Platform Session 4: Neural Bases of Language

159. Lesion Localization of Chronic Aphasia Syndromes

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Knowledge of the brain regions associated with the different types of aphasias has changed over the years since the advent of superior brain imaging techniques. Differences in lesion localization between acute and chronic patients have also become apparent with most current models being derived from patients in the acute stage of their illness. The present study evaluated the brain lesions associated with the major aphasia syndromes in a large group of carefully-controlled chronic aphasic stroke patients to evaluate these brain-behavior relationships once the aphasia has stabilized.

Methods
All patients had suffered a single left hemisphere infarction with a residual speech or language deficit. All were right-handed and native English-speaking with no prior neurological or psychiatric history, and were evaluated with the Western Aphasia Battery more than one year post onset. All had undergone structural neuroimaging, and patients' lesions were computer-reconstructed and normalized into MNI space. Patients classified into the different aphasia types were grouped together and their lesions overlapped to yield common areas of infarction.

Results (see figure)
Broca's aphasia. Results from 36 patients with chronic Broca's aphasia indicate a large region of common overlap primarily in the insula with involvement of surrounding tissue including white matter, motor cortex and the inferior frontal gyrus.

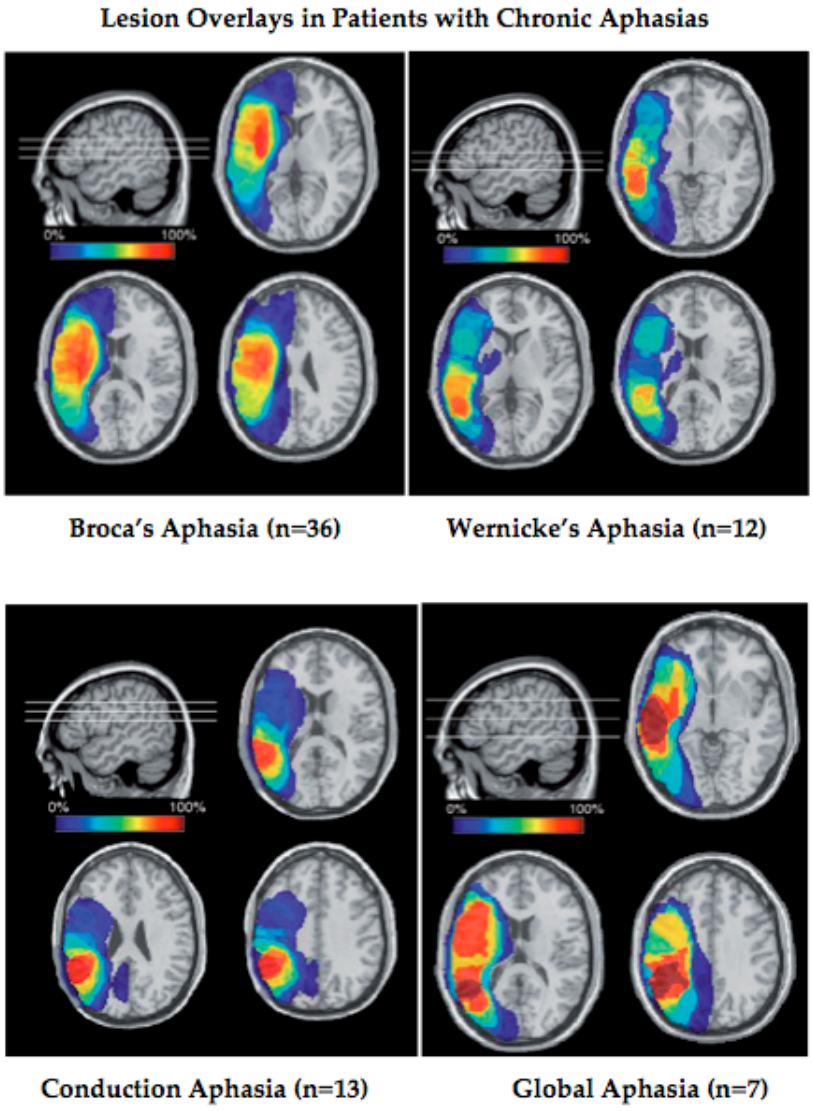
Wernicke's aphasia. The overlay of 11 patients' lesions reveals that the middle temporal gyrus is consistently infarcted in patients with persisting Wernicke's aphasia. Other areas commonly affected include the posterior, superior temporal gyrus and inferior parietal cortex.

Conduction Aphasia. The lesion overlay from 13 patients with chronic conduction aphasia shows the most common region of overlap is centered in inferior parietal cortex and the posterior superior temporal gyrus.

Global Aphasia. Overlays from 7 patients reveal that the lesion associated with a persisting, chronic global aphasia encompasses large portions of the left peri-Sylvian region. Key regions of common overlap include the middle and superior temporal gyri, insula and inferior frontal regions, the inferior parietal lobule, and white matter surrounding these areas.

Anomic aphasia. No single common region of overlap is found for this group of 37 patients. The lesions cover a wide range of areas extending over the middle and posterior cerebral artery distributions of the left hemisphere.

Discussion
Lesion overlays in chronic aphasic patients, whose behavior has stabilized, reveal consistent areas of infarction in the same general areas as derived from acute data, but also with some fundamental differences. Lesions in chronic Broca's aphasia involve primarily deeper areas than Broca's area and include the insula and underlying white matter. Lesions in chronic Wernicke's aphasia often include Wernicke's area, but the key region was the middle temporal gyrus. In chronic conduction aphasia, the area of common infarction is the inferior parietal cortex and posterior superior temporal gyrus, rather than the arcuate fasciculus. These results suggest important differences in the lesion patterns between acute and chronic patients that can significantly alter our perceptions of the key brain areas involved in the different aphasia syndromes.



Colored bars indicate the degree of lesion overlap across patients, from 0% (dark blue) to 100% overlap (dark red).

Presented by: **Dronkers, Nina**

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160. Areas of Ischemia Associated with Semantic vs. Phonological Errors in Auditory Comprehension

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Introduction
We previously reported data from 289 unselected acute left hemisphere stroke patients on a test of auditory word/picture verification showing that severe impairments of word comprehension (using signal detection methods

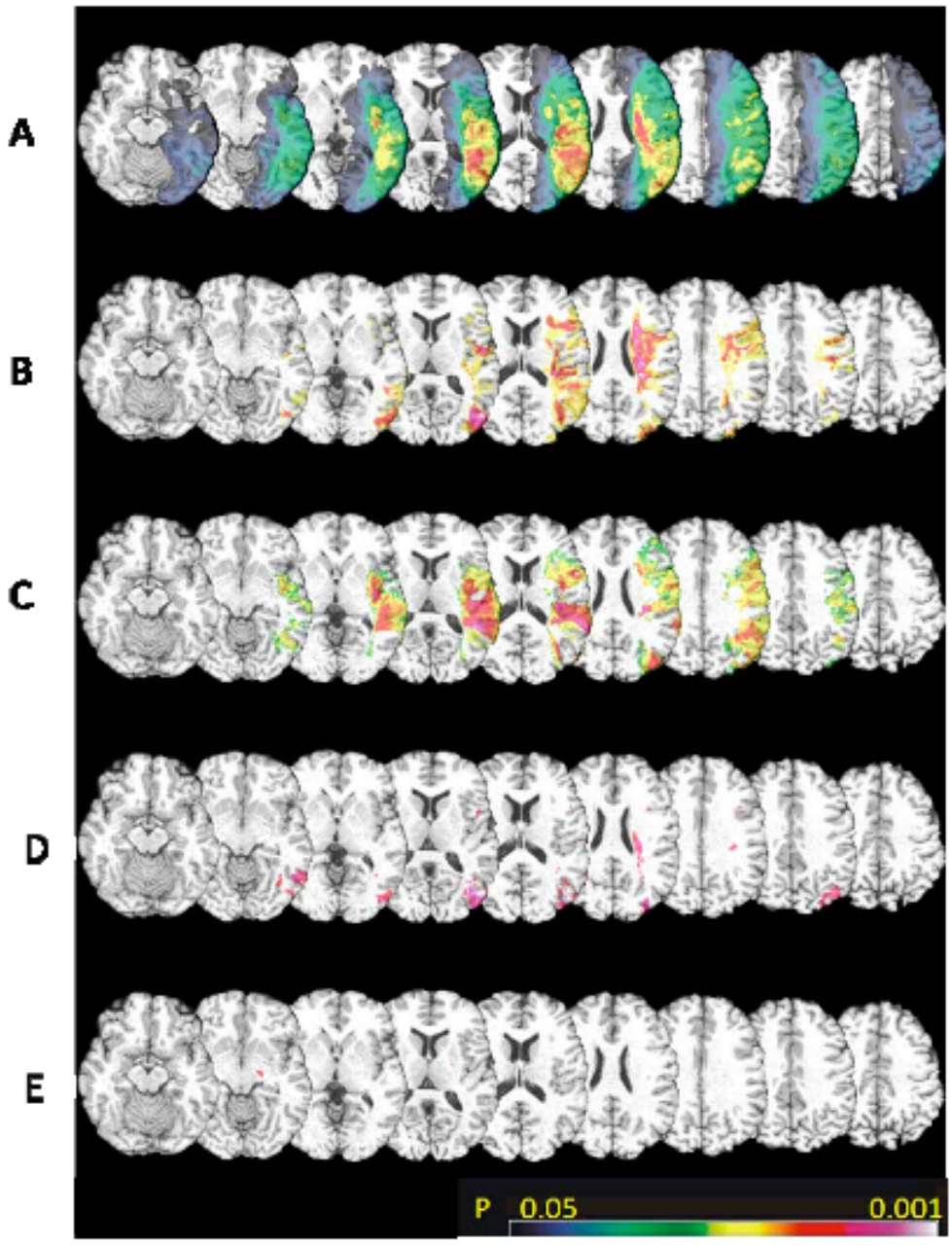
to control for response bias) are relatively uncommon, and that semantic errors are more common than phonological errors. A majority of patients showed higher proportions of correct responses, corrected for response bias (measured with a-prime) with phonologically related foils than with semantically related foils. In this study, we identified areas of dysfunctional (infarcted and/or hypoperfused) tissue associated with (1) a predominance of semantic errors, (2) equivalent performance with semantically and phonologically related foils, and (3) a predominance of phonological errors in patients who made more than 10% errors on the test (> 2 SD more than controls).

Method
We analyzed data from the subset of patients (n=120) from the previous study who had interpretable diffusion-weighted and perfusion-weighted MRI as well as assessment of spoken word comprehension within 24 hours of stroke onset. Dysfunctional tissue was defined as bright on diffusion weighted imaging (DWI) and dark on apparent diffusion coefficient maps, or hypoperfused as defined by greater than 4 second delay in time to peak arrival of contrast in a voxel, relative to the homologous voxel on the right. We used MRICroN to identify voxels associated with each pattern of errors, using a False Discovery Rate (FDR) analysis to correct for multiple comparisons.

Results
The figure shows the "prior probability map" - areas of hypoperfusion/infarct of all 120 included patients (Panel A), voxels associated with normal performance (<10% errors) (Panel B), as well as voxels most strongly associated with each error pattern. Normal performance (n= 34 patients) was associated with infarct/hypoperfusion in frontal and fusiform cortex and corona radiata. Production of equal numbers of errors with phonological and semantic foils (n= 9) was associated with infarct/hypoperfusion in left posterior superior temporal cortex. Production of more semantic than phonological errors (n= 65) was associated with infarct/hypoperfusion in inferior temporal and parietal cortex. There were few scattered subcortical voxels associated with more phonological errors than semantic errors (n= 12), but no clear region. This pattern was uncommon (14.0% of patients with deficits).

Discussion
Patients with the most severely impaired auditory word comprehension made errors equally with semantically related and phonologically related foils. These patients had tissue dysfunction (infarct/hypoperfusion) predominantly in Wernicke's area. Patients who accurately rejected phonologically related foils that were not semantically related to the target, but incorrectly accepted some semantic foils had more posterior and inferior temporal or inferior parietal tissue dysfunction. Few patients made more errors with phonological foils than semantic foils. Tissue dysfunction in posterior frontal cortex or corona radiata was associated with normal performance on word/picture verification. Future analyses of these data will evaluate the independent contributions of ischemia in various regions of interest and total volume of dysfunctional tissue in accounting for the rate of errors with semantic and phonological foils.

Figure. Voxels Where Tissue Dysfunction was Associated with each Pattern of Errors. Panels: A. Prior probability of lesion localization expressed as number of lesions per group, B. Voxels associated with normal performance,C. Voxels associated with equal numbers of semantic and phonological errors; D. Voxels associated with predominantly semantic errors; E. Voxels associated with predominantly phonological errors.



Presented by: **Hillis, Argye**

161. Anatomical Correlates of Spelling Errors in Primary Progressive Aphasia

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Objective
Primary progressive aphasia (PPA) has recently been divided into three clinical subtypes that appear to be associated with different regions of cortical atrophy and hypometabolism and loosely associated with different pathologies (Rabinovici, Jagust, Furst, Ogar, Racine, Mormino, O'Neil, Lal, Dronkers, Miller, Gorno-Tempini, 2008). One of the earliest symptoms of PPA can be spelling difficulties, arising before verbal features that distinguish between subtypes. At present, there is no way of predicting from their spelling behavior which clinical subtype a patient is likely to develop.

Methods
To identify regions where cortical loss predicts single word spelling difficulties, we acquired high-resolution structural MRI from 10 patients with a clinical diagnosis of PPA who had a range of severity of spelling impairment and other language impairments. Continuous measures of gray matter density were correlated with continuous measures of spelling error types on a voxel by voxel basis across the whole brain. The most common error types, phonologically plausible errors (PPEs; e.g. couch spelled kowtch) and phonologically implausible nonwords (PINs e.g. couch spelled cuopth), were included in the analyses.

Results
Damage to two discrete left hemisphere brain regions was significantly associated with spelling difficulties: head of the caudate (x -18, y 26; z 2; z score= 4.52; cluster size=119 voxels) and anterior temporal pole (x -30, y 14, z -38; z score= 4.58; cluster size 54 voxels), p=0.001 uncorrected for the whole brain; p=0.05 corrected at a cluster level (See Figure 1). In addition there was a double dissociation between patterns of gray matter loss and the types of spelling errors patients produced. Increasing gray matter damage to the caudate correlated with increasing numbers of PINs, whereas preservation of the caudate was correlated with PPEs. In contrast, increasing damage to the anterior temporal lobe was correlated with increasing numbers of PPEs, whereas preservation of the anterior temporal lobe region was correlated with PINs.

Interpretation
Patients who produce a high rate of PPEs but low rate of PINs on spelling tasks have a high likelihood of having gray matter loss in the left anterior temporal lobe. Semantic dementia (SD) is associated with left (>right) anterior and inferior temporal lobe atrophy, and are known to frequently have surface dyslexia and dysgraphia, with a high rate of PPEs. However, the dysgraphia may precede other features of SD, and may be helpful in predicting the eventual diagnosis. The association between a high rate of PINs and low rate of PPEs in spelling and gray matter loss in the left caudate is a novel finding and may be most common in patients who will progress to PNFA. However, longitudinal studies are required to evaluate these hypotheses.

Reference
Rabinovici, G.D., Jagust, W.J., Furst, A.J., Ogar, J.M., Racine, C.A., Mormino, E.C., O'Neil, J.P., Lal, R.A., Dronkers, N.F., Miller, B.L., Gorno-Tempini, M.L (2008). Aβ amyloid and glucose metabolism in three variants of primary progressive aphasia. Annals of Neurology, 68, 388-401.

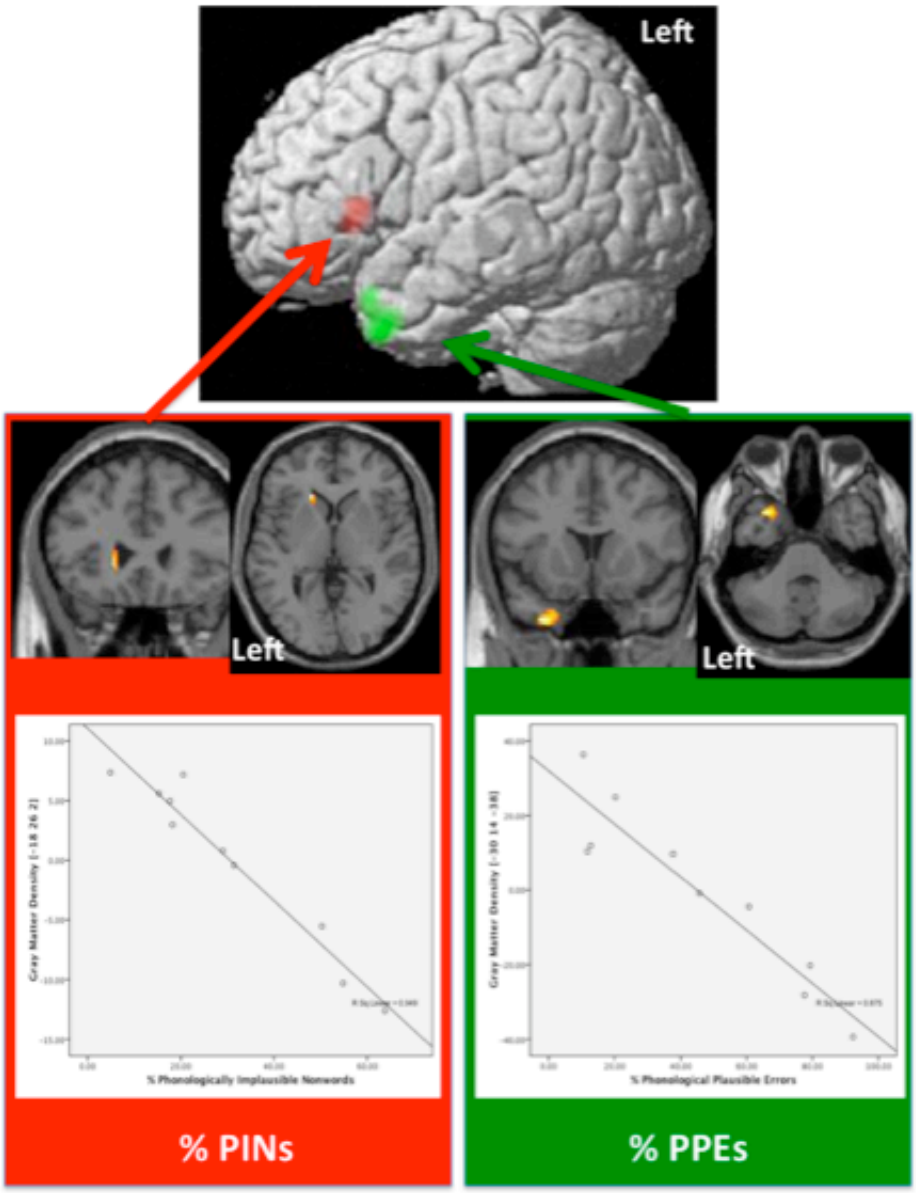

Figure: Regions where brain damage is associated with spelling difficulties.
The top image illustrates voxels where there were significant correlations between regional gray matter density and single word spelling in an analysis of 10 PPA patients. The results are rendered here on a SPM5 template brain. The colors relate to the type of spelling errors made: red= phonologically implausible nonwords (PINs) and green= phonologically plausible errors (PPEs). The left column (red background) of images and plot illustrate where gray matter loss in the head of the left caudate correlates significantly with increased PINs. The right column (green background) of images and plot illustrate where gray matter loss in the anterior temporal lobe correlates significantly with increased PINs. The results are displayed in these columns on sagittal and coronal slices of a SPM5 single-subject brain T1 template.

Presented by: **Crinion, Jenny**

162. Anterior Temporal Involvement in Semantic Word Retrieval: VLSM Evidence from Aphasia

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Introduction
The task of naming pictures invokes semantically-driven lexical retrieval, as shown by the occurrence of semantic errors in healthy speakers and, more prominently, people with aphasia. To examine the brain basis of semantic word retrieval, this study mapped the lesions associated with semantic naming errors in post-stroke aphasia using voxel-based methods.

Methods
We report on 64 right-handed English speakers (42% female; 48% minorities) with left hemisphere stroke and aphasia. Mean for age was 58 + 11, education, 14 + 3; months post onset, 68 + 78, and WAB AQ (76.8 +15.2). From the 175-item Philadelphia Naming Test (PNT), the semantic error score (SemErr) was computed as a proportion of total items. Additionally, standard scores on four semantic comprehension tests were averaged to create a measure of core semantic processing (CoreSem).
Lesions from patients with recent high-resolution MRI scans [n = 34] or CTs [n = 30] were segmented manually and registered to a standard 1x1x1mm template. In each voxel that was lesioned in at least 5 patients, a t-test was computed comparing SemErr scores between patients with and without lesions in the voxel. The resulting t-map was thresholded to control the False Discovery Rate (FDR) at 0.01. In a second analysis, errors arising during conceptualization were factored out by mapping the (SemErr – CoreSem) residuals.

Results
We found 25,669 voxels for which there was a significant correlation between lesion status and SemErr. The highest t-value voxels were in left anterior temporal lobe (ATL); the highest concentration was in the middle temporal gyrus and the temporal pole. Clusters of significant voxels were also found in the posterior portion of the middle temporal gyrus (lateral and superior portion of BA 37), and in the inferior and middle frontal gryi (BA 45 and 46). There were no significant voxels in the posterior superior temporal gyrus (Wernicke's area); peak t-values here were approximately 1.8, far below the critical t (3.86).
Filtering out CoreSem changed the strength of effects but not the pattern (see Figure 1). The majority of significant voxels (7,332) were in the mid- and anterior temporal lobe, thus implicating this region, specifically, in the mapping from semantics to lexical items during production.

Discussion
Aphasia lesion studies have long linked semantic word retrieval to left posterior temporal and parietal regions. Instead, we found the strongest effects in mid- and anterior temporal lobe. Drawing on evidence from semantic dementia (Patterson, Nestor & Rogers, 2007) and functional neuroimaging (Indefrey & Levelt, 2004), we suggest that this role is one of transmitting information from an ATL semantic hub to lexical representations localized in the mid part of the left middle temporal gyrus.

References
Indefrey, P., & Levelt, W. J. M. (2004). The spatial and temporal signatures of word production components. Cognition, 92(1-2), 101-144.
Patterson, K., Nestor, P. J., & Rogers, T. T. (2007). Where do you know what you know? The representation of semantic knowledge in the human brain. Nature Reviews Neuroscience, 8, 976-987.

Acknowledgements
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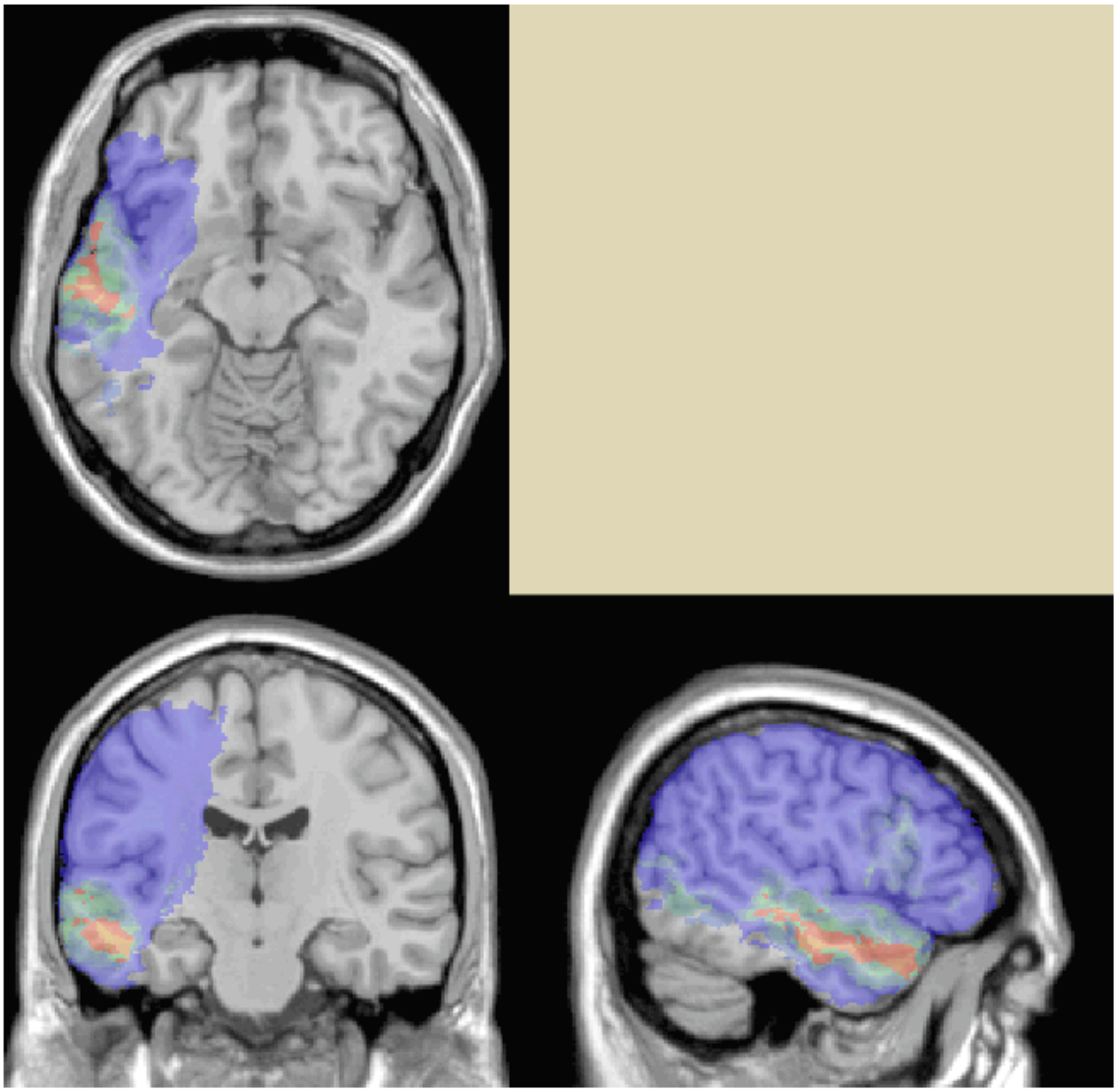

Figure 1. Representative axial, coronal, and sagittal views of a map of the reliability of the difference in SemErr (after factoring out CoreSem) between patients with and without lesions in each voxel (rendered on the MNI-space ch2 volume). Voxels with a statistically significant result after correction for multiple comparisons are rendered in a red ($t = 3.86$) to yellow ($t > 5.86$) scale, while non-significant values are rendered on a scale from green (t just below 3.86) to blue ($t < 1.86$).

Presented by: **Schwartz, Myrna**