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LESION CHARACTERISTICS RELATED TO TREATMENT IMPROVEMENT IN OBJECT AND ACTION NAMING FOR PATIENTS WITH CHRONIC APHASIA

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Abstract

Few studies have examined the relationship between degree of lesion in various locations and improvement during treatment in stroke patients with chronic aphasia. The main purpose of this study was to determine whether the degree of lesion in specific brain regions was related to magnitude of improvement over the course of object and action naming treatments.

Participants and Methods—Fifteen left-hemisphere stroke patients with aphasia participated in treatments for object and/or action naming. Two raters assessed extent of lesion in 18 left hemisphere cortical and subcortical regions of interest (ROIs) on CT or MRI scans. Correlations were calculated between composite basal ganglia, anterior cortical, and posterior cortical lesion ratings, on the one hand, and both pre-treatment scores and treatment change for both object and action naming, on the other hand.

Results—Unexpectedly, greater anterior cortical lesion extent was highly correlated with *better* object and action naming scores prior to treatment and with greater improvement during treatment when partial correlations controlled for total basal ganglia lesion extent (r ranging from .730 to .858). Greater total basal ganglia lesion extent was highly correlated with *worse* object and action naming scores prior to treatment and with less improvement during treatment when partial correlations controlled for total anterior lesion extent (r ranging from $-.623$ to $-.785$). Correlations between degree of posterior cortical lesion and naming indices generally were not significant. No consistent differences were found between the correlations of ROI lesion ratings with object naming versus action naming scores.

Conclusion—Large anterior cortical lesions and intactness of the basal ganglia may both contribute to more efficient re-organization of language functions.

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INTRODUCTION

The neural mechanisms driving improvement in the language functions of aphasic stroke patients are not well understood. Although much work has been done in studying the relationship between lesion characteristics and aphasia type (e.g., Cappa & Vignolo, 1999; Damasio, 1998; Kertesz, 1979; Kreisler et al., 2000), fewer studies have examined whether lesion characteristics are related to improvement in aphasia, and only a small percentage of those have looked specifically at the predictors of improvement in naming ability during treatment. The literature suggests a number of factors that might contribute to recovery and/or treatment outcome and, therefore, should be studied. These factors include degree and location of cortical lesions, the type of item being named, and degree of basal ganglia lesion.

With respect to degree and location of cortical lesions, Knopman, Selnes, Niccum, and Rubens (1984) examined a group of 54 left-hemisphere stroke patients with mild to severe naming deficits at one month and six months post-stroke. They found that patients with larger overall lesions showed less recovery of naming and that patients with lesions in Wernicke's area and inferior parietal cortex demonstrated the most severe naming impairments at six months post onset. Participants with lesions of the insula and putamen, extending into areas deep to the supramarginal gyrus, were noted to have significant but less severe naming impairments (compared to patients with Wernicke's area and inferior parietal lesions) by six months post onset. However, the precision for both language and imaging measures was not high, and it was unclear whether the patients participated in formal language therapy.

Using more precise measures, but fewer subjects, Cato, Parkinson, Wierenga and Crosson (2004a) and Cato, Parkinson, Wierenga and Crosson (2004b) examined improvement of naming ability in nine non-fluent subjects over the course of a novel naming treatment (Crosson et al., 2007). Unlike Knopman et al., Cato et al. (2004a) found that naming improvement was not correlated with overall lesion size, and subjects with large or small lesions could show significant improvement. Instead, poorer treatment response was found to be correlated specifically with greater lesion extent in Wernicke's area, the supramarginal gyrus, and the posterior one-third of the periventricular white matter (Cato et al., 2004b).

Another issue that has received little attention is whether predictors of treatment change will differ for object and action naming. Previous research has indicated that partially distinct neural systems may be involved in the naming of objects versus actions. Individual cases of stroke patients with specific naming deficits for either nouns or verbs have been reported (Caramazza & Hillis, 1991; Hillis & Caramazza, 1995; Zingeser & Berndt, 1990), and a double dissociation between anatomical regions supporting noun versus verb production has been proposed (Damasio & Tranel, 1993) based on such cases. Tranel, Adolphs, Damasio, and Damasio (2001) reported further evidence supporting this double dissociation in a group of 75 patients. In this group of patients with stable, chronic lesions, lesions related to action naming impairment had maximum overlap in the left frontal operculum, its underlying white matter, and in the anterior insula. Lesions in the left anterior temporal regions were associated with deficits in naming concrete entities, but not with deficits in naming actions. Hillis, Tuffiash, Wityk, and Barker (2002) addressed the object/action naming dissociation issue with a group of acute stroke patients using diffusion weighted and perfusion weighted MRI. Similar to previous studies with chronic patients, in 33 patients with acute left hemisphere stroke, left temporal cortex lesions were associated with object naming deficits, whereas left posterior frontal cortex lesions were associated with action naming deficits. The work of Lu et al. (2002) suggests that differences in naming objects and actions may be related in part to action semantics rather than the grammatical role of a word as a noun or a verb, respectively. Hence, it is possible that different lesion locations could affect recovery

of object and action naming differently. However, no studies have examined how lesion characteristics are related to improvements in object versus action naming over the course of language treatment.

Damage to the basal ganglia also may impact recovery. The effect of subcortical lesions on language in aphasia has long been debated (Nadeau & Crosson, 1997). Many case studies have reported the occurrence of aphasia following lesions restricted to subcortical areas, including the basal ganglia (e.g., Alexander, Naeser & Palumbo, 1987; D'Esposito & Alexander, 1995). More recently, perfusion weighted imaging studies (Hillis, Barker, et al., 2004; Hillis, Wityk, et al., 2002) have shown that aphasia following lesions restricted to the basal ganglia is more likely caused by the hypoperfusion of language cortex than the basal ganglia lesion itself. Nevertheless, there is evidence that when combined with cortical lesions, left basal ganglia lesions may decrease an individual's ability to recover language functioning. For example, Brunner, Kornhuber, Seemuller, Suger, and Wallesch (1982) found that patients with restricted subcortical lesions and aphasia usually had good spontaneous recovery. However, patients with both cortical and basal ganglia lesions experienced relatively more severe and longer lasting aphasia. Patients with cortical damage alone (unless the lesion involved Wernicke's area) generally displayed more transient aphasic syndromes, suggesting that when combined with lesions to cortical language areas, subcortical lesions appear to decrease language recovery potential.

A series of functional imaging studies suggest that the basal ganglia play a specific role in organizing or facilitating the recovery of language function. Based on results of an fMRI language study with normal (left language-dominant) subjects, Crosson et al. (2003) hypothesized that during a language task, the right basal ganglia served to suppress right frontal activity preventing right frontal areas from interfering with language production in the left hemisphere. In aphasic patients, Kim, Ko, Parrish, and Kim, (2002) observed different fMRI activation patterns during a language task depending on whether the patient's lesions were restricted to left frontal cortex or also involved subcortical lesions. Patients with restricted left frontal lesions displayed activation mainly in the right inferior frontal lobes, while patients with left frontal plus subcortical lesions displayed bilateral frontal and temporal activation. Taken with Crosson et al.'s (2003) findings, it appears that the intact left basal ganglia might suppress any peri-lesional left frontal activity which would interfere with re-organization of language production to the right hemisphere. Crosson et al. (2005) found further evidence for this hypothesis in two aphasic stroke subjects (one with a cortical-only lesion, and one with a lesion affecting cortex plus basal ganglia and thalamus) who showed contrasting functional activation patterns similar to those of the Kim et al. (2002) study.

No studies to date have examined lesion characteristics for chronic aphasia associated with improvement in both object and action naming over the course of naming therapy. In the current study, 15 patients with chronic aphasia received one of two semantically based naming treatments. Based on the literature reviewed above, we hypothesized that patients with large anterior cortical lesions would improve less in action naming than patients with small anterior cortical lesions, while patients with large posterior/temporal lesions would improve less in object naming than patients with small posterior/temporal lesions. Further, we hypothesized that in patients whose lesions generally involved cortical language areas, a high degree of basal ganglia lesion would lead to less improvement on naming than a lesser degree of basal ganglia lesion.

METHODS

Participants

Twenty-three participants with unilateral left-hemisphere stroke completed object and action naming treatments (Raymer et al., 2006; Raymer et al., 2007). Of those 23 participants, 16 participants had chronic MRI or CT brain scans available for analysis. One of these participants was later dropped because the participant had a brain shunt and clip which distorted images and interfered with the raters' ability to confidently assess the participant's lesion. Therefore, data from 15 participants were used in this study. Participants were recruited by investigators at medical and clinical facilities for neurology and speech-language pathology affiliated with Old Dominion University in Norfolk, Virginia, the Brain Rehabilitation Research Center of the Malcom Randall VA Medical Center in Gainesville, Florida, and the Brooks Rehabilitation Hospital in Jacksonville, Florida. All participants had major-vessel ischemic left-hemisphere strokes without hemorrhage covering variable portions of the middle cerebral artery distribution, with the following two exceptions. Participant #12 had a hemorrhagic lesion of the basal ganglia that was accompanied by an ischemic lesion in the middle MCA distribution superior to the basal ganglia lesion. Participant #13 had a major-vessel ischemic lesion in the posterior cerebral artery (PCA) distribution. Participants had no history of right-hemisphere stroke, other neurological illness, or developmental learning disabilities, and all were native English speakers. All participants were right-handed prior to stroke, and demonstrated significant difficulties in naming objects and actions [$<75\%$ accuracy on the Boston Naming Test (BNT; Kaplan, Goodglass & Weintraub, 1983) and the Action Naming Test (ANT; Nicolas, Obler, Albert & Goodglass, 1985)], with 10 of the participants being classified as having non fluent aphasia and 5 as having fluent aphasia, (classified according to the Western Aphasia Battery; Kertesz, 1982). Of the 15 participants, 12 were Caucasian and 3 were African American. There were 10 men and 5 women, with an average age of 65.2 years ($SD = 10.6$, range = 49 to 81 years) and average education of 13.4 years ($SD = 2.0$, range = 10 to 18 years). Participants varied in the time post stroke, with a mean of 30.7 months post onset ($SD = 35.6$; range = 5 to 128 months). Participants gave informed consent according to guidelines approved by the Institutional Review Board (IRB) of the University of Florida or Old Dominion University.

Aphasia Treatment

Participants took part in one of two naming treatments which have been previously described in detail; a gestural treatment (Raymer et al., 2006), or a semantic/phonologic treatment (Raymer et al., 2007). In brief, the semantic/phonologic treatment consisted of a series of steps encouraging the participant to activate and link information about the meaning and sound characteristics of a target picture/word, in keeping with the normal process of word retrieval. Specifically, the therapist presented a series of yes/no questions about the meaning and sound of a target picture (e.g., spoon; Is this similar to a ladle? Is this used to eat meat? Does this sound like moon? Does it start with /kr/?), followed by a rehearsal phase producing the target word several times. In gestural treatment, the therapist encouraged the participant to use gestural pantomimes to facilitate retrieval of spoken words, as a reorganization approach to word retrieval training. Therefore, the clinician modeled the correct gesture for imitation, the correct spoken word for imitation, and then required production of the word and gesture combined to facilitate the word retrieval process. Naming treatments were administered in two phases. Treatment phases differed by the type of treatment technique used (either semantic/phonologic or gestural) or by the type of word being trained (either objects or actions). Treatment order was counterbalanced across all participants. Some participants received treatments for both objects and actions using either the semantic or gestural technique. For these participants, data from both object

and action treatment phases were used in the current analysis. Other participants received both semantic/phonologic and gestural treatments for either objects or actions. For these participants, only the data from the first treatment phase was used in the current analysis. Among the 15 participants, the data were used from six semantic and seven gestural treatments for objects, and four semantic and eight gestural treatments for actions. Seven trained therapists from three sites provided the treatments based on the same established protocol.

Individualized picture/word probe sets were developed for each participant consisting of pictures of objects (n=40) or actions (n=40) that the participant had difficulty naming based on a pre-treatment assessment of noun (n=396) and verb (n=212) picture naming. Half of the probe words (n=20) were used in training and the other half served as untrained controls (n=20). Prior to each treatment phase, participants named stimuli from their individual word sets for between 4 and 10 sessions, or until their baseline performance appeared stable. Because treatment stimuli were individually-selected, performance levels were low and stable across baseline sessions. The treatment phase then began, with each session being initiated by the administration of two probe sets (comprised of trained and untrained words), with no feedback from the therapist, followed by the administration of the treatment word set under treatment conditions. Treatment phases lasted for 10 sessions. Participants received between three and five treatment sessions per week and had a month break between treatment phases. In addition to daily picture naming probes, the BNT and ANT were administered to participants at baseline and after each treatment phase.

Pre-treatment naming abilities were defined as a participant's percent correct on baseline BNT and ANT administrations. Improvements in the naming of objects and actions were calculated as range corrected gain scores for trained words on the picture naming probes [(mean number of words correct following treatment minus the mean number of words correct during baseline) divided by (total number of words minus mean number of words correct during baseline)]. See Table 1 for demographic and other data for individual participants.

One of the aims of the original treatment study was to compare improvement of object and action naming in participants who were randomly assigned to two separate treatment types. However, for the lesion analysis arm of the study, data were collapsed across treatment type in order to maximize the number of participants who could be included. It also should be acknowledged that the two treatments differ in the manner in which they attempt to treat naming deficits. This difference may be substantive since the success of these treatments may depend upon the integrity of different underlying neural mechanisms and brain regions. However, the two treatments contained the same frequency of sessions, the same number of sessions, the same treatment providers, the same outcome measures, and all participants were recruited using the same methods and criteria and are from the same geographical areas. Further, since the semantic/phonological treatment used semantic cuing and the gestural treatment used symbolic gesture, both treatments used strong semantic components. Considering (1) the lack of studies examining the effects of lesion location on treatment improvement of object and action naming, (2) the difficulty of obtaining large datasets involving a single standardized treatment, and (3) the similarities of the two treatments in question, it was felt that combining the treatment groups was justified as long as no obvious differences in effectiveness of treatments could be found.

In this regard, preliminary analysis with a mixed ANOVA showed that the semantic/phonological and gestural treatments resulted in similar improvements for both object and action naming. Participants improved on object naming treatments [$F(1, 11) = 16.391$, $p = .002$, partial eta squared = .598], with no significant main effect for treatment type [$F(1, 11)$

= .128, $p = .728$, partial eta squared = .011], and no significant interaction between improvement and treatment type [$F(1, 11) = 2.157$, $p = .170$, partial eta squared = .164]. Thus, although participants receiving the semantic treatment for object naming were somewhat older and more educated ($p < .05$) than participants receiving the gestural treatment, the two treatments did not produce different outcomes. Participants also showed improvement across action naming treatments [$F(1, 10) = 11.039$, $p = .008$, partial eta squared = .525], with no significant main effect for treatment type [$F(1, 10) = 1.470$, $p = .253$, partial eta squared = .128], and no significant interaction between improvement and treatment type [$F(1, 10) = 1.430$, $p = .259$, partial eta squared = .125]. Thus, although participants receiving the semantic treatment for action naming were somewhat older and had higher pre-treatment ANT scores ($p < .05$) than participants receiving the gestural treatment, the two treatments did not produce different outcomes for action naming. Since the treatments did not produce different outcomes, they were combined for the current data analyses.

Imaging and Lesion Analysis

Structural Images—Brain images for characterizing stroke lesions were acquired from each of the 15 participants. The average length of time between the stroke and scan was 32.6 months ($SD = 35.3$, range = 6 to 131 months). Seven of the 15 participants underwent functional MRI scans as part of the original treatment study. For these participants, three dimensional anatomical T1 weighted scans were acquired as part of the scanning protocol. These structural scans were imported into ANALYZE AVW format, and using ANALYZE 5.0 images were re-sliced in the axial plane to a common angle, 15 degrees from the canthomeatal line (as depicted in Matsui & Hirano, 1978). Axial slices were then screen-captured into tif files for later analysis.

Eight of the 15 participants were unable to be scanned as part of the original study, but were scanned as part of their clinical protocols following their strokes. Either CT or MRI films were obtained for these participants. Scan type depended on scanning preferences of the medical facility at which that participant had been treated as well as the participant's individual limitations. For example, participants with ferromagnetic metal implants would be administered a CT rather than MRI due to the danger of introducing such metal into the magnetic field of an MRI scanner. Of the eight clinical scans obtained, seven were CT, and one was an MRI (FLAIR sequence). These films were digitized using either a Microtek 9800XL flatbed scanner with a transparent media adapter or a Nikon D $\times$ 1 5 MP digital camera mounted over a standard clinical light box. All images were stored and analyzed as high resolution uncompressed tif files.

Lesion Analysis—Lesions were analyzed using a modified version of a protocol developed by Naeser and colleagues (Naeser et al., 1998; Naeser & Hayward, 1978; Naeser et al., 1989). According to the Naeser method, lesions are localized with the aid of a set of axial templates representing the angle at which CT scans are typically acquired (15 degrees from the canthomeatal line). Regions of interest (ROIs) drawn on the templates and defined by common landmarks such as major sulci, are visually compared with a participant's brain scan in order to determine the extent to which each ROI may have been lesioned. ROIs are primarily from the middle cerebral artery (MCA) distribution. Trained raters estimate the degree to which a given ROI is lesioned using these templates (0 = no lesion; 1 = equivocal lesion; 2 = small, patchy or partial lesion; 2.5 = patchy, less than half of area has lesion; 3 = half of area has lesion; 4 = more than half of area has solid lesion; 5 = total area has solid lesion). The Naeser templates were used to rate most subcortical ROIs whereas cortical ROIs (as well as the dorsal caudate and thalamus) were rated with the aid of a detailed photographic atlas of the brain (Matsui & Hirano, 1978).

One advantage of this method is that since ROIs were defined based on landmarks which would be easily recognized on both CT and MR and since the lesion ratings are relatively coarse, the method minimizes differences between scan types. More detailed descriptions of the lesion analysis technique, including templates, are available, and will not be reproduced here (Parkinson, 2006; Naeser et al., 1998). For scans which were not able to be viewed at the standard angle, landmarks were identified using alternative templates (Damasio & Damasio, 1989). All ratings were done independently by two raters (RBP and YC) who had been trained to an inter-rater correlation of $r = .887$ on a practice set of scans. When the ratings of the two trained raters differed by a point or less, the ratings were averaged, but when the ratings differed by more than a point the raters met to develop a consensus about the ratings. Raters were blind to patient performance in treatment.

Three composite ratings were created as measures of overall anterior cortical lesion extent (AC), overall posterior/temporal lesion extent (PTC), and total basal ganglia lesion extent (BG). The constituent ROIs of these composite regions are listed in Table 5 (see Results section). The composite rating consisted of the arithmetic sum of the ratings of the constituent ROIs. Hence, the maximum composite rating for AC was 35, the maximum composite rating for PTC was 40, and the maximum composite rating for the basal ganglia was 15.

RESULTS

Table 2 shows the composite AC, PTC, and BG ratings for each of the 15 participants. The mean anterior lesion rating across participants was 13.58 ($SD = 10.42$). The mean posterior lesion rating across participants was 17.98 ($SD = 9.15$). The mean basal ganglia lesion rating across participants was 6.38 ($SD = 4.29$). ANT, BNT, range correct gain scores (RCG) for object and action naming treatments, and treatment types for object and action naming treatments are also shown in Table 2.

Table 3 shows the means and standard deviations for the measures of pre-treatment naming ability and naming improvement used in the following analyses.

Naming and Left Cortical Lesions

Because a basal ganglia lesion can exacerbate the effects of a cortical lesion (e.g., Brunner et al., 1982; Crosson et al., 2005; Kim et al., 2002), it was necessary to control for extent of basal ganglia lesions to assess the relationship between naming and the degree of cortical lesion. It was expected that given equal extent of basal ganglia lesion, a greater degree of anterior cortical (AC) lesion would be correlated with lower pretreatment action naming scores and less improvement during action naming treatment. It was also expected that given equal extents of basal ganglia lesion, a greater degree of posterior/temporal cortical (PTC) lesion would correlate with lower pretreatment object naming scores and less improvement during object naming treatment. Correlations were therefore conducted between each individual naming measure and composite AC and PTC lesion ratings, each time controlling for the BG composite lesion rating. It should be recalled that pretreatment naming scores consisted of percent correct on standardized tests of object and action naming (BNT and ANT, respectively). Improvement indices consisted of range corrected gain scores for the specific object and action naming items trained during treatment. Correlations between degree of cortical lesion and range corrected gain scores for treated stimuli are shown in Table 4.

Both pretreatment naming scores and improvement during treatment showed strong, statistically significant correlations with AC lesion extent for both object and action naming. It should be noted that all naming correlations with AC were unexpectedly significant in the

positive direction. In other words, greater anterior lesion extent correlated with higher pretreatment naming scores and greater improvement in naming during treatment for both object and action naming. The meaning of these unexpectedly positive correlations will be addressed in the discussion section. PTC lesion extent showed a modest but significant correlation with pretreatment action naming, but no other significant correlations for pretreatment naming or improvement were noted for PTC.

When partial correlations between PTC and naming measures were carried out, controlling for AC, there were significant correlations for both the ANT ($r = -.673$, $p = .008$) and BNT ($r = -.539$, $p = .047$), but not for naming improvement in action naming ($r = -.428$, $p = .190$) or object naming ($r = -.530$, $p = .076$).

Follow-up analyses were also conducted for individual ROIs, and were found to overwhelmingly reflect the overall findings (Table 5), and will not be discussed in great detail here. Individual ROIs within AC were almost all positively and significantly correlated with all naming measures. Individual ROIs within PTC were generally negatively and not significantly correlated with naming measures.

Naming and Left Basal Ganglia Lesions

It was expected that basal ganglia lesion ratings would be significantly correlated with both object and action naming for both pre-treatment naming and change in naming during treatment. Given the reported effect of basal ganglia lesions combined with cortical lesions in aphasia (Brunner et al., 1982; Kim et al., 2002), correlations were carried out as partial correlations, controlling for the effects of anterior and posterior cortical lesions. Results are shown in Table 6. As can be seen, correlations between basal ganglia lesion ratings and naming scores or naming improvement were far from significant when PTC lesion ratings were controlled for, consistent with the relatively low correlations between PTC lesion extent and these variables. Correlations between naming scores/improvement and BG lesion extent (when neither AC nor PTC were controlled for) are not shown in Table 6 but were not significant. However, when AC lesion ratings were controlled for, correlations were highly significant. This latter finding most likely is related to the opposite effects of AC and BG lesions on naming and treatment outcome and will be addressed in the Discussion section.

In order to determine if lesion ratings in certain basal ganglia structures were more highly correlated than others to naming and change in naming during treatment, individual partial correlations were run for each basal ganglia structure, controlling for AC lesion extent. Results were generally consistent with the composite BG correlations (Table 5) and are not discussed in detail here.

DISCUSSION

The primary purpose of the present investigation was to study the relationship between lesion location/extent and treatment outcomes for object and action naming. The positive correlation between degree of AC lesion and pretreatment naming/naming improvement was not expected. It indicated that large AC lesions were associated with better pretreatment naming and greater improvement in naming performance during treatment. On the other hand, the negative correlation between degree of BG lesion and pretreatment naming/improvement was expected. It indicated that larger BG lesions were associated with poorer pretreatment naming and less improvement during naming treatment. Findings for both the AC and BG were consistent for object and action naming, contrary to expectations. The importance of these findings is discussed in detail below.

Degree of AC Lesion and Pretreatment Naming/Improvement

It was hypothesized that degree of PTC lesion would be negatively correlated with pretreatment object naming and object naming improvement. Further, it was hypothesized that degree of AC lesion would be negatively correlated with pretreatment action naming and action naming improvement. Unexpectedly, however, greater anterior lesion extent correlated robustly with better pretreatment naming scores ($r = .730$ for BNT, $r = .740$ for ANT) and with greater improvement during treatment ($r = .858$ for objects, $r = .821$ for actions). In other words, patients with larger AC lesions tended to show both better pretreatment scores on the BNT and ANT and greater range corrected gain scores for object and action naming probes during treatment than patients with smaller AC lesions. There was no significant relationship between PTC lesion and improvement in either treatment. To make certain that results could not be explained by a correlation between degree of AC and PTC lesion, we did a product-moment correlation and found no significant relationship between the two ($r = .207$, $p > .05$). Further, since items generally were selected for treatment that patients had difficulty naming at pre-treatment evaluation, all patients began treatment with substantial room for improvement, and no patient was close to ceiling regarding percentage of correct responses on treated items. Further, use of range-corrected gain scores, would negate any advantage one subject might have over another regarding baseline accuracy in naming. Yet, based on these data, it appears likely that the patients who have higher pre-treatment naming scores (and larger anterior lesions) are more able to benefit from treatment. However, this observation does not account for why patients with larger anterior lesions have better naming scores in the ANT and BNT prior to treatment, and it does not explain the mechanism underlying the greater improvement for patients with larger lesions. For heuristic reasons, a hypothesis regarding the underlying mechanism is offered.

Any theory claiming that a larger brain lesion leads to better cognitive functioning is likely to be controversial; however, the idea is not without precedent. For example, reports from the epilepsy literature have indicated that surgical lesions in the left anterior temporal lobe can be associated with improved complex language comprehension (Hermann, Wyler & Somes, 1991). Vargha-Khadem et al. (1997) also reported a case of Sturge-Weber Syndrome in which the patient was mute with little receptive vocabulary until his atrophic and diffusely calcified left hemisphere was removed at the age of nine, and he was taken off of anticonvulsant medication. Subsequently, this patient developed expressive and receptive language skills, many of which were within the low normal range for his age, and he spoke in complete sentences with a variety of grammatical forms. Both of these studies were with patients who had tissue removed for conditions other than stroke; hence, we should be somewhat cautious in generalizing from their cases to our sample. However, Monti et al. (2007) applied transcranial direct current stimulation (tDCS) to the left frontotemporal region of stroke patients with chronic nonfluent aphasia. Cathodal stimulation, thought to suppress cortical activity, improved naming accuracy, but anodal stimulation, thought to enhance cortical activity, had no effect on naming accuracy. Hence, suppression of left frontal activity in patients with aphasia may lead to improvement of language function in some cases. These latter data lend credence to the notion that left frontal activity can interfere with naming in some cases of aphasia, as can activity in right pars triangularis (Naeser et al., 2005).

The concept that suppression of activity in or removal of dysfunctional tissue can improve language function is relevant to the current data set. The strength of the correlations found in the present study between degree of AC lesion and both pretreatment naming and naming improvement indicates this idea should be given serious consideration. It should be remembered that all patients in the current study had chronic aphasias and it can therefore be inferred that their lesions, whether large or small in size, produced significant damage to the language production network. This damage may have been inflicted in different particular

areas of the language production network for different participants; however, each had the common effect of significantly disabling the system. On the other hand, patients who demonstrated good recoveries (see Crosson et al., 2007 for discussion of this matter) were excluded from the current sample because they did not demonstrate deficits requiring treatment. Given these characteristics of the current sample, one possible explanation for the positive correlation between naming indices and degree of AC lesion is that anterior cortex was damaged enough that it could only produce “noisy” output with poor correspondence to naming targets, and that its elimination in cases of larger anterior lesions removes the source of noise competing with other areas of the dominant hemisphere or with areas of the previously nondominant hemisphere, thereby allowing reorganization to occur. This conclusion should be considered a hypothesis requiring further empirical validation. Further, it would be useful to establish correlations between degree of frontal lesion and naming accuracy in a full range of lesion sizes and language deficits. Based upon the literature (e.g., Heiss et al., 1997), we suspect that patients with more modest deficits and, frequently, smaller lesions than patients in the current study may show a negative correlation between degree of frontal lesion and naming performance. Again, empirical validation of this assumption is needed.

Correlation of a greater degree of lesion with greater improvement during treatment is counter-intuitive from most available lesion models. Hence, alternative hypotheses are difficult to conceptualize. It is possible that frontal areas are not very important in naming processes; for example, the most common lesion in chronic Broca’s aphasia includes much more than frontal cortex (Alexander, 2003). However, a lack of importance of the frontal cortex in naming does not explain the strong positive correlation between lesion size and either naming scores or improvement during treatment in the current study.

Indeed, the most important conclusion to be drawn from this finding is that the impact of lesion location and extent on treatment outcome deserves further attention. Indeed, the current findings are based on a relatively small number of subjects for correlation studies, and until confirmed, they should be considered provisional. Further, it should be noted that correlations between lesion location/extent may differ for treatments relying on different underlying mechanisms. Nonetheless, understanding the relationship between cortical lesion variables and outcome for various treatments could be useful both for selecting treatment strategies in aphasia and for designing new, more effective treatments.

Basal Ganglia and Anterior Cortical Lesions

Basal ganglia lesion extent was significantly correlated with pre-treatment naming measures and naming improvement only when degree of AC lesion was controlled by statistical means (i.e., partial correlation). This finding is consistent with previous literature suggesting that basal ganglia lesion, when combined with cortical lesion, can produce more severe and long-lasting aphasia than a similar degree of cortical lesion without basal ganglia lesion (Brunner et al., 1982). A further implication is that the impact of basal ganglia lesion can be masked if the degree of anterior lesion is not controlled for by analysis techniques.

The fact that controlling for anterior lesion extent was important in revealing the influence of basal ganglia lesions (while controlling for posterior lesion extent had little if any effect), reflects a special relationship between anterior cortex and the basal ganglia. Indeed, Middleton and Strick (2000) have previously described several basal ganglia-thalamo-cortical circuits or loops involving anterior cortical regions, including Brodmann areas 46 and 9. Similar loops involving other anterior cortical regions such as Brodmann areas 44 and 45 may also exist (Ullman, 2004). As previously noted, Crosson et al. (2005, 2007) suggested that the left basal ganglia can suppress dysfunctional perilesional activity during word production, allowing other areas to assist without interference from the dysfunctional

cortex. Hence, language production may be more adeptly re-organized when the left basal ganglia are intact. Indeed, Kim et al. (2002) and Crosson et al. (2005) showed that patients with basal ganglia damage had prominent bilateral frontal activity during language production, but that patients with intact basal ganglia had predominantly right frontal activity, suggesting that an intact basal ganglia may suppress left frontal activity, allowing the language production to reorganize to right frontal cortex. Such a mechanism would be consistent with the idea that one function of the basal ganglia is to suppress activity competing with selected actions (e.g., Crosson, Benjamin, & Levy, 2007; Mink, 1996; Penney & Young, 1986). As the current results indicated that patients with smaller basal ganglia lesions both have higher pretreatment BNT and ANT scores and demonstrate greater range corrected gain scores for object and action naming, the current findings are consistent with this hypothesis.

It should be noted that basal ganglia lesions which produce aphasia have been associated in acute stroke with hypoperfusion of language cortex, which is not detected by standard structural imaging such as used in the current study (Hillis, Barker, et al., 2004; Hillis, Wityk, et al., 2002). In keeping with these findings, we are not suggesting a direct role for the basal ganglia in basic language functions. Rather, we believe that a more subtle influence that the basal ganglia normally exert on cognitive processes (see Crosson, Benjamin, & Levy, 2007 for details) can greatly facilitate reorganization of function after lesion.

Of course, alternative hypotheses to a role for the basal ganglia in suppressing interference from non-essential cortical activity should be considered. Dynamic diaschisis (Price & Friston, 2003) refers to the idea that an intact area of cortex may be affected in performing a specific function when it relies upon interaction with a damaged area to perform that function. The basal ganglia are known to be connected to a vast array of frontal as well as temporal and parietal cortices (Middleton & Strick, 2000). Yet, as noted above, basal ganglia lesion alone does not seem to be sufficient to cause aphasia (Hillis, Barker, et al., 2004; Hillis, Wityk, et al., 2002), which raises some doubts about functional diaschisis as an explanation for the current phenomenon. If the cortex were dependent upon the basal ganglia for naming functions, then basal ganglia lesion alone should cause more obvious disturbance in naming.

Another possibility is that inclusion of the basal ganglia in an ischemic infarct may be a sign that the entire middle cerebral artery (MCA) distribution has been compromised. Indeed, the lenticulostriate arteries are derived from the initial (M1) segment of the MCA, and therefore, the most common site of occlusion in striatocapsular infarct is the M1 segment of the MCA (Weiller et al., 1993), from which the other MCA segments are derived. In cases where M1 occlusion is not the cause of striatocapsular infarct, occlusion of the internal carotid artery is usually the culprit, which also compromises the entire MCA distribution. In isolated striatocapsular infarct, end-to-end anastomosis from other arterial territories is thought prevent cystic infarction of the type most easily visualized on clinical brain images, but ischemic neuronal dropout still may affect cognitive functions (Nadeau & Crosson, 1997). In a case of reading deficit in chronic basal ganglia infarction, Love, Swinney, Wong and Buxton (2002) used perfusion imaging to assess resting blood flow levels to various cortical structures. Although no damage was visible on structural imaging, the left inferior parietal lobule was hypoperfused, offering a possible explanation for the reading deficits. Hypoperfusion of this cortex may have represented ischemic neuronal drop-out that reduced resting metabolic needs driving regional cerebral blood flow and that could not be seen on clinical structural images. Extensions of the current study using imaging of resting cerebral blood flow or hypercapnic challenge to assess cerebrovascular reactivity would be beneficial in further exploring these relationships (Iannetti & Wise, 2007).

Degree of PTC Lesion and Naming

Extent of PTC lesion was not initially strongly correlated with either pretreatment naming or treatment outcome; however, the correlations between pre-treatment naming (but not treatment improvement) and PTC lesion extent became more highly significant when the effects of AC lesion were controlled. This effect was similar to that found with the basal ganglia correlations discussed in the previous section, and supported the notion that unless controlled for, the presence of large anterior cortical lesions can obscure the relationship between language functioning and lesions in other areas. The importance of PTC in both object and action naming has been found in previous studies (Knopman et al., 1984; Cato et al., 2004b; Tranel et al., 2005). It may be that the posterior language cortex plays a special role in the reorganization of naming ability in anterior regions post-stroke. For example, when left anterior cortex (ostensibly participating in neural networks representing the word production lexicon) is lesioned, perhaps the preservation of networks in the left posterior cortex representing aspects of a receptive lexicon could facilitate the reorganization of a new production lexicon. Therefore, when significant lesions affect the left posterior cortex, it would be less likely that such reorganization could take place. However, it should be emphasized that the correlations with PTC and treatment improvement were not significant even when extent of AC lesion was controlled.

Object and Action Naming

Previous literature has indicated that lesion location differentially affects object vs. action naming, with AC lesions affecting action more than object naming and PTC lesions affecting object more than action naming (Damasio & Tranel., 1993; Hillis, Tuffiash, et al., 2002; Tranel et al., 2001). Hence, it was hypothesized that AC lesion extent would be more negatively correlated with pretreatment action naming than object naming and more negatively correlated with improvement in action naming than object naming. Conversely, it was hypothesized that PTC lesion extent would be more negatively correlated with pretreatment object naming than action naming and more negatively correlated with improvement in object naming than action naming. The current data did not support this hypothesis. Rather, AC lesion extent demonstrated strong positive correlations with pretreatment naming and improvement in naming for both object and action naming. One potential reason that the expected pattern did not emerge is that participants in the current study were quite different in terms of level of language deficit than the patients of Damasio and Tranel (Damasio & Tranel, 1993; Tranel et al., 2001). Most participants in the current study were only included if they were impaired on both action and object naming whereas the participants in the Damasio and Tranel study had varying degrees of accuracy in their naming, but were not necessarily impaired in both areas. It is possible that the greater overall severity of aphasia in our participants and the selection bias in our patients toward impairment in both object and action naming obscured the pattern seen in less severely impaired participants, as demonstrated by Damasio and Tranel. On the other hand, not all studies have found dissociations between object and action naming, and some studies have found dissociations only when certain factors such as word-frequency, imageability, transitivity, and manipulability/action semantics are taken into account (see Arevalo et al., 2007; Lu et al., 2002; Luzzatti, et al., 2002, Jonkers & Bastiaanse, 1998).

Finally, the choice of Naeser's ROI-based technique for the current study should be briefly addressed. Her technique requires a relatively coarse estimate of degree of lesion in relatively large ROIs. Hence, the differences in image quality can be easily accommodated by this approach. Given the previous success of this technique in revealing important commonalities in lesions between aphasia patients (Naeser et al., 1998; Naeser & Hayward, 1978; Naeser et al., 1989), given the guidance of the Matsui and Hirano (1978) atlas in locating objective ROI boundaries for cortical ROIs, and given our ability to train raters to a

high degree of reliability ($r=.887$) on an independent set of images, we are confident that the degree of lesion was adequately captured by application of Naeser's technique. Finally, in the current study, use of the ROI method allowed for the statistical control of particular regions (using partial correlations) in order to more clearly observe correlations between other regions and various naming measures.

Conclusions

The results of the current study may be summarized by two major findings. First, when controlling for degree of basal ganglia lesion, greater anterior lesion extent correlated strongly with better pre-treatment naming and improved naming during treatment. Second, when controlling for anterior lesion extent, greater basal ganglia lesion extent was strongly correlated with both worse pre-treatment naming and less improvement during treatment. Based on these results, a unifying explanation was set forth to explain both of these findings: It was suggested that there are two relatively independent mechanisms which are able to suppress the "noisy" or non-functional left frontal output in the present group of chronically aphasic patients. The first mechanism is that left frontal cortex with the potential to produce such noisy output may be damaged by larger left frontal lesions, preventing them from competing with potentially more functional substrates during word production. The second mechanism is that the left basal ganglia, when left intact, can suppress activity in regions that produce "noisy" output, allowing more functional substrates to take over. It is simply a reversal of what happens in normal language, where left pre-SMA uses the right basal ganglia to suppress right frontal activity that might compete or interfere with left frontal activity during word generation (see Crosson et al., 2003). This second principle also is consistent with the observations of Brunner et al. (1982) that cortical plus basal ganglia lesions produce more severe and longer lasting aphasias than cortical lesions alone and consistent with the observations of Kim et al. (2002) and Crosson et al. (2005) that word production is re-organized to right frontal cortex only when the left basal ganglia are intact. These two mechanisms may operate in an orthogonal fashion, making it difficult to detect the effects of one unless the effects of the other are controlled. Given the relatively small number of subjects in this correlational study, this hypothesis about suppression of frontal activity should be considered as tentative until the findings are replicated.

Hence, future studies will be necessary to determine both the degree to which the current findings can be generalized and the validity of the theoretical propositions derived from the findings. It must be remembered that the current sample of patients was selected because they had chronic aphasias with substantial naming impairments. Patients who showed good recoveries did not meet inclusion criteria. Nonetheless, the sample can be considered representative of patients with chronic aphasia who may seek treatment for word production problems, and understanding the mechanisms that impact natural recovery and treatment outcome will be essential for selecting the best treatment option for an individual patient and for designing maximally effective treatments. Hence, the most important conclusion from the current investigation is that we must study factors contributing to recovery and treatment outcome. In particular, our knowledge of the relationship between lesion location and aphasia taxonomy does not always translate to knowledge of mechanisms underlying recovery and treatment outcome. Further, comparison of the current findings to those of Cato et al. (2004a, 2004b) suggests that factors influencing treatment response are not the same for all treatments. Hence, we must find the means to conduct these difficult but important studies on a variety of treatments.

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Table 1

Demographic and language data for individual participants

Subj #	Age	Ed	Sex	Race	Aphasia Type	Mos Post	ANT	BNT
1	70	10	M	C	nonfluent	17	0.158	0.083
2	68	14	M	C	nonfluent	128	0.474	0.433
3	49	12	F	C	nonfluent	29	0.614	0.450
4	81	NA	F	C	nonfluent	93	0.632	0.483
5	74	18	M	C	nonfluent	48	0.439	0.400
6	80	16	M	C	fluent	41	0.371	0.100
7	64	12	M	C	fluent	5	0.210	0.083
8	66	14	M	C	fluent	9	0.368	0.167
9	50	14	M	C	nonfluent	6	0.032	0.017
10	70	14	M	C	fluent	31	0.048	0.033
11	61	13	M	AA	nonfluent	13	0.694	0.333
12	52	12	F	C	fluent	14	0.158	0.050
13	51	12	F	C	nonfluent	6	0.491	0.300
14	72	12	M	AA	nonfluent	9	0.065	0.050
15	70	14	F	AA	nonfluent	11	0.048	0.000

Ges = Gestural treatment; Sem = Semantic/phonological treatment; RCG = range corrected gain score for treatment; ANT and BNT scores are at baseline and expressed as fraction of correct responses / total items.

Anterior, posterior, and basal ganglia ratings, baseline ANT and BNT scores, treatment type, and range corrected gain scores (RCG) for each participant

Table 2

Partic	AC (max = 35)	PTC (max = 40)	BG (max = 15)	ANT	BNT	Obj Tx- type	RCG Obj	Act Tx- type	RCG Act
1	7.75	23.25	4.00	0.158	0.083	Ges	0.18	Ges	0.08
2	26.25	16.75	7.75	0.474	0.433	Sem	0.42	Sem	0.25
3	14.50	27.00	5.50	0.614	0.450	Ges	0.38	Ges	0.26
4	26.00	10.00	6.00	0.632	0.483	Sem	0.66	Sem	0.77
5	28.00	22.50	12.00	0.439	0.400	Sem	0.31	Sem	0.24
6	1.00	13.00	0.00	0.371	0.100	Sem	-0.02	NA	NA
7	3.00	12.50	1.00	0.210	0.083	Ges	0.02	Ges	0.33
8	15.25	10.00	11.00	0.368	0.167	Sem	0.07	Sem	-0.03
9	20.50	27.00	11.25	0.032	0.017	Ges	0.30	Ges	0.21
10	0.00	28.50	2.25	0.048	0.033	Ges	0.01	Ges	-0.01
11	24.00	10.50	3.50	0.694	0.333	Sem	0.83	NA	NA
12	2.50	13.00	8.75	0.158	0.050	NA	NA	Ges	-0.04
13	0.00	0.50	1.00	0.491	0.300	Ges	0.38	Ges	0.28
14	15.25	20.75	9.75	0.065	0.050	NA	NA	Ges	0.02
15	19.75	34.50	12.00	0.048	0.000	Ges	0.15	NA	NA

Table 3

Descriptive statistics for language measures.

	N	Mean	Standard Deviation	Min	Max
Pretreatment BNT *	15	.199	.179	0	.483
Pretreatment ANT *	15	.320	.232	.032	.694
Object Naming Improvement **	13	.284	.256	-.02	.83
Action Naming Improvement **	12	.197	.225	-.04	.77

* fraction of correct responses / total items

** range corrected gain scores

Table 4
Partial correlations between naming measures and cortical lesions extent, controlling for basal ganglia lesion extent.

	Region	Pretreatment BNT & ANT		Improvement in Naming Probes	
		r	p	r	p
Object Naming	AC	.730	<.0005**	.858	<.0005**
	PTC	-.350	.141	-.373	.232
Action Naming	AC	.740	<.0005**	.821	.002**
	PTC	-.470	.042*	-.256	.448

* p ≤ .05
** p ≤ .01

Table 5

ROIs, their composite regions, and correlations with pre-treatment and treatment improvement measures

Composite Measure	ROI	<i>r</i> : pre-treatment			<i>r</i> : improvement		
		BNT	ANT	Object	Action		
Anterior Cortex (AC)	Anterior Brodmann area 9	.784**	.638**	.439	.672*		
	Brodmann area 46	.690**	.563*	.738**	.686*		
	Brodmann area 45	.644**	.633*	.701**	.757**		
	Brodmann area 44	.586*	.620*	.743**	.744**		
	Posterior Brodmann area 9	.717**	.694**	.746**	.602*		
	Precentral gyrus (non-mouth)	.654**	.667**	.886**	.791**		
	Precentral gyrus (mouth)	.623*	.629*	.878**	.794**		
	Anterior temporal lobe	-.630*	-.650*	-.398	-.369		
	Wernicke's area	-.516	-.660**	-.515	-.365		
	Brodmann area 37	-.476	-.543*	-.336	-.094		
Posterior/Temporal Cortex (PTC)	Primary sensory cortex (mouth)	.312	.194	.324	.002		
	Primary sensory cortex (non-mouth)	.296	.211	.357	.070		
	Anterior supramarginal gyrus	-.190	-.365	-.460	-.151		
	Posterior supramarginal gyrus	-.389	-.569*	-.527	-.303		
	Angular gyrus	-.382	-.433	-.487	-.323		
Basal Ganglia (BG)	Putamen	-.658**	-.731**	-.637*	-.851**		
	Globus pallidus	-.532*	-.629*	-.708**	-.650*		
	Caudate	-.474	-.528	-.661*	-.637*		

*
p ≤ .05,**
p ≤ .01

Partial correlations for AC and PTC corrected for degree of basal ganglia lesion; partial correlations for basal ganglia corrected for degree of AC lesion

Table 6
Partial correlations between naming measures and basal ganglia lesion extent controlling for cortical lesion extent.

	Partial correlations controlling for cortical lesion extent					
			Pretreatment		Improvement	
	Control variable	r	p	r	p	
Object Naming	AC	-.623	.004**	-.749	.005**	
	PTC	.040	.870	.249	.434	
Action Naming	AC	-.750	<.0005**	-.785	.004**	
	PTC	-.154	.530	-.159	.641	

**
p ≤ .01