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Neural Processing Critical for Distinguishing Between Speech Sounds

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Abstract

We aimed to identify neural regions where ischemia acutely after stroke is associated with impairment in phoneme discrimination, and to determine whether such deficits are associated with impairment of spoken word comprehension. We evaluated 33 patients within 48 hours of left hemisphere ischemic stroke onset with tests of phoneme discrimination and word-picture matching. We identified Pearson correlations between accuracy in phoneme discrimination and accuracy of word comprehension and identified areas where the percentage of infarcted tissue was associated with severity of phoneme discrimination deficit. We found that 54% had deficits in phoneme discrimination relative to healthy controls. Accuracy in phoneme discrimination correlated with accuracy on word comprehension tests. Damage to left intraparietal sulcus and hypoperfusion and/or infarct of left superior temporal gyrus were associated with phoneme discrimination deficits acutely, although patients with these lesions showed improvement or resolution of the deficit by six months.

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Keywords

phoneme discrimination; acute ischemic stroke; auditory processing; lesion-deficit mapping

1. INTRODUCTION

The earliest stages of spectrotemporal analysis of speech in auditory cortex appear to be bilateral, as indicated by roughly symmetric functional activation to speech (compared with rest) (Binder *et al.,* 1994), bilateral lesion patterns associated with pure word deafness (Buchman *et al.,* 1986; Poeppel, 2001), and the relatively spared ability of the isolated right hemisphere to recognize words (Zaidel, 1985; Hickok *et al.,* 2008); see (Hickok and Poeppel, 2007) for review. However, unilateral left hemisphere lesions have been shown to disrupt phonemic processing in the context of nonword syllable identification and same-different discrimination tasks (Blumstein *et al.,* 1977; Jauhiainen and Nuutila, 1977; Miceli *et al.,* 1978; Miceli *et al.,* 1980; Caplan *et al.,* 1995), with one study linking deficits to the supramarginal gyrus and parietal operculum (Caplan *et al.,* 1995). A similar finding emerged from a much larger study of chronic stroke that implicated not only the temporal-parietal junction area but also auditory cortex in the superior temporal gyrus (Rogalsky *et al.,* submitted). Impairments on such tasks have also been demonstrated with transcranial magnetic stimulation (TMS) to left motor-related regions (Meister *et al.,* 2007; D'Ausilio *et al.,* 2009). These and other findings have led to the proposal that discrimination and identification tasks rely to some extent on dorsal stream sensorimotor speech circuits, in contrast to word comprehension tasks, which rely on resources primarily in the temporal lobe (Hickok and Poeppel, 2000; Hickok and Poeppel, 2004; Hickok and Poeppel, 2007).

However, one study of 10 individuals with impaired phoneme discrimination chronically after stroke (time post stroke was not reported) also identified other potentially important areas (Caplan *et al.,* 1995). Of the 10 individuals with deficits, seven had lesions involving: posterior temporal gyrus, including Heschl's gyrus and planum temporale angular gyrus; anterior supramarginal gyrus (SMG); central operculum; and/or insula. Eight of 10 had damage to posterior SMG and parietal operculum. Only two individuals had no damage to any of these areas. The frequency of damage to these areas in left hemisphere stroke patients without deficits was not identified. The same paper reviewed published case reports of individuals with chronic phoneme discrimination deficits; in eight of nine cases with adequate description of the lesions, damage to left STG was reported; seven of nine cases had damage to left parietal cortex (in one case isolated to angular gyrus). However, only lesion extent in left posterior SMG and parietal operculum correlated with *severity* of deficit in phoneme discrimination.

One study with an effective sample of 90 individuals with predominantly subacute left hemisphere lesions (including stroke, tumor, and resection), found that 14 (15.6%) were impaired in phoneme discrimination. The deficits generally had resolved by four months post-stroke (Varney, 1984). Importantly, all of the participants with phoneme discrimination deficits had impaired spoken word comprehension, suggesting that phoneme discrimination may tap into processes needed for auditory word comprehension (as proposed by Luria,

1970). However, we analysed their published data and found that there was, in fact, no correlation between phoneme discrimination and auditory comprehension ($r^2 = .03$, $p = .56$) consistent with previous reports of the double-dissociability of discrimination and comprehension speech tasks (Hickok & Poeppel, 2004).

Analysis of phonological discrimination in *acute* stroke before compensatory reorganization can occur would be important to identify the brain regions that are normally critical for phonological discrimination. The study of acute stroke also allows assessment of all brain regions that are typically affected by stroke, to determine whether or not damage to the region causes impairment. Unlike the study of people with chronic aphasia, investigations of acute stroke also include patients with small lesions, to identify relatively selective deficit. Therefore, this paradigm is well suited to examine the relationship between phonological discrimination and spoken word comprehension.

The current study had three goals: 1) identify the frequency of phoneme discrimination deficits acutely after stroke (within 48 hours) and their relation to chronic deficits (at 6 months post-stroke or later); 2) identify the association between impairments in phoneme discrimination and spoken word comprehension acutely; and 3) identify areas of tissue dysfunction (infarct and/or hypoperfusion) associated with acute deficits in phoneme discrimination.

2. METHODS

2.1. Participants

A series of 33 patients with acute ischemic left hemisphere stroke were enrolled at Johns Hopkins Hospital or Johns Hopkins Bayview Medical Center upon meeting the following inclusion criteria: the presence of unilateral left hemisphere infarct on diffusion-weighted imaging (DWI); able to provide informed consent or indicate a decision-maker to provide informed consent; premorbid proficiency in English; premorbid right-handedness, and testable within 48 hours of stroke onset. Exclusion criteria were: history of dementia, previous symptomatic stroke, or other neurological disease affecting the brain; reduced level of consciousness determined by difficulty attending to tasks or ongoing sedation, hearing loss by medical records or self-report, or uncorrected vision loss; and hemorrhage on initial scan. Mean age was 57 (SD 16) years. A smaller subset of 12 patients had repeat language testing 3, 6, and/or 12 months later. Of these 12 participants, 11 also had perfusion weighted imaging (PWI) at onset. One person in this subset did not have PWI at onset, but had infarct in left STG. The study was approved by the Johns Hopkins Institutional Review Board, in accord with the Declaration of Helsinki.

We also enrolled 28 participants with no history of neurological disease, matched in age and education to the stroke survivors, as healthy controls. Control participants were recruited from Baltimore and San Diego.

2.2. Language Tests

2.2.1. Phoneme (Syllable) Discrimination Task—The syllable discrimination task (Rogalsky *et al.,* 2011; 2015) is modeled on previous discrimination tasks used with

individuals with aphasia (Blumstein *et al.,* 1977; Baker *et al.,* 1981; Caplan and Waters, 1995). This task contained 64 trials, each involving the presentation of a pair of one-syllable non-words. Each non-word was created by changing the vowel sound of a CVC or CV word (selected from those used in the word comprehension tasks below, plus an additional eight words) so that a phonologically possible but meaningless non-word was generated. The stimuli were recorded by a male talker and presented through headphones. The interstimulus interval between the two stimuli to discriminate was 1 second, and the time between trials was 5 seconds. Patients were instructed to determine if the two syllables presented were the same or different. "Different" trials contained two syllables that differed by one feature of the onset consonant (e.g. "piz" vs "kiz"). The 64 trials were comprised of 16 non-word pairs presented in four arrangements: A-B, B-A, A-A, and B-B such that for half of the trials the correct answer was "same", and for the other half the correct answer was "different". In the "same" trials, two different tokens of the same syllable were presented. Patients made their response either by saying "same" or "different" or by pointing to the words "same" or "different" written in large print.

2.2.2. Word Comprehension Tasks—Two forced choice word-to-picture matching tasks, with four picture options per trial, previously used by (Rogalsky *et al.,* 2011) and similar to Baker, Blumstein & Goodglass' (Baker *et al.,* 1981) paradigm, were administered. In each trial, an auditory word was presented after the appearance of a picture array depicting four objects. The participant was instructed to point to the picture (or otherwise indicate if the participant had motor deficits) that matched the auditory word.

In the *mixed foil word comprehension task,* there were 20 trials; and each picture array contained the target, one phonological foil, one semantic foil, and one unrelated foil (e.g. target was "coat", foils were "goat", "shoe", and "pig", (see Figure 2 in Rogalsky *et al.,* 2011). Ten of the 20 trials in the mixed foil test contained a phonological foil that represented a minimal pair to the target (four place of articulation contrasts, four voicing contrasts, and two manner contrasts). The auditory stimuli were counterbalanced such that within each variant, each picture in each array was presented once as the target.

In the *phonological foil word comprehension task*, the picture array contained the target and three phonological foils (e.g. target was "mail", foils were "nail," "tail" and "pail", see Figure 2 in Rogalsky et al. 2011). A subset of seven of the control subjects completed 24 trials of the phonological foil word comprehension task; the remaining 21 controls completed 20 trials due to differences in the testing protocol across collection sites. All stroke patients completed the 20 trial version. Twenty-one of the 24 trials and 16 of the 20 trials in the two phonological foil task versions contained at least one foil that represented a minimal pair to the target, with the contrasts distributed across place of articulation, voicing and manner. Percent correct for each subject's overall performance was calculated in each word comprehension task.

2.3. Imaging

Within 24 hours of language testing, all patients underwent MR imaging, including apparent diffusion coefficient (ADC) maps, DWI trace images, which together reveal infarct or dense

ischemia soon after stroke onset. A subset of individuals also underwent PWI, which reveals areas of hypoperfusion corresponding to dysfunction. Hypoperfusion was defined as >4 s delay in time to peak (TTP) arrival of contrast to the voxels relative to homologous voxels in the right hemisphere, based on evidence that delays of this threshold are associated with tissue dysfunction (Hillis *et al.,* 2001).

2.3.3. Image Analysis—Technicians blinded to the language evaluation results identified the presence or absence of tissue dysfunction. Tissue dysfunction was defined as dense ischemia/infarct (bright on DWI and dark on ADC maps) and/or significant hypoperfusion on PWI. These areas of tissue dysfunction were traced using MRIcron (http://www.sph.sc.edu/comd/rorden/mricron) and then co-registered using SPM12 (https://www.nitrc.org/projects/clinicaltbx/) to the Montreal Neurological Institute (MNI) atlas (http://www.bic.mni.mcgill.ca/ServicesAtlases/ICBM152NLin2009). This normalization allows for comparisons across the individuals in our study while preserving individual local features of each brain (Rorden and Brett, 2000). Lesion overlap maps were created in the larger group (those with DWI and ADC, but no PWI) using normalized DWI trace images and their associated lesion tracings, both for patients with impaired phoneme discrimination (n=18) and those with unimpaired phoneme discrimination (n=15).

2.4. Statistical Analysis

We compared differences between groups on continuous variables using one way ANOVA (for 3 groups) or t tests (for 2 groups), and differences between groups on dichotomous variables using chi square or Fisher's exact tests. We also identified the Pearson correlations between accuracy of phoneme discrimination and word comprehension tests (and each with lesion volume).

2.4.1. Behavioral analysis—Percent error for each participant was calculated along with A'. A' is based on signal detection methods to determine how well subjects could discriminate between the same and different pairs. It is a non-parametric version of the more familiar d' statistic. Measuring A' allows for the measurement of performance sensitivity independent of response bias or guessing strategies. For A' analyses, the proportion of hits (correctly saying both items were the "same") and false alarms (saying the items in the non-word pair were the "same" when the correct answer was "different") was calculated. We used the following formula (Zhang & Mueller, 2005) to calculate A':

$$A = \begin{cases} \frac{3}{4} + \frac{H-F}{4} - F(1-H) & \text{if } F \le 0.5 \le H; \\ \frac{3}{4} + \frac{H-F}{4} - \frac{F}{4H} & \text{if } F \le H < 0.5; \\ \frac{3}{4} + \frac{H-F}{4} - \frac{1-H}{4(1-F)} & \text{if } 0.5 < F \le H. \end{cases}$$

A' analyses included 27 of our 33 participants because responses to each item were not available for the remaining 6 participants, making it impossible to calculate their A' scores.

2.4.2. Lesion mapping—We initially used parcel-symptom lesion mapping to identify any parcels in the different anatomical regions on the AICHA atlas (Joliot *et al.,* 2015) where the percentage of infarcted voxels (on DWI, in the entire set of 33 patients) was associated with severity of phonological discrimination deficits (measured by percent error) using GLM (pooled-variance *t* test, linear regression). Each analysis only included regions where at least three patients had damage. All *t* scores were transformed to Z scores using SPM12's spm_t2z function, as interpreting Z scores excludes the need to know the degrees of freedom. Resulting statistical maps were thresholded to correct for multiple comparisons using 5,000 permutations (one-tailed $p < 0.05$, as we predicted injury would be associated with impairment) using the open source NiiStat (https://github.com/neurolabusc/NiiStat) routines and the methods described by (Rorden *et al.,* 2007). We repeated this mapping in the subset of 27 participants for whom we could calculate d' statistics.

We sought to identify areas where tissue dysfunction (infarct and/or hypoperfusion) were associated with phoneme discrimination deficits acutely and at follow up, in the smaller subset of 12 patients who had longitudinal testing (and PWI). Given the smaller number of patients, we used non-parametric statistics with dichotomized values of phoneme discrimination impairment and tissue dysfunction. Associations between the presence of phoneme discrimination deficits and the presence of tissue dysfunction (hypoperfusion and/or infarct) in five language network regions of interest (ROI: left superior temporal gyrus (posterior to the pole); supramarginal gyrus, angular gyrus, arcuate fasciculus, and inferior frontal gyrus) were tested with Fisher's exact tests. Additionally, participants were classified as having improved, not improved (no change), or declined on each of the language tests from the initial stage to either the chronic time point (>6 months post-stroke) using absolute values for change (not thresholded). We evaluated the association between improvement in phoneme discrimination and reperfusion of each the ROIs.

3. RESULTS

There were no significant differences between groups (healthy controls, stroke patients with impaired phoneme discrimination, and patients with normal phoneme discrimination) in age, education or racial distribution (see Table 1).

3.1. Behavioral Results

3.1.1. Control participants—made no or few errors in *phoneme discrimination*; the mean accuracy was 97.7% (SD 2.7). Therefore, we used a score of < 92.3% (> 2 SD below the mean) as the threshold for defining a phoneme discrimination deficit measured in error rate. Using A' data, the mean score for controls was 0.9951 (SD 0.0058). We used an A' of <0.9835 (>2 SD below the mean) to identify abnormal A'. For the *word-picture matching tasks,* all but one of the controls were 100% correct on both tasks; one participant scored 95%. Therefore, we used a cut off of <95% correct as the threshold for word comprehension deficit.

3.1.2. Among all individuals with acute ischemic stroke < 48 hours from onset—18/33 (54.5%) had deficits in phoneme discrimination. (See Table 2 for summary data) Participants with phoneme discrimination deficits were significantly more impaired in

word-picture matching with mixed foils (77.9% vs. 100% correct; t= −1.9; df=15; p=0.04) and more impaired in word-picture matching with only phonologically similar foils (78.8% vs. 98.3%; t= −2.6; df=21; p=0.009), compared to left hemisphere stroke participants without phoneme discrimination deficits (Table 2). The presence of phoneme discrimination deficit was associated with the presence of impairment in word-picture matching with phonologically similar foils (Fisher's Exact: p<0.0001), and with the presence of impairment of word-picture matching with mixed foils (p=0.04), although dissociations were also noted: phoneme discrimination impairment was found with unimpaired comprehension on the phonological foil comprehension test (N=1) and on the mixed foil comprehension test (N=2).

Accuracy on phoneme discrimination at the acute stage was significantly correlated with accuracy on word comprehension with mixed foils (r=0.51; p=0.018) and with phonological foils (r= 0.58; p=0.018). Infarct volume was not significantly associated with accuracy on phoneme discrimination (r=0.07), word comprehension with mixed foils (r=0.15) or with phonological foils (r= 0.13).

Very similar results were obtained when we used A' data from the controls (to identify deficits defined as 2 SD below the mean) and from the 27 stroke participants in whom we could calculate A'. Among this group of stroke patients, 14/27 (51.9%) had impaired phoneme discrimination, with a mean of A' of 0.8455 (SD 0.1200)). Participants with phoneme discrimination deficits were significantly more impaired in word-picture matching with only phonologically similar foils 84.3% vs 99.6% (t = 3.4; df=19; p= 0.003), compared to left hemisphere stroke participants without phoneme discrimination deficits by A' (Table 2). The presence of phoneme discrimination deficit was associated with the presence of impairment in word-picture matching with phonologically similar foils (FE: p<0.0001), and with the presence of impairment of word-picture matching with mixed foils (p=0.02).

Of the 14 participants with impaired phoneme discrimination, only one had normal performance on spoken word picture matching with mixed foils and two had normal performance with phonological foils.

3.2. Lesions associated with impairment of phoneme discrimination

Figure 1 shows the DWI lesion overlap for the entire group of 33 patients (top panel), and for patients with impaired phoneme discrimination (middle panel), and for patients with normal phoneme discrimination (bottom panel).

Most patients with impairments in phoneme discrimination (and word comprehension) had lesions in the left middle cerebral artery (MCA) territory, whereas most patients with normal phoneme discrimination had lesions in the territory of the left posterior cerebral artery (PCA) or recurrent artery of Huebner, a branch of the left anterior cerebral artery (ACA). All but one of the patients with impaired phoneme discrimination had left subcortical strokes; but the subcortical lesion site varied considerably. We hypothesized that their deficit in phoneme discrimination might be due to associated cortical hypoperfusion around the infarct rather than the subcortical infarct itself, as we have shown for other language deficits in non-

thalamic subcortical strokes (Hillis *et al.,* 2002). Unfortunately, not all patients had Perfusion Weighted Imaging (PWI) acutely to evaluate areas of hypoperfusion.

To test this hypothesis, we evaluated the relationship between the presence of a phoneme discrimination deficit and hypoperfusion in five cortical ROIs (based on (Caplan *et al.,* 1995; see 2.4.2 and Figure 2) in the 12 patients who completed testing and had both DWI and Perfusion Weighted Imaging (PWI) available at onset. This analysis allowed us to identify areas of acute tissue dysfunction on MRI. Of these 12 patients, 4 (33%) had significant impairment in phoneme discrimination at Day 1, in each case associated with both spoken word comprehension impairment (on both tests) and tissue dysfunction (hypoperfusion and/or infarct) in left superior temporal gyrus (STG) (see scores in Table 3). STG was the only ROI where infarct and/or hypoperfusion was significantly associated with a phoneme discrimination deficit; and only one participant had hypoperfusion of left STG but no significant phoneme discrimination deficit (FE: p=0.01). It is possible that this person had a less typical cytoarchitectural map or structure-function relationships, such as greater bilateral processing of phoneme discrimination.

All four participants with acute phoneme discrimination deficits (by accuracy and A') showed at least some improvement by the chronic stage (Table 3). Two of four with initial phoneme discrimination deficits showed hypoperfusion (but no infarct) in left STG, and recovered to normal phoneme discrimination by 6–12 months see Table 3 for scores). Two patients had infarct in left STG and showed improvement, but not recovery, of both phoneme discrimination and word comprehension by 6 months post-stroke. The scans of these four patients at the acute time point are shown in Figure 3.

The other eight patients had normal phoneme discrimination at acute and chronic time points, and only one of these individuals had hypoperfusion (but no infarct) in left STG. Impaired phoneme discrimination was significantly associated with dysfunction of left STG (p=0.010), but no other ROI. Although three of four participants with acute deficits had hypoperfusion (but no infarct) of left supramarginal gyrus (SMG), three of the eight participants with normal phoneme discrimination also had poor perfusion of SMG (p=0.54, ns).

There was one patient who was classified as unimpaired in phoneme discrimination using accuracy rate but impaired using A'. That individual's phoneme discrimination was 96.9% correct and A' was 0.9834 (normal is ≥0.9835). There is evidence of hypoperfusion (but no infarct) in both left STG and surrounding areas, including left SMG and intraparietal sulcus (Figure 4). This patient did not have follow up testing. There were no patients who were impaired using error rate and unimpaired using A'.

We also attempted to identify areas where the percentage of voxels with acute infarct (on DWI) was associated with severity of phoneme (syllable) discrimination impairment. However, there were no areas significantly related to accuracy on phoneme discrimination. Even when we dichotomized impairment (impaired versus no impairment using error rate), there were no areas where the presence of a lesion (on DWI) was significantly associated with low accuracy rate on phoneme discrimination.

However, when we used A' prime data from the subset of 27 patients, we found a significant association between percentage of infarcted voxels in left intraparietal sulcus and A' score, with lower scores in patients with more damage to intraparietal sulcus (Figure 5).

4. Discussion

We identified a higher incidence of deficits in phoneme discrimination after acute left hemisphere stroke in this study (>50%), relative to previous studies (e.g. 14/68 stroke patients or 20.6% and 14/19 or 15.6% for all lesions reported in Varney, 1984). This difference is likely because we studied patients more acutely after stroke (within 48 hours), and included only acute stroke (not tumor or other lesion). We and others have found that phoneme discrimination deficits recover rapidly after stroke in many cases (Varney, 1984). In some cases, the recovery is likely to be due to reperfusion of critical areas. However, in other cases, there is likely to be reorganization of structure-function relationships, such that intact brain regions are able to assume the role of damaged areas in phoneme discrimination. As other evidence indicates some degree of bilateral organization of early stages of speech analysis (Hickok and Poeppel, 2007), the contralateral (right) STG is a strong candidate for an increased role in speech processing in the face of damage to left STG.

We showed a statistical association between impaired phoneme discrimination and impaired word-picture matching. Accuracy of phoneme discrimination correlated with accuracy of word comprehension with mixed foils and with phonological foils. It might be somewhat surprising that the accuracy in word comprehension did not differ for the mixed foil condition and the phonological foil condition (77.9% vs 78.8%) among people with phoneme discrimination deficits. However, recall that the mixed foils condition always contained a phonologically similar foil; in half of the trials, the phonological foil was a minimal pair with the target. Of the 14 patients with impaired phoneme discrimination, only one had normal performance on spoken word picture matching with mixed foils and two patients had normal performance with phonological foils. If phoneme discrimination is required for word comprehension, we would expect no cases of intact word comprehension among those with impaired phoneme discrimination. A descriptive explanation of these dissociations is that the comprehension task is easier than the discrimination tasks. We have shown in previous work that a word-picture verification task (more comparable to the phoneme discrimination task) is more sensitive to comprehension deficits than a forced choice task (Breese and Hillis, 2004). But the question arises why this should be the case. One explanation is that the phoneme discrimination task requires use of mechanisms (e.g. short-term/working memory, decision) that are not required for the word-picture matching task (Hickok and Poeppel, 2000). Thus, damage to short-term/working memory processes, for example, could impair performance on the discrimination task without necessarily impacting acoustic phonetic analysis of speech for word comprehension, thus explaining the dissociations.

In contrast to previous studies of chronic stroke showing that impairment of phoneme discrimination is not always associated with impaired word comprehension, we found a correlation between the two deficits. Although one cannot infer causation, a straightforward interpretation is that performance on the two tasks share at least some neurocomputational

resources, thus leading to the correlated performance. Alternatively (or additionally), phoneme discrimination and word comprehension deficits in acute stroke may be due to hypoperfusion of distinct but parallel perisylvian networks engaged in phoneme discrimination and word comprehension. In acute stroke, there is often hypoperfusion of extensive areas of cortex surrounding the infarct, as shown in Figures 3 and 4. In contrast, the dysfunctional area in chronic stroke is generally limited to the infarct itself, which could explain discrepancies between our findings in acute stroke and the previously reported findings in chronic stroke. Even in acute stroke, the observed correlation, while significant, explained only 33.6% of the variance indicating that the two tasks either draw on partially dissociable resources or that the parallel networks for the two tasks are only sometimes equally affected by acute hypoperfusion. Hickok & Poeppel (2007) propose that discrimination and comprehension tasks share neural resources in the posterior STG and STS, which are critical for extracting phonological information from the speech signal. Beyond that stage, discrimination tasks tend to draw more on the dorsal, frontoparietal stream, which is important for working memory and explicit comparison of phonological forms, whereas comprehension relies more on the ventral stream to map a sound pattern onto word meaning. The critical association between acute dysfunction in left STG within the ventral stream of speech processing (Hickok and Poeppel, 2000) and acute impairment of phoneme discrimination is consistent with this view and with several case studies of impaired phonological processing associated with left STG lesions (Martin and Caramazza, 1982; Caramazza *et al.,* 1983; Friedrich *et al.,* 1984; Friedrich *et al.,* 1985) and several cases in Caplan, et al., 1995).

We also found an association between percent infarct in left intraparietal sulcus (which forms the superior border of the SMG and AG) and A’ score for phoneme discrimination, which is a more accurate assessment of impairment than error rate (because it accounts for response bias). Evidence from functional connectivity studies indicates that there is an anterior-posterior gradient in the intraparietal sulcus, with the anterior part specialized for sensorimotor functions involved in perception to action, and the posterior part involved in executive/attention functions such as working memory and cognitive flexibility (Cieslik, et al, 2015). Thus, we found that impairments on the phoneme discrimination task were associated with lesions in posterior intraparietal sulcus, likely because it has a role in directing attention to phonological level representations processed by the STG. That is, deficits on the task can arise either because of damage to left STG which affects perceptual mechanisms or because of damage to left posterior intraparietal sulcus, which affects attentional systems that enable conscious access to an otherwise unconscious process. Word comprehension is a more natural task that does not require conscious attention to phonological level representations, and so should not rely heavily on attentional systems in left intraparietal sulcus. The correlation we identified between phoneme discrimination and word comprehension may be driven by the dependence of both on left STG, whereas their dissociability is driven by damage to left intraparietal sulcus that does not affect word comprehension. This hypothesis is consistent with previous studies that reveal that word comprehension critically depends on left STG (see Hillis et al. 2017 for review).

We did not find an association between *percent infarct* in left STG (or SMG) and phoneme discrimination deficits, but it is likely that at least some patients with infarct in intraparietal

sulcus had hypoperfusion of nearby left STG and SMG, as indicated by the cases who had PWI (see Figures 3 and 4). We have shown in previous studies that the entire area of tissue dysfunction (the area of infarct plus the area of hypoperfusion) accounts for acute deficits more accurately than the area of infarct alone (Hillis *et al.,* 2001, 2017).

Studies of chronic stroke (Caplan *et al.,* 1995; Rogalsky *et al.,* submitted) have found that chronic infarct in the left SMG is associated with failure to recover phoneme discrimination. Rogalsky and colleagues (submitted) found left SMG and adjacent STG damage (temporoparietal junction) is associated with poorer non-word discrimination in 97 chronic stroke patients. It is possible that both left STG and left SMG/intraparietal sulcus are critical for phoneme discrimination, but right STG is able to assume the role of left STG over time, while right SMG cannot assume the role of left SMG (e.g. the phonological short term memory system required to compare two phonemes in the phoneme discrimination task). If this is the case, patients with dysfunction in left STG or SMG should cause acute deficits, while only lesions in left SMG would result in persistent deficits in the chronic stage. In the current study, two patients with hypoperfusion in left SMG had normal word comprehension; however, it may be that the entire SMG was not hypoperfused.

We noted that most participants with phoneme discrimination deficits had subcortical lesions, although the site of subcortical lesion was highly variable. Among all participants with PWI, we found a strong association between hypoperfusion of left STG and phoneme discrimination deficits, consistent with our hypothesis that acute dysfunction of left STG, rather than the subcortical lesion itself, was responsible for the deficit. Another the possible explanation for deficits in participants with purely subcortical infarcts is that the lesion disrupted white matter tracts critical for phoneme discrimination, such as the auditory radiations, as has been well reported in a single case of auditory agnosia in a patient with bilateral subcortical hemorrhages (Godefroy et al., 1995). Almost certainly, disruption of white matter tracts connecting various “hubs” of the networks underlying phoneme discrimination and word comprehension would affect one or the other task or both. For example, disconnection between posterior STG and frontoparietal regions critical for working memory and comparison of phonological representations via arcuate fasciculus would likely impair phoneme discrimination. Likewise, disruption of white matter tracts that connect left STG to ventral regions critical for mapping sound patterns onto word meaning would disrupt word comprehension. These accounts are not mutually exclusive; it is likely that both hypoperfusion of cortex and subcortical regions, as well as lesions of white matter tracts causing disconnection within critical networks, result in impaired performance on phoneme discrimination in acute stroke.

Limitations of this study include the relatively small number of participants, especially those who had adequate PWI to evaluate hypoperfusion. Reasons for failure to obtain PWI in many patients included: contraindication for Gadolinium contrast needed for PWI (usually due to renal dysfunction, in which Gadolinium increases the risk of nephrogenic systemic fibrosis), inadequate venous access for administration of intravenous contrast, and technical error (e.g. inadequate bolus administration; failure to follow stroke protocol MRI). For participants who had only DWI and ADC (no PWI), it is likely that the lesion map failed to include some areas of dysfunctional tissue (hypoperfusion beyond the infarct), as discussed

above. Another limitation is the relatively “easy” word comprehension task that may not have been sensitive to all word comprehension deficits. The absence of any data from Auditory Evoked Potentials is also a limitation.

Despite the limitations, this study shows that phoneme discrimination deficits are common acutely after left MCA stroke, and are associated with word comprehension deficits. For many patients, these impairments can be mild in absolute terms—average performance in the impaired group is still well above chance—consistent with claims for weaker hemispheric dominance in speech perception compared to expressive language tasks (Hickok & Poeppel, 2007). Nonetheless, measureable deficits in receptive language, even at the sound and word level are clearly present in some cases of acute stroke. This information is important for clinicians caring for individuals with stroke, as all care providers should be aware that the stroke survivor may have trouble understanding, especially in the absence of context. Bedside assessments of comprehension (e.g. following simple commands appropriate to the context) are not sensitive to these deficits. Studies of chronic stroke have indicated that word comprehension deficits are relatively rare after unilateral stroke (Hickok & Poeppel, 2004), but our findings indicate that they are fairly common, although recovery is relatively quick in most cases.

Our results also show that left STG dysfunction is associated with phoneme discrimination deficits and auditory word comprehension deficits acutely, often due to hypoperfusion; and these deficits recover by 6–12 months if there is no infarct in left STG. Lesions involving left posterior intraparietal sulcus also disrupt performance on the phoneme discrimination task, perhaps because such damage interferes with attention or cognitive control. Improvement in phoneme discrimination by the patients with initial deficits also provides evidence that their acute deficits were not (or at least not entirely) due to peripheral hearing loss. Results also confirm that impaired phoneme discrimination may underlie at least some cases of word comprehension deficits.

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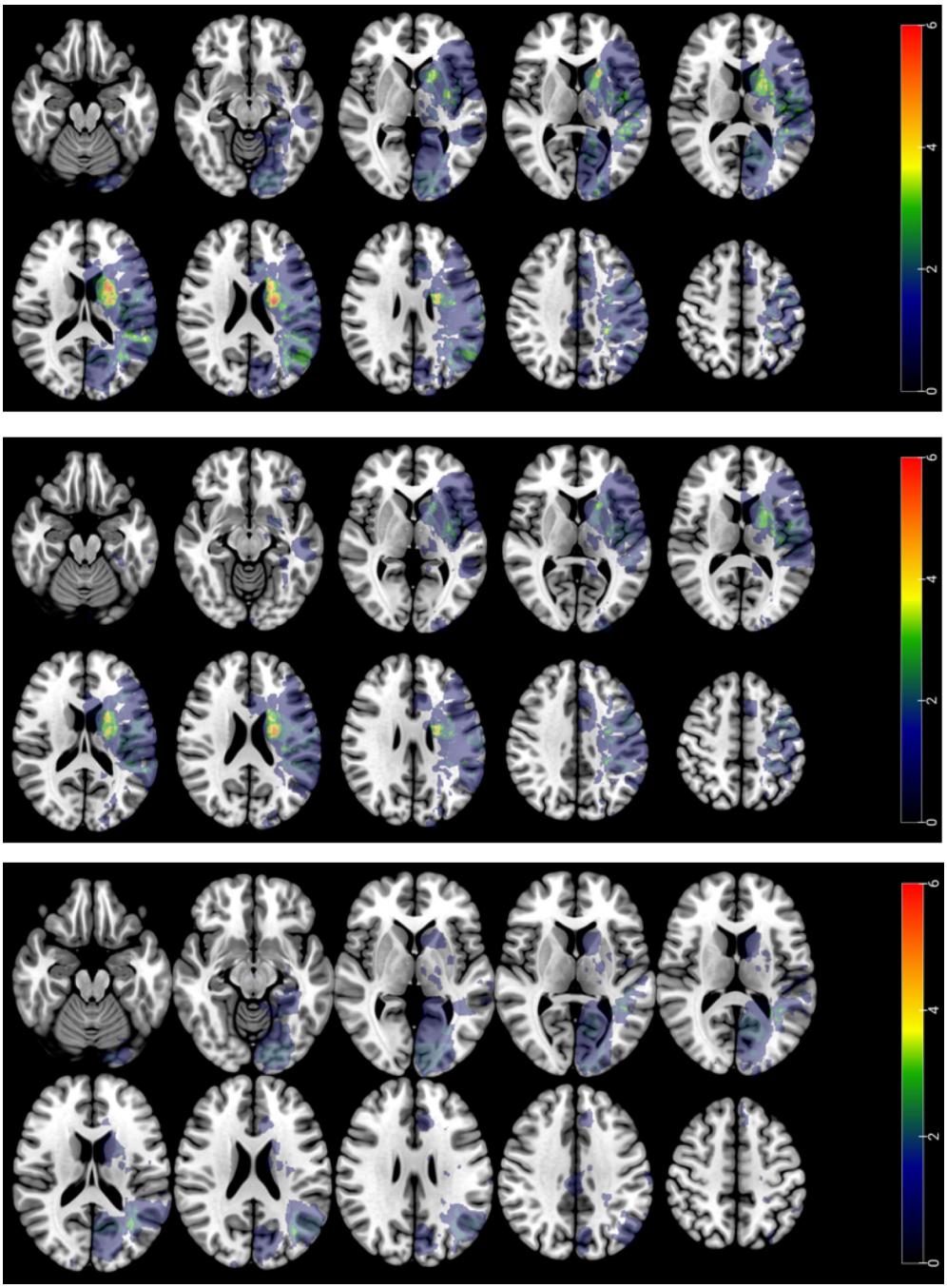

Figure 1.

Lesion overlap for patients all 33 patients (top panel), patients with impaired phoneme discrimination (middle panel; n=18) and with normal phoneme discrimination (lower panel; n=15). We used the 'radiological convention' of left hemisphere on the right in Figures 1–3. The white arrow in the top panel points to Heschl's gyrus. Green, yellow, and red voxels are those whereat least 3 participants had lesions.

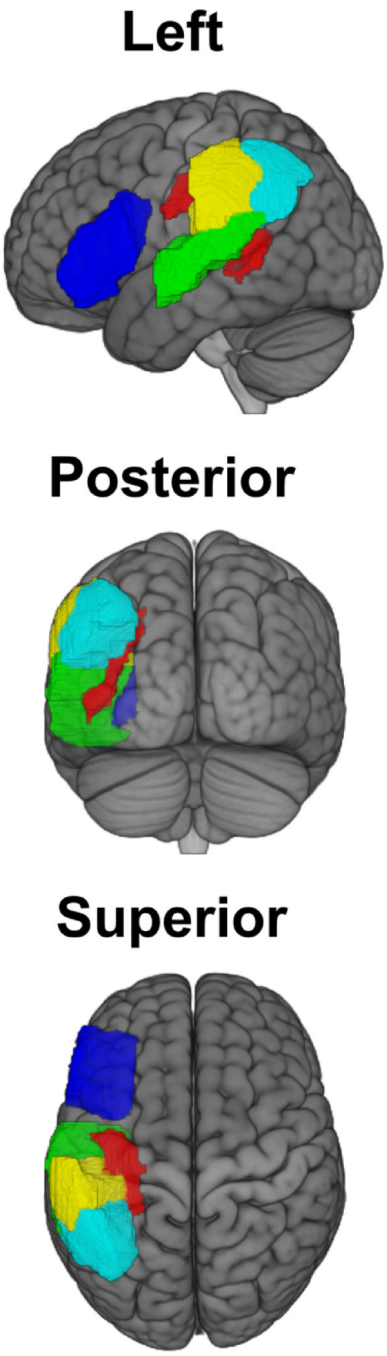

Figure 2.

Regions of interest used in analyses

Key: red=left AF (arcuate fasciculus); green=left STG (superior temporal gyrus); blue=left IFG (inferior frontal gyrus pars triangularis, pars opercularis, and pars orbitalis); cyan= left AG (angular gyrus); yellow=left SMG (supramarginal gyrus).

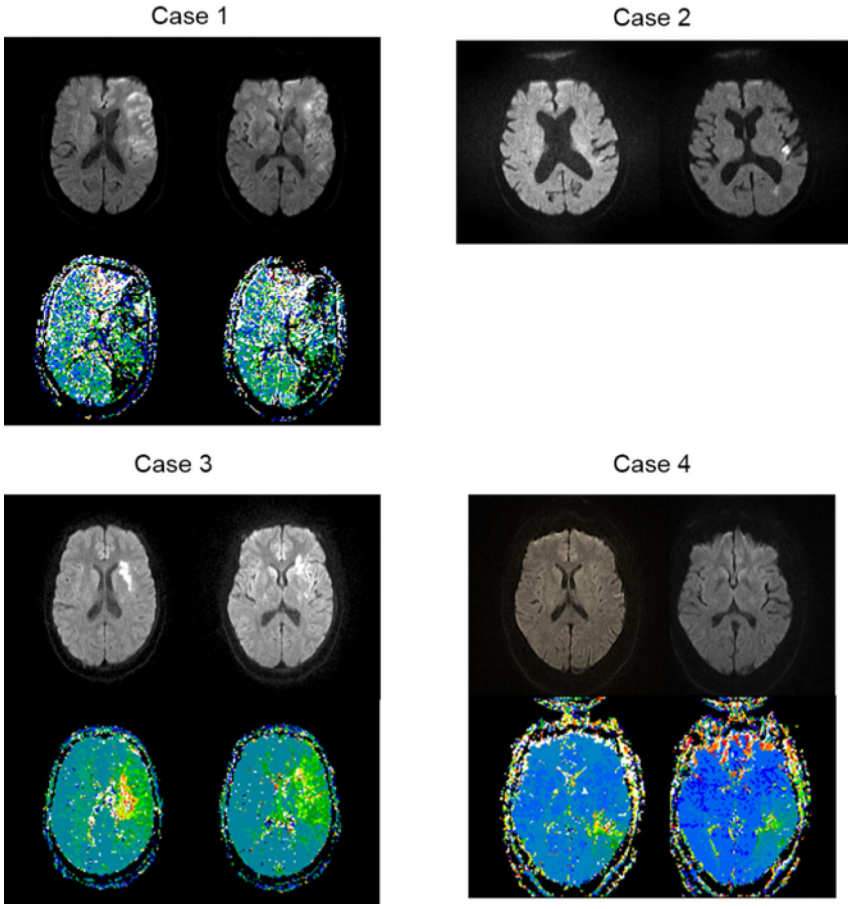

Figure 3.

Acute MRI scans of individuals with acute deficits in phoneme discrimination. Scans of patients with impaired phoneme discrimination (by percent error and d' score) at Day 1. Bright areas on DWI (top) are areas dense ischemia/infarct. Yellow/green areas in PWI (lower scans) are areas of significant hypoperfusion (>4 sec delay in TTP).

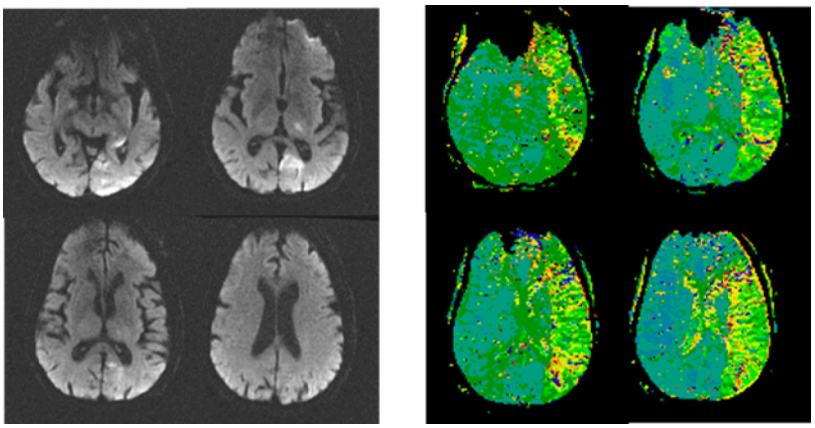

Figure 4.

DWI (left) and PWI (right) of Case 5 with impaired d' score for phoneme discrimination at Day 1. Bright areas on DWI (left) are areas dense ischemia/infarct. Yellow/green areas on PWI (right) are areas of significant hypoperfusion (>4 sec delay in TTP)

Figure 5.
Intraparietal sulcus (in red) where damage was significantly associated with impaired phonemic discrimination as measured by d' values in 27 participants with left hemisphere damage.

Table 1.

Demographics of Participants in Each Group

	Mean Age in Years (SD)	Mean Education in Years (SD)	Sex (%Female)	Race (%)
Healthy Controls (n=28)	56.8 (9.3)	14.8 (2.7)	30%	50% White 40% Black 10% Other
Patients with Phoneme Discrimination Deficits (n=18)	62.4 (15.4)	15.1 (4.9)	22%	59% White 41% Black
Patients with Normal Phoneme Discrimination (n=15)	52.1 (16.0)	13.6 (2.1)	40%	47% White 47% Black 6% Other

Table 2.

Mean (Standard Deviation; SD) and Range of Scores for Each Group

	Accuracy of Phoneme Discrimination	A' Score for Phoneme Discrimination	Accuracy of Word-Picture Matching-Mixed Foils	Accuracy of Word-Picture Matching-Phon. Foils
Controls	97.7 (SD 2.7) 93–100	0.9951 (SD 0.0058) 0.98–1.0	100 (SD 0) 100	99.8 (1.1) 95–100
Patients with Impaired Phoneme Discrimination	69.7 (SD 26.1) 0–90.6	0.8455 (SD 0.12) 0.5–0.98	77.9 (0.8) 55–100	78.8 (13.4) 50–100
Patients with Normal Phoneme Discrimination	98.6 (SD 1.7) 93.8–100	.9952 (SD 0.006) 0.98 – 1	100 (SD 0) 100	98.3 (1.3) 95.8–100

Table 3.

Percent Correct Phoneme Discrimination in Patients With Deficits who had Longitudinal Testing

	Acute (<24 hours)	Chronic >6 months
Case 1 *	0	40.6
Case 2 *	51.6	75.0
Case 3 **	79.7	100
Case 4 **	84.4	100

* Participants with infarction of left STG or both infarct and hypoperfusion of left STG (see Figure 4)

** Participants with hypoperfusion but no infarct in left STG