Behavioural and Neural Changes after a "Choice" Therapy for Naming Deficits in Aphasia: Preliminary Findings

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Preliminary Findings

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Abstract:
Background: Anomia, difficulty producing words, is a pervasive symptom of many individuals with aphasia. We have developed a treatment for naming deficits – the Phonological Components Analysis (PCA) protocol - that has proven efficacious for individuals with post-stroke aphasia.

Aims: The aim of the present investigation is to present preliminary findings exploring the potential influence of choice on our PCA treatment.

Methods & Procedures: Five individuals with aphasia were treated in one of two conditions – Choice or No Choice. Potential changes in neural activation as a function of the treatment were also investigated. Two individuals (one from each condition) underwent fMRI pre- and post-therapy.

Outcomes & Results: All individuals demonstrated a treatment effect immediately post-treatment and at 4- and 8-week follow-ups. Three also demonstrated generalization. Unfortunately, no clear-cut patterns emerged to allow us to make claims about the influence of choice, per se, on the behavioural manifestations of improved naming. Interestingly, the participant from the Choice condition showed neural activation changes post-treatment in frontal and parietal regions that were not evident for the participant in the No Choice condition. Moreover, these changes were accompanied by a larger treatment effect for that individual and generalization to a novel naming task.

Conclusion: The efficacy of PCA treatment for naming deficits is further supported. Also, continued exploration of task factors that may promote even better treatment effects using this protocol is warranted, as is continued investigation of the neural underpinnings associated with treatment effects.

Key words: stroke, aphasia, anomia, rehabilitation, neuroimaging, neuroplasticity

This report presents preliminary data exploring the potential influence of a particular task factor, the element of choice, on our phonologically-based treatment for anomia – the Phonological Components Analysis (PCA) protocol (Leonard, Rochon, & Laird, 2008). In addition, data addressing the neural changes that occur as a function of the therapy are presented, following upon our previous work addressing this topic (Rochon et al., 2010). The element of choice (or active engagement on the part of a participant in his/her therapy) has been raised as a potential factor that leads to better treatment effects. Hickin, Best, Herbert, Howard, and Osborne (2002) suggest that deeper processing during therapy may be promoted by an individual's engagement in the task through active choice and that treatment effects may, in turn, prove to be longer-lasting.

In Leonard et al. (2008), we demonstrated the efficacy of our PCA treatment for anomia in individuals with aphasia. Our PCA therapy is a modified version of Coelho, McHugh and Boyle's (2000) protocol for semantic features therapy, wherein participants are asked to name a picture and identify five phonological components of the target word (e.g., rhyming words). Using a single-subject multiple baseline across behaviours design, we found that the naming performance of seven of the ten participants improved, with very good maintenance of gains at 4-weeks follow-up, and evidence of generalization to untrained stimuli on a standardized naming test. While these results were encouraging, there were still three individuals for whom this treatment was not effective. We suggested that the notion advanced by Hickin et al. (2002), that active engagement on the part of the participant in his/her therapy is necessary to produce longer lasting effects may help to explain our results; phonological components (i.e., prompts) in our treatment were not simply supplied to the participants, but rather participants were provided with the opportunity to generate and/or choose their own for a given target word. Interestingly, five of

the seven patients for whom treatment was successful were able to generate the components independently at least 50% of the time (averaged across the 3 lists), as compared to 40% or less in the group for whom treatment was not successful.

As noted above, in addition to tracking changes in naming performance as a function of PCA treatment, we also investigated the neural processing characteristics associated with improved naming (Rochon et al., 2010). Using fMRI, we compared neural changes related to completing a phonological task and a semantic task before and after treatment. Two of the treated patients in Leonard et al. (2008) and two untreated patients were scanned. In both treated patients whose naming had improved post-treatment, we found changes associated with semantic processing in the left inferior frontal gyrus (LIFG) and left middle temporal gyrus, areas typically associated with semantic processing in healthy participants (e.g., Perani et al, 2003). In addition, consistent with some previous studies (e.g., Cornelissen et al., 2003; Meinzer et al., 2008) we found increased left hemisphere (LH) processing compared to right hemisphere (RH) processing post-treatment. This finding supports recent work by Fridriksson, Richardson, Baker, and Rorden (2011) who found, using transcranial magnetic stimulation of the LH in addition to behavioural anomia therapy, evidence to suggest that LH activation is extremely important to the recovery of naming abilities. We also found that activation post-treatment during the semantic task involved areas more typically associated with phonological processing; specifically the left supra-marginal gyrus and inferior parietal regions (e.g., Lurito, Kareken, Lowe, Chen, & Mathews, 2000). This finding led to the speculation that our phonologically-based treatment strengthened the connections between the lexical and phonological processing levels involved in naming. In addition, we suggested that perhaps, while our treatment focused on the phonological aspects of target words, semantic processing was also activated since pictures were used as

stimuli and correct production necessarily involved the activation of both semantic and phonological elements.

The present investigation represents a preliminary inquiry into the factor of active engagement or choice associated with the success of PCA treatment on naming performance in individuals with aphasia and associated neural underpinnings. In particular, we compared PCA treatment in two conditions: Choice and No Choice. The conditions differed as to whether the participant was allowed to *choose* the phonological components of the target word or whether he/she was simply provided with the response. We hypothesized that while the two conditions may result in similar immediate treatment effects, the Choice condition would lead to better effects of maintenance of targeted items and generalization to untrained lexical items. With respect to the neuroimaging results, we hypothesized that post-therapy, for individuals in both groups (Choice/No Choice) when performing both the phonological and semantic tasks, there would be a shift from greater RH processing to greater LH processing associated with improved performance in naming and more LH peri-lesional activation. Moreover, because the therapy specifically targets phonological processing, greater activation in the left supramarginal gyrus post- versus pre-therapy was expected. Associated increased activation by treated patients in the anterior LIFG and middle temporal areas during the semantic judgment task (and accompanying right to left hemisphere shift) would provide evidence of the influence of a phonological feature based therapy on semantic processing. In addition, based on the literature (e.g., Turner & Levine, 2004) emphasizing the importance of frontal regions to executive processing and active engagement, increased neural activation in frontal regions post-treatment was expected for individuals in the Choice condition.

Method for treatment phase

Participants: Five individuals with aphasia participated in this study. Participants were randomly assigned to one of two treatment conditions: Choice – comprised of two men and one woman (mean age: 81.3 years; mean level of education: 15 years); or No Choice condition – comprised of two men (mean age: 71.5 years; mean level of education: 9.5 years). All participants were right-handed individuals who were native English speakers or who had been educated in English, who had experienced a single left-hemisphere stroke and were at least 1-year post-onset at the time of enrollment. Classification of aphasia was based on the results of the *Boston Diagnostic Aphasia Exam* (Goodglass, Kaplan, & Barresi, 2001) and revealed 4 individuals with Broca's aphasia (3 in the Choice condition) and one with Wernicke's. All participants had a naming impairment defined by less than 75% correct on the *Boston Naming Test* (Goodglass et al., 2001) and had (corrected) normal vision and visual perceptual abilities within normal limits as defined by performance on the *Birmingham Object Recognition Battery* (Riddoch & Humphreys, 1993). Hearing was screened and found to be within normal limits for all. As well, no participant presented with a significant apraxia of speech and none was receiving formal speech-language therapy at the time of testing. Other exclusion criteria included a known history of drug or alcohol abuse, a history of major psychiatric illness and/or other neurological illness.

Treatment: The treatment stimuli were the same as those used in Leonard et al. (2008) and consisted of 105 coloured photographs.

Baseline testing: Participants were shown all of the pictures to name in three consecutive sessions. Words that were in error on at least 2 of the 3 sessions served as the potential pool of words to be targeted in therapy. Participants were asked to choose from this pool the items that they would like to have treated. Of those words, 30[1] were chosen and divided into 2 lists that

were equated as much as possible by category, word frequency, and number of syllables. Responses provided by the participants during the baseline sessions were also rated on a 4-point scale (0 = incorrect; 1 = semantic or phonological paraphasia; 2 = semantic or phonological paraphasia with immediate self-correction of target word; 3 = correct (Huber, Poek, Weniger, & Willmes, 1983).

Treatment: As noted, our PCA therapy is a modified version of Coelho et al.'s (2000) protocol for semantic features therapy. Participants were presented with a picture of the target word and asked to name it. Next, irrespective of the patient's ability to name the target, he/she was required to identify five phonological components of the target word (rhyming words, first sound, first sound associates, final sound, number of syllables), guided by the use of a chart. Identification of the components proceeded differently, depending on the treatment condition.

Choice Condition: For each of the five components to be identified, the participant was asked to provide a response. If the participant could not spontaneously provide a response, then he/she was asked to *choose* one from a list of up to four. The choices were visually presented on a card and read aloud by the examiner.

No Choice Condition: For each of the five components identified, the participant was *provided* with the response[2]. All other aspects of the treatment procedure were identical for the Choice and No Choice conditions (see Leonard et al. (2008) for complete details of the treatment protocol).

Treatment schedule: Treatment sessions (approximately one hour in duration) occurred approximately 3 times a week for 10 weeks (30 sessions in total). During each session, words in one of the two treatment lists were targeted. Target words were randomly presented at each session. Immediately following treatment and again at 4- and 8-week follow-up periods,

participants were asked to name all treated items and responses were rated on the 4-point scale. Scoring of these responses was carried out by a rater blind to the purpose of the study.

Reliability: Twenty percent of the treatment sessions were videotaped and all of the sessions were audiotaped. Point-to-point agreement was used as a measure of reliability for the administration of treatment and the scoring of responses and found to be high (administration of therapy 100%; scoring as correct/incorrect 93%; scoring on 4-point scale 81% and 88% pre- and post-therapy, respectively (see Leonard et al. (2008) for a detailed description of the procedures used).

Generalization: A comparison of performance on the *Philadelphia Naming Test (PNT)* (Roach, Schwartz, Martin, Grewal & Brcher, 1996) pre- and post-therapy provided a measure of the generalization of treatment effects to untreated items. Point-to-point agreement on scoring as correct/incorrect was 95% pre-therapy and 97% post-therapy.

Results of treatment phase

For each participant, the mean score (based on the 4-point scale) for naming treated items at baseline was compared to naming performance immediately post-treatment, and at 4- and 8-week follow-up periods using the Wilcoxon Signed Rank Test. For all participants, performance at all three post-treatment time points (i.e., post-treatment, 4- and 8-week follow-up) was significantly better than performance at baseline ($p<0.01$, one-tailed), with one exception; for P3, while performance at the 8-week follow-up period was better than baseline, this difference was not significant (see Figure 1).

(Figure 1 about here)

For each participant, treatment effect sizes were calculated and found to be medium to large (Busk & Serlin, 1992) (see Table 1) and performance on the PNT (Roach et al., 1996) was

compared pre- and post-therapy using the McNemar test. A significant difference ($p<0.01$, one-tailed) was found for P2, P3, and P5, with increased accuracy for all three patients post-treatment (see Table 2).

(Tables 1 and 2 about here)

Method for imaging phase

Participants: Two of the five participants in the treatment phase underwent neurological imaging. One participant (P2) was in the Choice Condition and the other one (P4) was in the No Choice Condition.

fMRI activation tasks: The two experimental tasks (semantic and phonological) and their corresponding control tasks were the same as those used in Rochon et al. (2010). In brief, a semantic judgment task, using the pictures from the *Pyramids and Palm Trees Test* (Howard & Patterson, 1992) was used as the experimental semantic task. Participants were presented with 3 pictures (one on top and two on the bottom) and were required to indicate, with a key press, which bottom picture was related in meaning to the one on top. The experimental phonological task was a rhyme judgment task using picture stimuli from a subtest of the *Psycholinguistic Assessments of Language Processing in Aphasia (PALPA)* (Kay, Lesser & Coltheart, 1992). Two pictures were presented side by side and the participant was required to indicate, with a key press, if the words rhymed or not. The computer automatically recorded reaction time and accuracy (see Rochon et al. (2010) for further details regarding the control tasks and baseline task).

fMRI protocol: For P2, scanning occurred 1 week prior to treatment and for P4 5 weeks. The second scans occurred 1 week post-treatment for P2 and 2 days post-treatment for P4.

Scans were obtained using a 3.0 Tesla system (Signa Eclipse, GE Medical Systems, Milwaukee, WI). A T1-weighted volumetric anatomical MRI was obtained for each participant (124 axial slices, 1.4 mm, FOV = 22cm). In addition, for each participant, T2*-weighted functional images were acquired using a spiral in/out pulse sequence (26 axial slices, 5 mm, TR = 2000 ms, TE = 30 ms, FOV = 20, 64 x 64 matrix). To assess brain activation the blood oxygenation level-dependent effect was used.

Acquisition of the fMRI data was done using a block design. For both the semantic and phonological tasks, 6 runs were used. Runs were divided into 3 blocks (experimental, baseline, control), with each block containing 4 trials. The stimulus presentation rate was one per 8 seconds; so each block was 32 seconds and each run 96 seconds. The total duration for the presentation of the 6 runs was 576 seconds. The 6 runs used for the semantic task were presented together as were those comprising the phonological task (see Rochon et al. (2010) for example trials).

fMRI data analysis: As in Rochon et al. (2010), fMRI images were preprocessed using the Analysis of Functional Neuroimages (AFNI) software (Cox, 1996). The images were motion-corrected, spatially coregistered, and smoothed. To further improve the signal-to-noise ratio in the patients' images we used Independent Components Analysis (ICA) (Kochiyama et al., 2005). Each participant's dataset was analyzed individually using Partial Least Squares (PLS) analysis (McIntosh & Lobaugh, 2004). PLS is a multivariate technique, which examines the covariance between activity in all brain voxels and experimental conditions, providing sets of mutually independent spatial patterns depicting brain regions that show the strongest relation to the contrasts across tasks. Using PLS, latent variables (LV), defined as cohesive patterns of neural activity associated with a task, were identified (the LV accounting for the most covariance is

extracted first) across conditions and Scans 1 and 2. A permutation test (McIntosh et al., 1996) determined the significance of each LV and a bootstrap estimation of the standard errors determined the reliability of each LV (Efron & Tibshirani, 1986). Note that this analysis reveals the contrasts that account for the most covariance between the experimental tasks and brain activity: contrasts are not specified in advance.

Results of imaging phase

Behavioural performance in the scanner:

Table 3(a) shows the reaction time (RT) data and Table 3(b) the accuracy data for P2 and P4 on the four tasks: phonological experimental, phonological baseline, semantic experimental and semantic baseline. The McNemar change test was used to assess the difference in accuracy between Scans 1 and 2 on both the phonological and semantic tasks for each patient. Only one comparison was significant ($p<0.01$; one-tailed), but it is in the wrong direction; at Scan 2 P4 was less accurate on the semantic task than at Scan 1. The Wilcoxon Signed Rank Test was used to examine the differences in reaction times between Scans 1 and 2 on both the phonological and semantic tasks for each patient for correct responses only. Two comparisons were significant, both for P4. For the both the phonological and semantic tasks, P4 was significantly faster ($p<0.05$; one-tailed) at Scan 2 than at Scan 1.

(Tables 3(a,b) about here)

fMRI results: PLS analyses were carried out comparing each participant's activity during the phonological and semantic tasks across both scans. For P2 comparison of the phonological to the baseline task yielded two significant LVs. LV1, accounting for 54% of the variance ($p=0.014$), is largely accounted for by patterns of activation at Scan 1, before treatment. LV2, accounting for 37% of the variance ($p=0.046$), represents changes in activation on this task at Scan 2 in left and

right prefrontal areas, thalamus, right middle occipital gyrus, and precuneus. Comparison of the semantic to the baseline task yielded a significant LV, which accounted for 80% of the variance ($p<0.001$). P2 showed changes in activation on the semantic task after treatment (i.e., Scan 2) in left and right prefrontal regions, left cingulate gyrus, left middle temporal gyrus, and right insula. Figure 2 shows the design scores for both of these analyses with representative cortical activity maps and Tables 4 and 5 show significant activations on the phonological and semantic tasks, respectively.

(Figure 2 about here)

(Tables 4 and 5 about here)

For P4, comparison of the phonological to the baseline task yielded one significant LV accounting for 68% of the variance ($p=0.002$). As for P2, this effect appears to be due to patterns of activation at Scan 1, before treatment. Comparison of the semantic to the baseline task yielded a significant LV, which accounted for 79% of the variance ($p<0.001$). In contrast to P2 where the effect occurred after treatment, this effect in P4 was evident both before and after treatment (i.e., no significant changes in activation seen after treatment). P4's imaging data can be seen in Figure 3 and Tables 4 and 5.

(Figure 3 about here)

Discussion

The purpose of the present investigation was to explore the potential influence of choice on the efficacy of our phonologically based treatment for anomia - Phonological Components Analysis - and to identify associated neural underpinnings. Results indicated that all five participants showed improved naming performance post-treatment, irrespective of the treatment condition. Moreover, the treatment effect was maintained at 4- and 8-week follow-up periods,

and generalization of naming to untrained items was noted for three participants, two of whom were in the Choice condition and one in the No Choice condition. Unfortunately, with this small number of participants, no clear-cut patterns emerged to suggest that the element of choice, per se, resulted in improved naming performance, nor that it particularly influenced the maintenance of treatment effects and generalizability to untrained items.

With respect to the imaging data, while acknowledging the limitation inherent in the small sample size, the results, nonetheless, are somewhat more intriguing. While it is true that both participants showed improved naming after treatment, P2 (from the Choice condition) showed neural activation changes post-treatment in a number of areas, most notably left and right frontal regions that were not evident for P4 (No Choice condition). Interestingly, these changes in neural activation were accompanied by a larger treatment effect size for P2 compared to P4 and generalization to a novel naming task (once again, not evidenced by P4). These findings speak to the issue of neuroplasticity associated with our treatment protocol and seem consistent with the results of Fillingham, Sage and Lambon Ralph (2005) and others (e.g., Turner & Levine, 2004) who have argued that frontal executive systems in particular are crucial for optimal gains in rehabilitation.

The results of the present study are mostly similar to those of other studies and to our previous study (Rochon et al., 2010) regarding the areas of activation that were identified after successful treatment for anomia. However, the current results also differ somewhat from our previous study (Rochon et al., 2010) even though we used the PCA treatment and the same fMRI tasks. In our first study, we found changes in activation after treatment only on the semantic task and predominately in the left hemisphere; in the present investigation changes in activation were found on *both* the phonological and semantic tasks. Moreover, for P2 while changes in activation

on the semantic task were also predominantly in the left hemisphere, changes on the phonological task were predominantly in the right hemisphere.

Based on these findings one might speculate that the element of 'choice' that was manipulated in this study led to post-treatment changes in activation in the phonological task in addition to changes on the semantic task. It is also of interest to note that it has been suggested that the right inferior frontal gyrus may play a more important role in language processing with larger lesions and where there is less pronounced ipsilesional activity (e.g., Sebastian & Kiran, 2011; Meinzer, Harnish, Conway & Crosson, 2011; Cappa, 2011). P2's relatively large lesion and the fact that the phonological task recruited a relatively large amount of right hemisphere activity even before treatment (i.e., see the first significant LV for P2) are in keeping with these suggestions. In addition, rhyming has been shown to activate areas in the right inferior frontal gyrus (Calvert et al., 2000). This points to the importance of considering the influence of the task (see Cappa, 2011; Meinzer et al., 2011) on our findings as the task used here was not one of overt naming but of rhyme judgment. Lastly, the preponderance of changes in brain activation after therapy in the left hemisphere on the semantic task is in line with the importance that has been ascribed to increased left hemisphere activation for recovery in anomia, which has been well documented (e.g., Fridriksson, 2010; see Meinzer et al., 2008; Rochon et al., 2010). We can also speculate that improvement on the semantic task after treatment is compatible with the notion that PCA treatment exerts its effect by boosting access to the semantic information necessary for word production (Leonard et al., 2008; Rochon et al., 2010; Van Hees, Angwin, McMahon, & Copland, 2013).

There is yet another intriguing difference between the present results and our previous ones. In Rochon et al. (2010), both treated patients who improved after PCA treatment showed

changes in activation patterns after treatment. In the present study, while both patients improved with PCA treatment, only one (P2) showed changes in activation after treatment. Although the reasons for this remain to be further explored, one possibility has to do with the magnitude of the treatment effects observed. The treatment effect size for P2 was 3.9, whereas for P4 it was 1.5. In Rochon et al. (2010), the treatment effect sizes for the two patients who improved were comparable to P2's (3.0 and 3.47), leading us to speculate that there may be a certain threshold of behavioural improvement that has to be exceeded in order for concomitant changes in neural activation patterns to be detected.

In terms of the behavourial performance of the participants in the scanner, the results are not very revealing. For P2, no changes were found between Scans 1 and 2 for either the phonological or semantic task in terms of both accuracy and reaction time. For P4, accuracy on the semantic task was poorer at Scan 2 than Scan 1. However, this may be attributable to a speed/ accuracy trade-off since reaction times at Scan 2 were also significantly faster than at Scan 1.

Some limitations of this study must be mentioned. Firstly, the small sample size precludes clear conclusions regarding the task factor that was manipulated in this study, the element of "choice". This and other task factors that may influence success in treatment for anomia remain to be further studied and elucidated. Secondly, the specific tasks used in the fMRI protocol no doubt influenced the findings. While the phonological and semantic judgment tasks employed here presumably reflected some of the underlying cognitive and linguistic processes involved in naming (Van Hees et al., 2013; see DeLeon et al., 2007), our results do not bear directly upon the task of overt naming per se. Although our use of a treatment approach targeted to a specific impairment allowed us to attempt to isolate the underlying cognitive operations involved in the treatment task (not often seen in larger, group studies), future work will include

larger numbers of patients and an overt naming task. Many other aspects related to brain plasticity associated with our aphasia treatment remain to be further examined, such as the areas of activation associated with correct versus incorrect responses (e.g., Fridriksson, Bonilha, Baker, Moser & Rorden, 2010; Postman-Caucheteteux et al., 2010), treatment maintenance (Menke, et al., 2009; Vitali, et al., 2010) and treatment dosage (Meinzer & Breitenstein, 2008). These and other studies may ultimately shed light on the types of aphasia that are likely amenable to remediation with a given treatment approach and to whether damage to specific areas of the brain and/or specific functional activation changes can help to predict response to treatment for anomia (e.g., Marcotte & Ansaldo, 2010; Fridriksson, 2010).

Importantly, the overall results further support the efficacy of PCA treatment for the remediation of naming deficits in aphasia. As well, they suggest that continued exploration of task factors that may promote even better treatment effects using this protocol in individuals with aphasia is warranted, as is continued investigation of the neural underpinnings associated with these treatment effects.

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Table 1. Mean effect size across treatment lists

Participant	Mean Effect Size
P1	1.70
P2	3.94
P3	1.85
P4	1.53
P5	3.28

All participants had a medium to large effect size according to Busk & Serlin, 1992

Table 2. Percent correct on the PNT pre- and post-therapy

Participant	Pre	Post
P1	67	63
P2	63	75*
P3	7	26*
P4	33	38
P5	45	72*

* Difference significant ($p < 0.01$, one-tailed), McNemar test;
PNT - Philadelphia Naming Test (Roach et al., 1996)

Table 3a. Accuracy and reaction time (RT msec) data for P2 and P4 on the phonological and baseline tasks at Scan 1 and Scan 2.

		Phonological Experimental Task				Phonological Baseline			
		SCAN 1		SCAN 2		SCAN 1		SCAN 2	
		RT	Accuracy	RT	Accuracy	RT	Accuracy	RT	Accuracy
Patients									
P2	Mean (SD)	3908 (949)	0.56	3970 (807)	0.54	745 (343)	1.00	629 (267)	1.00
P4	Mean (SD)	3339 (906)	0.42	2601 (613)	0.54	1047 (446)	1.00	505 (211)	1.00

Note. msec= milliseconds

Table 3b. Accuracy and reaction time (RT msec) data for P2 and P4 on the semantic and baseline tasks at Scan 1 and Scan 2.

		Semantic Experimental Task				Semantic Baseline			
		SCAN 1		SCAN 2		SCAN 1		SCAN 2	
		RT	Accuracy	RT	Accuracy	RT	Accuracy	RT	Accuracy
Patients									
P2	Mean (SD)	4336 (1099)	0.50	4060 (1377)	0.45	772 (418)	0.83	764 (436)	0.83
P4	Mean (SD)	3781 (1294)	0.88	2775 (1133)	0.46	817 (408)	0.83	755 (583)	0.83

Note. msec= milliseconds

Table 4. Activations for P2 and P4 on the phonological task.

Participant	Region	BA	MNI Coordinates			Ratio
			X(mm)	Y(mm)	Z(mm)	
P2 (LV1)						
(LH)	inferior frontal gyrus	45	-60	36	0.00	7.6018
	superior temporal gyrus	38	-36	4	-40.00	7.2574
	cingulate gyrus	31	-20	-48	24.00	7.0178
(RH)	middle occipital gyrus	18	28	-80	-4.00	11.1553
	orbitofrontal gyrus	11	20	44	-32.00	10.518
	inferior frontal gyrus	44	52	12	20.00	8.9544
	superior temporal gyrus	38	32	4	-36.00	8.2954
P2 (LV2)						
(LH)	inferior frontal gyrus	47	-55	36	-16.00	5.5315
(RH)	middle & inferior frontal gyrus	10	48	56	-4.00	19.5902
	medial frontal gyrus	10	16	52	-8.00	5.3883
	thalamus		24	-24	16.00	4.2289
	superior frontal gyrus	8	4	56	44.00	4.0466
	middle occipital gyrus	19	32	-60	16.00	3.7936
	precuneus	7	12	-40	48.00	3.6545
P4 (LV1)						
(LH)	cuneus	17	-16	-76	8.00	14.9999
	insula	13	-36	4	0.00	7.877
	inferior frontal gyrus	44	-48	4	16.00	6.5783
(RH)						
	inferior frontal gyrus	45	64	24	16.00	10.919
	superior frontal gyrus	10	12	68	-4.00	9.7921

Note. BA= Brodmann Area; MNI= Montreal Neurological Institute; LH= Left Hemisphere; RH= Right Hemisphere. (P2) LV1: p = 0.014; 54% covariance; LV2: p = 0.046; 37% covariance; (P4) LV1: p = 0.002; 68% covariance; Positive ratios correspond to regions with positive salience on the LV. Negative ratios correspond to regions with negative salience on the LVs. X (right/left): Negative values are in the left hemisphere; Y (anterior/posterior): negative values are posterior to the zero point (located at the anterior commissure); Z (superior/inferior): negative values are inferior to the plane defined by the anterior and posterior commissures. Ratio, salience/S.E. ratio from the bootstrap analysis, which is a measure of each voxel's reliability.

Table 5. Activations for P2 and P4 on the semantic task.

Participant		Region	BA	MNI Coordinates			Ratio
				X(mm)	Y(mm)	Z(mm)	
P2 (LV2)							
	(LH)	parahippocampal gyrus	35	-24	-12	-24	11.3868
		thalamus		-20	-16	16	7.7749
		cingulate gyrus	24	-12	-4	36	6.0772
		lingual gyrus	19	-20	-68	4	5.7634
		superior frontal gyrus	6	-8	-12	64	5.6704
		middle temporal gyrus	21	-64	8	-20	5.2785
		middle frontal gyrus	8	-32	12	36	4.9332
	(RH)	inferior frontal gyrus	9	60	16	24	12.542
		insula	13	36	-20	12	5.5609
		superior frontal gyrus	6	16	8	60	4.6445
P4 (LV1)		superior frontal gyrus	8	-16	44	44	7.0765
	(LH)	cingulate gyrus	32	-20	8	44	5.2219
		inferior frontal gyrus	9	-56	12	28	5.1105
		middle frontal gyrus	8	-28	28	40	4.8539
	(RH)	lingual gyrus	18	8	-76	0	13.8308
		middle frontal gyrus	6	20	0	56	7.032

Note. BA= Brodmann Area; MNI= Montreal Neurological Institute; LH= Left Hemisphere; RH= Right Hemisphere. (P2) LV2: $p < 0.001$; 80% covariance; (P4) LV1: $p < 0.001$; 79% covariance: Positive ratios correspond to regions with positive salience on the LV. Negative ratios correspond to regions with negative salience on the LVs. X (right/left): Negative values are in the left hemisphere; Y (anterior/posterior): negative values are posterior to the zero point (located at the anterior commissure); Z (superior/inferior): negative values are inferior to the plane defined by the anterior and posterior commissures. Ratio, salience/S.E. ratio from the bootstrap analysis, which is a measure of each voxel's reliability.

Figure Captions

Figure 1. Mean rating on a four-point scale naming treated words per participant at 4 time points: Baseline, post treatment, four-week follow-up and eight-week follow-up.

Figure 2. Results of the analysis comparing activation in the phonological and baseline tasks at Scans 1 and 2 for P2, as shown by the first latent variable (LV1) in Figure 2a and the second latent variable (LV2) in Figure 2b. Activations denoted in red represent brain regions that positively correlate with the phonological task and negatively correlate with the baseline task. Activations denoted in blue represent the brain regions that positively correlate with the baseline task and negatively with the phonological task. LV1 distinguishes the pattern of activation between these two tasks at Scan 1. LV2 distinguishes the pattern of activation between these two tasks at Scan 2. Figure 2c shows the results of the analysis comparing activation in the semantic and baseline tasks at Scans 1 and 2 for P2. This is shown by the first latent variable (LV1), which distinguishes the pattern of activation between these two tasks at Scan 2. Error bars denote 95% confidence intervals for the correlations calculated from the bootstrap procedure.

Figure 3. Results of the analysis comparing activation in the phonological and baseline tasks at Scans 1 and 2 for P4, as shown by the first latent variable (LV1) in Figure 3a. Activations denoted in red represent brain regions that positively correlate with the phonological task

and negatively correlate with the baseline task. Activations denoted in blue represent the brain regions that positively correlate with the baseline task and negatively with the phonological task. LV1 distinguishes the pattern of activation between these two tasks at Scan 1. Figure 3b shows results of the analysis comparing activation in the semantic and baseline tasks at Scans 1 and 2 for P4. This is shown by the first latent variable (LV1), which shows that the pattern of differences in activation between these two tasks is the same at Scans 1 and 2. Error bars denote 95% confidence intervals for the correlations calculated from the bootstrap procedure.

Footnotes

1. The responses used to represent the rhyming words were identified in a norming study of 10 healthy adults as the one that rhymed best.
2. P2 had only 21 target words as he did not have enough words in error at baseline.

Figure 1.

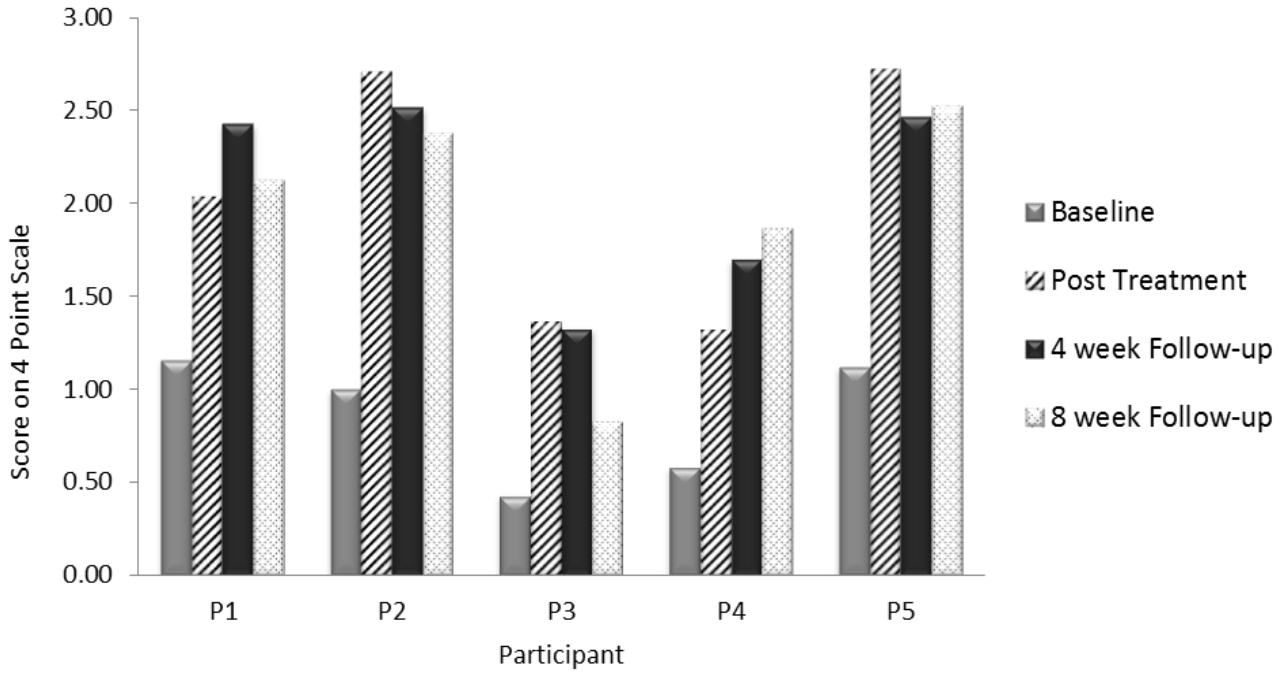
3.00
2.50
2.00
1.50
1.00
0.50
0.00
Score on 4 Point Scale
P1
P2
P3
P4
P5
Participant
Baseline
Post Treatment
4 week Follow-up
8 week Follow-up

Figure 2a.

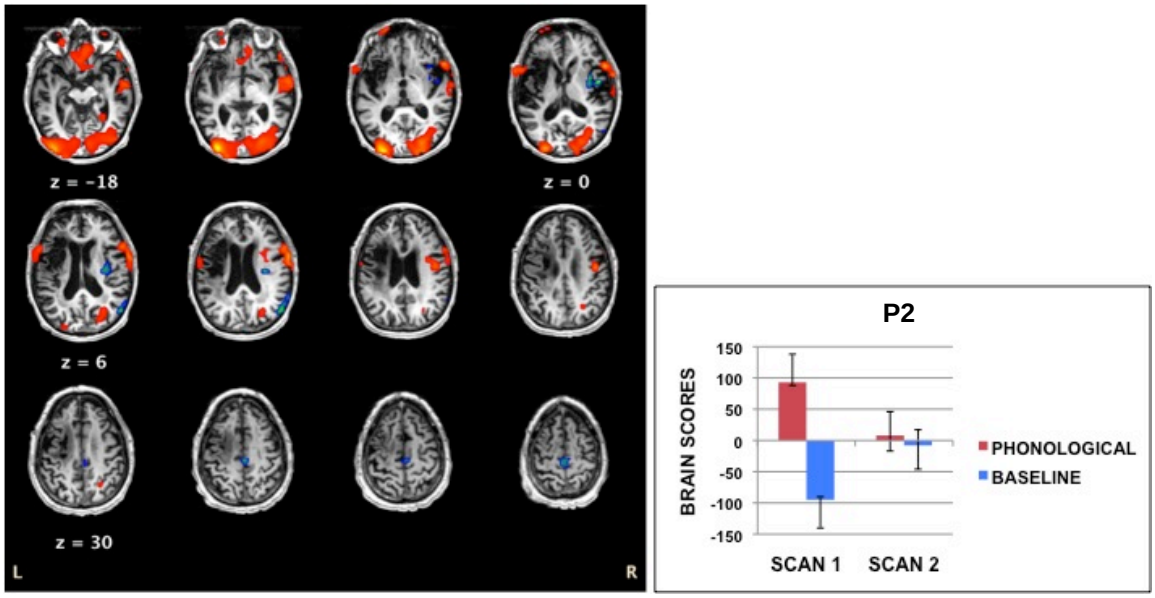

Figure 2b.

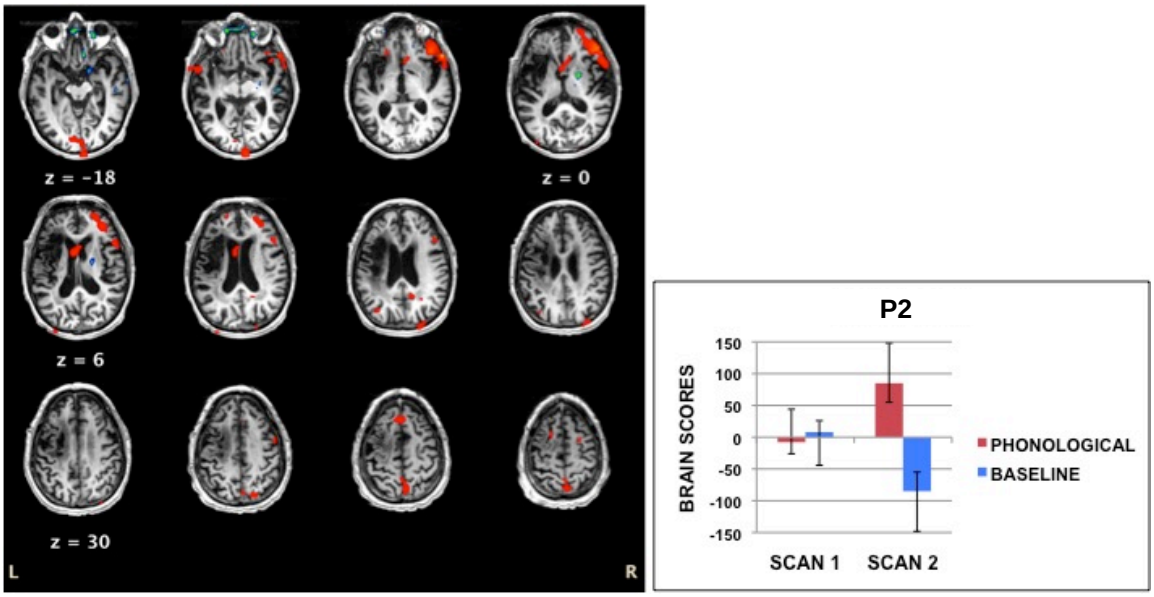

Figure 2c.

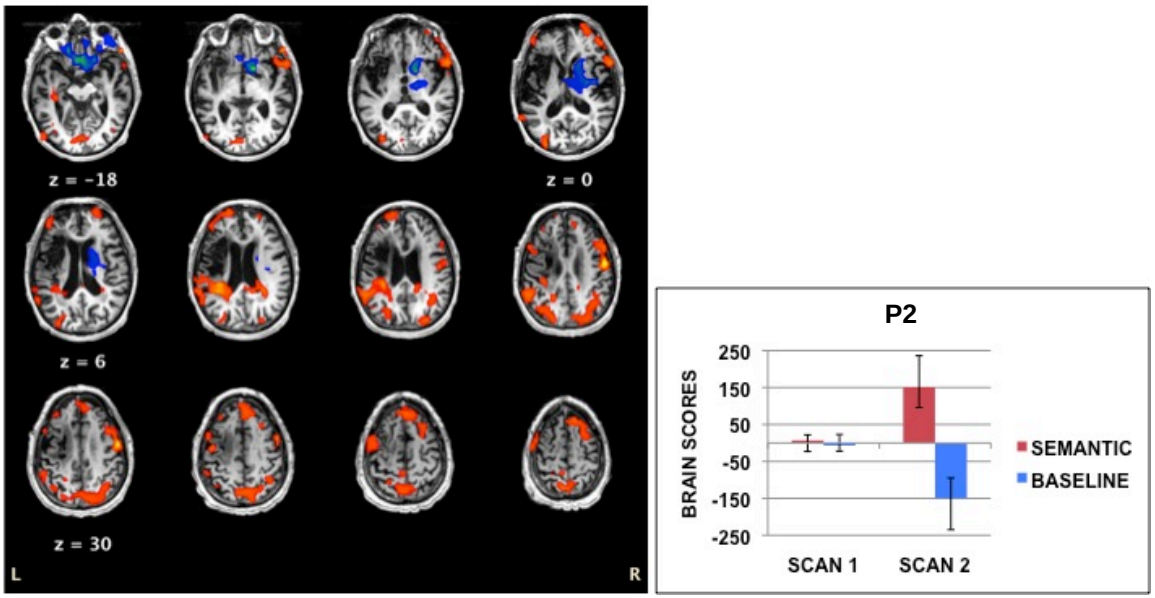

Figure 3a.

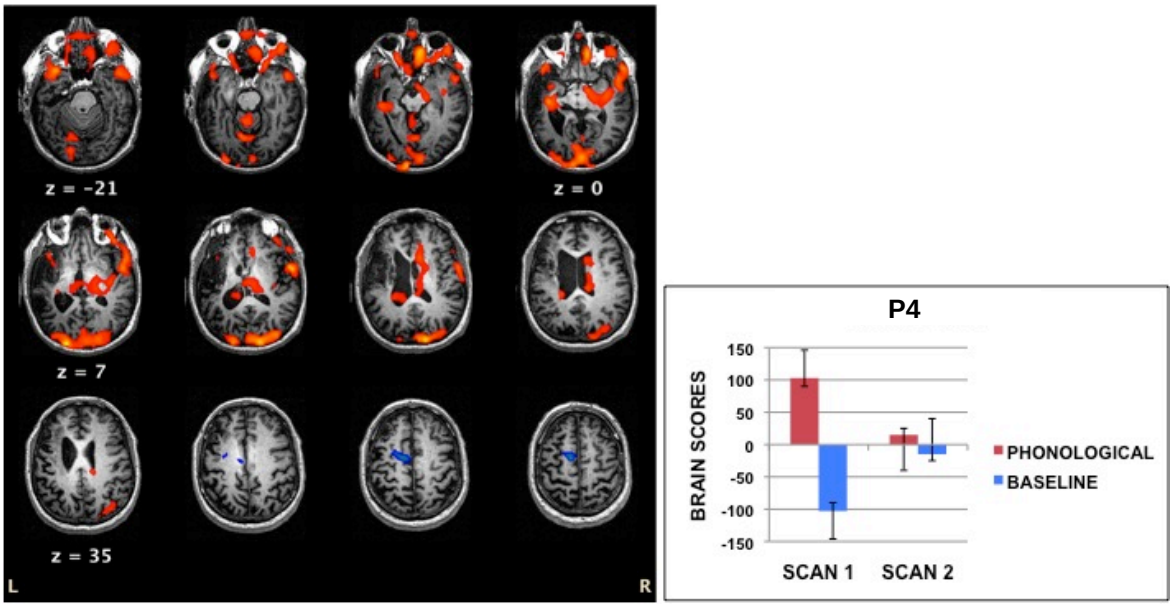

Figure 3b.