Magnetoencephalographic evidence of neural plasticity following aphasia therapy

Abstract

This study used magnetoencephalography (MEG) to investigate changes in the spatio-temporal patterns of neural activity following language treatment in 6 individuals with chronic aphasia. All participants produced agrammatic language with predominantly morphosyntactic deficits and responded positively to language treatment targeting verb morphology. MEG responses to an online morphological processing task were measure twice before initiation of treatment and once after cessation of treatment. All six participants demonstrated quantitative and qualitative changes in neural activity following aphasia therapy, and the spatiotemporal patterns were similar to those found in neurologically unimpaired participants. The results demonstrate that, in this study, neurophysiological changes following language therapy were specific to the linguistic process that was targeted, and not the result of general cognitive or compensatory mechanisms.

1. Introduction

The extent of recovery from stroke-induced aphasia varies from complete resolution of language deficits to severe and persistent deficits in 10-18% of individuals (Wade et al., 1986). Currently, there is little doubt that targeted and intensive language treatment plays a significant role in the recovery potential of aphasic individuals (Bhogal et al., 2003; Beeson & Robey, 2006). Numerous studies continue to investigate the neurobiological bases of treatment-induced language recovery in aphasia (for a recent review see Thompson & DenOuden, 2008). These studies, although significant in demonstrating changes in patterns of neural activity following language therapy, are yet to provide a clear answer to several crucial questions about the neural mechanisms underlying language recovery and neural plasticity. One such unresolved question is whether the neural regions that are more active after language treatment subserve any linguistic function targeted by the treatment or whether these regions are involved in non-linguistic cognitive operations (e.g., attention and effort) and compensatory strategies (e.g., Winhuisen et al., 2005). A majority of the neuroimaging investigations use tools such as functional magnetic resonance imaging (FMRI) or positron emission tomography (PET) that rely on hemodynamic patterns, which are spatially sensitive but reveal little about the underlying mechanisms. Given that a variety of linguistic functions activate a limited subset of perisylvian regions in a many-to-many relation in neurologically unimpaired and aphasic individuals, the functional role of these regions in the post-treated brain remains somewhat unanswered especially with hemodynamic neuroimaging techniques.

Electrophysiological (ERP) and magnetoencephalographic (MEG) investigations are relatively direct neurophysiological measures that could be used to investigate whether treatment-induced neural changes subserve a linguistically specific function. This is because relatively distinct and replicable spatio-temporal activity patterns are associated with specific linguistic processes such as syntactic or semantic processing (Kutas & Hillyard, 1983; Kwon et al., 2005). The primary purpose of this study was to investigate the nature of neurophysiological reorganization that accompanies improvement in language after aphasia treatment by taking advantage of the spatio-temporally sensitive information provided by MEG. More specifically, this study examined whether 1) neural activity related to processing of morphological information in sentences was altered following targeted treatment of verb morphology, and 2) if this post-treatment neurophysiological activity pattern resembled the spatio-temporal pattern demonstrated by neurologically unimpaired participants.

2. Methods

Participants

Seven individuals with agrammatic Broca's aphasia following a single left hemisphere stroke and at least one year post-onset (age range: 37-68 years, two female, all right-handed) participated. Their demographic and language details are provided in Table 1. All patients demonstrated severe difficulty in the production of morphosyntax in elicited and narrative speech.

Stimuli

A total of 360 sentences (70 each with semantic and tense anomalies; 150 correct) were audiorecorded by a native speaker of North American English. Examples are:

- *Yesterday the teacher ^graded the exams* (correct sentence)
- *Yesterday the honeybee ^graded the exams* (semanticaaly anomalous sentence)
- *Tomorrow the teacher ^graded the exams* (morphologically anomalous sentence).

^ represents the onset of the verb and the point at which neuromagnetic activity was extracted (see later for details). Semantically anomalous sentences were included as a control condition since individuals with agrammatic aphasia are known to process these sentences with high accuracy (Hagoort et al., 2003). If the changes in neural activity are specific to the treatment provided, then MEG responses to semantically anomalous sentence should remain unchanged after morphological treatment.

Procedure and Data analysis

Morphological Treatment. The primary purpose of the treatment was to improve production of contextually accurate verb morphology by learning to associate the tense conveyed by different morphological endings (for example, Tomorrow↔will drink, today/nowadays↔drinks, Yesterday↔drank). The treatment protocol is described in detail in

Faroqi-Shah (2008), and includes a variety of processing and generation tasks. One of the treatment steps (judgment of morphological accuracy of sentences) is similar to the task used for MEG, described below. Daily treatment probes were used to document acquisition of verb morphology. Treatment cessation criteria were treatment probe accuracy exceeding 80% on four consecutive sessions or less than 10% in accuracy after eight treatment sessions. Six aphasic individuals received this therapy for tense marking over a period of 2-4 weeks (3-4 sessions per week) until their tense marking accuracy was maintained at above 80% over four consecutive treatment sessions. The seventh aphasic individual served as a control and received therapy that was unrelated to tense marking over the same time frame.

MEG. The task involved judgment of sentence acceptability. Audiorecorded sentences were presented in a random sequence and participants were instructed to indicate whether the sentences were acceptable or not by pushing one of two buttons. Neuromagnetic signals were recorded with a 160-channel whole-head MEG device (Kawanaza Institute of Technology, Japan). Six out of seven aphasic individuals performed the experiment twice prior to the initiation of therapy (at least a week apart) in order to demonstrate test-retest consistency when no language treatment is administered. All aphasic individuals received a post-therapy MEG scan within three days of cessation of morphological treatment.

Following preliminary processing and filtering for artifacts, averaged root mean square (RMS) waveforms in the time window of 100-1000 ms (measured from verb onset) were statistically compared across the three sentence conditions for each hemisphere for every 100ms block. Dipole localization using single equivalent current dipole (ECD) was obtained for prominent peak components using the best fitting 20-30 channels.

3. Results & Discussion

The six participants who received tense-related verb morphology treatment improved in production of verb inflections from a mean accuracy of 25% pre-treatment to 93.3%post-treatment, while the control participant (AP2) remained at 20% accuracy. This is shown in Figure 1. The mean number of treatment sessions was 15.25. In the pre-treatment scans, the MEG responses of all seven participants were unremarkable and there was no difference between correct and morphological/tense violations for the pre-treatment sessions (Mann-Whitney U = 5.5, p>0.05). However, the pattern for semantic anomalies was similar to that of unimpaired participants[1] with a left lateralized N400 effect (400-500 ms) for semantic anomalies when compared with correct sentences (Hagoort et al., 2003; Kwon, et al., 2006). Post-treatment MEG changed to a significantly greater amplitude in the post-treatment session (Mann-Whitney U [correct sentences] =10.2 & [tense anomalies]=8.1, p<0.05) for all six participants who received morphological treatment and no change for the seventh (control-AP2) aphasic participant (see Figure 2a for AP12 as an example). For four out of six participants, this pattern was similar to that observed for neurologically unimpaired participants: a three-peaked pattern with peak amplitudes approximately corresponding to 400, 500 and 600 ms for morphological anomalies (t(11)= 3.1 & 2.2, p<0.05). As shown in Figure 3, MEG amplitudes in the 350-500 and 500-900 ms (after verb onset) range were significantly higher for post-treatment scans and quantitatively not significantly different from neurologically unimpaired participants (Mann Whitney U, all p<0.05). To summarize post-treatment MEG activity quantitatively and qualitatively (the latter for 4 out of 6 participants) increased after treatment and resembled that of the normal pattern for morphological processing. Dipole source localization for the post-treatment changes revealed left hemisphere cortical sources for four

[1] N=14, 8female, Mean age=21.6 years.

out of six participants (see Figure 2b) and bilateral source (with a stronger left hemisphere component) for two participants. The control participant showed no MEG change between her two pre and one post-treatment scans. The results reveal relatively unambiguously that, in this case of therapy-induced language reorganization, the newly recruited neural networks are likely performing linguistic functions similar to unimpaired networks and are primarily dominated by the perilesional left-hemisphere networks (consistent with a previous MEG study of word retrieval treatment, Cornelissen, et al., 2003).

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Table 1. Demographic and language data for study participants. AP2 was the control participant who received a different treatment and showed no improved in morphological accuracy.

	Age (yrs) Gender	Handedness	Y; MPO	Educ.	WAB AQ	Pre-Tx % Verb infl.	Post-Tx % Verb infl.
AP10	37/M	R	7;0	18	77.1	55	100
AP12	61/M	R	1;1	15	57.2	15	70
AP14	44/M	R	1;4	18	45.7	25	90
AP19	55/M	R	1;5	18	61.8	30	100
AP17	55/F	R	2;2	17	32.8	25	95
AP18	39/M	R	2;1	18	71.0	5	90
AP2	62/F	R	1;0	22.2	60	20	20

Legend: Y;MPO=Years Months post onset; Educ=years of education; WAB AQ= Western Aphasia Battery Aphasia Quotient (Kertesz, 1982); Pre-Tx %, Post-Tx %= Accuracy of treatment probes prior to and after morphological treatment.

Figure 1. Participants response to morphological treatment plotted as a function of accuracy of treatment probes in % over time. B=Baseline; T= Treatment.

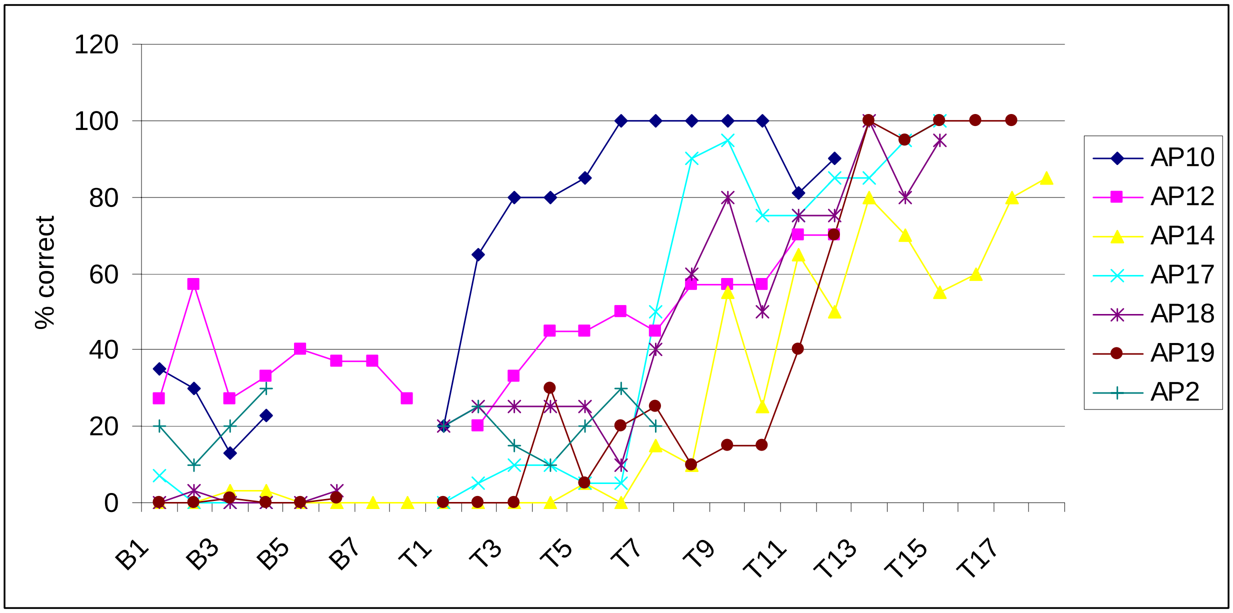

Figure 2. a Post-therapy MEG RMS waveform (red) compared to pre-treatment MEG response (black) in the time range of 300-700 ms time window after verb onset for one participant (AP12). **b.** Dipole source localization showing a peri-lesional source.

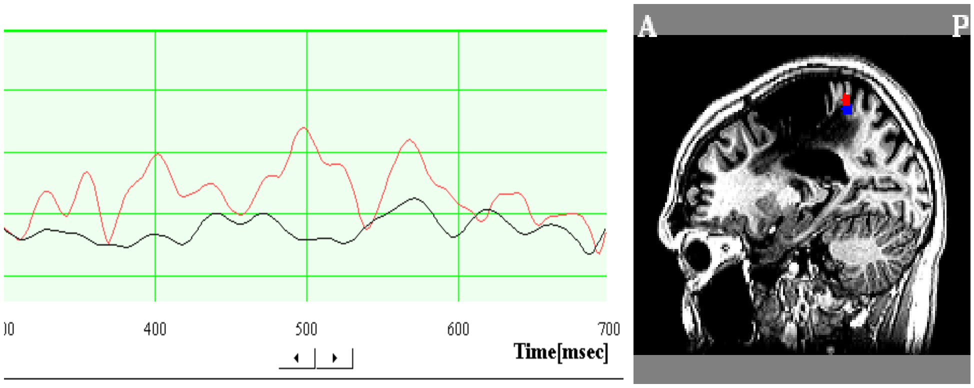

Figure 3. RMS amplitude in femtoTesla plotted for correct (green) and morphologically anomalous (blue) sentences in neurologically unimpaired young participants (Normal), all sic aphasic participants prior to treatment (Aphasia-pre) and after cessation of treatment (Aphasia-post).