# 1537: Large N Pooled Analyses of Neuroimaging Data on Speech Production


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## Introduction

- Speech production network characterized by neuroimaging is based largely on small-N studies or meta-analyses of such studies
- Picture may therefore be incomplete due to false negatives arising from relatively low power
- Here we describe efforts to improve our understanding of the brain regions involved in speech using a *mega-analysis* approach
- This approach (i) increases statistical power, (ii) can result in a more heterogeneous and representative sample, and (iii) provides a means to better characterize the sources of variability across subjects and studies (Costrafreda, 2009; Van Horn, 2004; )
- Functional imaging data pooled across 10 fMRI studies of speech production (See Table 1 for list of study designs)
- Results used to determine *functional ROIs* for speech processes

## Methods

### Functional Analyses

**Common pipeline:** 1st-level analysis of realigned functional images (no normalization or spatial smoothing) using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/). **Speech>Baseline** contrasts (all experiments) and **Perturbed Speech>Non-perturbed Speech** contrasts (three experiments) estimated for each subject.

**Inter-experiment equalization:** 1st-level contrast volumes normalized by *experiment-specific scaling factor:* standard deviation of *Speech-Baseline* contrast across entire brain, averaged across all subjects within each experiment.

**Surface-based analyses:** Cortical surfaces extracted from T1 volumes for each subject using FreeSurfer (https://surfer.nmr.mgh.harvard.edu; Dale et al, 1999; Fischl et al, 1999). Contrast values at the pial surface extracted after functional-anatomical coregistration and entered into vertex-level 2nd-level analyses. *Perturbed Speech>Non-perturbed Speech* contrast values spatially smoothed (approx. 8 mm FWHM kernel) prior to 2nd-level analyses.

2nd-level analyses controlled for false positives using vertex-level uncorrected $p<.001$ threshold, and a cluster-level whole-brain FWE-corrected $p<.05$ threshold, Cluster- and ROI- level statistics obtained using permutation analyses (10000 simulations, permutation of residuals; Still et al., 1981).

### Identifying Functional ROIs In Speech Network

**Average activity clustering:** Watershed segmentation of the group-level *Speech-Baseline* statistical maps leads to ROIs divided along local minima in average functional responses. Preprocessing with 6 mm spatial smoothing kernel on the cortical surface results in approximately 150 distinct regions in each hemisphere. Only ROIs with significant average *Speech-Baseline* (FDR-corrected $p<.05$) were retained.

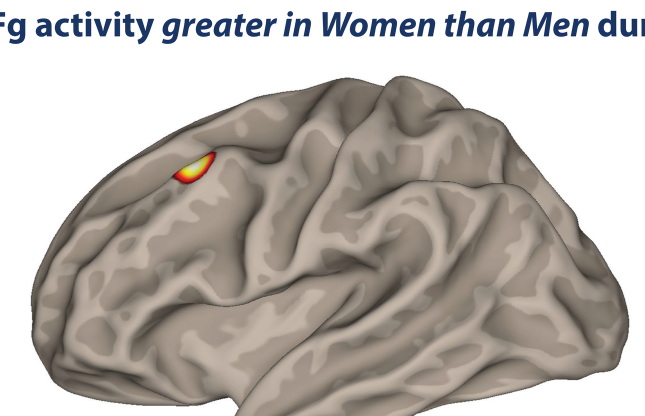
**Between-subjects variability clustering:** Neighboring vertices/ROIs sequentially grouped based on the similarity of their patterns of functional responses (minimization of within-ROI variability in *Speech-Baseline* contrast values across all subjects; Seghier et a., 2009). Resulting hierarchical tree trimmed to contain 100 ROIs per hemisphere. The average response within these ROIs accounted for 74% of the overall variability in responses across all vertices in the cortical surface. Only ROIs with significant average Speech-Baseline (FDR-corrected $p<.05$) retained.

## Summary

- Pooled analysis reveals distinct peaks within the Speech Production, network, characterized by *Average Activity Clustering.* In particular:
  - medial prefrontal/cingulate cortex; insular/opercular cortex
- *Between-Subjects Variability Clustering* indicated additional functionally distinct anterior-posterior bands in the core sensorimotor regions that subserve speech prodution
- Pooled analysis of *Perturbed>Non-perturbed* contrast revealed greater lateral frontal right hemisphere activity with distinct peaks in premotor cortex, inferior frontal gyrus, and anterior insula
- First step in building a functional-anatomical atlas for speech production

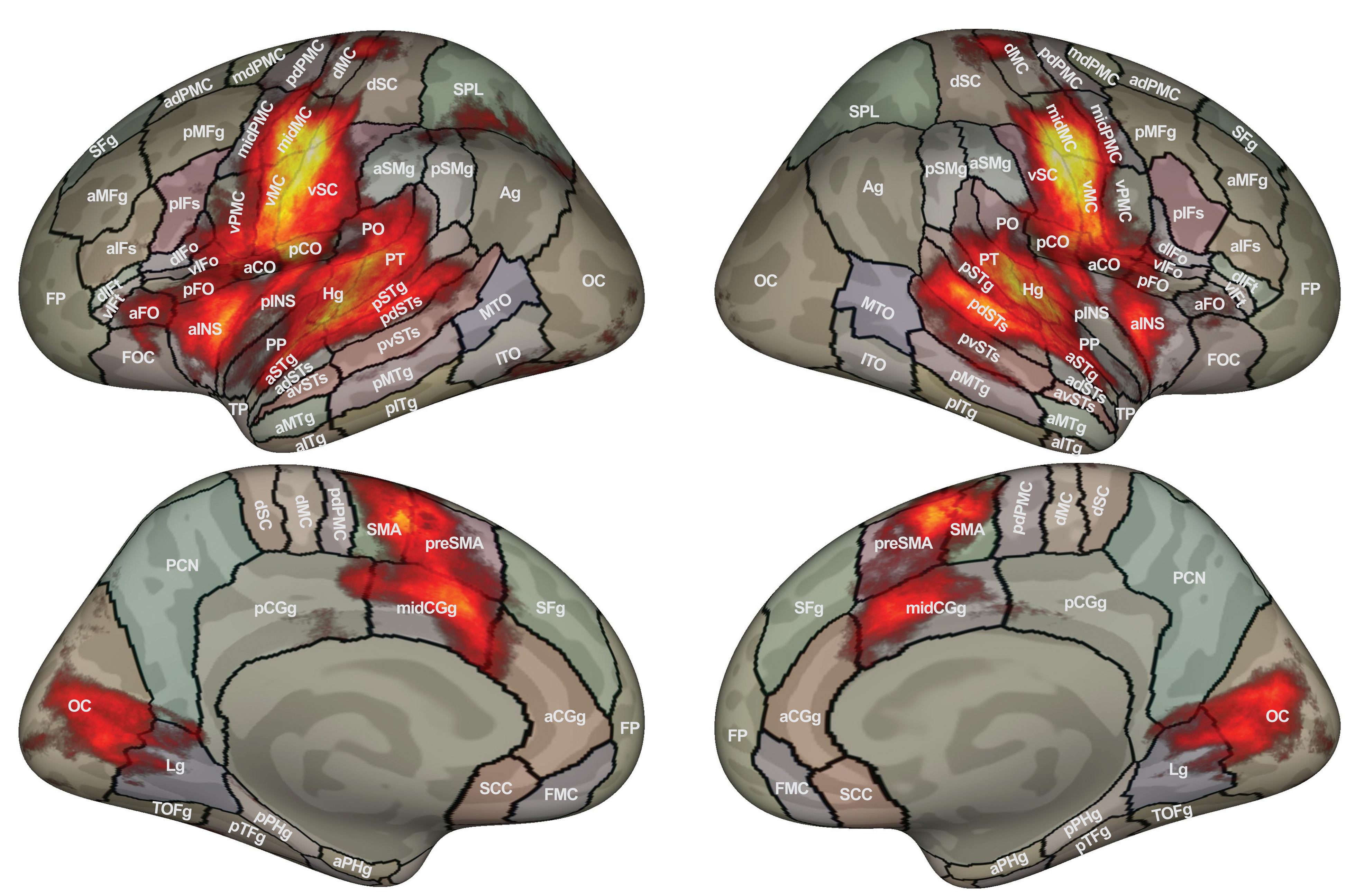
### Future Directions

- Integrate subcortical analysis
- Incorporate remaining studies (29 additional datasets) add more??
- Investigate functional and structural connectivity between functionally derived ROIs ... currently have ~90 DTI datasets
- Quantify functional-anatomical relationships
- Explore task, behavior, and demographic effects and compare to variability-based clustering to identify functional-anatomical relationships
  - e.g., **pMFg activity *greater in Women than Men* during speech:**



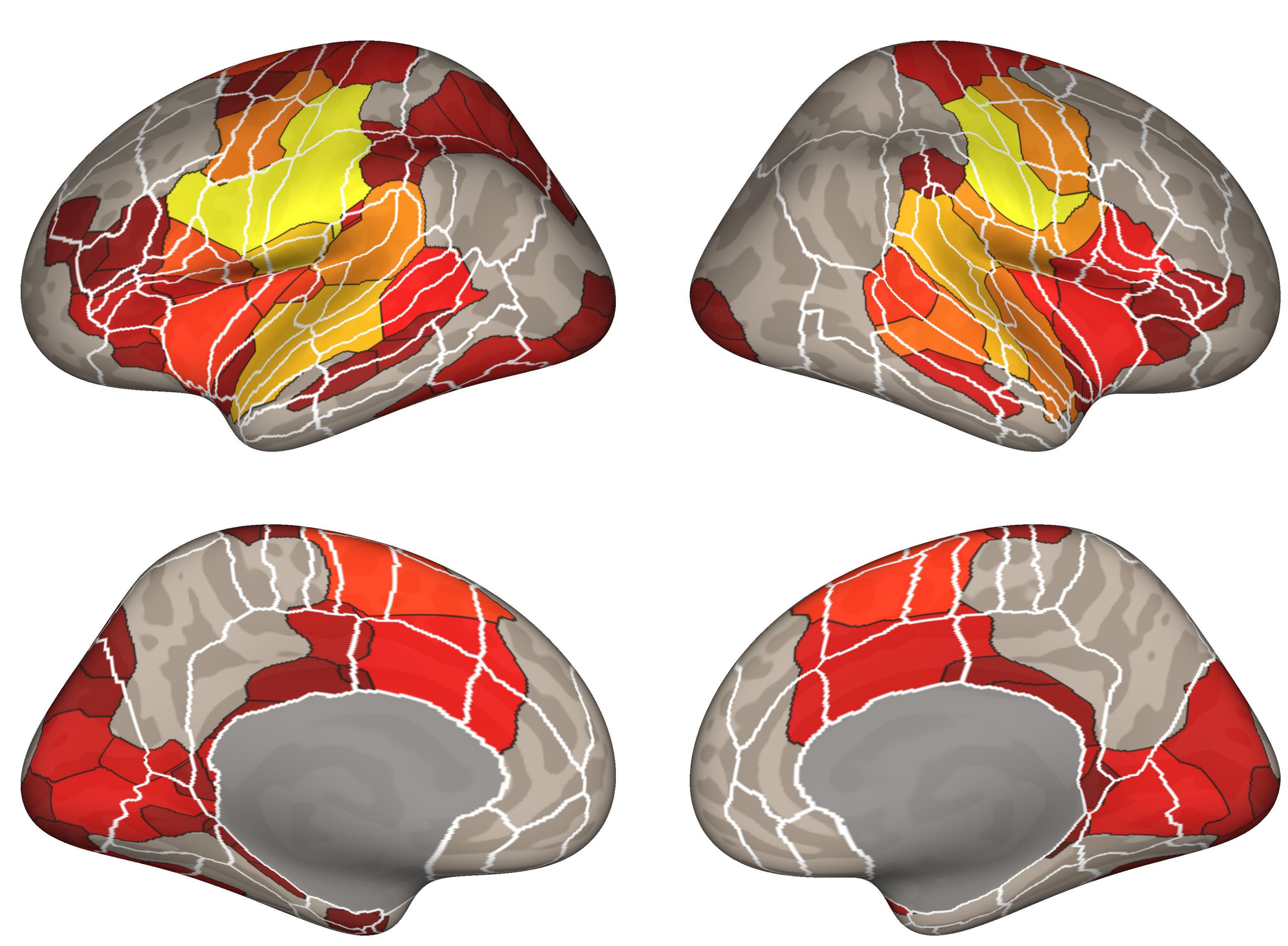
## Figure 1: Brain Regions Involved in Speech Production

*Speech-Baseline* Contrast, 130 subjects from 11 studies (51 Female; Median Age: 25, Range: 18-51). See Table 1 for details of individual study designs. Significant activity is overlaid on the inflated 'fsaverage' surface included in the FreeSurfer distribution. See Tourville & Guenther (2012) for anatomical region definitions.



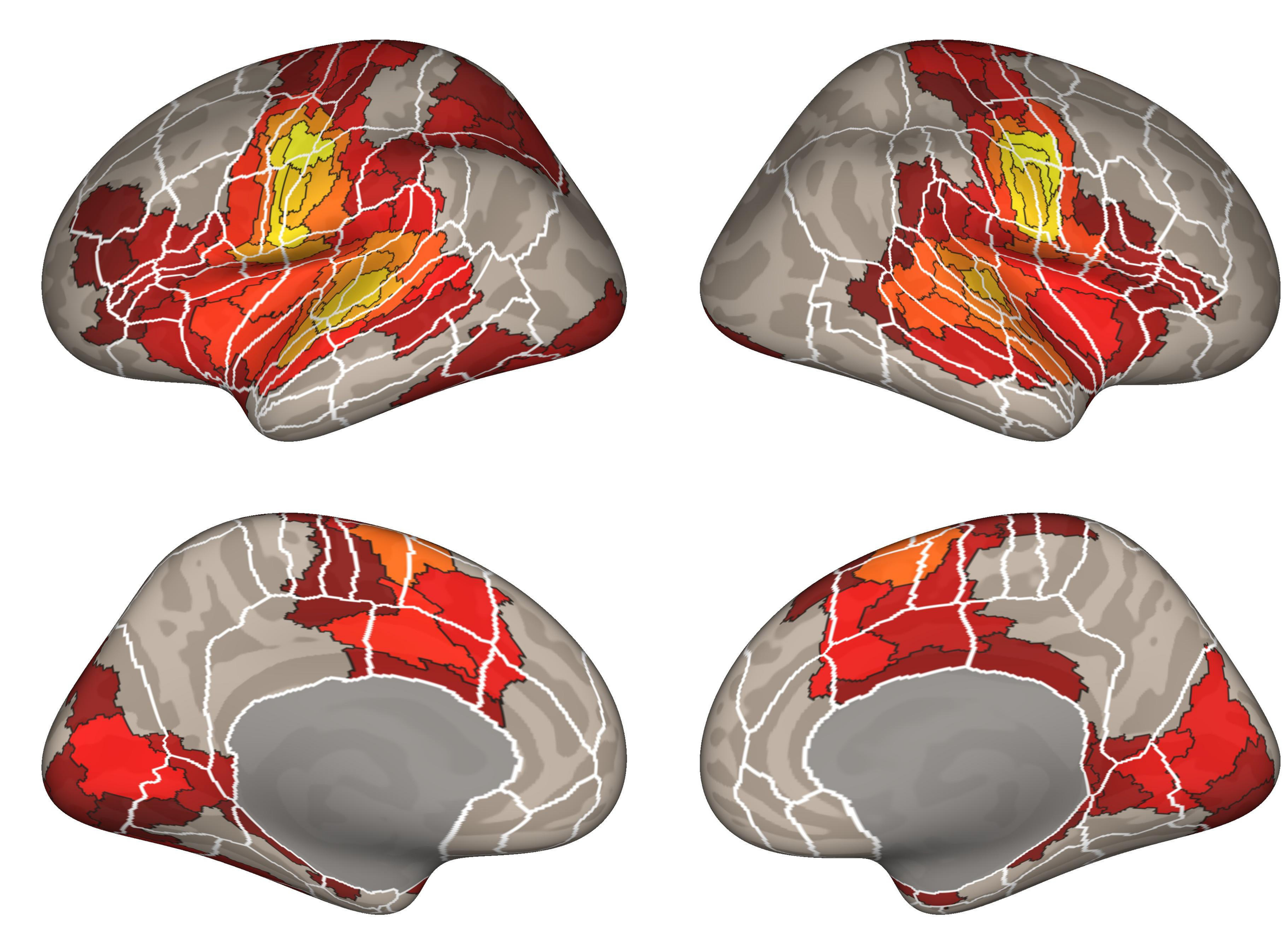

## Figure 2: Average Activity Clustering

155 ROIs in LH (69 significant), 166 in RH (45 significant)



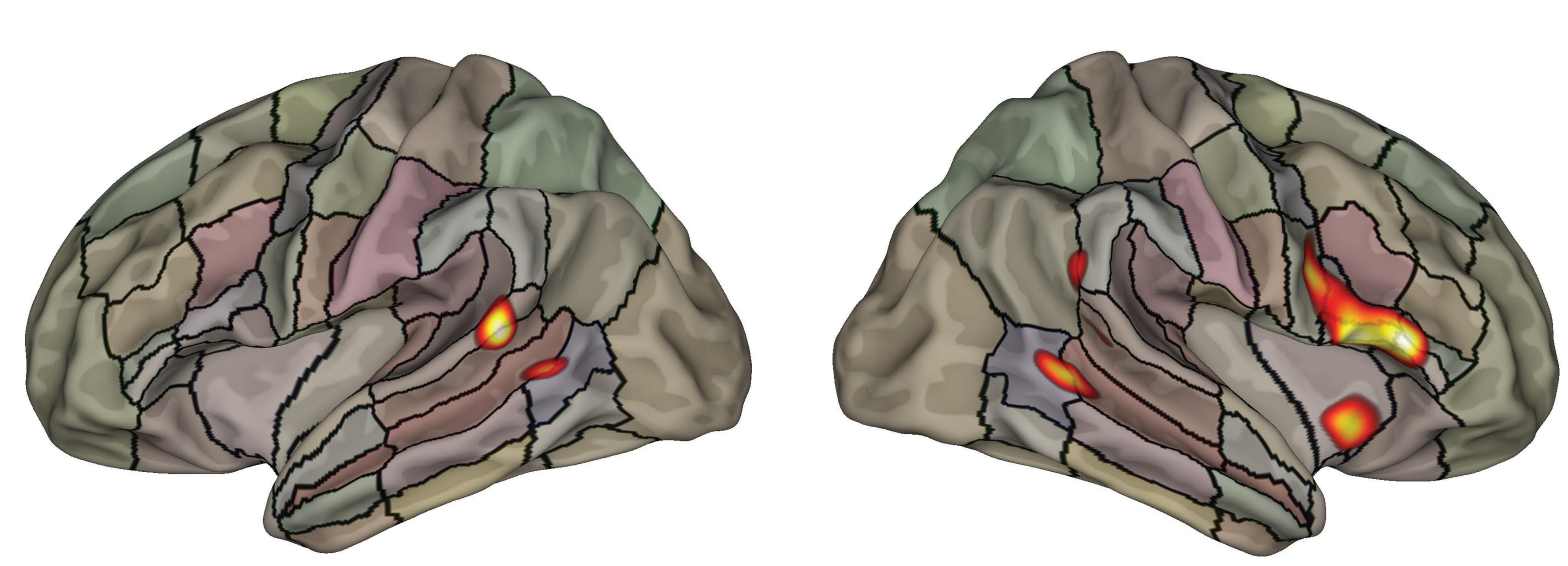
## Figure 3: Between-Subjects Clustering

100 ROIs in LH (59 significant), 100 in RH (52 significant)



## Figure 4: Feedback Control Network

*Perturbed Speech>Non-perturbed Speech* Contrast; 38 subjects from 3 studies (18 Female; Age Range: 19-51 ; Median: 26 ). See Table 1 (gray columns) for study designs.



### ROI-Level Cluster Activity

| | Activation Mass | ROI-Level *pFWE* |
|---|---|---|
| ***Left*** | | |
| pSTg | 1375 | .036 |
| ***Right*** | | |
| dIFo | 2148 | <.001 |
| vIFo | 1795 | <.001 |
| vIFt | 649 | .007 |
| vPMC | 2103 | .012 |
| pFO | 1277 | .017 |
| aFO | 1003 | .027 |
| aINS | 2344 | .031 |
| dIFt | 695 | .031 |

## Table 1: Studies In Analysis Pool

All subjects right-handed and speakers of American English unless otherwise noted. All data acquired on 3T scanners.

| | Sequence Learning | Sequence Learning in PWS | Speech Production in PWS | Speech Rate, Clarity, and Emphasis | Syllable Sequence Representation | Syllable Frame Representation | Consonant Cluster Representation | Overt Production | Auditory Shift | Auditory Category Shift | Somatosensory Perturbation |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Task** | Trisyllabic pseudowords with (legal/illegal) syllable frames that are novel/learned **Baseline:** "xxx" | Trisyllabic pseudowords with (legal /illegal) syllable frames that are novel/learned **Baseline:** "xxx" | Bisyllabic words (teacup", "topic" and "boutique") **Baseline:** "###" | 5-syllable sentences under fast, clear, emphatic, or normal conditions **Baseline:** Box characters | Bisyllabic pseudowords that varied in terms of their phonemic or suprasyllabic content **Baseline:** "XXXXX" | Monosyllabic pseudowords that varied in terms of their phonemic, frame, or syllabic content **Baseline:** "xxx" | Bisyllabic pseudowords that varied in terms of their phonemic, cluster, or syllabic content **Baseline:** "xxx" | Vowel (V), consonant–vowel (CV), or bi-syllabic (CVCV) pseudowords **Baseline**: "xxxxx" | Monosyllabic CVC words under normal or altered auditory feedback (F1 shifted up or down by 30%) **Baseline**: "yyy" | Monosyllabic CVC words under normal or altered auditory feedback (F1/F2 shift) resulting in within- or across-category change) **Baseline**: "***" | VV or VCV pseudowords under normal or perturbed somatosensory feedback (interdental block) conditions **Baseline:** "yyy" |
| **Subjects** | 12 (7F) Age: 26 (20-43) | 17 (2F) Age: 27 (18-43) | 16 (3F) Age: 26 (19-43) | 14 (7F) Age: 25 (18–35) | 18 (7F); *Fluent French* Age: 18-30 | 17 (9F) Age: 30 (20–43) | 16 (8F) Age: 30 (20-43) | 10 (3F) Age: 26 (19–47) | 10 (6F) Age: 28 (23–36) | 18 (9F) Age: 24 (19 – 33) | 13 (6F) Age: 30 (23–51) |
| **Equipment** | MGH Siemens Trio 32 Channel Coil | MGH Siemens Trio 32 Channel Coil | MIT Siemens Trio 32 Channel Coil | MIT Siemens Trio 12 Channel Coil | Marseille Bruker Medspec | MGH Siemens Trio 32 Channel Coil | MGH Siemens Trio 32 Channel Coil | MGH Siemens Allegra / Trio 12 Channel Coil | MGH Siemens Trio 12 Channel Coil | MGH Siemens Trio 32 Channel Coil | MGH Siemens Trio 12 Channel Coil |
| **Structural Acquisition** | 176 sagittal slices 1x1x1 mm | 176 sagittal slices 1 x 1 x 1 mm | 176 sagittal slices 1 x 1 x 1 mm | 171 sagittal slices 1 x 1.33 x 1.33 mm | 128 sagittal slices 1 x 1 x 1 mm | 176 sagittal slices 1 x 1 x 1 mm | 176 sagittal slices 1 x 1 x 1 mm | 128 sagittal slices 1 x 1 x 1.33 mm | 128 sagittal slices 1 x 1 x 1.33 mm | 176 sagittal slices 1 x 1 x 1.33 mm | 128 sagittal slices 1 x 1 x 1.33 mm |
| **Functional Acquisition** | **Sparse Sampled** 41 axial slices 3.1 x 3.1 x 3 mm 25% gap TA: 2.5 s; ITI: 10 s 1 Volume / Trial 40 Trials / Run 6-8 Runs / Subject | **Sparse Sampled** 41 axial slices 3.1 x 3.1 x 3 mm 25% gap TA: 2.5 s; ITI: 10 s 1 Volume / Trial 40 Trials / Run 6-8 Runs / Subject | **Sparse Sampled** 46 axial slices 3 x 3 x 3 mm 10 % gap TA: 2.4 s; ITI: 5 s 1 Volume /Trial 60 Trials / Run 3-4 Runs / Subject | **Sparse Sampled** 45 axial slices 3.1 x 3.1 x 3 mm 10 % gap TA: 2.75s; ITI: 14.75s 1 Volume / Trial 50 Trials / Run 4 Runs / Subject | **Block Design** 32 axial slices 3.1 x 3.1 x 3 mm 1 mm gap TR: 2.1 s Mean IBI: 14.5 s 35 Blocks / Run 3 Runs / Subject | **Block Design** 41 axial slices 3.1 x 3.1 x 3 mm 25% gap TR: 2.5 s IBI: 12 s 18 Blocks / Run 5-6 Runs / Subject | **Block Design** 41 axial slices 3.1 x 3.1 x 3 mm 25% gap TA: 2.5 s; IBI: 15 s 15 Blocks / Run 6-7 Runs / Subject | **Sparse Sampled** 30 axial slices 3.1 x 3.1 x 5 mm TA: 2s; Mean ITI: 16.5 s 2 Volumes / Trial 65 Trials / Run 2-3 Runs / Subject | **Sparse Sampled** 32 axial slices 3.1 x 3.1 x 5 mm TA: 2 s; ITI: 12 s 2 Volumes / Trial, 64 Trials / Run 3-4 Runs / Subject | **Sparse Sampled** 45 axial slices 3 x 3 x 3 mm 10 % gap TA: 2.75 s; ITI: 8 s 1 Volume / Trial 80 Trials / Run 5 Runs / Subject | **Sparse Sampled** 32 axial slices 3.1 x 3.1 x 5 mm No gap TA: 2 s; ITI: 11 s 2 Volumes / Trial 72 Trials / Run 3-4 Runs / Subject |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