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Neural Correlates of Phonological and Semantic Based Anomia Treatment in Aphasia

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Abstract

Most naming treatments in aphasia either assume a phonological or semantic emphasis or a combination thereof. However, it is unclear whether semantic or phonological treatments recruit the same or different cortical areas in chronic aphasia. Employing three persons with aphasia, two of whom were non-fluent, the present study compared changes in neural recruitment associated with phonologic and semantic based naming treatments. The participants with non-fluent aphasia were able to name more items following both treatment approaches. Although this was not the case for the participant who had fluent aphasia, her naming errors decreased considerably following treatment. Post-treatment fMRI revealed similar changes in neural activity bilaterally in the precuneus among the two non-fluent participants – increased activity was noted in the right entorhinal cortex and posterior thalamus on post treatment scans for the third participant. These findings imply that cortical areas not traditionally related to language processing may support anomia recovery in some patients with chronic aphasia.

Keywords

Cuing Hierarchy; fMRI; Naming; Neuroimaging; Recovery; Therapy

Although the ability to name common objects has limited ecological significance per se, it is commonly targeted in aphasia treatment based on the assumption that it ameliorates lexical-semantic processing deficits which in turn would drive aphasia recovery. While the underlying cause of anomia varies significantly among patients, most treatment approaches either include a phonological or semantic focus (for a review see Nickels, 2002 and Maher & Raymer, 2004).

Previous research has suggested that to be optimally effective, anomia treatment should be tailored to the needs of each patient – e.g., patients with primarily semantic deficits should be treated with regimens that emphasize semantic processing. However, other studies have shown that some patients who respond well to semantic-based anomia treatment also respond well to

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phonologically based approaches (Fridriksson, Holland, Beeson, and Morrow, 2005; Wambaugh et al., 2004). While several cognitive models of lexical processing might explain this effect, a particularly influential 'interactive activation model' has been suggested by Dell and colleagues (Dell and O'Seaghdha, 1991, 1992; Gagnon, Schwartz, Martin, Dell, and Saffran, 1997; Martin, Dell, Saffran, and Schwartz, 1994; Schwartz, Dell, Martin, and Saffran, 1994). This account posits spreading activation within three processing levels with semantic-lexical information being processed at the first two levels and phonological constructions occurring at a third level. However, processing between levels is highly interactive as suggested by mixed semantic and phonological naming errors (as in "cow" for *cat*). Since this model is highly interactive, stimulation at one level (e.g. the phonological level) also stimulates processing at the other (semantic-lexical). This interactive stimulation has been shown in several anomia treatment studies of persons with aphasia (Dell, Schwartz, Martin, Saffran, and Gagnon, 1997; Martin and Laine, 2000; Renvall, Laine, Laasko, and Martin, 2003).

Some recent studies suggest aphasia recovery following stroke is dependent on left hemisphere reorganization while increased right neural activity following stroke represents maladaptive disinhibition (Martin et al., 2004). Perhaps even more convincingly, studies by Naeser and colleagues (Martin et al., 2004; Naeser et al. 2005) have shown that repetitive transcranial magnetic stimulation (rTMS) of the pars triangularis in the right hemisphere in non-fluent aphasic patients' results in improved naming. Since rTMS generally leads to tonic inhibition of the stimulated area, this finding suggests that right hemispheric activity is maladaptive, as its inhibition in this study ameliorated symptoms. It is possible that damage to the left pars triangularis leads to transcallosal disinhibition of the homologous area of the right hemisphere, with this activity decrementing performance and that rTMS to the right pars triangularis suppresses activity that normally would be inhibited by an intact Broca's area. The key question is why right hemisphere activity should be maladaptive, and why reduction of this activity should improve symptoms. Heiss and Thiel (2006) suggested that right hemispheric activity may itself suppress left hemisphere activity, and therefore that disrupting right hemisphere function allows the residual regions of the left hemisphere to become more active. Although this work provides substantial evidence suggesting a maladaptive role for the right hemisphere in inhibiting recovery, numerous studies have revealed right hemisphere recruitment associated with recovery of speech production (Crinion and Price, 2005; Crosson et al., 2005; Meister et al., 2006).

With regard to treatment induced anomia recovery in aphasia, changes in neural activity have been reported in the left hemisphere (Cornelissen et al., 2003), right hemisphere (Peck et al., 2004), and both (Fridriksson, Morrow, Moser, Fridriksson, and Baylis, 2006). Employing two non-fluent and one fluent aphasic participant, the study by Cornelissen et al. (2003) used magnetoencephalography (MEG) to reveal anomia treatment related changes in neural modulation in the left perilesional parietal lobe. In contrast, the results by Peck et al. (2004) showed primarily right hemisphere changes in the temporal aspects of the hemodynamic response (HDR) in three patients who underwent anomia treatment. More recently, Fridriksson and colleagues (2006) also employed three participants who received naming treatment and pre- and post-treatment fMRI. This study employed three fMRI scanning session before and after anomia treatment focused on errorless learning of a closed set of words. The results revealed a bilateral increase in neural activity associated with improved naming ability in two participants while the third did not respond to treatment. These three studies included participants with a wide range of aphasia severity and type as well as different anomia treatment approaches; nevertheless, some gross similarities in treatment related neural modulation were noted. For example, one of the fluent participants in the Fridriksson study also showed left parietal peri-lesional modulation associated with anomia recovery much as the three participants studied by Cornelissen et al. (2003).

The purpose of the present study was to investigate the neural correlates of phonological and semantic based treatments of anomia in three persons with chronic aphasia. Each participant received five 2-hour treatment sessions with a phonological focus and five 2-hours sessions with a semantic focus. Treatment sessions for each of the two approaches were completed within a one week period and the order of approaches were counter-balanced, where two participants first received the phonological treatment and the third participant first received the semantic approach. Based on evidence suggesting less reliable fMRI data in persons with aphasia, (Fridriksson, Morrow, and Moser, submitted), two fMRI sessions testing picture naming were acquired before and after each treatment approach was completed. Thus, neurological activity associated with treatment was assessed in a higher level fMRI analysis within each participant.

Methods

Participants

This study included three persons with aphasia who regularly attend aphasia groups at a university clinic. The first participant – NS – was a 63 year old woman who retired as a librarian following a left hemisphere ischemic stroke approximately one year prior to study inclusion. To classify aphasia type and assess specific language problems, the Western Aphasia Battery (WAB; Kertesz, 1982) was administered to each participant. NS' overall score on the WAB suggested that her language impairment was most consistent with conduction aphasia. Her speech was marked by frequent phonemic paraphasias and hesitant attempts at self-correction; she was very aware of her speech errors, something that is common in conduction aphasia (Table 1). She scored 33 out of 100 on the confrontation naming subtest of the WAB; errors consisted of both phonemic and semantic paraphasias while tactile and phonemic cues provided minimal support in naming attempts. During the word fluency task, she was able to name three animals (i.e., dog, cat, and zebra). Repetition on the single word level was moderately impaired, and her performance worsened at the phrase and sentence levels. Auditory comprehension was relatively spared although she had mild difficulty following two- and three-step directions. To more specifically test naming performance, the Philadelphia Naming Test (PNT; Roach, Schwartz, Martin, Grewal, & Brecher, 1996) was administered. The PNT includes 175 picturable nouns that were selected from a word frequency list compiled by Frances and Kucera (1982). Pictures are presented on a computer screen and responses are video-recorded and later scored by two clinicians. The mean number of correctly named pictures by NS on two baseline PNT sessions was 24. She also produced frequent semantic and phonemic (formal) paraphasias as well as non-words (Table 1).

An MRI examination of NS including T1 weighted MRI (T1-MRI) revealed a chronic infarct involving areas within the territory of the left middle cerebral artery (Figure 1). The lesion involved the cortex and underlying white matter of the left inferior frontal gyrus (Brodmann's area - BA - 44), left insula, left superior temporal gyrus (BA 41/42), left inferior parietal lobe (BA 39/40), and left occipital lobe (BA19). The T1-MRI also showed asymmetry of the lateral ventricles, with ex-vacuo left ventricular enlargement. T2 weighted MRI (T2-MRI) revealed mild diffuse focal white matter hyperintensity, in addition to the chronic stroke lesion (see anatomical scans used for fMRI reference in Figure 4).

The second participant – EG – was a 42 year old woman who suffered a left ischemic stroke 22 months before study enrollment. Prior to her stroke, she worked full time as a pharmacy technician; she has returned to work on a part-time basis. Her performance on the WAB suggested Broca's aphasia, characterized by short sentences and phrases (Table 1). Although her auditory comprehension was below normal limits, it was less affected than her speech production. Her ability to repeat even single words was considerably impaired. Naming of common objects was characterized by phonemic and semantic paraphasias, and she did not

benefit from either tactile or phonemic cues. The two baseline PNT sessions revealed severe anomia mostly marked by non-responses, occasional semantic, phonemic, or mixed paraphasias and perseverations (Table 1).

The MRI exam of EG revealed the following findings: T1 weighted MR imaging showed a chronic infarct of the left middle cerebral artery territory, involving the cortex and underlying white matter of the left and middle inferior frontal gyri (BA 9, 46, 44, posterior portion of 45), left insula, left superior temporal gyrus (BA 41, 42), left inferior parietal lobe (BA 7/39/40), and left occipital lobe (BA19). There was asymmetry of the lateral ventricles, with ex-vacuo left ventricular enlargement. T2 weighted images revealed that the lesion also included most of the white matter adjacent to left frontal horn, underlying Broca's area, and adjacent to left body of lateral ventricle underlying the sensorimotor cortex for the mouth.

The final participant with aphasia – CH – was a 63 year old retired minister who sustained a left ischemic stroke approximately eight years prior to study inclusion. CH also participated in another recent study of treatment-assisted anomia recovery (Fridriksson et al., 2006). Administration of the WAB revealed speech mostly marked by one- and two-word utterances and very few paraphasias (Table 1). Although not within normal limits, his auditory comprehension was much less affected than speech production. He responded well to yes/no questions, but demonstrated more difficulty when asked to point to the object or picture named by the clinician. Shapes, letters, colors, and body parts proved to be most difficult for him during this auditory comprehension task. Comprehension deficits were most pronounced during the sequential commands task; he was unable to complete all of the multi-step commands in full. Repetition was judged to be intact at the single word and short phrase levels with increased difficulty noted at the sentence level. During object naming on the WAB, he produced some semantic paraphasias but responded well to phonemic cueing. Similarly, he was able to name 22% of the PNT pictures correctly, also producing frequent semantic paraphasias. Although EG and CH were both characterized as having Broca's aphasia based on their WAB scores, CH presented more typically than EG. Unlike EG, CH produced frequent stereotypical utterances and agrammatical phrases. This was rarely the case with EG, who was much less likely to attempt words she was not certain she could produce correctly. Moreover, her short phrases and sentences were never agrammatical, something that is not typically seen in Broca's aphasia.

The MRI examination (T1-MRI) of CH revealed a large chronic stroke lesion involving almost the entire territory of the left middle cerebral artery (Figure 1). There was widespread destruction of the dorsolateral part of left hemisphere including frontal, temporal, and parietal lobes. The lesion also affected the left insula and left components of the basal ganglia, such as the caudate, pallidum, and putamen. There was asymmetrical ex-vacuo dilation of the lateral ventricles, which was more pronounced in the left side. T2 weighted image showed mild diffuse focal and periventricular white matter hyperintensities in addition to the frank lesion (Figure 4).

To examine cortical activity associated with naming common objects, ten normal participants underwent fMRI scanning while performing the same naming task as the persons with aphasia. The controls were recruited within the local community where the study took place. None reported a history of neurological or psychiatric problems. The average age of the group was 58.3 and the range was 35 to 77.

Procedure

Each participant received testing with the WAB within two weeks preceding their participation in this study. The PNT was administered the day of the first fMRI session and again the following day when the second fMRI session took place; then, five days of treatment ensued

utilizing either the semantic or the cueing hierarchy treatment approach. At one week following completion of the first treatment phase, two fMRI sessions were conducted on two consecutive days. The PNT was also administered on these two days. Two days later, the other treatment approach was utilized for five days, followed by the final two fMRI sessions at one week after the end of the second treatment phase. As before, the PNT was also administered during the last two days of scanning. Hence, each participant with aphasia received six fMRI sessions and six PNT sessions.

Naming treatment

The present study used an anomia treatment protocol similar to that described by Wambaugh et al. (2001). Using phonemic and semantic cueing hierarchies with increasing cueing strength, this study suggested that aphasic participants with either primarily phonemic or semantic naming errors could benefit from both cueing approaches. Except where noted, our protocol followed the phonemic cueing hierarchy of Wambaugh et al., that proceeded as follows: 1) at the first level the participant was presented with and asked to name a picture; 2) following an incorrect response, the clinician would verbally provide a non-word that rhymed with the target item ("it rhymes with..."); 3) the next level of the hierarchy included an phonemic cue in the form of the initial phoneme of the target; 4) in case of an incorrect response, the fourth level combined the cues from levels two and three ("it rhymes with... and starts with a /?/"); 5) the final level included repetition of the target word modeled by the clinician. The semantic cueing hierarchy proceeded in a similar manner: 1) confrontation naming; 2) verbal description of the target item; 3) sentence completion including a non-specific sentence; 4) sentence completion with a semantically-loaded sentence; 5) repetition. Wambaugh et al. also included a prestimulation phase where the target was presented among three foils and the participant was asked to point to the picture that matched the verbally presented word provided by the clinician. This step was not included in the present study as it was found to significantly decrease the time available for direct naming stimulation.

Each participant received five treatment sessions using the phonemic cueing hierarchy and five sessions with the semantic cueing hierarchy. Each session lasted two hours and each approach was employed for five consecutive days. Following a one-week break, the other cueing hierarchy was applied for five consecutive days. NS and EG first received treatment using the phonemic cueing hierarchy while treatment for CH started with the semantic approach. A total of 160 picturable nouns were selected for treatment using the Frances and Kucera (1982) word list. This stack of picture cards was divided into two stacks to be used as stimuli in the phonological or semantic cueing hierarchies. The cards were split based on word frequency, phonological complexity, semantic category, and typicality. To assess typicality, the 160 words were presented to a group of 30 individuals who were asked to rate the typicality of each word within a given semantic category on a 10-point scale. The PNT was utilized to chart treatment outcome and was administered twice before naming treatment was initiated, twice following completion of the first treatment approach, and twice when the second approach was completed. To test generalization, no PNT items were included in the corpus of 160 treatment items.

Behavioral data analyses

The behavioral analysis examined whether there was a reliable improvement following treatment sessions. Each individual was tested twice before and after each of the two treatment phases, and the difference between these scores allowed us to estimate the normal variability between sessions (due to learning or general variability in performance). Specifically, the within-treatment variability allowed us to estimate the standard deviation across testing sessions (variation between testing sessions one and two, between sessions three and four, and between sessions five and six), and this was used to determine the Z-scores for the observed

between-treatment variability. Five participants with aphasia were tested to assess the normal variability on these tests (this group included the three participants in the current study and two additional patients with similar etiology were included in an unrelated study of anomia recovery). The within-treatment standard deviation (SD) for the number of items correctly named in the fMRI naming task was 2.67 items. The within-treatment SD for correct naming on the PNT was 4.14 items and the SD for PNT errors was 4.21 items. Thus, this test-retest variance was utilized to estimate the effect of treatment measured as the increase in correct naming on the fMRI task (trained items) and the PNT (untrained items). Similarly, the change in errors was measured for the PNT.

Neuroimaging

All MRI data were collected using a Siemens Trio 3T scanner. Participants performed a confrontation naming task during sparse fMRI scanning to assess functional brain changes associated with treatment. A sparse fMRI paradigm was chosen as it allows for clear recording of participants' speech without the concomitant scanner noise in the background. On rare occasions, participants did speak during fMRI volume collection; however, these volumes were not removed from the data analysis since very minimal motion related noise was present in the fMRI data and overlap between speaking and fMRI data collection only occurred about once or twice per session. Stimuli were projected on a wide screen located at the end of the scanner bore and viewed via a back-projected mirror that was mounted on the head coil. A total of 80 pictures were presented at an average rate of one every 10 seconds. For fMRI baseline purposes, 40 abstract pictures were presented randomly throughout the paradigm. Each of the abstract pictures showed multiple colors and a mixture of geometrical and non-geometrical shapes. Prior to scanning, participants were instructed not to try to name these pictures. Throughout this study, no attempts at naming were observed during following baseline items. Responses were recorded using a non-ferrous optical microphone connected via an optical cable to a computer outside the scanner room – naming accuracy was scored off-line. To improve modeling of the hemodynamic response (HDR), the inter-stimulus-interval (ISI) was jittered with a mean of 6 seconds and a range of ± 3 seconds. Sparse imaging was employed as it reduces head motion artifact during overt speech and allows for clear recording of naming attempts (Bohland and Guenther, 2006; Fridriksson et al., 2006; Naeser et al. 2004). The fMRI data collection utilized an echo planar imaging (EPI) sequence with a TR of 10 seconds and a TA of 2 seconds, yielding an 8 second period between volume acquisitions when no scanner noise is present. We have found that the predictability of the timing between volume acquisitions significantly reduces the chance of speaking during fMRI data collection. This is especially important as it decreases the influence of motion artifacts associated with overt speech. Other EPI parameters were as follows: TE=35 ms; matrix=64×64; voxel size=3.25×3.25×3.5; number of slices=36. For lesion analysis, each participant was scanned using high-resolution 1mm isotropic T1- and T2-MRI (as previously described). Each participant underwent a total of six fMRI sessions: two before treatment initiation; two at one week following completion of the first cueing hierarchy, and two at one week following the completion of the second cueing hierarchy. Each fMRI session was completed on separate days.

fMRI Analysis

First level analysis of each fMRI session was carried out using FMRI Expert Analysis Tool (FEAT) Version 5.63, part of FMRIB's Software Library (FSL; www.fmrib.ox.ac.uk/fsl). The following pre-statistics processing was applied; motion correction (Jenkinson, Bannister, and Smith, 2002); non-brain removal (Smith, 2002); spatial smoothing using a Gaussian kernel of FWHM 8 mm; mean-based intensity normalization of all volumes by the same factor; highpass temporal filtering (Gaussian-weighted LSF straight line fitting, with sigma=50.0 s). Time-series statistical analysis was carried out using general linear modeling (GLM) (Woolrich,

Ripley, Brady, and Smith, 2001) and a Gamma function. All presented stimuli were modeled in the analysis and the number of correctly named items was used as a co-variate in a higher level analysis of pre- and post-treatment brain activity associated with naming. Thus, greater weight was given to correctly named items. Z (Gaussianised T/F) statistic images were thresholded using clusters determined by $Z > 2.3$ and a (corrected) cluster significance threshold of $P = 0.05$ (Worsley, Evans, Marrett, and Neelin, 1992). Data for each participant with aphasia were analyzed and co-registered in native space for intra-subject comparisons. However, for later verification of local maxima, their statistical maps were co-registered in Montreal Neurological Institute (MNI) space using FMRIB's Linear Image Registration Tool and cost functions to mask brain lesions (Jenkinson and Smith, 2001; Jenkinson et al., 2002). Similarly, data for each of the normal participants were analyzed in native space but the results of the higher level analysis depicting group activation was registered in MNI space.

To estimate mean cortical activity associated with the pre- and post-treatment performance within each participant with aphasia, a higher-level analysis was carried out using a fixed effects model, by forcing the random effects variance to zero in a local analysis of mixed effects (Beckmann, Jenkinson, and Smith, 2003; Woolrich, Behrens, Beckmann, Jenkinson, and Smith, 2004). Z (Gaussianized T/F) statistic images were generated using a cluster threshold of $Z > 2.3$ and a (corrected) cluster significance threshold of $P = 0.05$ (Worsley et al., 1992). Because naming accuracy was employed as a covariate in the higher level analysis, cortical activity associated with naming more items contributed more to the final statistical maps than when fewer items were named. To determine the effects of the naming treatment on changes in cortical activity within each participant, the following contrasts were examined: 1) Phonological treatment compared to baseline; 2) Semantic treatment compared to baseline; and 3) Phonological treatment compared to semantic treatment.

Results

Participant 1: NS

Following treatment utilizing either approach (semantic or phonological), NS was not able to name more treatment items during the fMRI sessions (Figure 2). In fact, the number of her successful naming attempts remained remarkably stable (10 and 13 items in the two baseline sessions; 8 and 11 items in sessions three and four following completion of the phonological treatment approach; and 11 and 13 items in sessions five and six at the end of the semantic treatment). This was also the case for her accuracy on the PNT across the six testing sessions (Figure 3). However, her number of errors on the PNT decreased as the study progressed; especially following completion of the phonological treatment approach. She made 66 and 64 errors during the two initial baseline PNT sessions; 29 and 33 errors in sessions three and four following the phonological treatment ($p < .0001$); and 28 and 28 after completion of the semantic approach ($p = ns$). NS's baseline fMRI sessions revealed bilateral neural activation associated with naming common objects (Figure 4); local maxima were mainly noted in the frontal lobes including the spared section of Broca's area and its right hemisphere homologue (Table 2). Although her successful naming attempts did not increase, the higher-level fMRI analysis revealed changes in cortical activity following administration of both treatment approaches. After completion of the phonological cueing hierarchy, increased neurological activity was noted in the right thalamus and left cerebellum. Increased neural modulation associated with the semantic approach was revealed in the right inferior temporal lobe specifically in the area of the entorhinal cortex.

Participant 2: EG

EG was able to name more trained and untrained items following both treatment approaches. Her naming ability during fMRI scanning improved greatly from the baseline to the post-

treatment sessions: 2 and 3 items during baseline scanning; 19 and 27 in sessions three and four following the phonological treatment ($p < .0001$); and 28 and 35 in the two sessions after the semantic treatment ($p = .0007$) (Figure 2). Similarly, the PNT revealed considerable generalization to untrained items (Figure 3); her mean number of named items in the post-phonological treatment sessions improved on average by six items compared to baseline, a difference that was approaching statistical significance ($p = .07$), and by eight items following the semantic approach ($p = .026$). In spite of extensive left hemisphere damage to EG's frontal and parietal lobes, her naming of common objects recruited left frontal motor and premotor areas as well as the supplementary motor areas and inferior temporal gyrus (Figure 4). This was also the case for the spared right hemisphere where a somewhat similar pattern of activity was noted. With regard to pre- and post-treatment fMRI contrasts, increased neural activity was noted in the superior medial parietal lobe – specifically bilaterally in the precuneus – following both treatment approaches compared to baseline. In addition, increased neural activity was revealed in the right anterior superior frontal gyrus when the semantic treatment approach was contrasted with the phonological approach (Table 2).

Participant 3: CH

CH also benefited from both treatment approaches even though generalization to untrained items was noted only following the phonological approach. Compared to his performance during the baseline fMRI sessions (26 and 24 items named correctly), his naming improved by an average of six items ($p = .012$) following the semantic based treatment (30 and 32 items in sessions three and four, respectively), and by 6.5 items ($p = .006$) following completion of the phonological treatment phase (37 and 38 in the final two sessions) (Figure 2). On average, CH named an equal number of pictures correctly during the two baseline PNT sessions and in the two sessions following the semantic treatment. However, his PNT score improved by eight items following the phonological treatment ($p = .026$) (Figure 3). His baseline fMRI revealed task related increase in neural activity in the left anterior, inferior frontal gyrus and the inferior temporal lobe (Figure 3 and Table 2). Right hemisphere baseline modulation was noted in the motor and premotor cortex as well as the middle temporal gyrus. As with EG, increased neural activity associated with the phonological treatment approach compared to baseline was noted bilaterally in the precuneus. Other contrasts for CH were not statistically significant.

Region of Interest Analysis

To examine whether anomia recovery was associated with activity in the right homologue of Broca's area, the mean z-score was calculated under a mask (representing BA 44 and 45) derived from a standard template and transformed into native space for the first two, the middle two, and final two fMRI sessions. For NS and EG, a consistent increase or decrease was not noted across the sessions (Figure 5). However, the mean z-score for CH's Broca's area homologue decreased fairly steadily from the first to the last fMRI session.

Control Group

The higher-level analysis including the single fMRI naming sessions for the normal participants revealed activity in the bilateral motor and premotor cortex, as well as Broca's and Wernicke's areas. Subcortical activity was noted in the bilateral thalamus and the left putamen. The mean z-values for the right homologue of Broca's area in the control group was .84 ($sd=.59$).

Discussion

This study focused on neural modulation associated with semantic and phonemic cueing naming treatments in aphasia. All three participants benefited from both treatment approaches; albeit, to very different degrees with regard to correct responses, errors, and generalization to untrained items. Interestingly, both participants whose number of correct naming attempts

increased had Broca's aphasia while the third participant whose overall naming errors decreased had fluent (conduction) aphasia. Below is a discussion of each case outcome.

Participant 1: NS

Although NS received two weeks of intensive anomia treatment, her naming of common objects – either trained or untrained – did not increase. Unlike EG and CH whose naming increased steadily from one treatment session to the next throughout both treatment phases, NS's correct naming attempts remained stable. Nonetheless, NS completed each two-hour treatment session despite persistent production of paraphasias. Her total naming attempts was reduced following each of the treatments compared to baseline. This did not result in fewer successful naming attempts; rather, her overall naming errors decreased steadily. This finding may be suggestive of improved ability to predict her naming errors or better recollection of failed naming attempts during previous testing sessions.

The higher-level fMRI analysis revealed changes in cortical activity for NS following each treatment compared to baseline scanning. Along with impaired repetition and abundant phonemic paraphasias, one of the main features of conduction aphasia is the intact ability to self-monitor speech production. For example, unlike in Wernicke's aphasia, people with conduction aphasia are very aware of the speech errors. Increased left cerebellar and right thalamic activity following the phonological treatment could possibly reflect increased reliance on motor feedback to predict naming errors (Nasir & Ostry, 2006). It is also of note that the higher-level analysis for the normal participants revealed strong bilateral thalamic activity, something that was not seen in any of the three participants with aphasia. Following the semantic treatment phase, NS showed increased neural activity in her right inferior temporal lobe. Given that her error rate decreased slightly more following the semantic treatment, this finding may reflect a strategy relying on episodic memory to reduce failed attempts by recalling the pictures that she could consistently name correctly (Simic et al., 2005; Squire, Stark, & Clark, 2004).

Given that NS showed a severely impaired ability to repeat, her inability to name more treatment items is perhaps not surprising. Even if all the cues in either approach failed to elicit the correct response, at least correct repetition of the target picture should provide stimulation at the lexical level of processing. However, in contrast to EG and CH, NS usually could not repeat the target item. A participant studied by Wambaugh et al. (2001) with conduction aphasia who was treated with the same phonological and semantic based cueing hierarchies as NS showed a considerable increase in correct naming. However, the current study did not include the pre-stimulation phase used by Wambaugh and colleagues. Because the pre-stimulation does not depend on overt naming, it is possible that lexical and/or phonological stimulation without the negative reinforcement associated with repeated naming errors could result in overall increase in naming.

Participant 2: EG

EG's naming performance improved during the fMRI sessions, and this improvement generalized to naming of untrained items on the PNT. The increased neural activity in the precuneus that was revealed following the phonological treatment remained when she was scanned two weeks later after completion of the semantic treatment. Implication of the precuneus in phonological processing comes from a study of patients with left temporal lobe epilepsy (Voets et al, 2006). This study showed a bilateral increase in precuneus activity associated with an overt phonological speech fluency task when patients were contrasted with normal controls. This effect was only seen for the phonological task, not on the overt semantic fluency task. Musso and colleagues (1999) found increased activity in the left precuneus associated with auditory comprehension treatment in four persons with aphasia and posterior

lesions caused by stroke. Compared to the activation seen in EG, their local maximum was somewhat more ventrally located (-14,-62-20).

A recent review of the functional role of the precuneus by Cavanna and Trimble (2006) proposes that it plays a particularly important role in episodic memory retrieval. Thus, increased precuneus activity following treatment could reflect reference to specific stimuli presented during the treatment. According to this account, one might speculate that improvement to EG's naming ability used information from episodic memory, rather than consolidated lexical-semantic memory. On the other hand, it is important to note that EG showed improvement not only on rehearsed items (as tested during the fMRI session), but also on untrained items. It is probable that episodic memory is one (but only one) of the strategies that allowed EG to improve her naming performance.

Not only was EG's improved naming ability demonstrated during the post-treatment fMRI and PNT sessions, but she also experienced steady naming improvement from one treatment session to the next. In spite of this recovery, perseverations of previously named pictures increased along with treatment success. It is possible that the increased medial frontal lobe activity in EG reflected an attempt to prevent these perseverations, by inhibiting the retrieval of previously produced words. Indeed, a similar treatment-related increase in neural activation was noted in the medial frontal lobe by Fridriksson et al. (2006) in a person with anomic aphasia who produced frequent perseverations during post-treatment naming.

Participant 3: CH

In spite of improved naming by CH during the two fMRI sessions following the semantic treatment phase, no difference in neural activity was revealed in the higher level statistical analysis. This was perhaps not surprising given that no generalization was revealed from trained to untrained items. In contrast, treatment related modulation was noted bilaterally in the precuneus following completion of the phonological treatment phase; and at this stage the treatment effect generalized to untrained items on the PNT. Although the increase in activity was noted in the precuneus, the local maxima were noted somewhat dorsally compared to EG. Rather than being language specific per se, it is possible that this effect is related to retrieval of specific item presentations during the treatment sessions.

Compared to the normal controls, only CH showed greater activity in the right homologue of Broca's area. Previous studies in this area have reported increased neurological activity in this area in persons with non-fluent aphasia compared to controls (Blank, Bird, Turkheimer, & Wise, 2003; Naeser et al., 2004). As we discussed earlier, even though EG was non-fluent, her neurological and language profile was very different than CH who presented with typical Broca's aphasia. Thus, while CH showed substantially complete ablation of Broca's area, EG showed sparing of the anterior portion of Broca's area and much of left motor cortex. The gradual decrease in neural activity in CH's right Broca's homologue – something that was not seen in NS or EG – could reflect reduced effects of pathological disinhibition as a result of treatment. This finding would support Naeser et al. (2005) and Martin et al. (2004) who found decreased activity induced by rTMS in the right hemisphere homologue of Broca's area to correlate with improved naming performance in non-fluent aphasia.

General Discussion

The present findings revealed increased neurological activity associated with aphasia recovery in cortical areas not typically associated with language processing; moreover, the location of increased neural modulation overall (excluding increased right thalamic activity in NS) did not mirror the activity seen in the normal subjects performing the same language task. Previous studies have suggested that spared left hemisphere language areas are the primary mechanism

supporting successful long term recovery, while right hemisphere activation reflects maladaptation in the chronic phase of the disorder (Naeser et al., 2005; Saur et al., 2006). In contrast, the present study implicates non-linguistic cortical areas. As discussed by Musso et al. (1999), non-linguistic (attention, working memory, and/or inhibition) processing may represent compensatory cortical adaptation rather than specific repair of the pre-morbid language network. In other words, aphasia recovery in adults may depend on utilizing brain regions that were not previously crucial to language.

It is important to note that the current study only employed three participants with different aphasia profiles; thus, generalizing the present results to the greater population of aphasic patients is not warranted at this time. However, our findings provide important preliminary findings for future studies in this area. For example, it remains to be answered whether increased precuneus activity is associated with improved speech production in non-fluent aphasic patients. In deed, our results suggest this to be the case but these findings need to be extensively replicated before we can conclusively determine that the precuneus plays a role in speech recovery in aphasia.

A recent review of neuroimaging studies of aphasia recovery by Price and Crinion (2005) suggested increased neurological activity in the right superior temporal lobe to correlate with improved auditory comprehension in aphasia. In contrast, increased right hemisphere activity was found to have a negative effect on speech production in aphasia. In spite of this comprehensive review, a holistic picture of neuro/anatomical changes associated with aphasia treatment is incomplete. Obviously, the current findings of increased bilateral precuneus activity do not quite fit within this account. What is clearly needed is a large scale study focused on brain changes related to treatment induced aphasia recovery that includes a large homogenous sample of patients. However, increasing sample size also has significant practical disadvantages: many aphasic patients are inherently medically fragile and may not be able to complete long treatment studies that include extensive MRI scanning. Moreover, repeated failure in treatment (as in the case of NS) may lead participants to prematurely terminate study participation. Finally, implementation of intensive treatment regimen that is administered every day (or even every other day) mandates that participants be willing to spend extensive time on aphasia treatment. We find that most patients with chronic aphasia welcome the chance to participate in language treatment research; nevertheless, this usually requires extensive (although temporary) alteration of their daily lives – something that may not be possible due to extraneous factors such as employment, routine medical and rehabilitation appointments, transportation issues (including distance to the MRI facility), and other personal issues that may be impossible to work around. In addition, as suggested by in a meta-analysis study by Bhogal, Teasell, and Speechley (2003) aphasia treatment studies that resulted in positive outcome utilized, on average, 98.4 hours of treatment. Clearly, it would be quite difficult to dispense that many hours in a treatment study that included periodic MRI scanning and extensive post-treatment testing. Of equal importance, though, Bhogal et al found that a positive treatment effect was strongly associated with at least 8.8 hours of treatment per week. The current study utilized 10 hours of treatment per week which resulted in positive treatment outcome for all three participants.

While a large scale study may be more difficult to implement, future studies in this area need to incorporate greater numbers of participants with similar cognitive and neurological profiles. Based on previous research that included fewer patients, these studies can rely on methods that have been shown to work in the past. For example, it is likely that a clearer picture of treatment induced brain changes in aphasia will emerge when patients with similar cortical lesions and aphasia profiles are studied. It is also possible that modeling of different types of paraphasias may provide more homogeneous results among aphasic patients with different aphasia profiles – something that we are currently working towards.

So far, we are not aware of any studies providing neurophysiological evidence that either supported or detracted the utility of a given aphasia treatment approach. Thus, current research in this area has not yielded evidence beyond more traditional aphasia treatment studies (only including behavioral data) that might guide clinicians in choosing the most optimal treatment approach for given patient with aphasia. Traditionally, aphasia treatment has been dispensed on trial-and-error basis. While aphasia treatment studies may provide basis for what treatment works with a particular patient profile, an exact treatment approach is usually tailored specifically to the needs and abilities of a given patient. Accordingly, aphasia treatment studies including structural and fMRI data may provide more comprehensive data as to what kind of patient is likely to benefit from a given aphasia treatment approach. Predicting treatment induced recovery from aphasia based on neuroimaging data – both structural and functional – is premature at this time. Along with behavioral data, it is possible that neurophysiology may be used to predict aphasia treatment success. However, the evidence is simply not available and collecting such a dataset would tax extensive resources.

With regard to the relationship between left/right hemisphere recruitment in aphasia recovery, we speculate that there may be a parsimonious explanation for the apparently paradoxical findings reported by different groups. Specifically, recovery in patients with small injuries who experience mild anomia may largely rely on spared perilesional language areas. On the other hand, patients with even larger and more debilitating strokes may need to recruit brain areas that were not originally required for language. This model may also inform rehabilitation, suggesting that patients with more severe aphasia require different training regimes than individuals with milder aphasia.

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References

- Beckmann CF, Jenkinson M, Smith SM. General multi-level linear modeling for group analysis in FMRI. *NeuroImage* 2003;20:1052–63. [PubMed: 14568475]
- Blank SC, Bird H, Turkheimer F, Wise RJ. Speech production after stroke: the role of the right pars opercularis. *Annals of Neurology* 2003;54(3):310–320. [PubMed: 12953263]
- Bohland JW, Guenther FH. An fMRI investigation of syllable sequence production. *Neuroimage*. 2006Epub ahead of print
- Cavanna AE, Trimble MR. The precuneus: A review of its functional anatomy and behavioural correlates. *Brain* 2006;129(Pt 3):564–83. [PubMed: 16399806]
- Cornelissen K, Laine M, Tarkiainen A, Järvensivu T, Martin N, Salmelin R. Adult brain plasticity elicited by anomia treatment. *Journal of Cognitive Neuroscience* 2003;15(3):444–61. [PubMed: 12729495]
- Crinion J, Price CJ. Right anterior superior temporal activation predicts auditory sentence comprehension following aphasic stroke. *Brain* 2005;128:2858–71. [PubMed: 16234297]
- Crosson B, Moore AB, Gopinath K, White KD, Wierenga CE, Gaiefsky ME, et al. Role of the right and left hemispheres in recovery of function during treatment of intention in aphasia. *Journal of Cognitive Neuroscience* 2005;17(3):392–406. [PubMed: 15814000]
- Dell GS, Schwartz MF, Martin N, Saffran EM, Gagnon DA. Lexical access in aphasic and non-aphasic speakers. *Psychological Review* 1997;104(4):801–38. [PubMed: 9337631]
- Dell GS, O'Seaghdha PG. Mediated and convergent lexical priming in language production: a comment on Levelt et al. (1991). *Psychological Review* 1991;98(4):604–14. [PubMed: 1961775]
- Dell GS, O'Seaghdha PG. Stages of lexical access in language production. *Cognition* 1992;42(13):287–314. [PubMed: 1582160]
- Frances, WN.; Kucera, H. *Frequency Analysis of English Usage*. Houghton Mifflin; Boston: 1982.

- Fridriksson J, Holland A, Beeson P, Morrow KL. Spaced retrieval treatment of anomia. *Aphasiology* 2005;19:99–109. [PubMed: 16823467]
- Fridriksson J, Morrow KL, Moser D. Examining test-retest reliability of fMRI data in aphasia. submitted
- Fridriksson J, Morrow L, Moser D, Fridriksson A, Baylis G. Neural correlates of anomia recovery in aphasia. *NeuroImage* 2006;32:1403–1412. [PubMed: 16766207]
- Gagnon DA, Schwartz MF, Martin N, Dell GS, Saffran EM. The origins of formal paraphasias in aphasics' picture naming. *Brain and Language* 1997;59(3):450–72. [PubMed: 9299072]
- Heiss WD, Thiel A. A proposed regional hierarchy in recovery of post-stroke aphasia. *Brain and Language* 2006;98(1):118–23. [PubMed: 16564566]
- Jenkinson M, Smith SM. A global optimization method for robust affine registration of brain images. *Medical Image Analysis* 2001;5(2):143–56. [PubMed: 11516708]
- Jenkinson M, Bannister M, Smith S. Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage* 2002;17(2):825–41. [PubMed: 12377157]
- Kertesz, A. *Western Aphasia Battery*. New York: Grune & Stratton; 1982.
- Martin PI, Laine M. Effects of contextual priming on word retrieval in anomia. *Aphasiology* 2000;14(1):53–70.
- Martin PI, Naeser MA, Theoret H, Tormos JM, Nicholas M, Kurland J, et al. Transcranial magnetic stimulation as a complementary treatment for aphasia. *Seminars in Speech and Language* 2004;25(2):181–91. [PubMed: 15118944]
- Maher LM, Raymer AM. Management of anomia. *Topics in Stroke Rehabilitation* 2004;11(1):10–21. [PubMed: 14872396]
- Martin N, Dell GS, Saffran EM, Schwartz MF. Origins of paraphasias in deep dysphasia: testing the consequences of a decay impairment to an interactive spreading activation model of lexical retrieval. *Brain and Language* 1994;47(4):609–60. [PubMed: 7859057]
- Martin PI, Naeser MA, Theoret H, Tormos JM, Nicholas M, Kurland J, et al. Transcranial magnetic stimulation as a complementary treatment for aphasia. *Seminars in Speech and Language* 2004;25(2):181–91. [PubMed: 15118944]
- Meister IG, Sparing R, Foltys H, Gebert D, Huber W, Topper R, et al. Functional connectivity between cortical hand motor and language areas during recovery from aphasia. *Journal of the Neurological Sciences*. 2006pub ahead of print
- Musso M, Weiller C, Kiebel S, Muller SP, Bulau P, Rijntjes M. Training-induced brain plasticity in aphasia. *Brain* 1999;122(Pt 9):1781–90. [PubMed: 10468516]
- Naeser MA, Martin PI, Baker EH, Hodge SM, Sczerzenie SE, Nicholas M, et al. Overt Propositional Speech in Chronic Nonfluent Aphasia Studied with the Dynamic Susceptibility Contrast fMRI Method. *NeuroImage* 2004;22:29–41. [PubMed: 15109995]
- Naeser MS, Martin PI, Nicholas M, Baker EH, Seekins H, Kobayashi M, et al. Improved picture naming in chronic aphasia after TMS to part of the right Broca's area: an open-protocol study. *Brain and Language* 2005;93(1):95–105.
- Nasir SM, Ostry DJ. Somatosensory precision in speech production. *Current Biology* 2006;16:1918–1923. [PubMed: 17027488]
- Nickels L. Therapy for naming disorders: Revisiting, revising, and reviewing. *Aphasiology* 2002;16(1011):935–79.
- Peck KK, Moore AB, Crosson BA, Gaiefsky M, Gopinath KS, White K, et al. Functional magnetic resonance imaging before and after aphasia therapy: shifts in hemodynamic time to peak during an overt language task. *Stroke* 2004;35:554–9. [PubMed: 14739418]
- Renvall K, Laine M, Laakso M, Martin N. Anomia treatment with contextual priming: A case study. *Aphasiology* 2003;17(3):305–28.
- Roach A, Schwartz MF, Martin N, Grewal RS, Brecher A. The Philadelphia Naming Test: Scoring and Rationale. *Clinical Aphasiology* 1996;24:121–33.
- Saur D, Lange R, Baumgaertner A, Schraknepper V, Willmes K, Rijntjes M, et al. Dynamics of language reorganization after stroke. *Brain* 2006;129:1371–1384. [PubMed: 16638796]
- Schwartz MF, Dell GS, Martin N, Saffran EM. Normal and aphasic naming in an interactive spreading activation model. *Brain and Language* 1994;47:391–4.

- Simic G, Bexheti S, Kelovic Z, Kos M, Grbic K, Hof PR, Kostovic I. Hemispheric asymmetry, modular variability and age-related changes in the human entorhinal cortex. *Neuroscience* 2005;130:911–925. [PubMed: 15652989]
- Smith S. Fast robust automated brain extraction. *Human Brain Mapping* 2002;17(3):143–55. [PubMed: 12391568]
- Square LR, Stark CEL, Clark RE. The medial temporal lobe. *Annual Review of Neuroscience* 2004;27:279–306.
- Voets NL, Adcock JE, Flitney DE, Behrens TE, Hart Y, Stacey R, et al. Distinct right frontal lobe activation in language processing following left hemisphere injury. *Brain* 2006;129(Pt 3):754–66. [PubMed: 16280351]
- Wambaugh JL, Linebaugh CW, Doyle PJ, Martinez AL, Kalinyak-Fliszar M, Spencer KA. Effects of two cueing treatments on lexical retrieval in aphasic speakers with different levels of deficit. *Aphasiology* 2001;15(1011):933–50.
- Woolrich MW, Behrens T, Beckmann C, Jenkinson M, Smith S. Multi-level linear modeling for fMRI group analysis using Bayesian inference. *NeuroImage* 2004;21(4):1732–1747. [PubMed: 15050594]
- Woolrich MW, Ripley BD, Brady JM, Smith SM. Temporal autocorrelation in univariate linear modeling of fMRI data. *NeuroImage* 2001;14(6):1370–86. [PubMed: 11707093]
- Worsley KJ, Evans AC, Marrett S, Neelin P. A three-dimensional statistical analysis for CBF activation studies in human brain. *Journal of Cerebral Blood Flow and Metabolism* 1992;12:900–18. [PubMed: 1400644]

Figure 1.
T1-MRI for the participants with aphasia presented in axial view and neurological orientation.

Figure 2.
Naming accuracy during each of the fMRI sessions.

Figure 3.

Treatment outcome measured using the PNT (C = correct response; s = semantic paraphasia; f = formal paraphasia; n = non-word; m = mixed paraphasia; u = unrelated response).

Figure 4.

Cortical activity maps overlaid on high resolution isotropic (1 mm) T2-MRI scans for the three participants with aphasia and normal controls. The color scales represent the following maps: 1) red-to-yellow = baseline; 2) blue = phonological treatment > baseline; 3) green = semantic treatment > baseline; 4) yellow = semantic treatment > phonological treatment; 5) cyan = overlap of baseline and contrasts 2 and 3 above.

Figure 5.

Mean z-values in the right hemisphere homologue of Broca's area in the three participants with aphasia across the six fMRI sessions.

Table 1

Biographical and language related information for each of the three participants with aphasia.

	NS	EG	CH
Gender	Female	Female	Male
Age	63	42	63
Time Post Onset	12 months	22 months	98 months
Current Aphasia Type	Conduction	Broca's	Broca's
<i>Western Aphasia Battery</i>			
Spontaneous Speech	16/20	11/20	7/20
Comprehension	140/200	140/200	141/200
Repetition	24/100	12/100	76/100
Naming	33/100	25/100	37/100
Aphasia Quotient	57.4	43.4	50.7
<i>Philadelphia Naming Test</i> *			
Correct Response	24	46	38
Semantic Paraphasia	23	10	22
Phonemic Paraphasia	18	9	3
Mixed Paraphasia	2	1	1
Unrelated	10	1	4
Nonword	12	3	0
No Response	86	105	107

* Scores represent a mean performance on the first two PNT sessions before treatment initiation

Table 2

Local maxima and cluster size (CS; for each hemisphere) for baseline cortical activity and treatment related contrasts.

	Baseline	Phonological > Baseline	Semantic > Baseline	Semantic > Phonological
NS (left hemisphere)	CS = 115217 Z = 6.32 – BA 6 Supplementary motor area (-8,8,48) Z = 5.65 – BA 32 Anterior Cingulum (-8,14,42) Z = 4.87 – BA 44 <i>Area opercularis</i> (-50,12,22) Z = 4.5 – BA na Putamen (-24,6,2) Z = 4.46 – BA 6 Precentral gyrus (-52,2,38)	CS = 2058 Z = 2.88 – BA na Cerebellum (-10,-82,-20)		
NS (right hemisphere)	CS = 21094 Z = 6.43 – BA 47 Insula (38,22,-6) Z = 5.04 – BA 45 <i>Area triangularis</i> (56, 24,0)	CS = 2482 Z = 3.04 – BA na Thalamus (8,-24,12)	CS = 2716 Z = 3.2 – BA 36 Parahippocampal gyrus	
EG (left hemisphere)	CS = 33412 Z = 4.03 – BA 6 Supplementary motor area (-4,4,50) Z = 2.76 – BA 36 Temporal pole (-24,16,-34) Z = 2.71 – BA 4 Precentral gyrus (-36,-18,54)	CS = 1794 Z = 2.58 – BA na Precuneus (-6,-50,42)	CS = 2286 Z = 2.97 – BA na Precuneus (-8,-48,40)	
EG (right hemisphere)	CS = 56890 Z = 3.82 – BA 4 Precentral gyrus (32,-22,58) Z = 3.02 – BA 48 Insula (30,28,10) Z = 3.01 – BA na Cerebellum (54,-70,-32) Z = 2.95 – BA 45 <i>Area triangularis</i> (56,36,16) Z = 2.64 – BA 21 Middle temporal gyrus (56,-34,0)	CS = 967 Z = 2.59 – BA na Precuneus (6,-52,50)		CS = 2115 Z = 3.06 – BA 10 Superior frontal gyrus (8,56,6)
CH (Left hemisphere)	CS = 69238 Z = 8.08 – BA 20 Inferior temporal gyrus (-48,8,-42) Z = 7.48 – BA 47 <i>Area orbitalis</i> (-36,28,-8)	CS = 10965 Z = 3.12 – BA 5 Precuneus (-6,-48,74)		
CH (Right hemisphere)	CS = 161557 Z = 9.04 – BA 3 Postcentral gyrus (58,-18,46) Z = 8.54 – BA 48 Supramarginal gyrus (62,-16,28) Z = 6.58 – BA 21 Middle temporal gyrus (64,-20,-8)	CS = 13402 Z = 3.3 – BA 5 Precuneus (6,-44,74)		
Normals (Left hemisphere)	CS = 48401 Z = 4.58 – BA 6 Superior frontal gyrus (-2,12,60) Z = 4.58 – BA 43 Postcentral gyrus (-64,-10,22) Z = 4.39 – BA 42 <i>Trnasverse</i> temporal gyrus (-64,-16,10) Z = 4.37 – BA 22 Superior temporal gyrus (-52,8,-8)			
Normals (Right hemisphere)	CS = 26062			

Baseline	Phonological > Baseline	Semantic > Baseline	Semantic > Phonological
Z = 4.45 – BA 6 Precentral gyrus (42,-2,34)			