	**2.145**	**0.037**	**2.296**	**0.015**	**-4.048**	**32**	**0.000**	**82.362**	0.006
lh_parsorbitalis	2.265	0.033	2.295	0.029	-0.686	32	0.498	0.396	1.679
lh_parstriangularis	**2.072**	**0.027**	**2.207**	**0.016**	**-4.465**	**32**	**0.000**	**224.868**	0.002
lh_pericalcarine	**1.598**	**0.026**	**1.676**	**0.022**	**-2.268**	**32**	**0.030**	**2.225**	0.228
lh_postcentral	**1.865**	**0.029**	**1.943**	**0.020**	**-2.261**	**32**	**0.031**	**2.203**	0.230
lh_posteriorcingulate	**2.068**	**0.041**	**2.176**	**0.032**	**-2.103**	**32**	**0.043**	**1.722**	0.297
lh_precentral	**2.148**	**0.049**	**2.383**	**0.029**	**-4.328**	**32**	**0.000**	**161.093**	0.003
lh_precuneus	2.077	0.033	2.123	0.021	-1.225	32	0.230	0.587	0.962
lh_rostralanteriorcingulate	2.418	0.054	2.336	0.026	1.466	32	0.152	0.749	8.761
lh_rostralmiddlefrontal	**2.007**	**0.026**	**2.170**	**0.016**	**-5.643**	**32**	**0.000**	**4459.581**	0.000
lh_superiorfrontal	**2.182**	**0.035**	**2.426**	**0.023**	**-5.969**	**32**	**0.000**	**10384.251**	0.000
lh_superiorparietal	1.946	0.029	2.015	0.025	-1.810	32	0.080	1.136	0.458
lh_superiortemporal	2.274	0.037	2.342	0.024	-1.595	32	0.120	0.868	0.613
lh_supramarginal	**2.139**	**0.028**	**2.225**	**0.022**	-2.436	**32**	**0.021**	**2.937**	0.172
lh_frontalpole	2.342	0.050	2.375	0.033	-0.570	32	0.573	0.375	1.871
lh_temporalpole	2.936	0.077	2.837	0.044	1.177	32	0.248	0.562	7.178
lh_transversetemporal	2.162	0.053	2.166	0.039	-0.064	32	0.949	0.331	**2.875**
lh_insula	2.609	0.036	2.571	0.031	0.800	32	0.429	0.423	5.505
lh_Overall_Mean	**2.104**	**0.017**	**2.189**	**0.012**	**-4.210**	**32**	**0.000**	**121.203**	0.004

Supplementary table 1: Cortical thickness estimates from Freesurfer by group, related to Figure 2. Mean and standard error are followed by the t-score, degrees of freedom, and p-value for a two sample t-test with unequal variances. Given the illustrative nature of this table, p-values are not corrected for multiple comparisons. In our frontal regions of interest (lh_parstriangularis, lh_parsopercularis, and lh_ precentral) p values were all <=0.01 even after Bonferroni correction across 35 regions. BF10 is the Bayes Factor for a group difference in either direction (i.e. a two-tailed test), while BF_null is the Bayes Factor for no atrophy in the patient group (i.e. the inverse of a one-tailed test).