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Changes in N400 topography following intensive speech language therapy for individuals with aphasia

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ABSTRACT

Our goal was to characterize the effects of intensive aphasia therapy on the N400, an electrophysiological index of lexical-semantic processing. Immediately before and after 4 weeks of intensive speech-language therapy, people with aphasia performed a task in which they had to determine whether spoken words were a 'match' or a 'mismatch' to pictures of objects. Pre-therapy, people with aphasia exhibited an N400 mismatch effect that started over right hemisphere electrodes. Post-therapy, gains were seen in clinical measures of language ability, and the onset of the N400 was left-lateralized. No changes in the scalp distribution of the N400 were observed in healthy controls tested twice over the same 4 week interval. Since the distribution of the N400 after aphasia therapy differed from that of healthy controls, we conclude that it reflects the engagement of compensatory neural mechanisms for language processing rather than a return to a "normal" pattern of brain activation.

1. Introduction

Understanding how language processes are affected in individuals with aphasia is of considerable interest to both clinicians and neuroscientists. While many investigations have been directed at clarifying the efficacy of language therapy via clinical test batteries, work has also been done in an effort to better understand how the neural substrates that underlie language processing are affected in individuals with aphasia. These studies have used non-invasive imaging techniques such as MEG, ERP, and fMRI. This study sought to add to this body of literature using an ERP component, the N400, as a measure of change in the underlying neural processes related to language function as a result of undergoing intensive language therapy.

The N400 (Kutas & Hillyard, 1980), a well established ERP component, has been used extensively to study language function in aphasia patients (Connolly, Phillips, & Forbes, 1995b; Friederici, Hahne, & von Cramon, 1998; Hagoort, Brown, & Swaab, 1996; Kawohl et al., 2009; Kitade, Enai, Sei, & Iorita, 1999; Kotz & Friederici, 2003; Swaab, Brown, & Hagoort, 1997; Swaab, Brown, & Hagoort, 1998; Wassenaar & Hagoort, 2005). In the classic paradigm participants are presented with semantically congruent and semantically incongruent sentences. The result is a larger N400 for incongruent sentences than for congruent sentences. Thus the N400 is a marker of sensitivity to semantic violations. Collectively these studies have demonstrated that individuals with aphasia produce N400s that have longer latencies and smaller amplitudes, compared to healthy controls, and that the more severe the language impairment the more aberrant the N400 (Swaab et al., 1997). Thus the N400 appears to be sensitive to an individual's ability to access lexical information and may be able to discriminate the severity of language impairment in individuals with aphasia.

Other paradigms, such as a computer-adapted version of the Peabody Picture Vocabulary Test-Revised (PPVT-R; Minnesota: American Guidance Service, 1981) have also been successfully employed with aphasia patients whose communication impairments are so severe they are unable to complete the traditional sentence completion task (Byrne, Dywan, & Connolly, 1995a; Byrne, Dywan, & Connolly, 1995b; Connolly, Byrne, & Dywan, 1995a; D'Arcy et al., 2003; Marchand, D'Arcy, & Connolly, 2002). In the adaptation of the PPVT-R, the individual must determine whether an auditorily-presented label matches a just-presented image. The N400 is larger when the auditory label is incorrect, relative to when the label is correct – which we term the N400 mismatch effect. Critically, for people without language impairments the N400 is only apparent for items within the participant's vocabulary level (Byrne et al., 1995b; Connolly et al., 1995a), and people with aphasia show N400s to mismatches only for more

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commonly known words and not less common words that they may not know (D'Arcy et al., 2003; Marchand et al., 2002). These studies support the use of ERPs as a useful clinical tool for the assessment of language ability. ERPs may be particularly useful for assessing the effects of aphasia treatments because they can provide implicit and specific measures of language comprehension – in this case, the N400 component indexing lexical-semantic processing – independent of (possibly impaired) speech production abilities. Thus ERPs may provide greater neurocognitive specificity than behavioral assessments, as well as insight into the neural systems supporting language processing and how they may change with recovery.

Longitudinal designs have been used to describe therapy-induced changes to language processes of individuals with aphasia using ERP (Laganaro, Morand, Schwitter, Zimmermann, & Schnider, 2008; Léger et al., 2002; Menke et al., 2009; Musso et al., 1999; Pulvermüller, Hauk, Zohsel, Neininger, & Mohr, 2005; Pulvermüller, Mohr, & Lutzenberger, 2004), MEG (Cornelissen et al., 2003), PET (Belin et al., 1996) and fMRI (Fridriksson et al., 2007; Léger et al., 2002). Pulvermüller et al. (2005) compared ERPs elicited by pseudo-words and real words before and after intensive therapy (Pulvermüller et al., 2004). The authors found that, after therapy, individuals with aphasia produced larger evoked potentials to words (latency 250–300 ms) but ERP responses to pseudo-words did not change. These findings suggest that ERPs can reflect therapy-related improvements in lexical access.

Laganaro et al. (2008) observed similar changes in the early ERP components (i.e., before 250 ms) of four anomic patients who underwent 2–4 weeks of language therapy. In their task, Laganaro et al. used a delayed picture-naming task in which participants had to say out loud the name of presented line drawings. Post-therapy the early ERP waveform (0–300 ms) of the anomic patients was similar to that of the controls. However, abnormal amplitudes (i.e., larger amplitudes for anomic patients relative to controls) and scalp distributions (larger right lateralized activations for anomic patients relative to controls) of later components, including the N400, persisted for some patients. Consistent with other imaging studies examining the effects of therapy on language processes, Laganaro et al. attributed this to inter-individual variability as a result of differences in lesion location, and thus the brain areas that could be recruited to aide in the recovery of function (e.g., Fridriksson et al. (2007)).

The goal of this study was to determine if the N400 of people with aphasia is sensitive to therapeutic change arising from an intensive rehabilitative intervention. Building on the work of Pulvermüller et al. (2005); who investigated changes in ERPs associated with early lexical access as result of intensive treatment we examined the effects of intensive treatment on later lexical semantic processing via the N400. Participants with aphasia were recruited from the Intensive Residential Aphasia Communication Theraprogram (InteRACT Carey, Kostopoulos, & Belanger, 2006). This intensive therapy program delivers 100 h of structured Speech-Language Pathologist led language therapy and training over the course of four weeks (i.e.; more than 25 h/week) and offered an ideal opportunity to study therapy-induced change. people with aphasia and healthy controls completed a picture–label-matching task while ERPs were recorded; on two occasions 4 weeks apart (which was immediately before and after therapy in the case of people with aphasia).

Our hypothesis was that prior to therapy, the N400 of people with aphasia to picture-label mismatches, if present at all, would be have minimal amplitude relative to the healthy controls. We also predicted that post-therapy, the N400 violation effect (i.e., the difference between the N400 for congruent and incongruent picture/labels) would be larger, and thus more similar to the healthy controls, than pre-therapy.

2. Results

2.1. Clinical measures

Of the nine participants with aphasia, six demonstrated clinically significant gains on at least one of the clinical scales. Half of these participants showed clinically significant improvement on the Western Aphasia Battery (WAB-AQ), a routinely used scale that measures the level of impairment. All of the participants who did not show clinically significant gains on this scale were already performing at a very high level at the baseline measure (i.e., greater than 90/100). Four of the participants showed significant gains on the Communicative Effectiveness Index (CETI), a functional-level scale used to assess communication disability ability associated with aphasia. Two of the participants who showed significant improvement on the WAB-AQ also showed significant gains on the second function-level scale used, the Communication Activities of Daily Living −2 (CADL-2). These data are presented in Table 2.

2.2. Behavioral measures

Accuracy on the picture-naming task for the healthy controls group was 96.00% correct (sd. = 5.85%) for session 1 and 99.23% (sd. = 0.88%) for session 2. The people with aphasia group scored 91.05% correct (sd. = 17.10%) pre-therapy and 91.62% correct (sd. = 16.55%) post-therapy. Paired *t*-tests, using the *R* statistical software package (Development Core Team, 2011), indicated there was no significant difference between the session 1 and session 2 measurements (healthy controls) or the pre-treatment and post-treatment measurements (people with aphasia; $p > .05$). There were no between group differences ($p > .05$).

2.3. Event-related potentials

Visual inspection of the grand average ERP waveforms revealed a P1-N1-P2 pattern characteristic of auditory stimuli for both healthy controls and people with aphasia, in both testing sessions, as seen in the different waveform shown in Fig. 1. In all subjects at both testing sessions, this was followed by a centro-parietal negativity characteristic of the N400. For healthy controls, N400 amplitude appeared lower in session 2 than in session 1. For people with aphasia, amplitude generally appeared constant across sessions, however the onset of the N400 appeared to be differently distributed across the scalp post-therapy compared to pre-therapy. As can be seen in Fig. 2, the onset of the N400 (at around 350 ms) had higher amplitude over the right hemisphere pre-therapy relative to post, while over the left hemisphere onset amplitudes were larger post-therapy. This can also be seen in the plots of the scalp distributions of the N400 for each group and testing session in Fig. 3.

Examination of the scalp topographies of the data, shown in Fig. 3, revealed that the N400 had a typical scalp distribution, maximal over the central-temporal electrodes. Thus we restricted our analyses to the 3 ROIs over these electrodes (left, middle, and right). To characterize the time course of the ERP effects, the analyses were applied to mean amplitudes calculated over each 100 ms time window from 100–900 ms.

Statistical analysis using linear mixed effects (LME) modeling (Baayen, Davidson, & Bates, 2008) was employed to characterize the N400 violation effect. LME is an extension of the general linear model that is well-suited for ERP data (Newman, Tremblay, Nichols, Neville, & Ullman, 2011; Moratti, Clementz, Gao, Ortiz, & Keil, 2007; Pritchett et al., 2010; Wierda, Van Rijn, Taatgen, & Martens, 2010; Bagiella, Sloan, & Heitjan, 2000; Davidson & Indefrey, 2007). We used function *lmer* from package *lme4* (Bates, Maechler, &

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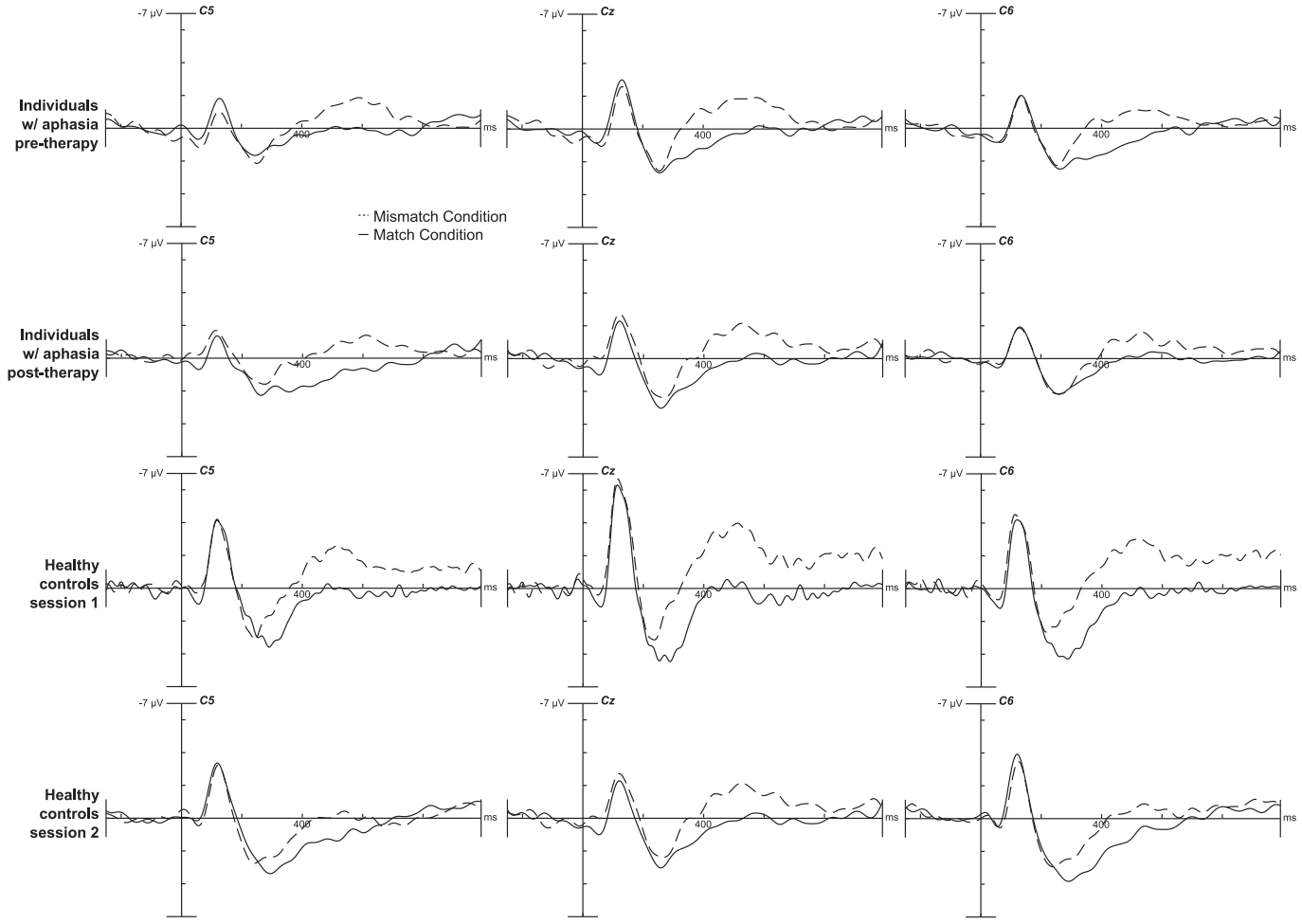

Fig. 1. ERP waveforms for match and mismatch trials, averaged across all subjects in each group, at representative electroles of the left (C5), middle, (Cz), and right (C6) ROIs both pre- and post-therapy. Negative is plotted up.

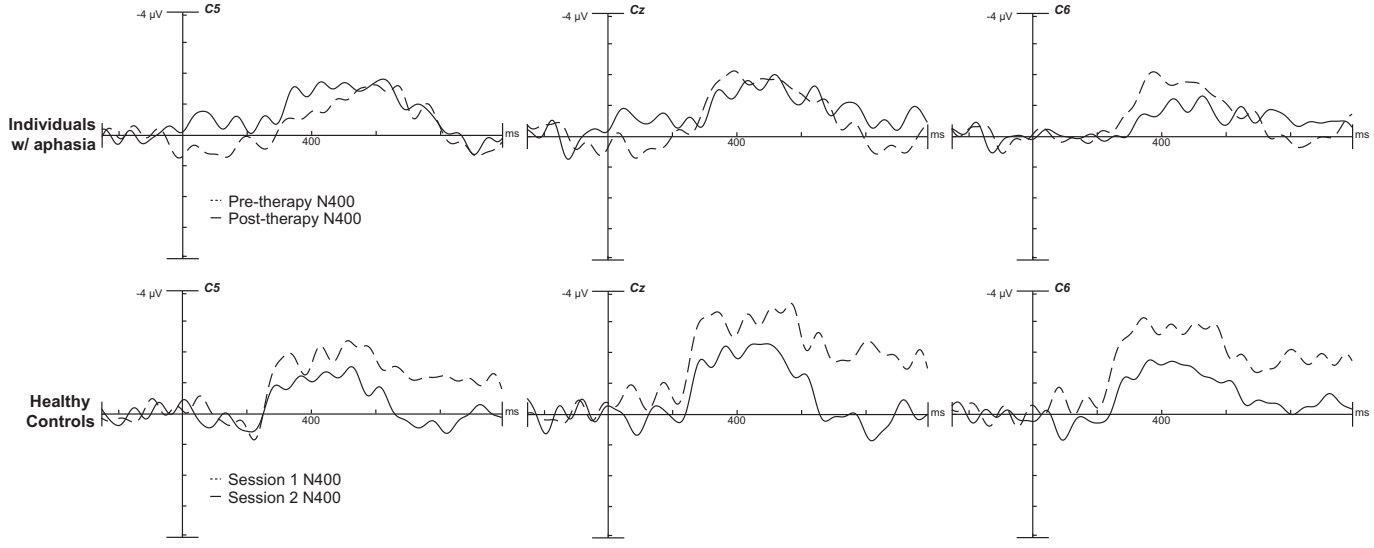

Fig. 2. ERP difference waveforms (calculated as mismatch–match), averaged across all subjects in each group, at representative electrodes of the left (C5), middle (Cz), and right (C6) ROIs. Negative is plotted up, thus deviations of the waveforms above the horizontal axis represent a stronger negativity for trials on which the auditory label did not match with the presented picture relative to match trials; the vertical axis represents the time at which the auditory label was presented. The N400 mismatch effect is seen as the prominent negativity sustained from roughly 300 to 500 or 600 ms.

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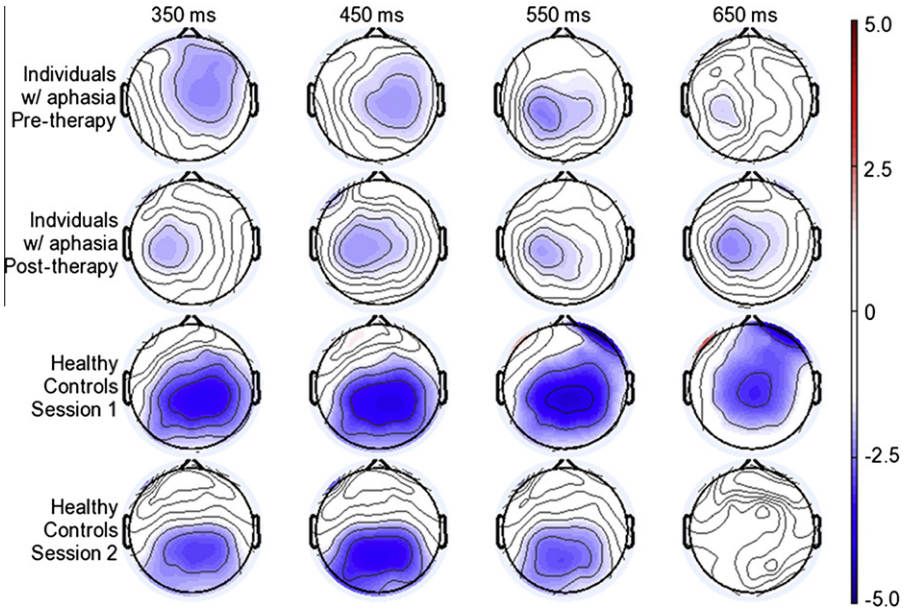

Fig. 3. Topographical maps showing the scalp distribution of the N400 mismatch effect (i.e., difference waves calculated as plotted in Fig. 2) at the midpoint of each time window when the effect was significant.

Bolker, 2011) implemented in *R* version 2.13.0 (Development Core Team, 2011) to fit our models to each subject's averaged ERP violation effect (calculated as mismatch–match) amplitudes. For each time window, modeling proceeded in a series of steps. (1) We fit an initial LME model with session (session 1 vs. session 2, which corresponded to pre- and post-therapy, respectively, in patients) and ROI as fixed effects, and subjects as a random effect. Data from each electrode within an ROI were included individually as repeated measures of that ROI. (2) To remove data points with undue leverage, those with a residual value 2.5 standard deviations above and below the residuals mean were removed (roughly 2% of the data in each case), and the model was re-fitted. (3) The addition of by-subject adjustments for session and for ROI into the model were evaluated using log-likelihood ratio tests. (4) The significance of interactions and main effects was evaluated by way of *F* tests; those that did not reach significance and that were not part of higher-order interactions were removed from the models, as long as such removal did not significantly reduce the explained variance of the model. This procedure, which is implemented in R package *LMERConvenienceFunctions* (Tremblay, 2011), is described in more detail in (Tremblay & Tucker, 2011). The denominator degrees of freedom (*df*) for assessing the significance of the resulting *F* values were calculated as the number of data points minus the number of *df* used up by the fixed effects and the number of random effects in the model. These were used to compute lower-bound (conservative) *p* values (Newman et al., 2011). To control for Type I error, the *p* values for *F* tests were corrected for the number of time windows investigated (eight tests). Within each time window, if there was a significant effect of session, and/or a significant session × ROI interaction, *t* tests used to evaluate the existence of a significant N400 violation effect (i.e., violation amplitudes significantly different form 0) at each of the three ROIs. For these tests *p* values were Bonferroni-corrected for the number of tests performed within each time window (6). Given that we observed possible changes in the laterality of the N400 in patients between sessions, we also performed post hoc tests to assess laterality. Rather than a complex set of pairwise comparisons between ROIs, we characterized the laterality of the N400 using polynomial contrasts (linear + quadratic terms). This was done for each session separately, as well as between sessions. Accordingly, *p* values for the polynomial contrasts were Bonferroni-corrected for the six comparisons (linear/polynomial × session 1/session 2/between-session).

The results of these analyses are summarized in Table 1. The fitted models are plotted in Fig. 4, which helps reveal the changing patterns of amplitude and laterality over time. In people with aphasia, the N400 mismatch effect was significant in all time windows from 300 to 700 ms both pre- and post-therapy. Post-therapy a significant effect was also obtained at the midline ROI from 700 to 800 ms. Significant Session × Laterality effects were obtained in all of these time windows except from 600 to 700 ms, indicating changes in laterality from pre- to post-therapy. In the first two epochs in which the N400 mismatch effect was significant, 300–500 ms, the effect was only significant over the middle and right ROIs. However, post-therapy the early phase of the N400 mismatch effect was significant only over the middle and *left* ROIs. This change from a more rightward to leftward laterality is reflected in the polynomial contrasts: pre-therapy there was a significant negative linear trend (indicating a rightward asymmetry owing to how the levels of ROI were coded) from 300–400 ms, and a significant difference in the linear trend between sessions. In the 400–500 ms time window, there was a continued (though non-significant) negative linear trend pre-therapy, and again a robust difference in the linear slope between sessions which persisted through the 500–600 ms time window. There was also a significant quadratic trend across the ROIs from 300 to 500 ms pre-therapy, reflecting similar amplitude negativities at the right and middle ROIs but a weaker negativity 400–500 ms and reflected over the left. Post-therapy, a significant quadratic trend was present from 400 to 500 ms indicating similar negativities at left and middle ROIs, but weaker over the right. Thus to summarize, in the early phase of the N400, from 300 to 600 ms, the N400 mismatch effect showed a rightward lateralization in people with aphasia before therapy, but a leftward lateralization after intensive speech-language therapy. Later however, from 600 to 700 ms, there were no differences in N400 amplitude or laterality before and after therapy. Some differences were observed from 700 to 800 ms, which reflected a somewhat more sustained N400 post-therapy at the middle ROI.

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Table 1

Summary of linear mixed effects analyses of ERP difference waveforms (mismatch–match). Mean amplitudes were tested in consecutive 100 ms time windows from 100–900 ms after the onset of the spoken label. Alpha (p) values are provided only for significant results. *Full Model* provides main effects and interactions; the threshold for significance was Bonferroni-corrected for the number of time windows analyzed (8) to provide a family-wise alpha of $p < .05$. *N400 Mismatch effects* provide planned t tests at each cell comparing the voltage against zero, to assess whether there was a significant difference between match and mismatch at each combination of scalp location and testing session. The threshold for significance was Bonferroni-corrected for the number of comparisons within that time window (6) to provide a family-wise alpha of $p < .05$. *Polynomial contrasts for laterality* assess the distribution of the violation effect across the three levels of laterality (left/mid/right). The threshold for significance was Bonferroni-corrected for the number of comparisons within that time window (6) to provide a family-wise alpha of $p < .05$. A significant positive linear trend indicates a left-lateralized N400 while a negative linear trend indicates a right-lateralized N400. A significant positive quadratic trend alone indicates an N400 maximal over midline electrodes; a combination of significant linear and quadratic trends represents a more complex pattern that is best interpreted with reference to the figure showing the scalp maps of the N400 effects, and Fig. 4. ∗ indicates values that would be redundant between sessions 1 and 2, when there was no between-session difference.

	Model	100–200 ms		200–300 ms		300–400 ms		400–500 ms		500–600 ms		600–700 ms		700–800 ms		800–900 ms	
		F or t	p	F or t	p	F or t	p	F or t	p	F or t	p	F or t	p	F or t	p	F or t	p
Individuals with aphasia	Full model	$F_{(1,517)}$		$F_{(1,516)}$		$F_{(1,514)}$		$F_{(1,515)}$		$F_{(1,516)}$		$F_{(1,533)}$		$F_{(1,518)}$		$F_{(1,516)}$	
	Main effect: prepost	2.50	–	1.37	–	0.26	–	0.01	–	0.12	–	–		0.50	–	2.23	–
		$F_{(2,541)}$		$F_{(2,516)}$		$F_{(2,514)}$		$F_{(2,515)}$		$F_{(2,516)}$		$F_{(2,533)}$		$F_{(2,518)}$		$F_{(2,516)}$	
	Main effect: laterality	0.65	–	1.26	–	4.53	–	8.96	0.001	7.52	0.006	2.80	–	0.78	–	0.08	–
	Interaction: prepost × laterality	20.81	0.001	39.40	0.001	74.56	0.001	68.20	0.001	11.78	0.001	–		11.85	0.001	10.57	0.001
	N400 mismatch effects	$t_{(570)}$		$t_{(569)}$		$t_{(567)}$		$t_{(568)}$		$t_{(569)}$		$t_{(567)}$		$t_{(571)}$		$t_{(569)}$	
	Left laterality																
	pre-therapy	1.35	–	0.54	–	−1.06	–	−2.10	–	−4.06	0.001	−4.06	0.001	−1.16	–	0.49	–
	post-therapy	−1.71	–	−1.49	–	−2.76	0.006	−6.10	0.001	−5.87	0.001	§	§	−1.89	–	−0.35	–
	Middle laterality																
	pre-therapy	1.27	-	−0.54	–	−3.04	0.001	−4.46	0.001	−4.39	0.001	−2.12	–	−0.48	–	1.00	–
	post-therapy	−2.00	–	−1.20	–	−2.72	0.006	−7.08	0.001	−4.93	0.001	§	§	−2.83	0.002	−0.93	–
	Right laterality																
	Pre-therapy	0.42	–	−0.94	-	−3.50	0.001	−4.12	0.001	−3.29	0.001	−1.19	–	−0.11	–	0.95	–
	Post-therapy	−0.24	–	−0.09	–	−1.87	–	−3.99	0.001	−2.61	0.005	§	§	−2.29	–	−1.33	–
	Polynomial contrasts for laterality	$t_{(570)}$		$t_{(569)}$		$t_{(567)}$		$t_{(568)}$		$t_{(569)}$		$t_{(567)}$		$t_{(571)}$		$t_{(569)}$	
	Pre-therapy																
	linear	–	–	–	–	−3.09	0.001	−2.43	–	−0.22	–	0.98	–	1.44	–	–	–
	quadratic	–	–	–	–	3.54	0.001	4.39	0.001	1.99	–	0.78	–	−0.69	–	–	–
	Post-therapy																
	Linear fit	–	–	–	–	1.47	-	1.49	-	1.01	-	§	§	0.12	–	–	–
	Quadratic fit	–	–	–	–	2.05	-	3.09	0.001	2.27	-	§	§	1.49	–	–	–
	Pre-therapy:Post-therapy																
	Linear fit	–	–	–	–	12.04	0.001	11.59	0.001	4.84	0.001	–	–	−4.06	0.001	–	–
	Quadratic fit	–	–	–	–	−2.19	–	−1.40	–	0.391	–	–	–	2.70	0.007	–	–
Healthy controls																	
	Full model	$F_{(1,653)}$		$F_{(1,644)}$		$F_{(1,665)}$		$F_{(1,538)}$		$F_{(1,632)}$		$F_{(1,540)}$		$F_{(1,631)}$		$F_{(1,640)}$	
	Main effect: prepost	0.61	–	2.72	–	–	–	–	–	3.24	–	–	–	5.16	-	10.19	0.001
		$F_{(2,653)}$		$F_{(2,644)}$		$F_{(2,665)}$		$F_{(2,539)}$		$F_{(2,632)}$		$F_{(2,565)}$		$F_{(2,631)}$		$F_{(2,640)}$	
	Main effect: laterality	2.17	–	6.04	0.003	12.66	0.001	10.33	0.001	12.87	0.001	–	–	2.89	–	4.82	–
	Interaction: prepost × laterality	15.69	0.001	15.09	0.001	–	–	–	–	6.09	0.003	–	–	–	–	39.05	0.001
	N400 mismatch effects	$t_{(718)}$		$t_{(709)}$		$t_{(707)}$		$t_{(707)}$		$t_{(569)}$		$t_{(567)}$		$t_{(571)}$		$t_{(569)}$	
	Left laterality																
	Session 1	−0.04	–	−1.26	–	−4.90	0.001	−3.71	0.001	−3.42	0.001	–	–	−1.75	–	−2.25	–
	Session 2	0.44	–	−0.74	–					−2.34	–	–	–	1.68	–	0.75	–
	Middle laterality																
	Session 1	−1.24	–	−2.99	0.003	−6.03	0.001	−4.71	0.001	−4.78	0.001	–	–	−2.24	–	−2.63	0.006
	Session 2	−0.14	–	−1.44	–					−3.03	0.003	–	–	0.35	–	1.11	–
	Right laterality																
	Session 1	−0.97	–	−3.17	0.002	−5.77	0.001	−5.1	0.001	−3.92	0.001	–	–	−2.60	–	−2.77	0.005
	Session 2	0.90	–	−1.19	–					−2.66	–	–	–	−0.32	–	0.03	–

(*continued on next page*)

Table 1 (*continued*)

Model	100–200 ms		200–300 ms		300–400 ms		400–500 ms		500–600 ms		600–700 ms		700–800 ms		800–900 ms	
	F or *t*	*p*	*F* or *t*	*p*	*F* or *t*	*p*	*F* or *t*	*p*	*F* or *t*	*p*	*F* or *t*	*p*	*F* or *t*	*p*	*F* or *t*	*p*
Polynomial contrasts for laterality	$t_{(570)}$		$t_{(569)}$		$t_{(567)}$		$t_{(568)}$		$t_{(569)}$		$t_{(567)}$		$t_{(571)}$		$t_{(569)}$	
Session 1																
Linear fit	–	–	−4.39	0.001	−3.07	0.002	−2.39	–	−1.78	–	–	–	–	–	−2.84	0.005
Quadratic fit	–	–	3.31	0.001	4.87	0.001	3.98	0.001	6.04	0.001	–	–	–	–	2.49	–
Session 2																
Linear fit	–	–	−1.19	–	§	§	§	§	−1.06	–	–	–	–	–	−1.83	–
Quadratic fit	–	–	1.88	–	§	§	§	§	3.16	0.001	–	–	–	–	−2.08	–
Session 1:Session 2																
Linear fit	–	–	5.13	0.001	–	–	–	–	0.97	–	–	–	–	–	1.99	–
Quadratic fit	–	–	−2.05	–	–	–	–	–	−3.37	0.001	–	–	–	–	−8.62	0.001

The data from healthy control participants showed a different pattern. Firstly, N400 mismatch amplitudes were noticably larger in healthy controls. Further, there were no significant between-session differences in the laterality or amplitude of the N400 mismatch effect in the 300–500 ms time window, where the effects were observed for people with aphasia. The N400 mismatch effect was robust across ROIs and sessions from 300 to 600 ms, and again from 800 to 900 ms. It was also significant from 200 to 300 ms in session 1 only. The N400 mismatch effect in healthy controls was maximal at the middle ROI throughout its duration, reflected in the significant quadratic polynomial contrasts. As well, the early phase of the N400 had a somewhat rightward lateralization as indicated by the significant negative linear trend from 300 to 400 ms (and 200–300 in session 1). The patterns of laterality can be seen clearly in Fig. 4. While there were no differences between sessions in scalp distribution, there was a significant main effect of Session from 500 to 600 ms. This was due to higher amplitudes in the first session than in the second. This difference in sessions was also reflected in the significant difference between sessions in the quadratic trend.

3. Discussion

We conducted an ERP study aimed at assessing whether the N400, an index of lexical-semantic processing, was altered after intensive speech-language therapy in people with aphasia. The results indicated that while the amplitude of the N400 did not change after therapy, its laterality did: the early phases of the N400 were right-lateralized pre-therapy but more left-lateralized after. This was accompanied by improvements on clinical assessments of language function in all therapy recipients. This change in laterality could not be attributed simply to the effects of repeating the ERP mismatch testing after therapy, since healthy control subjects tested twice with the same 4-week intervening time period did not show these effects. N400 mismatch amplitudes were somewhat smaller in the second session among healthy controls – presumably due to habituation to the paradigm (although no stimuli were repeated between sessions) – but did not change in laterality. A further between-group difference was that while N400 had a similar onset latency in both groups (though perhaps slightly earlier in session 1 for controls), it was more sustained in people with aphasia – an effect that did not change after therapy.

Our findings are consistent with the hypothesis that the N400 picture/label mismatch effect is a sensitive index of change in language processing associated with intensive speech-language therapy. These findings extend those of Pulvermüller et al. (2005), who found that the early components of the ERP waveform (i.e., 250–300 ms) became larger after an intensive 2-week aphasia therapy. In contrast we found that the amplitude of the N400 did not change after therapy but rather its scalp distribution did, becoming less right-lateralized relative to the pre-therapy assessment.

This shift in the scalp distribution of the ERP waveform suggests that there is a change in the relative contribution of different neural generators of the N400. However, we must be cautious in interpreting these changes since the inverse problem of localizing sources from scalp distributions is mathematically ill-posed. We did not attempt source localization in this study due to the limited coverage of the scalp by our recording electrodes, as well as the inevitably variable patterns of brain damage in our subjects. However, we do know that the N400 is most likely generated by a distributed network of regions including the left, and to a lesser extent right, inferior parietal, middle/inferior frontal, and inferior temporal lobes (Newman, Pancheva, Ozawa, & Neville, 2001; Ni et al., 2000; Nobre & McCarthy, 1995; Simos, Basile, & Papanicolaou, 1997). The change in scalp distribution

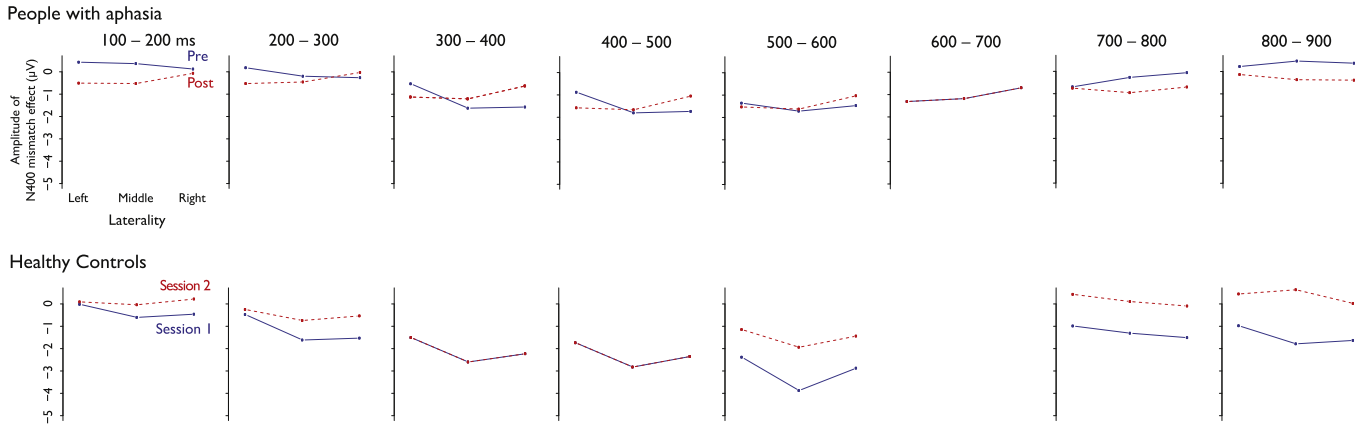

Fig. 4. Model-derived plots showing the linear mixed effects model fits for each time window and group. Note that negative is plotted down, so in contrast to the ERP waveforms in Fig. 2, here a larger N400 mismatch effect is reflected in a value plotted closer to the horizontal axis. There is no plot for healthy controls from 600 to −700 ms because neither factor explained any significant amount of the variance in the data, and thus the optimal linear mixed effects model contained only an intercept (i.e., the same amplitude at all levels of Session and Laterality).

observed after intensive aphasia therapy in this study may be seen as consistent with previous fMRI (Léger et al., 2002; Menke et al., 2009; Saur et al., 2006), TMS (Winhuisen et al., 2005) and ERP Pulvermüller et al. (2004) studies that have reported recovery from aphasic symptoms being associated with reduced right hemisphere activity and the re-engagement of left-sided "classic" language areas. Indeed, although accuracy in the ERP match/mismatch task was at ceiling both pre- and post-therapy, the majority of patients demonstrated clinically significant gains on standardized tests of language such as the WAB. Thus to the extent that the laterality of the N400 may reflect the laterality of the underlying activation generating this potential, our results suggest that therapy-induced recovery from aphasia is associated with a return to more leftward laterality of language processing.

However, it is interesting to note that this apparent leftward shift in N400 laterality was not a "normalization" of the N400 scalp distribution. As in the majority of previous studies (Van Petten & Luka, 2006), the scalp distribution of the N400 mismatch effect in healthy controls was maximal at the midline but with a significant linear trend towards the right. Thus it seems unlikely that the observed change in N400 lateralization in people with aphasia was due to a shift towards a more normal distribution of activation among the generators of the N400. Rather, the change we observed here might be interpreted as being compensatory, reflecting a change towards a more effective pattern of neural activation for successful lexical-semantic processing after intensive speech-language therapy.

One important caveat when considering the current results is the participant sample. All of the people with aphasia who participated in this study were relatively high functioning, as reflected by their standardized test scores (see Results, above, and Table 2). This had the benefit of good task performance during ERP testing, ensuring that the observed changes in ERPs are unlikely to be due to greater task difficulty during the first testing session relative to the second testing session. However, we cannot predict from the present data whether similar results would be observed in people with more severe aphasia.

4. Method

4.1. Participants

For this study, 15 people with aphasia, as clinically assessed by a neurologist or a speech-language pathologist, were recruited. All patients developed aphasia as a result of a primary stroke or a stroke secondary to a traumatic event. All patients were by self-report right handed prior to the event that caused their aphasia, however three individuals reported using their left hand for most activities post event. Although left handedness coincides with a greater propensity for bilateral or right lateralized language processing, the "left-handed" participants in our study were only recently so (max 2 years post trauma), and as reported by Rasmussen and Milner (Rasmussen & Milner, 1977), even early left hemisphere lesions are unlikely to change lateralization of language function. Thus, for the purposes of this study the left handed participants can reasonably be expected to have been left lateralized for language prior to the event that caused their aphasia. See Table 2 for further details. This research was reviewed and approved by the Research Ethics Boards of the National Research Council and the Capital District Health Authority. Patients were invited to participate in this research project after they had registered for the InteRACT program, by the speech-language pathologists running the program. Informed consent was conducted using both written and oral communication, with the assistance of a speech-language pathologist and a friend or relative of the patient if desired. It was emphasized that this study was being conducted independent of patients' therapy, that participation was completely optional, and that they were free to quit the study at any time for any reason, without penalty. No additional incentive was provided.

4.2. Therapeutic intervention

The InteRACT program is available to people with aphasia who are medically stable and who are deemed cognitively and physically able to endure the intensity of the program. A communication partner (family member or friend) must accompany the patient to support carry-over of new skills when the patient returns home. Each InteRACT session ran for 4 weeks, and consisted of speech language therapy, recreation therapy, and community integration exercises. The 100 h (5 h daily) of speech-language therapy were delivered in the following structured manner: 1 h of individual therapy was devoted to language production and comprehension (e.g., Cuing Verb Treatments, Visual Action Therapy), and motor speech (e.g., Rosenbek's Eight Step Continuum; Rosenbek, Lemme, Ahern, Harris, & Wertz (1973)). One hour of individual therapy was devoted to reading and writing (e.g., Parallel Oral Reading). One hour of individual therapy was devoted to functional

Table 2
Demographic information and clinical scores for all participants.

Patient	Gender	Age	Yrs Ed.	Aphasia Duration	Cause of Aphasia	Lesion Site	Type of Aphasia	Handedness	max 100 CETI		max 100 CADL-2		max 9 CADL-stanine		max 100 Western - AQ		Spontaneous		Aud Verbal		Western subtests (see below) Repetition		Name & Word		Western Classification	
									pre	post	pre %	post %	pre	post	pre	post	pre	post	pre	post	pre	post	pre	post	pre	post
A02	Male	62	15	3 years	Stroke	Left Temporal	nonfluent	Right-20% (Ambidextrous)	53	62	27	54	4	5	38.6	48.8	3	5	7.5	7.1	7.2	9.8	1.6	2.5	transcortical motor	transcortical motor
A03	Male	55	15	1 year	Stroke	Left Anterior	Conduction (nonfluent)	Left -83% Left handed	51	65	32	65	4	6	46	61.8	8	12	8	8	4.7	5.6	2.3	5.3	conduction	conduction
A07	Male	53	18	1 year	Stroke	Left	Anomic/apraxic	Right- 100% Righthanded	56	56	93	93	8	8	79.6	93.4	13	19	9.3	9.8	8.1	8.6	9.4	9.3	anomic	anomic
A08	Male	53	19	5.5 years	Stroke	–	Anomic	Right- 42.8% Righthanded	x	x	98	98	9	9	96.8	94.4	19	18	9.9	9.8	10	10	9.5	9.4	anomic	anomic
A09	Female	59	18	2 years	Stroke	–	Anomic	Right- 100% Righthanded	73	78	89	86	7	7	90.6	90.1	18	18	10	9.75	9.1	9	8.2	8.3	anomic	anomic
A11	Male	50	13	1 year	Stroke	Occipital lobe	Alexic/Anomic	83% Right	77	93	95	96	8	8	92.5	95.6	19	19	9.35	9.8	9.6	10	8.3	9	anomic	anomic
A12	Male	28	14	2 years	Stroke via MVA	–	Anomic	100% Left	53	68	93	98	8	9	93.1	97.5	19	20	9.35	9.75	9.6	10	8.6	9	anomic	anomic
A14	Male	55	13	6 mo	Stroke	Frontal, Parietal Lobe	Expressive, Receptive, Apraxia	91% Right	25	30	7	18	2	3	17.1	26.3	2	3	5.35	6.35	0.6	2.4	0.6	1.4	broca	broca
A15	Male	55	14	1 year	AVM - Secondary Stroke	Left Frontal Lobe	Global	100% Left	42	70	90	97	8	9	74.9	76.9	14	15	9.75	9.75	8	8	5.7	5.7	anomic	anomic

CETI clincially significant = 12 points or more, SACS clinically sig = 1 point or more, CADL-2 clinically sig = 1 stanine or more, Western clinically sig = 5 points or more.
Western Subtests: Spontaneous speech/20, Auditory Verbal Comprehension/10, Repetition/10, Naming & word finding/10

communication skills (e.g., PACE, phone use). One hour of individual therapy was devoted to computer skills (e.g., e-mail and internet usage). Finally, one hour of group therapy focused on conversation based activities (e.g., weekly newspaper, language constraint games). Recreation therapy focused on a return to previous leisure activities, or the introduction of new leisure pursuits (e.g., sports, arts and crafts) in both individual (1/week), and group sessions (2/week; Carey et al. (2006)).

4.3. Clinical measures

Clinical measures were selected to assess patients across all three spheres of the World Health Organization International Classification of Functioning, Disability and Health (ICF): Impairment Level, Participation Level, and Activity Level. Level of impairment was assessed via the Western Aphasia Battery (WAB-R; Kertesz (1982)). Participation level was measured via the Communicative Effectiveness Index (CETI; Lomas et al. (1989)) and Activity level was assessed via the Communication Activities of Daily Living-2 (CADL-2; Holland, Frattali, & Fromm (1999)).

4.4. Stimuli

The stimuli were colored pictures (281 × 197 pixels) selected from a set created by Rossion and Pourtois (2004), based on line drawin Snodgrass and Vanderwart (1980). Digital audio recordings of a male voice speaking the labels of each picture, using the most common name given in normative naming studies (Rossion & Pourtois, 2004), were made, and processed using Soundtrack Pro software (Apple Inc, Cupertino, CA) to attenuate fricatives, sibilants and volume fluctuations. The stimuli were arranged into four unique sets of 60 items each, with items across the sets balanced in terms of overall frequency, *H* score a measure of the consistency with which a picture is given a particular name; see Snodgrass and Vanderwart (1980), phonology (onset and syllable length), and frequency of various categories (e.g., animals and food) across lists.

4.5. Procedure

Healthy control participants completed the picture-name matching task at two time points, four weeks apart. people with aphasia entering the study completed the baseline assessment just prior to, or within the first 3 days after the beginning of the InteRACT program, and completed the post-treatment assessment on the last two days of the treatment program (approximately 4 weeks apart). All participants were tested in a sound-attenuating booth at the School of Human Communication Disorders or the Psychology Department at Dalhousie University. Both sessions were identical in nature. ERPs were recorded while participants completed the picture-name matching task, composed of a total of 120 trials presented in a pseudorandom order (60 matched and 60 mismatched). Stimulus presentation was controlled by a PC laptop running DirectRT software (Empirisoft Corp., New York, NY). Participants initiated each trial, which consisted of a picture displayed on a computer monitor for 1 s accompanied by an auditory label presented 1 s after the onset of the picture, through stereo speakers. A visual response cue then appeared and the participant had 3 s to indicate whether the label and picture pair matched or not via a response pad held in the left hand. Participants were provided with verbal instructions and a set of 16 practice trials to ensure the task demands were understood.

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4.6. ERP recording and preprocessing

EEG from 64 Ag–AgCl scalp electrodes (WaveGuard caps, Advanced Neuro Technologies BV – ANT – Enschede, The Netherlands), arranged according to the International 10–20 System (for locations see below) was acquired at a rate of 250 Hz using a Cognitrace 72-channel EEG amplifier and ASA recording software (ANT), with a 69 Hz lowpass filter and no high-pass filter. Horizontal and vertical electrooculogram (EOG) were also recorded to allow for detection and rejection of trials containing eye movements and blinks. Impedance of all electrodes was lowered to <10 kΩ prior to recording. Offline ERP processing was performed using EEGLAB (Delorme & Makeig, 2004). Data were band-pass filtered with a finite impulse response filter using a high-pass cutoff of 0.5 Hz, a low-pass cutoff of 50 Hz, and re-referenced to the average of the left and right mastoid electrodes. Epochs were extracted around the onset of each auditory stimulus, including a 250 ms pre-stimulus baseline and 900 ms post-stimulus. Epochs were visually inspected and trials with excessive noise (e.g., due to movement or other muscle activity) were rejected from further processing. Independent component analysis was used to detect and remove artifacts including eye blinks, DC drift, and noise localized to individual electrodes (Makeig, Jung, Bell, Ghahremani, & Sejnowski, 1997). Nine regions of interest (ROIs) were defined by dividing the electrode array into a 3×3 grid, which produced the following electrode groupings: anterior-left (AF7, F3, F5, and F7), anterior-middle (Fp1, Fpz, Fp2, AF3, AFz, AF4, F1, Fz, and F2), anterior-right (AF8, F4, F6, and F8), center-left (FT7, FC5, FC3, T7, C5, C3, TP7, CP5, and CP3), center-middle (FC1, FCz, FC2, C1, Cz, C2, CP1, CPz, and CP2), center-right (FC4, FC6, FT8, C4, C6, T8, CP4, CP6, and TP8), posterior-left (P3, P5, P7, P05, and P07), posterior-center (P1, Pz, P2, PO3, POz, PO4, O1, Oz, and O2), and posterior-right (P4, P6, P8, PO6, and PO8). Electrodes within each cell were grouped together for statistical analysis.

References

Baayen, R., Davidson, D., & Bates, D. (2008). Mixed-effects modeling with crossed random effects for subjects and items. *Journal of Memory and Language, 59*(4), 390–412.

Bagiella, E., Sloan, R. P., & Heitjan, D. F. (2000). Mixed-effects models in psychophysiology. *Psychophysiology, 37*(1), 13–20.

Bates, D., Maechler, M., Bolker, B. (2011). lme4: Linear mixed-effects models using S4 classes. R package version 0.999375-39.

Belin, P., Van Eeckhout, P., Zilbovicius, M., Remy, P., François, C., Guillaume, S., et al. (1996). Recovery from nonfluent aphasia after melodic intonation therapy: A PET study. *Neurology, 47*(6), 1504–1511.

Byrne, J. M., Dywan, C., & Connolly, J. F. (1995a). An innovative method to assess the receptive vocabulary of children with cerebral palsy using event-related brain potentials. *Journal of Clinical and Experimental Neuropsychology, 17*(1), 9–19.

Byrne, J. M., Dywan, C., & Connolly, J. F. (1995b). Asessment of children's receptive vocabulary using event-related potentials: Development of a clinically valid test. *Child Neuropsychology, 1*(3), 211–223.

Carey, L., Kostopoulos, E., Belanger, S., 2006. Functional Outcomes of an Intensive Aphasia Treatment Program.

Connolly, J. F., Byrne, J. M., & Dywan, C. (1995a). Asessing adult receptive vocabulary with event-related potentials: An investigation of cross-modal and cross-form priming. *Journal of Clinical and Experimental Neuropsychology, 17*(4), 548–565.

Connolly, J. F., Phillips, N. a., & Forbes, K. a. (1995b). The effects of phonological and semantic features of sentence-ending words on visual event-related brain potentials. *Electroencephalography and Clinical Neurophysiology, 94*(4), 276–287.

Cornelissen, K., Laine, M., Tarkiainen, A., Järvensivu, T., Martin, N., & Salmelin, R. (2003). Adult brain plasticity elicited by anomia treatment. *Journal of Cognitive Neuroscience, 15*(3), 444–461.

D'Arcy, R. C. N., Marchand, Y., Eskes, G. A., Harrison, E. R., Phillips, S. J., Major, A., et al. (2003). Electrophysiological assessment of language function following stroke. *Clinical Neurophysiology, 114*, 662–672.

Davidson, D. J., & Indefrey, P. (2007). An inverse relation between event-related and time-frequency violation responses in sentence processing. *Brain Research, 1158*, 81–92.

Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods, 134*(1), 9–21.

Development Core Team, R., 2011. R: A language and environment for statistical computing.

Fridriksson, J., Moser, D., Bonilha, L., Morrow-Odom, K. L., Shaw, H., Fridriksson, A., et al. (2007). Neural correlates of phonological and semantic-based anomia treatment in aphasia. *Neuropsychologia, 45*(8), 1812–1822.

Friederici, a. D., Hahne, A., & von Cramon, D. Y. (1998). First-pass versus second-pass parsing processes in a Wernicke's and a Broca's aphasic: Electrophysiological evidence for a double dissociation. *Brain and Language, 62*, 311–341.

Hagoort, P., Brown, C. M., & Swaab, T. Y. (1996). Lexical-semantic event-related potential effects in patients with left hemisphere lesions and aphasia, and patients with right hemisphere lesions without aphasia. *Brain, 119*, 627–649.

Holland, A. L., Frattali, C., Fromm, D. (1999). *Communication activities of daily living.* Austin, Texas.

Kawohl, W., Bunse, S., Willmes, K., Hoffrogge, a., Buchner, H., & Huber, W. (2009). Semantic event-related potential components reflect severity of comprehension deficits in aphasia. *Neurorehabilitation and Neural Repair, 24*(3), 282–289.

Kertesz, A. (1982). *The Western Aphasia Battery*. New York: Grune & Stratton.

Kitade, S., Enai, T., Sei, H., & Iorita, Y. (1999). The N400 event-related potential in aphasia. *Journal of Medical Investigation, 46*, 87–95.

Kotz, S., & Friederici, A. D. (2003). Electrophysiology of normal and pathological language processing. *Journal of Neurolinguistics, 16*, 43–58.

Kutas, M., & Hillyard, S. A. (1980). Reading senseless sentences: Brain potentials reflect semantic incongruity. *Science, 207*(4427), 203–205.

Laganaro, M., Morand, S., Schwitter, V., Zimmermann, C., & Schnider, A. (2008). Normalisation and increase of abnormal ERP patterns accompany recovery from aphasia in the post-acute stage. *Neuropsychologia, 46*(8), 2265–2273.

Léger, A., Démonet, J.-F., Ruff, S., Aithamon, B., Touyeras, B., Puel, M., et al. (2002). Neural substrates of spoken language rehabilitation in an aphasic patient: An fMRI study. *NeuroImage, 17*(1), 174–183.

Lomas, J., Pickard, L., Bester, S., Elbard, H., Finlayson, A., & Zoghaib, C. (1989). The communicative effectiveness index: Development and psychometric evaluation of a functional communication measure for adult aphasia. *Journal of Speech and Hearing Disorders, 54*(1), 113–124.

Makeig, S., Jung, T. P., Bell, A. J., Ghahremani, D., & Sejnowski, T. J. (1997). Blind separation of auditory event-related brain responses into independent components. *Proceedings from the National Academy of Science, 20*, 10979–10984.

Marchand, Y., D'Arcy, R. C. N., & Connolly, J. F. (2002). Linking neurophysiological and neuropsychological measures for aphasia assessment. *Clinical Neurophysiology, 113*, 1715–1722.

Menke, R., Meinzer, M., Kugel, H., Deppe, M., Baumgärtner, A., Schiffbauer, H., et al. (2009). Imaging short- and long-term training success in chronic aphasia. *BMC Neuroscience, 10*, 118.

Moratti, S., Clementz, B. A., Gao, Y., Ortiz, T., & Keil, A. (2007). Neural mechanisms of evoked oscillations: Stability and interaction with transient events. *Human Brain Mapping, 28*(12), 1318–1333.

Musso, M., Weiller, C., Kiebel, S., Müller, S. P., Bülau, P., & Rijntjes, M. (1999). Training-induced brain plasticity in aphasia. *Brain, 122*, 1781–1790.

Newman, A. J., Pancheva, R., Ozawa, K., & Neville, H. J. (2001). An event-related fMRI study of syntactic and semantic violations. *Journal of Psycholinguistic Research, 30*(3), 339–364.

Newman, A. J., Tremblay, A., Nichols, E. S., Neville, H. J., & Ullman, M. T. (2011). The influence of language proficiency on lexical semantic processing in native and late learners of english. *Journal of Cognitive Neuroscience*.

Ni, W., Constable, R. T., Mencl, W. E., Pugh, K. R., Fulbright, R. K., Shaywitz, S. E., et al. (2000). An event-related neuroimaging study distinguishing form and content in sentence processing. *Journal of Cognitive Neuroscience, 12*(1), 120–133.

Nobre, A. C., & McCarthy, G. (1995). Language-related field potentials in the anterior-medial temporal lobe: II. Effects of word type and semantic priming. *Journal of Neuroscience, 15*(2), 1090–1099.

Pritchett, S., Zilberg, E., Xu, Z. M., Myles, P., Brown, I., & Burton, D. (2010). Peak and averaged bicoherence for different EEG patterns during general anaesthesia. *BioMedical Engineering Online, 9*(1), 76.

Pulvermüller, F., Hauk, O., Zohsel, K., Neininger, B., & Mohr, B. (2005). Therapy-related reorganization of language in both hemispheres of patients with chronic aphasia. *NeuroImage, 28*, 481–489.

Pulvermüller, F., Mohr, B., & Lutzenberger, W. (2004). Neurophysiological correlates of word and pseudo-word processing in well-recovered aphasics and patients with right-hemispheric stroke. *Psychophysiology, 41*(4), 584–591.

Rasmussen, T., & Milner, B. (1977). The role of early left-brain injury in determining lateralization of cerebral speech functions. *Annals of the New York Academy of Sciences, 299*, 355–369.

Rosenbek, J. C., Lemme, M. L., Ahern, M. B., Harris, E. H., & Wertz, R. T. (1973). A treatment for apraxia of speech in adults. *Journal of Speech and Hearing Disorders, 38*, 462–472.

Rossion, B., & Pourtois, G. (2004). Revisiting Snodgrass and Vanderwart's object pictorial set: The role of surface detail in basic-level object recognition. *Perception, 33*(2), 217–236.

Saur, D., Lange, R., Baumgaertner, A., Schraknepper, V., Willmes, K., Rijntjes, M., et al. (2006). Dynamics of language reorganization after stroke. *Brain, 129*(6), 1371–1384.

Simos, P. G., Basile, L. F. H., & Papanicolaou, A. C. (1997). Source localization of the N400 response in a sentence-reading paradigm using evoked magnetic fields and magnetic resonance imaging. *Brain Research, 762*(1–2), 29–39.

Snodgrass, J. G., & Vanderwart, M. (1980). A standardized set of 260 pictures: Norms for name agreement, image agreement, familiarity, and visual complexity. *Journal of Experimental Psychology: Human Learning, 6*(2), 174–215.

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Swaab, T. Y., Brown, C., & Hagoort, P. (1997). Spoken sentence comprehension in aphasia: Event-related potential evidence for a lexical integration deficit. *Journal of Cognitive Neuroscience, 9*(1), 39–66.

Swaab, T. Y., Brown, C., & Hagoort, P. (1998). Understanding ambiguous words in sentence contexts: electrophysiological evidence for delayed contextual selection in Brocas aphasia. *Neuropsychologia, 36*(8), 737–761.

Tremblay, A., 2011. *LMERConvenienceFunctions: A suite of functions to back-fit fixed effects and forward-fit random effects, as well as other miscellaneous functions*. R package version 1.6.2. Comprehensive R Archive Network.

Tremblay, A., & Tucker, B. V. (2011). The effects of N-gram probabilistic measures on the recognition and production of four-word sequences. *The Mental Lexicon, 6*(2), 302–324.

Van Petten, C., & Luka, B. J. (2006). Neural localization of semantic context eVects in electromagnetic and hemodynamic studies. *Brain and Language, 97*, 279–293.

Wassenaar, M., & Hagoort, P. (2005). Word-category violations in patients with Broca's aphasia: An ERP study. *Brain and language, 92*, 117–137.

Wierda, S. M., Van Rijn, H., Taatgen, N. A., & Martens, S. (2010). Distracting the mind improves performance: An ERP study. *PLoS ONE, 5*(11), 7.

Winhuisen, L., Thiel, A., Schumacher, B., Kessler, J., Rudolf, J., Haupt, W. F., et al. (2005). Role of the contralateral inferior frontal gyrus in recovery of language function in poststroke aphasia: A combined repetitive transcranial magnetic stimulation and positron emission tomography study. *Stroke; A Journal of Cerebral Circulation, 36*(8), 1759–1763.

Please cite this article in press as: Wilson, K. R., et al. Changes in N400 topography following intensive speech language therapy for individuals with aphasia. *Brain & Language* (2012), http://dx.doi.org/10.1016/j.bandl.2012.06.005