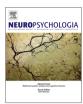
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# Neural underpinnings for model-oriented therapy of aphasic word production



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#### ABSTRACT

Model-oriented therapies of aphasic word production have been shown to be effective, with itemspecific therapy effects being larger than generalisation effects for untrained items. However, it remains unclear whether semantic versus phonological therapy lead to differential effects, depending on type of lexical impairment. Functional imaging studies revealed that mainly left-hemisphere, perisylvian brain areas were involved in successful therapy-induced recovery of aphasic word production. However, the neural underpinnings for model-oriented therapy effects have not received much attention yet.

We aimed at identifying brain areas indicating (1) general therapy effects using a naming task measured by functional magnetic resonance imaging (fMRI) in 14 patients before and after a 4-week naming therapy, which comprised increasing semantic and phonological cueing-hierarchies. We also intended to reveal differential effects (2) of training versus generalisation, (3) of therapy methods, and (4) of type of impairment as assessed by the connectionist Dell model.

Training effects were stronger than generalisation effects, even though both were significant. Furthermore, significant impairment-specific therapy effects were observed for patients with phonological disorders (P-patients). (1) Left inferior frontal gyrus, pars opercularis (IFGoper), was a positive predictor of therapy gains while the right caudate was a negative predictor. Moreover, less activation decrease due to therapy in left-hemisphere temporo-parietal language areas was positively correlated with therapy gains. (2) Naming of trained compared to untrained words yielded less activation decrease in left superior temporal gyrus (STG) and precuneus, bilateral thalamus, and right caudate due to therapy. (3) Differential therapy effects could be detected in the right superior parietal lobule for the semantic method, and in regions involving bilateral anterior and mid cingulate, right precuneus, and left middle/superior frontal gyrus for the phonological method. (4) Impairment-specific changes of activation were found for P-patients in left IFGoper. Patients with semantic disorders (S-patients) relied on right frontal areas involving IFG, pars triangularis. After therapy, they revealed less activation decrease in areas involving left STG, caudate, paracentral lobule, and right rolandic operculum.

Regarding naming performance, the present study corroborates previous findings on training and generalisation effects and reveals differential therapy effects for P-patients. Moreover, brain imaging results confirm a predominance of (1) general effects in the left brain hemisphere. (2) Brain regions related to visual strategy, monitoring/feedback, and articulatory patterns were characteristic for the familiar trained items. (3) Distinct regions associated with strategies, monitoring capacities, and linguistic information indicate the specific therapeutic influence on word retrieval. (4) While P-patients relied more on preserved phonological functions in the left hemisphere, S-patients revealed right-sided compensation of semantic processing as well as increased strategic efforts in both hemispheres.

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#### 1. Introduction

The model-oriented approach, which targets language treatment at impaired processing components or stages, has high priority in aphasia therapy (Cicerone et al., 2000). Clinically, word-finding difficulties are the most common symptom in aphasia (Laine & Martin, 2006). The lexical impairment is usually attributed to the semantic and/or phonological stages of processing, as explained in cognitive-functional models of word production (e.g., Howard & Gatehouse, 2006; Schwartz, Dell, Martin, Gahl, & Sobel, 2006), Metaanalyses revealed (1) that treatments of aphasic word-finding difficulties are efficacious (Wisenburn & Mahoney, 2009)—with (2) higher gains for trained compared to untrained words. Moreover, (3) impairment-specific therapy effects could be found for the group of patients with phonological deficits only (Wisenburn, 2010), (4) with the respective literature being inconclusive regarding which type of therapy is best designed for which type of patient. Both semantic and phonological treatments considered in the two meta-analyses involved a variety of techniques and inter-individual comparisons. An intraindividual comparison of parallelized methods at the group level should be well suited to reveal differential therapy effects. In the present study, we aimed to illuminate the neural underpinnings of model-oriented therapy of word production in aphasia, focussing on all four aspects mentioned.

Neural correlates of spontaneous and therapy-induced aphasia recovery have been investigated using functional brain imaging (for overviews, see Meinzer, Harnish, Conway, & Crosson, 2011; Zahn, Schwarz, & Huber, 2006; Crosson et al., 2007; Crinion & Leff, 2007). Both hemispheres were reported to subserve word production in healthy participants (Abel et al., 2011; Vigneau et al., 2011) as well as recovery of word production deficits in aphasia (Crosson et al., 2007). The right hemisphere (RH) appears be less efficient than the usually language-dominant left hemisphere (LH). The RH nevertheless tends to take over language functions, if LH capacities have become insufficient (Heiss & Thiel, 2006; Crosson et al., 2007).

Changes of brain activations related to therapy effects were rarely reported for RH activations (Crosson et al., 2005; Raboyeau et al., 2008) and more frequently for bilateral (Fridriksson, Morrow-Odom, Moser, Fridriksson, & Baylis, 2006; Fridriksson et al., 2007; Meinzer, Obleser, Flaisch, Eulitz, & Rockstroh, 2007; Menke et al., 2009) and LH (peri-lesional) activations (Leger et al., 2002; Cornelissen et al., 2003; Meinzer et al., 2008; Vitali et al., 2007; Fridriksson, Richardson, Fillmore, & Cai, 2012). Brain imaging studies on training effects have been dominated by (multiple) single-case studies, and only recently a few group studies have been conducted (Meinzer et al., 2011; Fridriksson et al., 2012).

To date, specific therapy effects and impairment type have not received much attention in brain imaging studies (Meinzer et al., 2008; Rochon et al., 2010). In a study including 11 patients with aphasia, Meinzer et al. (2008) investigated changes of fMRI activity in regions of interest showing abnormally slow wave activity as identified by magnetoencephalography (MEG). Cortical plasticity for picture naming was mainly observed in peri-lesional areas with dysfunctional processing. Despite behavioural generalisation effects, these brain areas correlated with therapy success for trained, but not for untrained items. Moreover, only in a few patients the brain activations for naming trained versus untrained items were partially overlapping. A direct comparison of both item sets might have helped to reveal the underlying differences assumed by the authors. Rochon et al. (2010) examined neural correlates of a semantic versus phonological fMRI task before and after phonological therapy. Both of the two patients improved in naming and revealed left frontal and temporal activation changes for the semantic task in the post-therapy scan.

In order to further enlighten neural underpinnings of modeloriented therapy, larger patient groups and a detailed characterisation of brain damage and language performance are considered to be crucial (Crinion & Leff, 2007). Among fMRI treatment studies, the present patient sample of 14 patients stands among the larger group studies executed to date. We aim to report each patient's brain damage to characterise the lesion, and to inform about pre-test naming abilities and type of lexical impairment to characterise his/ her language performance. The computer-assisted assessment of impairment type in a model-oriented framework, as featured by the interactive and connectionist lexical model of Dell (Fovgel & Dell. 2000), provides an easy to use, automated, and objective classification of the disorder as semantic (S) or phonological (P) (Abel, Huber, & Dell, 2009b). An application of parallelised cueing-hierarchies, a wellknown and effective stimulation technique, is optimal for a comparison of therapy methods guided by impairment type (e.g., Abel, Willmes, & Huber, 2007; Abel, Schultz, Radermacher, Willmes, & Huber, 2003). In this approach, cues with increasing semantic or phonological information about the target word are delivered and assist the patient's attempts to name depicted objects short-term and improve word finding long-term.

Fridriksson et al. (2007) investigated neural correlates of semantic and phonological cueing-therapy in three single cases. The two non-fluent patients showed significant improvements after both methods, while performance of the fluent patient remained relatively stable. The semantic method yielded differential activation in right superior frontal gyrus (Brodmann area (BA) 10) in one non-fluent patient. All in all, changes of activation were found in brain regions that are unrelated to language processing per se, e.g., in precuneus or thalamus. Even though patient error patterns were left unclassified by the authors, the predominance of semantic paraphasias over non-words is indicative for an S-disorder according to the Dell model. Our analysis at the group level might help to reveal language-related brain areas in response to semantic versus phonological cueing-therapies. Moreover, our group study intended to include lexical disorders both of the semantic and phonological type.

The two basic error types according to the Dell model have been localised by the research group of Schwartz et al. (2009), Schwartz, Faseyitan, Kim, and Coslett (2012). They found distinct structural left-hemisphere lesions to be associated with either semantic or phonological errors, namely anterior to mid portions of temporal and frontal gyri for the former and postcentral, supramarginal (SMG) and posterior portions of the inferior frontal gyrus (IFG) for the latter error type according to the Dell model. Moreover, Fridriksson, Baker, and Moser (2009) found compensatory activations for the production of semantic errors in left posterior peri-lesional occipital and temporal regions, while for the production of phonological errors nearly homologuous areas in the right hemisphere were detected. However, activations of patients classified as predominantly semantic or phonological have not been investigated yet. Thus, we were set to examine the relation between impairment type and brain activations.

To summarise, we applied lexical therapy, which was evaluated both with behavioural performance measures and with fMRI activation contrasts, to a group of 14 patients with aphasic word retrieval deficits after left-hemisphere stroke. We looked for possible correlations between changes of brain activations due to the therapy regimen and subsequent therapy gains (1). Moreover, we intended to investigate activation changes associated with specific therapy effects for trained versus untrained items (2) and semantically versus phonologically trained items (3). Finally, we aimed to detect activations related to the type of lexical impairment (semantic (S) versus phonological (P)) (4).

We expected to find especially left-hemisphere brain areas related to therapy gains (1), as well as distinct brain areas related

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