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1 Introduction

"Learning by doing". Many of us know this saying from parents, teachers or coaches, who emphasized the role of practice after observing our early failures in technical endeavours, for example: learning how to ride a bicycle, how to play an instrument or how to use a surfboard (i.e. *motor-skill learning*). The saying is based on the observation that for many tasks mere verbal instructions are not sufficient. In many occasions task performance can be significantly improved if one gets physically involved: in order to learn surfing it makes a major difference if we listen to somebody else, who describes how to keep the balance, or if oneself actually stands on the surfboard, directly realizing the consequences of every little movement. Thus for motor-skill learning active self-involvement is often crucial. But what about highly demanding cognitive tasks? Can cognitive performance be improved by taking an active stance?

With proceeding globalization foreign language skills have become a central requirement for many jobs. Second-language acquisition is extremely important, but often the learning process is cumbersome and difficult. Thus for many people alternative word-learning approaches are an attractive option. Bearing in mind the relevance of active self-involvement for motor-skill learning, it is interesting to investigate whether the same principle might also apply for the cognitive domain of word-learning. But how could active self-involvement be incorporated in word-learning? A promising idea refers to the facilitation of word-learning by gestures (e.g. Macedonia, Müller and Friederici, 2010a). Gesture-based word-learning exploits the semantic overlap between certain words (e.g. *cup*, *bow* or *hammer*) and congruent *iconic gestures* (i.e. hand movements, reflecting the meaning of those words). However, the effect of *grooming-gestures*, which do not reflect speech content (i.e. body-focused movements, such as scratching), remains unclear. Thus, one goal of this dissertation is to investigate how different gesture-types affect word-learning. Behaviorally this question is examined in a word-learning study, comparing the efficiency of iconic gestures and of grooming-gestures with a classical verbal-only learning condition.

In a clinical context gestures are frequently used during the rehabilitation of aphasia, a language impairment after stroke. They can be used instead of verbal communication (i.e. for compensation) but also to improve verbal communication (i.e. for restoration). Whereas some studies reported facilitating effects of gesture-based therapy on lexical retrieval (for a review see Rose, 2006), the role of gestures in word-learning remains unclear. Thus, a second goal of

this dissertation is to investigate on a clinical level whether patients with residual aphasia benefit from gesture-based word-learning. In addition to the behavioral data, the lesion-data of the patients are analyzed to investigate the implications of brain lesions for gesture-based word-learning.

Finally, with the advance of modern neuroimaging techniques, such as *functional magnetic resonance imaging (fMRI)*, it has become possible to identify brain regions involved in cognitive processes. In a recent review Friederici (2012) presented the *cortical language circuit*, a model on the left-hemispheric basis of sentence comprehension. Friederici (2012) described the involvement of the primary auditory cortex in the acoustic analysis of stimuli and the relevance of the middle temporal gyrus (MTG) and the anterior temporal lobe (ATL) for semantic processing. In particular the functional specialization within the inferior frontal gyrus (IFG) was emphasized: Friederici (2012) suggested that ventral back-projections from anterior Brodman area (BA) 45 to anterior superior temporal gyrus (STG) support semantic top-down processes and that dorsal back-projections of posterior BA 44 to posterior superior temporal brain regions subserve syntactic top-down processes.

Whereas scientific progress concerning the brain basis of language is advancing quickly (for reviews see Price, 2010; Friederici 2012), the neural correlates of gesture and speech are less clear. During comprehension of speech accompanied by iconic gestures, a differential contribution of the left IFG (e.g. Willems, Özyürek and Hagoort, 2007) and left superior temporal brain regions (Holle, Gunter, Rüschemeyer, Hennenlotter and Iacoboni, 2008) is currently discussed. Moreover, in the context of word-learning, Davis and Gaskell (2009) suggested that the hippocampus plays a crucial role, supporting rapid initial acquisition and episodic memory processes. However, the interaction and neural basis of gesture and speech has yet to be investigated for word-learning. Thus, the third goal of this dissertation is to use fMRI to localize neural correlates of gesture-based word-learning.

In sum, this dissertation investigates gesture-based word-learning on three levels: a) behaviorally, in a word-learning study the efficiency of different gesture-trainings is compared with a classical verbal-only learning condition, b) clinically, it is investigated whether stroke patients with residual aphasia benefit from gesture-based word-learning and whether certain brain lesions can be associated with gesture-benefit or with no gesture-benefit, c) on a neuroimaging level, fMRI is used to localize neural correlates of gesture-based word-learning. Before the actual experiments are described in the empirical part of this dissertation the specific topic of gesture-based word-learning will be situated into a broader

scientific context (Chapter 1). Following the introduction, the characteristics of blood-oxygen-level-dependent (BOLD-) fMRI are described (Chapter 2). The empirical part begins with a pilot study, which is followed by a behavioral study, a clinical study and a fMRI-study (Chapter 3). The last section highlights the main results and discusses them in a broader context (Chapter 4).

1.1 The relationship between gesture and language

Following an introduction about different kinds of gestures, this section describes the role of gestures in speech production and in verbal memory. This section ends with a paragraph evaluating the potential of gestures for word-learning.

What do we mean by gesture?

Speech is often accompanied by gestures. Giving a talk at a conference, speakers might use their hands to illustrate a steep correlation in their data (i.e. *iconic gestures*), to show the audience the location of peak activity in a figure (i.e. *deictic gestures*) or to emphasize the relevance of their final conclusions (i.e. *beat gestures*). All of these different hand movements occur during speech and are thus referred to as *co-speech gestures*. Co-speech gestures are spontaneous hand movements which are neither conventionalized nor contain linguistic properties (McNeill, 2000). As was described in the example above, co-speech gestures can fulfill different functions: Iconic gestures, for example, are hand movements, illustrating the semantic content of speech/words in a pictorial way. Deictic gestures are pointing gestures, directing attention to another person or object of shared interest. Finally, beat-gestures enrich the pragmatic function of speech and might be used to emphasize the content of speech by repeating simple hand movements synchronously with the speech prosody.

But gestures are also used in the absence of speech. Imagining the conference-example described above, the speaker might produce an 'OK-sign' with his hand to symbolize that his microphone works fine and that he is ready to start the talk. Those *emblematic gestures* are partly culture dependent and may also contain linguistic properties. Finally, for deaf people gestures entirely replace speech. *Sign languages* are complete linguistic systems, fully conventionalized and are sharing the same components with language (segmentation, lexicon, syntax).

In the present dissertation the focus is on meaningful hand movements which illustrate the semantic content of speech/words. These gestures have also been called *illustrators* (Ekman and Friesen, 1972), *iconic/metaphoric gestures* (for a concrete action/for an abstract idea; McNeill, Levy & Pedelty, 1990), *representational gestures* (McNeill, Cassell & McCullough, 1994), *ideational gestures* (Hadar, Burstein, Krauss & Soroker, 1998) and *lexical gestures* (Krauss, Chen & Gottesman, 2000). As the gestures used in this dissertation illustrate actions, they could be also called *pantomime*. However, in the present dissertation meaningful hand movements illustrating actions will be referred to as iconic gestures, because they underline the semantic content of speech/words in a pictorial way.

A completely different gesture-type are body-focused movements such as grooming, scratching, twitching and self-touching movements. In contrast to the gesture-types discussed above, body-focused movements are not timed with speech and do not reflect speech content. In the present dissertation meaningless *grooming-gestures* were chosen as a control-condition for meaningful iconic gestures.

The role of co-speech gestures in speech production

Despite the variety of different gesture-types most researchers agree that the primary function of co-speech gestures is to improve communication (e.g. De Ruiter, 2000). Based on Levelt's model of word production (Levelt, 1989), De Ruiter suggested the *Sketch Model* which explains the process of gesture production (see Figure 1a). According to the Sketch Model gestures originate during conceptual preparation at an early stage of speech production. Simultaneously with the activation of a lexical concept a spatio-temporal representation (i.e. sketch) is generated using imagistic information from working memory. Then the sketch is sent from the conceptualizer to the gesture planner, which is responsible for the selection of an appropriate gesture and the subsequent initiation of a specific motor program. The Sketch Model underlines the communicative function of gestures. An alternative view is suggested in the hypothesis of *lexical retrieval facilitation*, (Krauss et al., 2000). The hypothesis of lexical retrieval facilitation is also based on Levelt's model of speech production. However, in contrast to the Sketch model, the hypothesis of lexical retrieval facilitation does not assume a common origin of gestures and words at the level of conceptualizing.

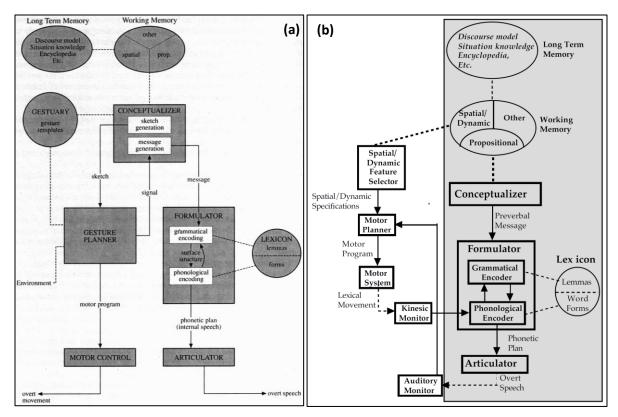


Figure 1 - Models of gesture production. (a) The Sketch Model (adopted from de Ruiter, 2000) assumes a common origin of gestures and speech at the level of conceptual preparation and suggests that the main function of gestures is to improve communication. **(b)** An alternative model proposes that the main function of iconic gestures is lexical retrieval facilitation (adopted from Krauss et al., 2000).

According to the hypothesis of lexical retrieval facilitation, there is a separate process, called the spatial/dynamic feature selector, which transforms spatio-dynamic features into a motor program and then facilitates lexical retrieval by cross-modal priming during phonological encoding at a late stage of speech production (see Fig. 1b).

Although both models share the view that gestures are derived from spatio-dynamic working memory, they differ considerably with regard to the subsequent steps following the stage of conceptual preparation. Whereas the Sketch Model suggests potentially independent and parallel development of gesture and word production, the hypothesis of lexical retrieval facilitation assumes a direct influence of iconic gestures on lexical retrieval. A critical point for the hypothesis of lexical retrieval facilitation is the question whether the meaning of a gesture could relate to multiple words or whether there is a single word (i.e. *lexical affiliate*) for a gesture. According to de Ruiter (2000) most iconic gestures activate a whole concept, such as a phrase or an entire sentence. Thus in contrast to Krauss et al. (2000), de Ruiter suggested that a facilitated speaking process could also be explained by iconic gestures activating conceptually related imagery. With regard to the present dissertation it is important

to note that the gestures used for word-learning were selected according to the criterion how well they represented manipulable objects such as *piano*, *cup*, *hammer* and so forth. This criterion was chosen, because the probability for these gestures to activate a single lexical affiliate is much higher compared to ordinary iconic gestures, which are spontaneously produced during speech (e.g. hand movements illustrating the steepness of a hill).

To summarize, two models describing the process of gesture production were presented, resulting in two different hypotheses about the role of co-speech gestures in speech production. According to the Sketch Model the main function of co-speech gestures is to improve communication. On the other hand, Krauss et al. (2000) emphasized a specific facilitating role of iconic gestures for lexical retrieval. It was shown that there is a close relationship between the production of gestures and words, although the exact details remain a matter of discussion. The models were presented, because they provide a framework for one of the main questions of this dissertation, regarding the effect of different gestures on pseudoword-learning. Further models of gesture production include the *Interface Model* (Kita & Özyürek, 2003), the *Growth Point Theory* (McNeill, 1992, 2005), the *Gesture-in-Learning-and-Development Framework* (Goldin-Meadow, 2003) and the *Gesture-as-Simulated-Action* (GSA) Framework (Hostetter & Alibali, 2008). With regard to the topic of the present dissertation it is important to note that all these models examined the role of gestures during speech production and not the role of gestures on verbal learning and memory, which will be discussed in the following paragraphs.

The role of gestures in verbal memory

In the early 1980s Engelkamp and Krumnacker (1980) investigated how different instructions affected memory for verbal phrases describing simple actions, for example "brush the teeth". They compared an action-condition (perform the action), with an imagination-condition (imagine the action) an observation-condition (observe the action in a video) and a control-condition (memorize the phrase). Engelkamp and Krumnacker (1980) were able to show that memory was improved for verbal phrases learned in the action-condition compared to verbal phrases learned in the imagination-condition. The result was considered relevant because of its implications for the *dual coding theory* (Paivio and Csapo, 1969; Clark and Paivio, 1991). The dual coding theory assumes that verbal and visual information are processed separately and that learning can be improved by combining both codes. The result of several studies (e.g.

Engelkamp and Krumnacker, 1980; Woodall and Folger, 1985) emphasized the role of motor processes for verbal memory and thus Engelkamp and Krumnacker proposed to extend the dual coding theory by a third motor code. Performing congruent actions for verbal phrases become known as (verbal) enactment and its positive effect on memory was termed *enactment effect*. The enactment effect was demonstrated in children (Thompson, Driscoll & Markson, 1998), young and old adults (Feyereisen, 2009). Crucial for the enactment effect is the semantic content of the gesture which needs to be congruent with the verbal phrase. Mismatching or non-iconic gestures do not facilitate verbal recall (Feyereisen, 2006). To summarize, behavioral research has shown that enactment of verbal phrases can facilitate verbal memory performance if the gesture is semantically congruent with the verbal phrase.

Can the enactment effect be used to support lexical learning?

Lexical learning (e.g. vocabulary-learning) becomes increasingly important as globalization proceeds at a high pace, requiring pupils and university students to prepare for jobs in international contexts. However, as many find lexical learning cumbersome and difficult, alternative learning strategies, promising facilitated learning, become increasingly attractive. Motivated by the enactment effect a few studies investigated whether gestures can be used to facilitate lexical learning (Macedonia, Müller & Friederici, 2010a; Kelly, McDevitt & Esch, 2009; Tellier, 2008; Allen, 1995). Allen (1995) examined the effect of emblematic gestures on the acquisition of French phrases (e.g. phrase: "Ca ne serait pas à prendre avec des pincettes" - "I wouldn't touch it with a 10-foot pole"; emblematic gesture: Touch index finger and thumb toward floor, other three fingers extended). It was shown that recall was greater for French phrases learned with emblematic gestures compared to French phrases learned without gestures. In contrast to Allen (1995), who used emblematic gestures, another study (Tellier, 2008) used iconic gestures to investigate whether learning of foreign English words (e.g. house, snake, book) could be facilitated in young French children (mean age 5;5). Tellier (2008) demonstrated that recall of foreign words was higher if these were learned with iconic gestures compared to foreign words learned with pictures. The results of both studies are in line with the enactment effect and show that iconic and emblematic gestures can be used to facilitate lexical learning. More recently two studies compared the effects of different gesture-types on lexical learning to exclude the possibility that improved gesture-based learning could be explained by the ability of any gesture to capture attention (Kelly et al., 2009; Macedonia et al. 2010a). Consistently both studies revealed that only meaningful iconic

gestures facilitate lexical learning whereas learning with incongruent gestures (Kelly et al. 2009) or grooming-gestures (Macedonia et al., 2010a) resulted in a reduced learning performance.

To summarize, studies investigating gesture-based word-learning indicate that the principle underlying the enactment effect can be successfully applied to lexical learning. In particular it was shown that successful gesture-based word-learning requires semantic congruence between gesture and word. However the interpretation of improved learning with iconic gestures remains difficult. Do iconic gestures facilitate lexical learning? Or is it more likely that grooming gestures interfere with lexical learning? In the behavioral part of this dissertation these questions were investigated in a word-learning study, comparing the efficiency of different gesture-training conditions with a classical verbal-only learning condition. If iconic gestures facilitated lexical learning, more words should be learned with iconic gestures compared to learning with grooming gestures and learning in the verbal-only condition. On the other hand, if grooming gestures interfered with lexical learning, the learning performance should be better with iconic gestures than learning with grooming gestures but not different from learning in the verbal-only condition.

1.2 The use of gestures in aphasia therapy

This section begins with a description of aphasia from a neurological perspective, introducing the classical *Wernicke-Geschwind model*. Next, the *Logogen-model* is presented, a patholinguistic model of word processing in aphasia. Finally a short overview about the use of gestures in aphasia therapy is provided, emphasizing possible facilitation effects of gestures on lexical retrieval. This section ends with the clinical research question of this dissertation.

What is aphasia? – A classical neurological perspective

One third of all stroke patients suffer from aphasia and its prevalence in Germany is between 70.000 – 100.000 (incidence rate 25.000/year, according to the Gesellschaft für Neurologie in Deutschland). Aphasia refers to acquired impairments of language processing including comprehension and/or production deficits. Depending on the size and location of the brain lesion, the symptoms and the severity vary dramatically in aphasia. In its most extreme form aphasic patients suffer simultaneously from receptive and expressive speech impairments and are unable to communicate (global aphasia). Other patients present predominantly impairments either at the level of speech comprehension or speech production. In 1861 the French neurologist Paul Broca described a patient whose speech comprehension seemed to be mainly intact but at the same time his speech production was greatly reduced (Broca's aphasia). This patient become known as 'Monsieur Tan', because 'Tan' was the only syllable he could produce. Examining his brain it was revealed that Monsieur Tan had a lesion in the frontal lobes. Based on this and similar findings in other patients Broca suggested that there is a critical brain region for speech production in the left frontal lobe, a region that has become subsequently known as *Broca's area*. Broca's work is of major significance because he was the first who demonstrated that impaired brain functions are associated with specific brain lesions. In 1874 the German neurologist Carl Wernicke discovered that normal speech is also disrupted following lesions in the left STG. This temporal brain region, located between the auditory cortex and the angular gyrus, become known as Wernicke's area. It was associated with a different type of aphasia which was mainly characterized by fluent speech but poor comprehension (Wernicke's aphasia).

The Wernicke-Geschwind model

Based on the observation that language impairments can be associated with specific brain lesions, the Wernicke-Geschwind model was suggested to describe the role of several brain regions for language processing. Its key regions include a left inferior frontal area (i.e. Broca's area), a left posterior superior temporal region (i.e. Wernicke's area), a connecting fibre tract (i.e. the arcuate fasciculus) and the angular gyrus (see Figure 2). According to the Wernicke-Geschwind model, speech sounds are acoustically analyzed in the auditory cortex, but further processing in Wernicke's area is needed to understand sounds as meaningful words. The model suggested that repetition of a spoken word requires that the acoustic signal is passed on to Broca's area via the dorsally located arcuate fasciculus. Further, in Broca's area the signal is then converted to a code for muscular movements enabling speech. Finally motor cortical areas activate lips, tongue and larynx to produce speech. The Wernicke-Geschwind model offered simple explanations for the symptom complex of aphasia as it was understood at the time. Based on the Wernicke-Geschwind model a lesion in Broca's area should result in impairments of speech production because the full signal cannot be sent to the motor cortex, while at the same time speech comprehension is unaffected (Broca's aphasia). On the other hand a lesion in Wernicke's area should not affect speech production but should result in impaired speech comprehension because the transformation into meaningful words is disturbed (Wernicke's aphasia). Finally Wernicke suggested that disconnecting Broca's and Wernicke's area should produce a speech disorder that is characterized by impaired repetition of auditory speech but intact comprehension (i.e. *conduction aphasia*).

However, subsequent research revealed several limitations of the Wernicke-Geschwind model (e.g. Poeppel and Hickok, 2004; Dronkers, Wilkins, van Valin, Redfern, & Jaeger, 2004; Ben Shalom and Poeppel, 2008; Bear, Connors & Paradiso, 2006). The model does not account for the fact that severity of aphasia depends on how much cortex is damaged beyond Broca's and Wernicke's area. Furthermore, the model does not include subcortical structures, such as the thalamus and caudate nucleus, which are often affected by stroke causing more serious speech deficits. Moreover, the Wernicke-Geschwind model does not offer an explanation for language recovery after stroke. The fact that 44% of all surviving aphasia patients show spontaneous remission of symptoms within 6 months after the stroke (*Gesellschaft für Neurologie in Deutschland*) suggests that intact cortical regions can compensate for destroyed brain regions.

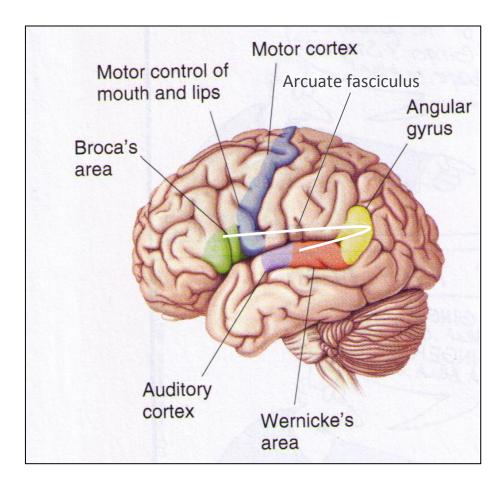


Figure 2 – Left-hemispheric brain regions involved in language processing. Key areas include Broca's area in the frontal lobe which lies next to the area that controls the mouth and lips in the motor cortex and Wernicke's area which lies on the superior surface of the temporal lobe, between the auditory cortex and the angular gyrus. The arcuate fasciculus is a dorsally located fibre tract connecting temporal and frontal regions (adapted from Bear et al. 2006).

Finally, the differentiation between Broca's and Wernicke's aphasia is not as clear as it was implied by the model, because both types of aphasia involve comprehension and speech deficits. It was demonstrated that isolated lesions to Broca's area do not cause Broca's aphasia (Mohr, Pessin, Finkelstein, Funkenstein, Duncan & Davis et al. 1978; Dronkers, Wilkins, Van Valin, Redfern & Jaeger, 1994) and that Broca's aphasic patients do not necessarily show lesions in Broca's area (Dronkers, Shapiro, Redfern & Knight, 1992). Dronkers et al. (2004) noted that "[...] lesions to Broca's area alone are known to produce only a transient mutism that resolves within 3-6 weeks" (p. 170). Reviewing the neural basis of syntactic comprehension Kaan & Swaab (2002) summarized that "[...] lesions in Broca's area are neither sufficient nor necessary to induce syntactic deficits" (p. 351). Furthermore, it was shown that Wernicke's aphasia is not caused by damage to Wernicke's area (Bogen & Bogen,

1976) and that conduction aphasia is not caused by damage to the arcuate fasciculus (Anderson, et al. 1999).

To summarize, based on neurological investigations the Wernicke-Geschwind model was the first model which described brain areas involved in language processing. Although subsequent research showed that it is an oversimplification, the Wernicke-Geschwind model has been useful both as a heuristic model to stimulate research and as a clinical model to guide diagnosis.

Aphasia from a linguistic perspective: the Logogen-model

In the previous paragraph aphasia was described from a neurological perspective, focusing on the consequences of specific brain lesions for language processing. A different approach is based on the analysis of errors in healthy volunteers and aphasic patients. From a neurolinguistic perspective aphasia is frequently described by the Logogen-model which focusses on language processing at the word level (see Figure 3). The Logogen-model (Morton, 1969; Pattersson, 1988) makes three core-assumptions: (a) independent processing of spoken and written language, (b) a lexical system to process words, (c) a non-lexical segmental system to process pseudowords (non-words such as *bafo*). The main components of the Logogen-model are four different lexica and one semantic system. For each modality (i.e. phonologic and visual) there is a receptive input-lexicon and an expressive output-lexicon. The model assumes that each of the single lexica could be impaired in isolation without affecting the activation of word forms in the other lexica. Whereas the lexica contain representations of word forms, the semantic system stores representations of the meanings of words.

According to the Logogen-model there are three possibilities of how spoken words are repeated following the auditory analysis of the stimulus: normal *lexico-semantic processing*, *lexico-non-semantic processing* and *non-lexical semantic processing*. Normal lexico-semantic processing implies that the auditory stimulus is recognized as a word in the phonological input lexicon. Subsequently the meaning of the word is realized by the semantic system and the appropriate phonemes are selected in the phonological output-lexicon, followed by overt articulation. Furthermore, the Logogen-model also provides an explanation for patients who correctly repeat a spoken word without knowing its meaning (i.e. lexico-non-semantic processing).

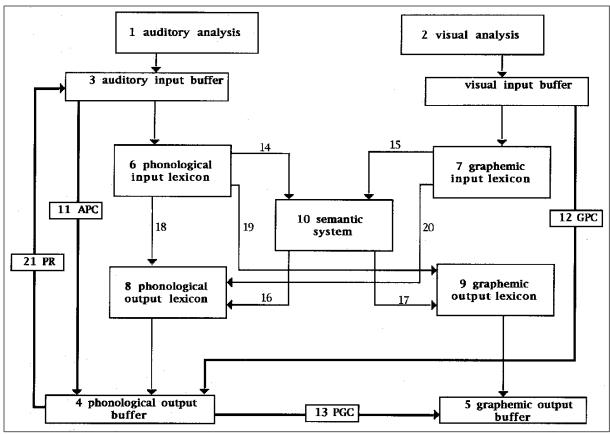


Figure 3 - Logogen-model for the processing of words. (adopted from De Bleser, Cholewa & Tabatabaie, 1997).

It is assumed, that following its recognition as a word, the word form can be passed on directly to the output-lexicon, without activating meaning in the impaired semantic system. In this case, overt articulation of the correct word-form is still possible, but due to the missing semantic analysis, the patient might not understand the meaning of the word. Finally non-lexical segmental processing implies that the patient successfully repeats a spoken word, without being able to distinguish it from a pseudoword (e.g. *bafo*). The Logogen-model suggests that, even if no entry is found in the phonological input-lexicon, speech-sounds can still be processed segmentally and repeated via the auditory-phonological correspondence.

To summarize, in contrast to classical neurological approaches which focus on brain lesions causing aphasia, modern patholinguistic models of word-processing emphasize the value of analyzing speech errors in the individual. Thus patholinguistic models of language processing are more flexible and can account for different symptoms. Furthermore, based on the Logogen-model a test-battery was developed (*lexicon and morphology*, i.e. *LEMO*, de Bleser et al., 1997) to investigate specific hypotheses concerning the underlying basis of the speech deficit and to provide a detailed description of the individual patholinguistic profile. Besides the frequently used Logogen-model which assumes modular and serial processing of

language, also other models were suggested, emphasizing the interactivity of language processes (*spreading activation*, e.g. Dell, 1986) or two sequential separate stages of speech production (Levelt, 1989; Levelt, Roelofs & Meyer, 1999). However, a common distinction which is found in all models of language processing refers to the separation of a phonological and a semantic level. In the next paragraph the use of gestures in aphasia therapy is summarized showing that a differentiated view on the underlying basis of aphasic symptoms is necessary to predict treatment outcomes.

The use of gestures in aphasia therapy

In the previous paragraphs aphasia was described from a neurological perspective focusing on the consequences of brain lesions and also from a linguistic perspective emphasizing the variability of aphasic symptoms within and between patients. The present paragraph describes the use of gestures in aphasia therapy and provides details about studies reporting a facilitation effect of gestures on lexical retrieval.

Gesture-based treatments in aphasia aim to enhance speech production. In particular two goals can be distinguished: compensation and restoration (for a review see Rose, 2006). In compensation-approaches gestures are used to replace impaired verbal communication. As Rose (2006) summarized:

[...] these compensation studies offer considerable support for the notion that individuals with moderate to severe non-fluent or global aphasia are capable of acquiring a repertoire of communicative gestures. The evidence addressing whether these gestures are generalized to a more natural communicative settings is less conclusive [...], (p. 101).

However, more interesting with regard to the topic of the present dissertation is the second approach which uses gestures to facilitate or re-establish verbal communication (restoration-approach). As was described above, Krauss and colleagues (2000) suggested that the main function of iconic gestures is to facilitate lexical retrieval. This hypothesis was supported by neuropsychological studies which showed that aphasic patients with lexical-retrieval difficulties produced more gestures than controls, patients with conceptual impairments (Hadar & Yadlin-Gedassy, 1994; Hadar, Wenkert-Olenik, Krauss & Soroker, 1998) and non-

aphasic patients with right hemisphere brain damage and visuo-spatial deficits (Hadar, Burstein, Krauss & Soroker, 1998; Hadar & Krauss, 1999).

Further support for the hypothesis of lexical retrieval facilitation comes from a study which did not focus on gesture-production but compared the effect of several conditions on picture naming (Rose and Douglas, 2001; but see de Ruiter 2006). It was demonstrated that picture naming was facilitated after the production of iconic gestures but not after pointing, cued articulation or visualization. The facilitation effect was only seen in patients with impairments on the phonological encoding level but not for patients with a semantic level impairment or a phonetic impairment. The authors argued that if gestural facilitation effects on speech production were dependent on early stages of conceptualization (Sketch model, de Ruiter 2000), there should have been facilitation effects in the visualization-condition. As the gestures had to be produced for a facilitation effect, Rose and Douglas (2001) see their result in line with the view that gesture- and speech-production interact at a late stage (hypothesis of lexical retrieval facilitation, Krauss et al. 2000).

Subsequently, gesture-based treatment-studies were conducted to investigate whether aphasic patients with lexical retrieval deficits might benefit from gesture-based treatments. Accumulating evidence suggests that gestures might be particularly helpful for aphasia patients with phonological speech deficits. This has been shown for noun retrieval deficits (Rose, Douglas and Matyas, 2002), for verb retrieval deficits (Rodriguez, Raymer and Gonzales Rothi, 2006; Rose and Sussmilch, 2008) in a natural setting (Lanyon and Rose, 2009) and for action observation and execution (Marangolo et al., 2010). However, facilitation effects of gestures were also found in a patient with apraxia of speech (Rose & Douglas, 2006) and even in a patient with mild semantic impairment (Rose & Douglas, 2007). There are also studies reporting no differential efficiency with regard to the underlying basis of the speech deficit (Raymer et al. 2011, Raymer et al., 2006) and no improvement in naming for items that received gesture therapy (Marshall et al., 2012).

To summarize, in line with a restoration approach many treatment-studies showed that a facilitating effect of gestures on lexical retrieval depends on the basis of the underlying speech deficit. Gesture-based treatments were shown to be in particular helpful for aphasic patients with mainly phonological speech impairments.

Do iconic gestures facilitate lexical learning in aphasic patients?

Whereas several clinical treatment studies reported facilitation effects of gesture-based trainings on lexical retrieval for aphasia patients, the effect of iconic gestures in lexical learning has not been addressed so far. Thus in the clinical part of this dissertation chronic aphasia patients were asked to learn the meaning of pseudowords (e.g. to learn the pseudword *krulo* for the rootword *piano*). One goal was to investigate whether gesture-based treatments can also be used to facilitate lexical learning in patients with residual aphasia. As aphasia is a very heterogeneous syndrome, encompassing comprehension and production deficits, it was further investigated whether there is a differential effect of gesture-based pseudoword-learning in aphasia patients, depending on their level of speech impairment. We assumed that impaired lexico-semantic processing will interfere with gesture-training. Therefore patients with lexico-semantic based deficits should not benefit from word-learning with iconic gestures. On the other hand, we hypothesized that aphasia patients with phonologically based speech impairments will benefit most from gesture-based word learning because their lexico-semantic processing capabilities are spared.

1.3 The neural basis of gesture and speech

In the previous sections an overview was provided, summarizing the relationship between language and gestures at a behavioral level and the use of gestures in aphasia therapy. The present section focuses on brain regions involved in the processing of gesture and speech. The dual-stream model was chosen to describe the brain basis of language comprehension, but note that alternative models exist, emphasizing different aspects of language processing, for example the cortical language circuit by Friederici, (2012) and models focusing on lexical-level processing (Price, 2000) and speech production (Indefrey and Level, 2004), (for a review see Ben Shalom and Poeppel, 2008). After introducing the dual-stream model of language processing, a second model is presented describing the role of the hippocampus in word-learning. Then studies are reviewed suggesting a neural overlap of gesture and speech. Finally neural correlates for the role of gestures in word-learning are described before the neuroimaging research question will be presented.

The neural basis of speech processing: the dual-stream model

Dual-stream models of language processing date back to the 1870s when the Wernicke-Geschwind model, which was based on lesion-data, emphasized the crucial role of Broca's area for speech production and the role of Wernicke's area for speech comprehension, with the arcuate fasciculus as the central pathway connecting both regions via the angular gyrus. Sharing basic assumptions about the functional roles of frontal and temporal brain regions with the Wernicke-Geschwind model, a recent model on the neural basis of speech processing incorporates modern neuroimaging data and describes two processing-streams: a ventral stream processing speech signals for comprehension and a dorsal stream which maps acoustic speech signals to frontal articulatory networks (see Figure 4; Hickok and Poeppel, 2000, 2004, 2007). According to the dual stream model the dorsal stream for speech production is strongly left dominant and involves a region in the Sylvian fissure at the parieto-temporal boundary which is proposed to be a sensorimotor interface and two frontal regions (Broca's area, premotor area) which correspond to the suggested articulatory network. However, for the present dissertation the ventral stream is more relevant, because in the fMRI-part of this dissertation (see section 3.3) comprehension of speech stimuli was investigated. According to the dual stream model the ventral stream for speech comprehension is bilaterally organized and involves four key regions.

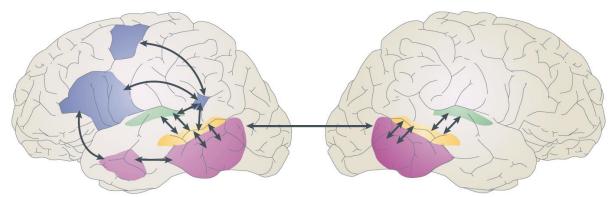


Figure 4 – Dual stream model of language processing (adopted from Hickok & Poeppel, 2007). Pink areas represent the ventral stream for speech comprehension including middle and inferior temporal regions. Blue areas represent the left-lateralized dorsal stream subserving articulation of speech, including *area Spt* at the left parieto-temporal boundary, Broca's area and the premotor cortex.

Initial spectro-temporal analysis of speech is assumed to take place in both auditory cortices in the dorsal superior temporal gyri. Processes at the phonological level are assumed to be represented in the posterior half of both superior temporal sulci. A lexical interface connecting phonological with semantic information is assumed to be located in the posterior middle and inferior portions of the temporal lobes with a weak left-hemisphere bias. Finally it was suggested that the ATL is involved in syntactic and compositional semantic operations, representing a combinatorial network. The crucial role of the bilateral ATL for semantic processing is also known from semantic dementia, a disease in which focal degeneration of the bilateral ATL is strongly associated with semantic degradation (Hodges, Patterson, Oxbury & Funell, 1992; for a review see Patterson, Nestor & Rogers, 2007). For language-related fibre tracts see Box 1.

Box 1 - Language pathways in the brain

With regard to language-related fibre tracts recent neuroimaging studies described a ventral pathway in addition to the well known dorsal pathway (Friederici, Bahlmann, Heim, Schubotz and Anwander 2006; Sauer et al. 2008; Friederici, 2009). Saur et al. (2008) used an approach combining fMRI with a probabilistic diffusion tensor imaging-based fiber tracking method to reveal the most probable anatomical pathways linking functionally specified language areas. Using two prototypical language tasks they described a dorsal pathway, connecting the superior temporal lobe and premotor cortices in the frontal lobe via the arcuate and superior longitudinale fascicle and a ventral pathway connecting the middle temporal lobe and the ventrolateral prefrontal cortex via the extreme capsule. With regard to the arcuate fasciculus Saur et al. (2008) showed that only the frontal seeds in the premotor cortices (frontal operculum, dorsal premotor cortex BA 6) are connected with the temporal lobe via the dorsal pathway. The authors suggested that the function of the dorsal pathway is restricted to sensory-motor mapping of sound to articulation, whereas the ventral route permits linguistic processing of sound to meaning (Saur et al., 2008).

A neural model of word-learning

Recently a neural model of word-learning was suggested integrating knowledge about brain regions involved in speech perception with the approach of complementary learning systems (Davis and Gaskell, 2009). In line with other researchers (e.g. Hickok and Poeppel, 2007) the assumptions about the functions of STG, inferior temporal gyrus (ITG) / MTG and inferior parietal lobe in speech perception are shared. However with regard to word-learning the differential roles of hippocampal and neocortical structures are emphasized (see Figure 5). Davis and Gaskell suggested two stages of word-learning: In the first stage of rapid initial familiarization novel words are encoded like other novel experiences as episodic memories and supported by the hippocampus. In the second stage of slow lexical consolidation, knowledge of words becomes independent of the hippocampus and dependent on neocortical temporal and temporoparietal brain regions. The model assumes that the process of slow consolidation from episodic memory towards long term memory requires sleep.

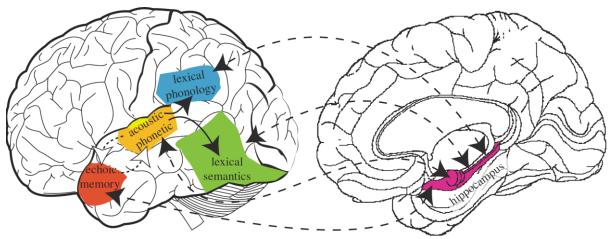


Figure 5 – Brain regions involved in learning and representing spoken words (adopted from Davis and Gaskell, 2009). Bidirectional arrows describe the interaction of the hippocampus with neocortical brain regions which are known to be involved in speech perception.

The neural basis of gesture-speech integration

Investigating the neural basis of action and speech is complex and can be pursued at different levels. Recently Willems and Hagoort (2007) reviewed neuroimaging studies on motor representations of speech sounds, action-related language, sign language and co-speech gestures. They concluded that there is a strong interaction between speech and gestures in the brain and that neural overlap between language and action is not restricted to speech and accompanying co-speech gestures.

On the sentence level Willems, Özyürek and Hagoort (2007) investigated if similar neural systems are involved when semantic information, conveyed through gesture or language, needs to be integrated into the preceding context. They demonstrated that a semantic mismatch between the sentential context and a sentence-final word and/or gesture increased activation of the left anterior IFG (BA 45 / 47). Willems et al. (2007) concluded that the left IFG is not restricted to language processing but also involved in the integration of gesture and meaning. Moreover, the premotor cortex was modulated by action information mismatching to a language context. Another study confirming the relevance of the IFG as an overlapping brain region for speech and gestures emphasized its role in semantic retrieval/selection (Skipper, Goldin-Meadow, Nusbaum & Small, 2007). Functional connectivity of Broca's area was compared with other brain regions, when participants listened to stories while watching congruent meaningful gestures, incongruent grooming-gestures or no hand movements. In line with the assumption that Broca's region plays an important role in semantic retrieval/selection, it was shown that Broca's area exerted the weakest influence on (pre)motor, superior temporal and inferior parietal regions during the meaningful gesture condition. Holle, Gunter, Rüschemeyer, Hennenlotter and Iacoboni (2008) used a disambiguation paradigm to study the neural system involved in the interaction of gesture and speech during comprehension. During fMRI-scanning participants watched videos in which ambiguous sentences (e.g. She touched the mouse) were accompanied by either meaningless grooming gestures or meaningful iconic gestures supporting the dominant meaning (i.e. animal) or the subordinate meaning (i.e. computer device) of the ambiguous word. Holle et al. (2008) showed that contrasted with grooming-gesture, both meaningful gesture-types activated a system of brain regions including the left posterior superior temporal sulcus (STS), the inferior parietal lobule bilaterally and the ventral precentral sulcus bilaterally. They suggested that the left STS reflects multimodal semantic interaction between a gesture and its co-expressive speech unit.

In sum, neural overlap of speech and gestures was found in different brain regions. Currently the contributions of the left IFG and left STS/STG are discussed regarding their role for the integration of speech and gesture (see also General Discussion, section 4.2)

Neural correlates of enacted words

While several studies investigated the neural basis of gestures and speech during comprehension, little is known about the neural correlates of verbal memory that was acquired with accompanying gestures.

Straube, Green, Weis, Chatterjee & Kircher (2009) investigated memory performance for abstract sentences which were accompanied with metaphoric gestures, unrelated gestures or no gestures. Behaviorally the discrimination performance (d') between conditions was comparable but fMRI revealed distinct memory-related left-hemispheric activations. Learning with metaphoric gestures was associated with activity in the IFG, the premotor cortex and the MTG. Furthermore, learning with metaphoric gestures correlated with hippocampal activation. On the other hand, learning with unrelated gestures or without gestures was processed in a network comprising the left occipito-temporal and cerebellar region and the right IFG. Straube et al. (2009) concluded that the left-hemispheric brain activations in the metaphoric gesture-condition reflect semantic integration of gesture and speech.

Gestures do not only facilitate memory for verbal material, but gestures can be also used to facilitate learning of novel words. Recently Macedonia and colleagues (2010a) demonstrated that learning of pseudowords (e.g. *ruzanego* = *bridge*) was improved if iconic gestures were performed during learning. Contrasting brain activity for pseudowords learned with iconic gestures versus pseudowords learned with grooming gestures revealed stronger activity in the premotor cortex. The opposite contrast (grooming vs. iconic) showed activity in a network reflecting cognitive control. Macedonia and colleagues (2010a) suggested that the premotor cortex activity reflects motor imagery for the meaning of those pseudowords, which were learned with iconic gestures.

In the fMRI-part of this dissertation neural correlates of gesture-based word-learning were further investigated to improve our understanding of the brain-mechanisms underlying multimodal word-learning. Which brain regions are involved in gesture-based word-learning? Are different brain regions involved in word-learning with and without gestures? To address these questions, pseudowords were learned in different training conditions. Thereafter fMRI was used to measure brain-activity, while participants listened to previously trained and untrained pseudowords.

1.4 Summary and research questions

The previous paragraphs provided theoretical background information for the empirical part of this dissertation. Behavioral research has shown that gestures and language are tightly linked with each other. It was described that gestures support memory for verbal material and might also affect learning of novel words. However, the specific roles of different gestures in word-learning remain unclear. Research on the roles of gestures was not able to disentangle whether the results show a facilitation effect of iconic gestures or whether they point to interference of grooming-gestures with word-learning. The behavioral part of this dissertation aimed to clarify this problem.

Gestures also have a long tradition in aphasia therapy. They can be used instead of verbal communication (i.e. for compensation) but also to improve verbal communication (i.e. for restoration). Several studies reported a facilitation effect of iconic gestures in lexical retrieval and this effect seems to be strongest in aphasic patients with phonological speech impairments. However, the role of gestures for word-learning in aphasic patients remains unclear. Furthermore the implications of brain lesions for gesture-based word-learning have not been addressed so far.

Models describing the brain basis of speech comprehension emphasize the role of both auditory cortices for spectrotemporal analysis, the posterior part of the STS for phonological processing, the middle and inferior portions of the temporal lobe for lexico-semantic processing, and a left parieto-temporal region as a sensorimotor interface. However, different accounts exist regarding the brain basis of gesture and speech. A relevant brain region for gesture-speech integration might be the left IFG, but also an involvement of the left STS/STG is currently discussed. In terms of word-learning it is known that the hippocampus plays an important role for the initial acquisition of novel word forms. However, only very little is known about the neural correlates of novel words, which were recently trained in different conditions.

To summarize the research questions, which are addressed in the empirical part (Chapter 3) of this dissertation:

- 1. How do different types of gestures affect pseudoword-learning? Do iconic gestures facilitate pseudoword-learning or do grooming gestures interfere with pseudoword-learning? (see *Pilot Study*, p. 36)
- 2. Does successful gesture-based pseudoword-learning depend on the overall level of learning performance? Do high performers benefit from gesture-based pseudoword-learning because they can easily integrate multimodal information? Or is gesture-based pseudoword-learning in particular helpful for low performers who use gestures as an elaborated learning-strategy? (see *Behavioral Study*, p.43)
- 3. Are iconic gestures helpful for pseudoword-learning in patients with residual aphasia? Is it possible to recommend gesture-based word-learning for aphasia patients based on their brain lesions or, alternatively, based on their patholinguistic profile? (see *Clinical Study*, p.53)
- 4. Which brain regions are involved in gesture-based pseudoword-learning? Do neural correlates of pseudowords differ depending on the training condition? (see *fMRI-Study*, p. 74)

2 General Methods (BOLD-fMRI)

This section provides background information about BOLD-fMRI, a technique which was used to investigate neural correlates of gesture-aided word-learning (see fMRI-study, section 3.3). Following a short introduction about the neurobiological basis of BOLD-fMRI, the characteristics of the hemodynamic response are described. Then the spatial and temporal resolution of fMRI is discussed and different experimental designs in fMRI are presented. Finally a short and precise overview on fMRI-data processing is given.

BOLD-fMRI

Neuronal activity requires energy to restore membrane potentials of neurons. Thus glucose and oxygen must be supplied by the vascular system. Crucially for BOLD-fMRI are the magnetic properties of hemoglobin: whereas oxygenated hemoglobin (oxy-Hb) is diamagnetic and weakly repulsed from a magnetic field, deoxygenated hemoglobin (deoxy-Hb) is paramagnetic and attracted to a magnetic field. Deoxy-Hb disturbs the magnetic field and experiencing different magnetic field strengths nearby protons will precess at different frequencies, which results in a rapid decay of transverse magnetization (Pauling and Coryell, 1936). Thus deoxy-Hb suppresses magnetic resonance (MR) signal intensity. After stimulus presentation the vascular system increases blood flow to the activated brain regions in an overcompensatory way (see Figure 6). In a famous analogy this principle was compared to "[...] watering the entire garden for the sake of one thirsty flower" (Malonek and Grinvald, 1996, p. 554). As oxygen supply is higher than oxygen consumption, deoxy-Hb is displaced by oxy-Hb (i.e. more rapid washout) and an increase in local MR signal can be observed (Ogawa, Lee, Kay and Tank, 1990). The BOLD-contrast is the difference in signal on T2*weighted images and depends on the cerebral blood volume and the absolute amount of deoxy-Hb present in a brain region (Huettel, Song & McCarthy, 2008).

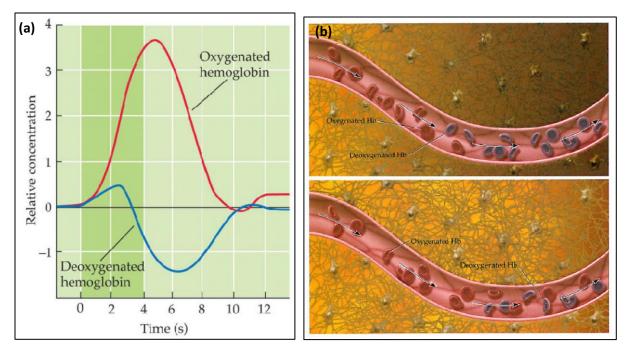


Figure 6 – BOLD-fMRI. (a) This graph shows changes of the relative concentration of oxygenated (oxy-Hb) and deoxygenated hemoblobin (deoxy-Hb) over time. The overcompensatory response of the vascular system is reflected in the high proportion of oxy-Hb. The HDR is defined by the timecourse of deoxy-Hb reaching its peak around 6s after stimulus onset. **(b)** This figure shows the ratio between deoxy-Hb and oxy-Hb within the blood vessels under normal conditions (top right) and the displacement of deoxy-Hb by oxy-Hb following neuronal activity (bottom right) (adopted from Huettel et al. 2008).

The hemodynamic response (HDR)

The HDR causes the change of MR signal on T2* images following local neuronal activity and results from a decrease of deoxy-Hb within a voxel (Huettel, et al. 2008). However, the exact relationship between neuronal activity and the BOLD-signal remains unclear (see Logothetis, Pauls, Augath, Trinath and Oeltermann, 2001; Logothetis, 2008). In contrast to neuronal activity which follows within milliseconds after stimulus onset, observable hemodynamic changes occur 1-2 seconds after the stimulus. The shape of the HDR is characterized by distinct phases (Huettel, et al. 2008): some studies have reported an initial decrease in MR signal directly after the stimulus (i.e. *initial dip*) which was attributed to a transient increase in deoxy-Hb in the voxel. During the displacement of deoxy-Hb the HDR rises, and crossing baseline at 2 seconds, the HDR reaches its maximum (i.e. *peak*) about 4 to 6 seconds after the presentation of a single stimulus. If multiple stimuli are presented an extended peak period (i.e. *plateau*) can be observed. As neuronal activity stops, blood flow is rapidly reduced and the MR signal drops below baseline. This *undershoot* has been attributed

to biophysical effects. According to the *balloon model* (Buxton, Wong and Frank, 1998), there is initially a greater inflow of blood than outflow which causes the venous system to expand like a balloon. As blood flow decreases more rapidly than blood volume, there is a higher amount of deoxy-Hb compared to oxy-Hb, and the HDR falls below baseline causing the undershoot.

Spatial resolution of fMRI

Whereas hemodynamic properties limit the temporal resolution of fMRI to several seconds, fMRI is an excellent technique to localize brain activity at the level of millimeters and less (Kim and Ogawa, 2002). Spatial resolution in fMRI is defined by the voxel-size (Huettel et al. 2008). The size of the three-dimensional voxels depends on three scanner parameters: field of view (FOV), matrix size and slice thickness. In the fMRI-study of this dissertation (see section 3.3) the chosen parameters (FOV = 19.2 cm, matrix size = 64 x 64, slice thickness = 3mm) defined a voxel-size of 3x3x3 mm. Voxel sizes can be adjusted by the researcher according to the brain region which is investigated. Whereas larger voxel sizes are used to cover the whole brain, it is also possible to reduce voxel-sizes to investigate specific brain regions, such as the visual cortex. Decreasing the voxel size also reduces *partial volume effects*, which occur in particular in larger voxels, containing several tissue types or different functional brain regions. Whereas the received signal in such a large voxel could be based on a mix of different signal contributions prohibiting exact localization, partial volume effects are reduced in smaller more homogeneous voxels.

However, there are two major limitations which prevent the use of very small voxel sizes: reduced *signal to noise ratio* (SNR) and increased acquisition time. Decreasing the voxel size implies that the total amount of deoxy-Hb in a single voxel is also reduced and thus resulting BOLD-changes will be smaller in a single voxel. Furthermore, acquisition time must be increased, because reducing the slice thickness requires an increase in slice-number to cover the same volume. Another disadvantage of increased acquisition time is T2* blurring. These distortions in T2* images occur if data acquisition is long enough that significant T2*decay occurs during that interval.

Temporal resolution of fMRI

Temporal resolution is defined as the ability to discriminate events in time. Whereas temporal resolution in BOLD-fMRI is not as high as in electroencephalography (EEG) / magnetoencephalography (MEG) (i.e. milliseconds), it is no problem to distinguish events, that are separated by a few seconds (Huettel, et al. 2008). In contrast to EEG/MEG, which measure electrical voltages and magnetic fields directly associated with neuronal activity, BOLD-fMRI measures the delayed HDR following neuronal activity. As previously explained, following the presentation of a single stimulus the HDR evolves over a period of more than 10 seconds. In blocked designs the HDR is even longer (see plateau, described above). The repetition time (TR) defines the sampling rate of the HDR. During slow TRs of 3 seconds and more very little data is acquired to describe the onset and the shape of the HDR. On the other hand, very fast TRs of 750ms and less allow a very precise sampling of the HDR. However, often medium TRs of 2 seconds are sufficient to adequately describe the HDR because BOLD-fMRI depends on slow physiological processes which are unlikely to vary wildly within short intervals of 100ms (Huettel et al. 2008). However, the effective sampling rate of the HDR can be increased by interleaved stimulus presentation. Using this technique a certain stimulus event is presented at different points within a TR over trials (e.g. +0 TR, +1/3 TR, +2/3 TR). Combining the data for the same event measured at different time points within a TR improves the sampling rate of the HDR. A disadvantage of this technique is the reduced number of trials. To achieve optimal temporal resolution the fMRI-study of this dissertation was conducted with a medium TR of 2 seconds combined with interleaved stimulus presentation.

Experimental designs in fMRI

The experimental design is a crucial part of every fMRI-study. Depending on the research question it must be considered whether a *blocked design* or an *event-related design* is more appropriate. In its simplest form a blocked design consists of only two conditions: stimulation and baseline. For example to investigate which part of the brain is involved in vision a blocked design can be used alternating between periods of stimulation (light on) and baseline (light off). Contrasting brain activation for both conditions (stimulation vs. baseline) reveals those brain regions which are associated with the stimulus. Another important issue in blocked designs concerns the duration of stimulation. To minimize noise from scanner drift,

the duration of each block should be kept as short as possible. On the other hand the physiological characteristics of the HDR require a minimum duration of around 10 seconds per block. Shorter blocks would prevent the HDR to return to baseline and the differences between conditions would be reduced. If the cognitive process of interest can be investigated in a blocked design, this design offers excellent detection power.

However, blocked designs are rather rigid and cannot be used to answer all research questions. The implementation of specific tasks and post-hoc analyses (e.g. lexical decision task, oddball-task or the analysis of response accuracy during a task) requires flexible eventrelated designs. Whereas in typical blocked designs many stimuli of the same type are presented consecutively within a block, in event-related designs only single discrete stimuli of short-duration are presented, whose timing and order may be randomized. Thus a main advantage of event-related designs is that responses to events are not systematically influenced by prior events nor confounded by differences in the subject's cognitive state. To minimize scanning-time without reducing statistical power by limiting the amount of trials per condition, rapid even-related designs use very short time intervals between successive stimuli. As the BOLD-signal saturates if intervals become too short (< 2s) the time interval between successive stimuli is often jittered (Dale, 1999). It is recommended to choose a mean interval of 4s to 6s for successive events of the same type to allow recovery from refractory effects (Huettel et al. 2008). In the fMRI-study of this dissertation an event-related design was used with a mean interstimulus interval of 6 seconds to investigate neural correlates of pseudowords (mean duration = 1.28 s). Event-related designs offer a lot more flexibility for the researcher because the same events could be analyzed in different ways. Furthermore event-related designs provide good estimation power for shape and timing of the HDR.

Analyzing fMRI-data

This section provides a general processing stream for the analysis of fMRI-data using the software *Statistical Parametric Mapping (SPM)* 8 (Figure 7). The following paragraphs explain the necessity of several pre-processing steps. Furthermore detailed background information is provided about the analysis of the fMRI-data of this dissertation.

Preprocessing

Following image reconstruction a series of computational procedures is applied to the raw fMRI-data. The main goals of preprocessing are: (a) to remove uninteresting variability from the data and (b) to prepare the data for statistical analysis. Preprocessing usually involves: motion correction, slice-time correction, spatial normalization and smoothing.

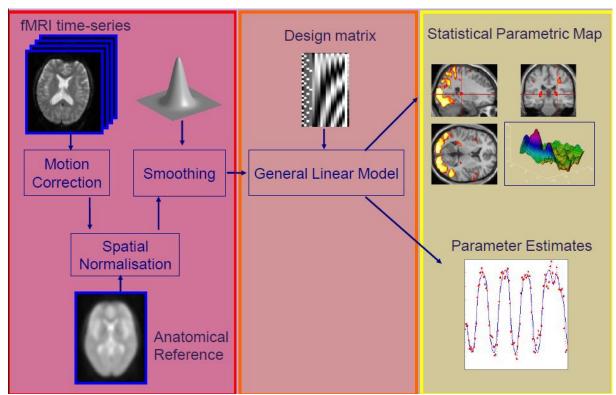


Figure 7 – Flow-chart of fMRI-data processing. Following several steps of preprocessing the investigator creates a design matrix and uses the general linear model to identify the relative contribution of the manipulated factors for the observed fMRI-data. After correction for multiple comparisons the results for each voxel are displayed at a certain alpha-niveau in a statistical parametric map.

Motion correction

Often there is head motion during fmri-data acquisition, which can be a problem for further data-analysis because a voxel might represent different parts of the brain across time points, introducing artefacts. To correct for head motion SPM 8 offers a routine called *realignment and unwarp* in which successive image volumes in the time-series are spatially aligned with a single reference volume and subsequently unwarped to account for non-linear distortions due to inhomogeneities in the magnetic field. The realignment routine in SPM 8 uses a least squares approach and a linear rigid-body transformation with six parameters (3 rotations, 3 translations). Realignment involves two stages: registration and transformation. During *registration* the 6 parameters are estimated that describe the rigid-body transformation between each image and the reference image. In a next step, during *transformation*, images are resampled according to the previously determined transformation parameters. For the fMRI-data of this dissertation a non-linear 4th degree B-spline interpolation was used. Although being slower, the non-linear B-spline interpolation was preferred over linear interpolations (nearest neighbour, bilinear, trilinear) because of its higher precision.

Choosing a linear rigid-body transformation during realignment is justified because the brain's size and shape do not change during the experiment (Huettel et al. 2008). However, tissue differences in the brain distort the signal and require unwarping, a process that estimates how distortions change as the subject moves. Furthermore, as a considerable amount of motion-induced variance remains in the data even after realignment, the estimated motion parameters can be included as covariates in the design matrix (realignment-parameter).

Slice-time correction

In the fMRI-study of this dissertation a TR of 2 seconds was used to acquire a full volume of the whole brain. During this TR of 2 seconds 30 slices were acquired in ascending order. Thus data for one volume are collected serially and there is a time interval of 1 second between acquisition of the first and the middle slice. Without correction, data for each slice will not correspond to the same point in time, introducing artefacts which are in particular problematic for time-sensitive event-related designs. Thus, after motion correction, the fMRI-data were slice-time corrected using temporal non-linear sinc interpolation with the middle slice as reference slice (number 15). Following slice-time correction the fMRI-data have values that

would have been obtained had each slice been acquired simultaneously at the same time as the reference slice.

Spatial normalization

To understand how the functional activation relates to the underlying brain anatomy the functional low-resolution images need to be *co-registered* with structural high-resolution images. Even after successful co-registration of functional and structural images for the individual, comparing brain activity between individuals is difficult due to the high variability of head sizes, shapes, orientation and gyral anatomy (Huettel et al., 2008). Thus participants' brains must be spatially normalized so that shape and size of the brain is the same for all. *Normalization* is a form of co-registration but the required transformations are much more complicated than for realignment during motion correction or intra-individual co-registration. Normalization into standard space requires affine-linear and non-linear transformations.

The fMRI-data of this dissertation were spatially normalized into Montreal Neurological Institute (MNI) space using parameters which were estimated based on the *unified segmentation approach*. Unified segmentation is an iterative process which aligns the tissue probability maps of grey matter, white matter and cerebrospinal fluid (CSF) with the segmented image until convergence. Following registration, trilinear interpolation was used to resample images with the previously determined normalization parameters obtaining an effective resolution of 3mm for the functional images and 1mm for the anatomical images.

Temporal filtering

System noise (e.g. scanner drift) and physiological noise (e.g. motion, respiration, cardiac activity) cause fluctuations in MR signal intensity over space and time (Huettel et al., 2008). To increase the SNR, these artefacts can be removed with temporal filters. The threshold for filtering depends on the experimental design and the time interval between two events of the same condition. To ensure that the frequency of interest is not filtered out a minimum duration of 2 epochs is recommended for highpass-filtering (Woolrich, Riplex, Brady and Smith, 2001). In line with this recommendation the fMRI-data of this dissertation were highpass-filtered, removing low frequencies under 100 seconds.

Spatial filtering

Spatial filtering (i.e. *smoothing*) refers to the blurring of fMRI-data across adjacent voxels. Usually a Gaussian filter is applied and the width of the kernel size is expressed in millimeters at half of the maximum value (i.e. full-width-half-maximum, FWHM). Advantages of spatial low-pass filtering are a reduction of variability between subjects and an increased SNR. Furthermore, smoothing also improves the validity of statistical tests because multiple comparisons are reduced and the normality of data is increased. Obviously the main disadvantage of smoothing is the reduced effective spatial resolution. The fMRI-data of this dissertation were smoothed using a Gaussian kernel of 8mm FWHM.

Statistical modeling and analysis

The *general linear model (GLM)* is a class of statistical tests that assume that the experimental data are composed of the linear combination of different model factors, along with uncorrelated noise (Huettel et al., 2008). The formula for a linear model is given in the following equation (for each voxel):

$$y_i = \beta_0 + x_{i1} \beta_1 + x_{i2} \beta_2 ... + x_{ij} \beta_j + \varepsilon_i$$
, $i = 1...n$

The basic idea behind a linear model is that the observed data (y_i) is equal to a weighted combination of model factors (x_{ij}) plus an additive error term (ε_i) . To account for all measured time points in an fMRI-data set there is also an equivalent matrix notation:

$$Y = X\beta + \varepsilon$$

The GLM estimates the experimental parameters (β) for a design matrix (X) that best accounts for the measured data (Y) while reducing noise (ε). Those estimated parameters (betas) reflect the relative contribution of the different model factors to the observed data within a given voxel. The higher the beta-value the stronger is the contribution of this factor for the observed fMRI-data in a given voxel. The design matrix (X) is constructed by the researcher and contains the factors which are manipulated in the study design, associated with specific hypotheses (experimental factors). Furthermore, other factors can be included that are not related to the experimental hypotheses but still might help to explain the measured fMRI-data by reducing noise, for example movement-parameters, respiration-artefacts or scanner drift (i.e. nuisance factors).

In order to model the observed fMRI-data (BOLD response), usually a box car function is specified in the design matrix (X). However, a more realistic model of the BOLD response can be obtained by incorporating knowledge about the HDR. Thus to adapt the GLM for fMRI-data the boxcar function can be convolved with a *basis function* (e.g. Gamma function), specifying properties of the HDR, such as peak and undershoot (see above).

Once parameters (beta-values) are estimated for each condition contrasts can be computed between two conditions of interest for each participant. Voxel-wise *t*-tests across all contrast images yield results (e.g. T-values, Z-values) which can be displayed in a *statistical parametric map*. Due to the high amount of univariate *t*-tests for all voxels in the brain, there is a considerable amount of false positive results. Thus it is important to correct for *multiple comparisons*. The most conservative way to correct for multiple comparisons is to use *Bonferroni corrections*, in which the alpha-niveau is decreased proportionally to the number of independent statistical tests. However, in fMRI-research this method is rarely used because it is very conservative and real activity might be missed. An alternative way to correct for multiple comparisons is to evaluate the size of a cluster containing several activated voxels. Whereas a single voxel might be activated by chance, it is much less likely that a group of contiguous voxels will also be activated by chance. Two common methods to correct for multiple comparisons on the cluster-level are: *family-wise-error correction* and *false-discovery-rate*, which is a little bit less conservative.

Finally statistical parametric mapping refers to the labeling of all voxels within the image according to the outcome of a statistical test. It is usually color-coded according to the probability value for each voxel. Depending on the chosen alpha-threshold only voxels will be displayed with an alpha-probability-value of p < .01 or p < .001 and so forth.

3 Empirical Part

Gesture-based word-learning was investigated on three levels. The behavioral part consists of a pilot study, exploring the effects of different training-conditions on word-learning, and a second behavioral study which includes a larger sample and investigates whether a facilitating effect of iconic gestures depends on the overall learning performance. In the clinical part of this dissertation gesture-based word-learning was investigated in 14 patients with residual aphasia. In addition to the clinical learning data, brain lesions of the patients were analyzed to investigate possible implications for gesture-based word-learning. In the neuroimaging part fMRI was used to examine neural correlates of gesture-based word-learning in 14 healthy participants.

3.1 Behavioral Investigations on Gesture-Based Word-Learning: Facilitation or Interference?

The behavioral part of this dissertation examines how different learning conditions affect pseudoword-learning (e.g. to learn the pseudoword *krulo* for the rootword *piano*). The paradigm models the acquisition of a foreign language. But in contrast to learning real words of a foreign language pseudoword-learning implies that prior experience with stimuli can be excluded, thus improving experimental control. Recently it was suggested that pseudoword-learning can be facilitated by performing gestures during learning (Macedonia et al. 2010a). Participants' learning performance was higher with iconic gestures compared to learning with grooming-gestures. Although this result could be expected, its interpretation is not trivial: Do iconic gestures facilitate lexical learning? Or is it more likely that grooming gestures interfere with lexical learning?

To examine these questions a paradigm with three learning-conditions was developed. In analogy to the paradigm of Macedonia et al. (2010a), it included a learning condition with iconic gestures and a second learning condition with grooming-gestures. A third verbal-only learning-condition was introduced in which no gestures were implemented. Thus, comparing the learning-performance for both gesture-conditions with the verbal-only condition will show whether iconic gestures facilitate pseudoword-learning (i.e. better learning with iconic gestures than in the verbal-only and grooming condition), or whether grooming-gestures interfere with pseudoword-learning (i.e. better learning with iconic gestures than with

grooming gestures, but similar learning with verbal-only condition). In contrast to the study of Kelly et al. (2009), participants were required to perform the gestures during learning (i.e. enactment). This is in line with earlier results, which showed that enactment of verbal phrases leads to improved recall compared to observation- or imagination-conditions (e.g. Engelkamp and Krumnacker, 1980). Thus the active performance of gestures should result in stronger effects on pseudoword-learning than passively observing gestures.

Moreover, aphasia-research suggests that iconic gestures facilitate lexical retrieval especially in patients with mainly phonological impairments (e.g. Rose & Douglas, 2001; Rose et al. 2002). Therefore we additionally varied the *phonological complexity* of the pseudowords by adding a legal (kr-ulo) or illegal consonant cluster (tk-edi) to the beginning of each pseudoword. The next section describes the Pilot Study.

3.1.1 Pilot Study

The Pilot Study was conducted for two main reasons:

- (i) To explore the effect of different gesture-types on pseudoword-learning
- (ii) To validate the experimental design and stimuli

3.1.1.1 Methods

3.1.1.1.1 Participants

Eight healthy volunteers participated in this pilot study (5 females, 24-32 years). They were financially compensated and provided written informed consent according to the protocol of the local ethics committee (University of Leipzig). All participants were right-handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971).

3.1.1.1.2 Stimulus material

The stimulus material for the training consisted of 45 sound files of pseudowords, 45 written German words, 45 videos of meaningful iconic gestures and 15 videos of meaningless grooming gestures (for all items see Table 1).

Pseudowords

The 45 pseudowords were bisyllabic, meaningless and had no strong resemblance with any existing German word. Pseudowords differed in terms of phonological complexity, including 15 simple (i.e. no consonant onset-cluster, e.g. *kela*), 15 medium (i.e. legal German onset-cluster, e.g. *vrebu*) and 15 complex items (i.e. non-German consonant-cluster, e.g. *bdumi*). A rating of pronounceability (N=25) confirmed the increasing difficulty of pseudowords (Krönke, Friederici & Obrig, *Poster at HBM*, 2010a). All pseudowords were spoken by a German/Slovak early bilingual female speaker in a soundproof booth and were digitally recorded with 16 bits at a sampling rate of 44 kHz. Mean duration of the pseudowords was 0.82 s [*SD* = 0.07].

Table 1 - Stimuli of Pilot Study

No	Rootword	PW - Simple	No	Rootword	PW - Medium	No	Rootword	PW - Complex
1	Angel [fishing rod]	/kela/	16	Buerste [brush]	/griba/	31	Bogen [bow]	/tkela/
2	Besen [broom]	/geda/	17	Cello [cello]	/vrebu/	32	Gabel [fork]	/vdosu/
3	Floete [flute]	/buka/	18	Diskus [discus]	/blire/	33	Glocke [bell]	/bdumi/
4	Gewehr [gun]	/bafo/	19	Frisbee [frisbee]	/brafi/	34	Hammer [hammer]	/bzope/
5	Guertel [belt]	/belu/	20	Geige [violine]	/trobe/	35	Harfe [<i>harp</i>]	/bzogu/
6	Jacke [jacket]	/dati/	21	Hacke [pick]	/brapu/	36	Hose [trousers]	/tkamo/
7	Loeffel [spoon]	/desa/	22	Lupe [magnifier]	/vresi/	37	Kanne [pot]	/dlefi/
8	Mixer [mixer]	/beki/	23	Mantel [coat]	/blino/	38	Klavier [piano]	/tkabu/
9	Pinsel [paintbrush]	/dule/	24	Muetze [cap]	/vrine/	39	Messer [knife]	/bduro/
10	Schere [scissors]	/voni/	25	Pfanne [pan]	/drobe/	40	Nadel [needle]	/dlesu/
11	Schnorchel [snorkel]	/dumo/	26	Pumpe [pump]	/krulo/	41	Peitsche [whip]	/tkedi/
12	Schraube [screw]	/gabo/	27	Schaufel [shovel]	/drofu/	42	Rechen [rake]	/bzola/
13	Spaten [spade]	/bome/	28	Schluessel [key]	/blegu/	43	Saege [saw]	/bdaki/
14	Tasse [cup]	/keto/	29	Spritze [syringe]	/grule/	44	Socke [sock]	/vdube/
15	Waage [scale]	/bonu/	30	Zange [pliers]	/blefo/	45	Trommel [drum]	/bzifu/

Note. 45 rootword-pseudoword pairs used for training are listed in alphabetical order. Pseudowords (PW) differ in phonological complexity (simple, medium, complex) and are only presented as a sound file, as indicated by //. English translation of rootwords is provided in [*italics*].

Rootwords

The 45 bisyllabic German words used during learning referred to manipulable objects such as *drum*, *bow* and *cup*. They will be referred to as rootwords. Lexico-semantic familiarity of the rootwords was controlled for frequency (classes 11-17, mean: 14), according to the German word frequency counter which is provided online by the University of Leipzig (http://wortschatz.Uni-Leipzig.de). Additionally, the chosen rootwords were rated by 9 volunteers, not participating in the learning study, in terms of gestureability, definability, manipulability and imageability in a test prior to the experiment. Pseudowords and rootwords were paired excluding that vowel structure and initial phonemes of any word pair were identical.

Gesture-videos

Videos of 45 meaningful iconic gestures show an actress who performs gestures illustrating the meaning for each of the 45 rootwords (see Appendix A). The most iconic and simple gesture was chosen from a set of alternative gestures offered by the actress. Another 15 videos

show different meaningless grooming gestures performed by the same actress (seven left-handed). To avoid distraction by facial expressions, the face of the actress was covered by a stocking mask (see Figure 8). Mean duration of all videos was 3.46 s (SD = 1.04).

3.1.1.3 Experimental design and training conditions

In a within-subject design 45 pairs of pseudoword-rootword were pseudorandomly assigned to 3 different learning conditions, balanced for phonological complexity of the pseudoword and word-frequency and gestureability of the rootwords. Depending on the learning condition a word-pair was either presented (a) without any gesture-video (15 pairs, verbal-only), (b) with a meaningful congruent iconic gesture (15 pairs, iconic gesture), or (c) with a neutral grooming-gesture (15 pairs, grooming-gesture). Each learning condition included five simple, five medium and five complex pseudowords. In sum, a within-subject design with nine conditions was used to investigate (a) whether learning performance is better in the gesture-condition than in the verbal-only or grooming conditions, (b) whether phonologically simple pseudowords are easier to learn than medium or complex pseudowords and (c) whether the iconic gesture condition is particularly helpful when learning complex pseudowords (see Figure 8).

3.1.1.1.4 Training procedure and learning assessment

The training was performed in a silent behavioral laboratory. Visual stimuli were presented on a computer monitor and auditory stimuli were delivered via headphones (Sennheiser HD600) using the software Presentation® (Neurobehavioral Systems 14.7). Each trial started with the presentation of the written rootword for 1000ms, followed by the auditory presentation of the pseudoword (see Figure 9). In the gesture-conditions the pseudoword was either accompanied by a video of a meaningful iconic gesture or a neutral grooming gesture and participants were instructed to perform the respective gesture while repeating the pseudoword aloud. In the verbal-only condition the participant simply had to repeat the pseudoword aloud.

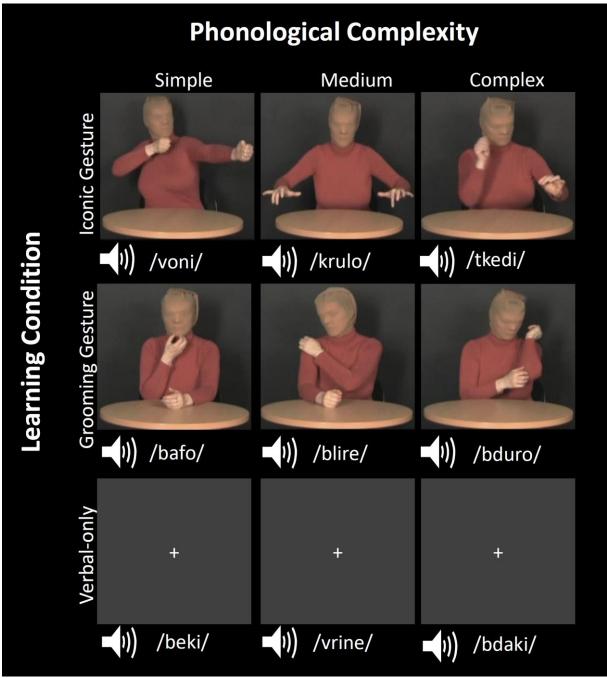


Figure 8 - Experimental design of the Pilot Study. Pseudowords differing in phonological complexity (simple, medium, complex) were learned with iconic gestures, grooming gestures or in a verbal-only condition without any gestures.

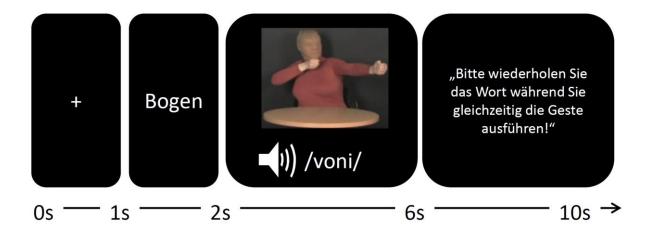


Figure 9 – Training-trial. This exemplary training trial shows the temporal sequence of pseudoword-learning. Following the written presentation of the German rootword (i.e. *Bogen*), the pseudword (i.e. *voni*) is presented via headphones. At the same time participants see a video of an iconic gesture (iconic gesture condition), or a video of a grooming-gesture (grooming-gesture condition). Then the participant is requested to repeat the pseudoword (*voni*), while imitating the gesture (iconic or grooming). No gesture was shown or repeated in the verbal-only condition.

The training program consisted of 7 blocks. One block comprised the presentation of all 45 pseudoword-rootword pairs and lasted approximately 8 minutes. Thus, overall training duration was 56 min. The order of items was pseudo-randomized, to ensure that the same training condition was not presented more than twice in a row. In addition, to exclude primacy/recency effects, the stimulus-sequence changed between blocks on the same day. Participants' learning performance was assessed after blocks 1, 3, 5 and 7. Participants were given the German rootword and should produce the trained pseudoword. Answers were registered by paper and pencil.

3.1.1.1.5 Statistical Analysis

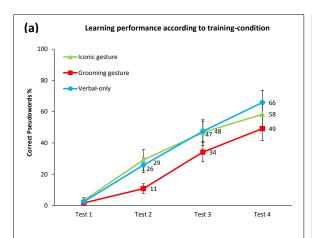
Data were analyzed using a 4 x 3 x 3 repeated-measurements analysis of variance (ANOVA) with the factors: time (1-4), learning condition (iconic, grooming, verbal) and phonological complexity (simple, medium, complex). Greenhouse-Geisser corrected degrees of freedom were used if the assumption of spherecity was violated. A significant main effect was further investigated with pairwise comparisons using Bonferroni corrections.

3.1.1.2 Results

Learning performance of pseudowords differed significantly in terms of learning condition (F(2, 14) = 16.26, p < .001) and phonological complexity (F(2, 14) = 17.71, p < .001). The interaction between learning condition and phonological complexity was not significant (F(4, 28) = 1.32, p = .29, ns).

The effect of learning condition is displayed in Figure 10a. The final learning performance with iconic gestures (M = 58%, SE = 9%) was higher than learning with grooming-gestures (M = 49%, SE = 9%). Interestingly, learning performance in the verbal-only condition was similar high as with iconic gestures and even slightly higher in the last assessment (M = 66%, SE = 8%). Pairwise comparisons confirmed that significantly more pseudowords were learned with iconic gestures than with grooming-gestures (p < .05) and that learning was similar with iconic gestures and in the verbal-only condition (p = 1.0, ns)

The effect of phonological complexity is displayed in Figure 10b. As expected, significantly more simple words were learned (M = 73%, SE = 9%), than medium (M = 60%, SE = 9%), or complex words (M = 41%, SE = 9%). Pairwise comparisons revealed that learning performance for simple and medium words was similar high (p = .14, ns), but significantly higher (p < .05) than learning performance for complex words.



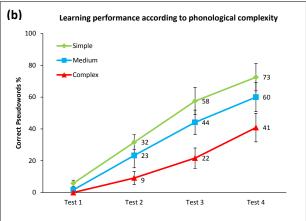


Figure 10 - Learning performance in the Pilot Study. (a) The mean learning performance (N=8) of pseudowords (PW) according to the learning condition is displayed. Learning performance was higher with iconic gestures than with grooming gestures but not different from learning in the verbal-only condition. **(b)** The mean learning performance according to phonological complexity of PW is shown. Learning performance was highest for simple PW, followed by medium and complex PW.

3.1.1.3 Summary and conclusions

One goal of this Pilot Study was to explore the effects of different gesture-types on pseudoword-learning. Consistent with previous results (Macedonia et al. 2010a), significantly more pseudowords were learned with iconic gestures than with grooming-gestures. Interestingly, learning performance in the verbal-only condition was similar high as with iconic gestures. Thus, these results are not in line with a facilitation effect of iconic gestures. Rather, the results of this Pilot Study indicate that different learning rates with iconic and grooming-gestures must be explained by an interference effect of grooming-gestures with pseudoword-learning.

As expected, the learning performance was affected by the phonological complexity of the pseudowords. Simple pseudowords were better learned than medium or complex pseudowords. Since there was no interaction between learning condition and phonological complexity, the data of this Pilot Study did not support the assumption that iconic gestures are in particular helpful for the acquisition of complex pseudowords.

Due to the small sample size of the Pilot Study (N=8) it is possible that a small facilitation effect for iconic gestures over the verbal-only condition could not be discovered because statistical power was too low. Thus for the next Behavioral Study it was decided to use the same learning paradigm again and to boost statistical power by increasing the sample size, extending the learning time and improving the stimulus material.

3.1.2 Behavioral Study – Does a Facilitating Effect of Iconic Gestures Depend on the Overall Learning Performance?

This behavioral study is based on the previously described Pilot Study and uses the same learning paradigm to further investigate the effects of different learning-conditions on pseudoword-acquisition. The Pilot Study revealed that learning performance is higher with iconic gestures compared to learning with grooming-gestures, but not different from learning in the verbal-only condition (Krönke et al., *Poster at HBM*, 2010a). However, due to the small sample size of the Pilot Study, it is possible that statistical power was too low to discover a small effect in favor for learning with iconic gestures over learning in the verbal-only condition. Thus, the goal of this Behavioral Study is to re-examine the effect of different gestures in pseudoword-learning, but in contrast to the Pilot Study statistical power is boosted by:

- increasing the sample size from N = 8 to N = 23
- extending the learning time from one day to three days
- exchanging weakly controlled stimuli

Highest learning performance is predicted in the iconic-gesture condition, followed by the verbal-only condition and learning with grooming-gestures. Again, the current design is also used to investigate whether iconic gestures are in particular helpful to learn phonologically complex pseudowords.

Furthermore a larger sample size allows to analyze whether a facilitating effect of iconic gestures depends on the general learning performance of participants. It is suggested that participants who show little learning at all (low performers) should benefit more from iconic gestures because their learning strategies are inefficient and performing iconic gestures provides an elaborated learning strategy that should support memory consolidation. On the other hand, participants with high learning performance (high performers) might not need additional gesture-based learning strategies and still excel the task without problems.

3.1.2.1 Methods

3.1.2.1.1 Participants

Twenty-three healthy volunteers participated in the Behavioral Study. They were financially compensated and provided written informed consent according to the protocol of the local ethics committee (University of Leipzig). All participants were right-handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). The monolingual native German speakers had some knowledge in 2 - 5 foreign languages (median: 3). Due to extremely bad learning-performance (more than 2 standard deviations below average performance), two participants were excluded. Thus all analyses reported below were performed on 21 participants (11 females, 21-32 years)

Neuropsychological testing was performed in all volunteers. This comprised (a) reading-span, (b) word list learning (German version of the California Verbal Learning Tests), (c) phonemic and semantic word fluency (subtests of the German version of the Controlled Oral Word Association Test), (d) digit block span (forward and backwards, respectively). The results of the neuropsychological tests were not used for further analyses (for mean scores of the participants see Appendix B).

3.1.2.1.2 Stimuli, experimental design and training conditions

As in the Pilot Study, stimulus-material consisted of 45 written German rootwords, 45 videos of meaningful iconic gestures, 15 videos of meaningless grooming gestures and 45 soundfiles of pseudowords (for a detailed description of stimulus-generation see section 3.1.1.1.2). Whereas German rootwords and gesture-videos were identical as in the Pilot Study, the stimulus-material was further improved by exchanging 29 weakly controlled pseudowords and adapting rootword-pseudoword pairings (see Table 2). The new pseudowords were taken from the same pool of audiofiles which were already used in the Pilot Study. Mean duration of the pseudowords was 0.82 s [SD = 0.07 s]. The same training conditions were applied as in the Pilot Study (for a detailed description see section 3.1.1.1.3).

Table 2 - Stimuli of Behavioral Study

No	Rootword	PW - Simple	No	Rootword	PW - Medium	No	Rootword	PW - Complex
1	Angel [fishing rod]	/voba/	16	Buerste [brush]	/krado/	31	Bogen [bow]	/kmifa/
2	Besen [broom]	/kedu/	17	Cello [cello]	/blire/	32	Gabel [fork]	/bdaki/
3	Floete [flute]	/voni/	18	Diskus [discus]	/bralo/	33	Glocke [bell]	/bziko/
4	Gewehr [gun]	/vime/	19	Frisbee [frisbee]	/brake/	34	Hammer [hammer]	/bzope/
5	Guertel [belt]	/tume/	20	Geige [violine]	/trodu/	35	Harfe [harp]	/tkedi/
6	Jacke [jacket]	/beki/	21	Hacke [pick]	/brapu/	36	Hose [trousers]	/tkela/
7	Loeffel [spoon]	/tubi/	22	Lupe [magnifier]	/vrego/	37	Kanne [pot]	/vdomi/
8	Mixer [mixer]	/bipa/	23	Mantel [coat]	/kruti/	38	Klavier [piano]	/tkase/
9	Pinsel [paintbrush]	/tulo/	24	Muetze [cap]	/krulo/	39	Messer [knife]	/vdosu/
10	Schere [scissors]	/vigu/	25	Pfanne [pan]	/krapu/	40	Nadel [needle]	/kmoda/
11	Schnorchel [snorkel]	/vole/	26	Pumpe [pump]	/blefo/	41	Peitsche [whip]	/vduli/
12	Schraube [screw]	/kafu/	27	Schaufel [shovel]	/vrema/	42	Rechen [rake]	/bduge/
13	Spaten [spade]	/tade/	28	Schluessel [key]	/vrine/	43	Saege [saw]	/kmope/
14	Tasse [cup]	/bafo/	29	Spritze [syringe]	/bregi/	44	Socke [sock]	/bduro/
15	Waage [scale]	/boga/	30	Zange [pliers]	/bliku/	45	Trommel [drum]	/bzifu/

Note. The same 45 German rootwords as in the Pilot Study were paired with 45 pseudowords, differing in phonological complexity (simple, medium, complex). Based on the experience of the Pilot Study several pseudowords were exchanged and rootword-pseudoword pairings were updated. Pseudowords were only presented as a sound file, as indicated by //. English translation of rootwords is provided in [italics].

3.1.2.1.3 Training procedure and learning assessment

Whereas learning-conditions and single training trials were identical with the Pilot Study (see section 3.1.1.1.3), learning time was significantly increased from 7 blocks during one day to 18 blocks distributed over three consecutive days (6 blocks per day, see Figure 11). Accordingly, overall training time increased from 56 minutes to 2 hours 24 minutes.

In contrast to the Pilot Study, an additional measure was introduced to assess participant's learning performance: prior to the *cued-recall* task, in which participants were given the German rootword and should produce the learned pseudoword, there was also a *free recall* task in which participants were asked to name all word-pairs they could remember without any help. The reason to include the free recall task was the assumption that a potentially facilitatory effect of iconic gestures on pseudoword-acquisition might only occur in a more difficult task in which normal learning mechanisms are not sufficient.

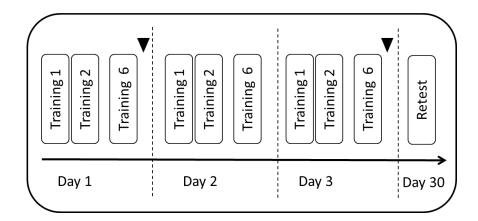


Figure 11 - Training schedule of the Behavioral Study. 18 training sessions were distributed over 3 consecutive days. The behavioral assessments reported here are indicated by triangles.

The free recall task requires that participants retrieve the complete word-pair without any help. Performing an iconic gesture is an elaborated learning strategy and should support consolidation and retrieval of the word-pair. Answers were registered by paper and pencil and additionally recorded digitally. Then responses were classified according to one of the following categories: a) *correct* (errorless), b) *almost correct* (answers include substitution, addition, elision or metathesis), c) *wrong* (more than one error), d) *no answer*. Subsequent analyses were performed for *correct* responses of the *free recall* task only.

3.1.2.1.4 Statistical Analysis

Data were analyzed using a 2 x 3 x 3 repeated-measurements ANOVA with the factors: time (day 1, day 3), learning condition (iconic, grooming, verbal-only) and phonological complexity (simple, medium, complex). Greenhouse-Geisser corrected degrees of freedom were used if the assumption of spherecity was violated. A significant main effect was further investigated with pairwise comparisons using Bonferroni corrections. The median of the learning performance was used to split the sample into two subgroups of high and low performers. Paired-samples *t*-tests were used to compare means between conditions within the whole group and within the group of low performers.

3.1.2.2 Results

Learning performance of pseudowords differed in terms of learning condition (F(2,40) = 8.36, p < .005) and phonological complexity (F(2,40) = 9.72, p < .001). There was a trend for an interaction between learning condition and time (F(2,40) = 2.68, p = .081). The interaction between learning condition and phonological complexity was not significant (F(4,28 = 1.32, p = .29, ns).

The effect of learning condition

Consistent with the Pilot Study, learning performance of pseudowords differed in terms of learning condition (F(2, 40) = 8.36, p < .005). Pairwise comparisons showed that learning performance with iconic gestures (ICON) was significantly higher than learning in the grooming-condition (GROOM) (p < .05). It was also superior to learning in the verbal-only condition (VERB) but did not reach statistical significance (p = .17, ns).

Furthermore, there was a trend for an interaction between learning condition and time (F(2,40) = 2.68, p = .081) indicating that learning performance differed between conditions over time (see Figure 12). On day 1, paired samples t-tests showed that learning with iconic gestures is significantly higher than learning with grooming-gestures (ICON: M = 23%, SE =3% vs. GROOM: M = 16%, SE = 3%; t(20) = 2.25, p < .05), but not different from learning in the verbal-only condition (ICON: M = 23%, SE = 3% vs. VERB: M = 22%, SE = 3%; t(20) = 1000.23, p = .82, ns). Learning performance in the verbal-only condition was significantly higher than learning with grooming-gestures (VERB: M = 22%, SE = 3% vs. GROOM: M = 16%, SE= 3%; t(20) = -2.1, p < .05). However, as revealed by paired-sample t-tests, on day 3 learning performance was significantly better with iconic gestures than learning with groominggestures (ICON: M = 78%, SE = 3% vs. GROOM: M = 65%, SE = 5%; t(20) = 3.89, p < .05). In contrast to day 1, learning with iconic gestures was also better than learning in the verbalonly condition (ICON: M = 78%, SE = 3% vs. VERB: M = 69%, SE = 4%; t(20) = 2.93, p < 0.00.05). Further, in contrast to day 1, learning performance in the verbal-only condition was not significantly better than learning with grooming-gestures (VERB: M = 69%, SE = 4% vs. GROOM: M = 65%, SE = 5%; t(20) = -1.27, p = .22, ns).

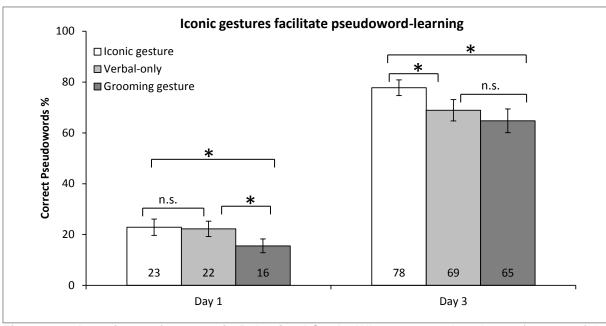
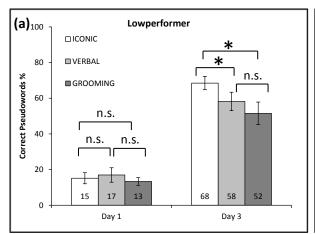


Figure 12 – Learning performance in Behavioral Study. Whereas mean learning performance (N = 21) with iconic gestures and in the verbal condition is similar on day 1, learning with iconic gestures is significantly higher than learning in the verbal condition or with grooming-gestures on day 3.

Level of performance and the effect of learning-condition

To investigate whether a facilitation effect of iconic gestures in pseudoword-learning might be driven by the overall level of learning performance, the sample was split into two groups (median-split): low performers (N = 11; mean performance 58%, SE = 4.3%) and high performers (N = 10; mean performance 82%, SE = 2%). Then the same statistical analysis as mentioned above was applied. Low performers showed an effect of learning-condition (F(2, 20) = 3.71, p < .05) that was in line with the result of the whole group: learning performance was best with iconic gestures, followed by the verbal-only and grooming-conditions. Furthermore, in the group of low performers, there was also a significant interaction between training and time (F(2, 20) = 4.14, p < .05): On day 1, learning performance was not different between conditions. However, paired-samples t-tests revealed that on day 3 learning performance was significantly higher with iconic gestures compared to the grooming (ICON: M = 68%, SE = 4% vs. GROOM: M = 52%, SE = 6%; t(10) = 2.9, p < .05) and verbal-only (ICON: M = 68%, SE = 4% vs. VERB: M = 58%, SE = 5%; t(10) = 2.28, p < .05) conditions (see Figure 13a).



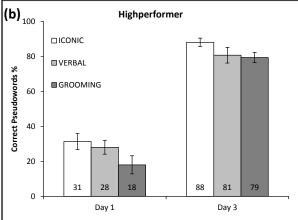


Figure 13 – Learning performance of subgroups. (a) Low performers (N = 11): consistent with the whole group the final learning performance is higher with iconic gestures than with grooming-gestures or in the verbal condition. (b) High performers (N = 10): learning performance does not interact with time. Learning performance was consistently higher with iconic gestures than in the grooming-condition, but in contrast to the group of low performers it was similar to learning in the verbal-only condition.

On the other hand, high performers showed an effect of learning-condition (F(2, 18 = 4.27, p < .05)) which is reflected in better learning with iconic gestures than in the grooming-condition (p < .05), but in contrast to low performers, similar performance as in the verbal-only condition (p = .46, ns). The interaction between time and training was not significant for the group of high performers (see Figure 13b).

Thus the overall result that final learning performance is significantly higher for learning with iconic gestures compared to the verbal and grooming conditions is driven by the group of low performers.

The effect of phonological complexity

As in the Pilot Study, learning performance differed also in terms of phonological complexity (F(2, 40) = 9.72, p < .001). Best learning performance occurred for simple words, followed by significantly decreased performances for medium and complex pseudowords (p < .05).

3.1.2.3 Summary

The Behavioral Study re-examined the effect of different gestures on pseudoword-learning in a larger sample of 23 healthy participants. Consistent with the Pilot Study (see section 3.1.1) more pseudowords were learned with iconic gestures than with grooming-gestures. However, in contrast to the Pilot Study, final learning performance for iconic gestures was also significantly higher than learning in the verbal-only condition. Thus the results of this larger study support the hypothesis of a facilitation effect of iconic gestures in pseudoword-learning.

Furthermore, splitting the whole sample into two groups, based on their overall learning performance, revealed different learning patterns for both groups. The facilitation effect of iconic gestures was not seen in participants with a high overall learning performance: high performers learned equally well with iconic gestures and in the verbal-only condition. Low performers on the other hand learned significantly more words with iconic gestures than in the verbal-only condition. Confirming our hypothesis, the comparison between high and low performers revealed that this facilitating effect was driven by the group of low performers.

Consistent with the Pilot Study, phonologically simple pseudowords were better learned than medium or complex pseudowords. Again, the assumption that iconic gestures are in particular helpful for the acquisition of complex pseudowords was not supported by the data.

3.1.3 Discussion

The behavioral results showed that gestures influence learning and memory of novel words. It was demonstrated that the success of gesture-based word-learning depends on the gesturetype. The behavioral results revealed that memory performance was better for pseudowords learned with iconic gestures compared to pseudowords learned with grooming-gestures. This is in line with two recent studies which have shown decreased memory performance for novel words learned with incongruent gestures (Kelly et al., 2009) or grooming-gestures (Macedonia et al., 2010a). The results suggest that in order to support the acquisition of novel words there must be a match between the semantic content of the gesture and the concept of the underlying novel word. If there is a semantic match between the gesture and the novel word, learning could be improved because integrating the information from both sources should create stronger and more multimodal memory representations (Kelly et al., 2009). The crucial role of semantic congruence between gesture and verbal material is further supported by a study investigating memory recall for short sentences in the mother-tongue (Feyereisen, 2006). Verbal recall for sentences in the mother-tongue was improved if they were accompanied by meaningful representational (i.e. iconic) gestures but not if sentences were accompanied by non-representational or incongruent gestures (Feyereisen, 2006).

The Pilot Study failed to reveal a facilitation effect of iconic gestures in pseudoword-learning compared with learning in the verbal-only condition (see section 3.1.1). However, the small sample size and the limited amount of learning time might have limited the statistical power of the Pilot Study. Consequently, in the Behavioral Study the sample size and learning time were significantly increased and using the same experimental design a different result was obtained (see section 3.1.2). In contrast to the Pilot Study, memory performance for novel words learned with iconic gestures was not only better than memory for novel words learned with grooming-gestures, but it was also better than memory for novel words learned in the verbal-only condition. This result is consistent with the original finding that enactment of verbal phrases leads to improved recall compared to observation- or imagination conditions (Engelkamp and Krumnacker, 1980). Furthermore, it is also in line with a study conducted by Kelly et al. (2009), who showed that learning of Japanese words is supported by combining speech and congruent gestures but not by speech alone or repeated speech. Finally, this result supports the dual coding theory (Paivio and Csapo, 1969; Clark and Paivio, 1991) which assumed that learning could be improved if in addition to verbal information nonverbal/visual information can be used.

Interestingly our results showed that learning behavior differed between high and low performers. Whereas both groups showed similar learning behavior in terms of improved learning with iconic gestures compared to reduced learning with grooming-gestures, they differed with regard to learning in the verbal-only condition. The results of the Behavioral Study revealed that only low performers showed significantly improved learning with iconic gestures compared to learning in the verbal-only condition. Thus we suggest that low performers benefit especially of iconic gestures because, lacking efficient learning strategies, they might use gesture-based pseudoword-learning as an elaborative learning strategy to support memory consolidation of pseudowords. A recent study, also comparing the learning behavior of high and low performers, reported similar learning behavior for both subgroups: superior learning performance with iconic gestures compared to grooming-gestures (Macedonia et al., 2010b). Our results confirmed this finding and further extended it by showing that for the group of low performers learning with iconic gestures is more helpful than learning in the verbal-only condition.

Based on the efficiency of gesture-based pseudoword-learning in the group of low performers it was decided to investigate the same effect in a clinical study with aphasia patients. Given that participants with limited verbal learning strategies benefit from iconic gestures, gesture-based pseudoword-learning should be in particular helpful for aphasia patients.

3.2 Clinical Study – Differential Efficiency of Gesture-Based Word-Learning in Patients With Residual Aphasia

This clinical study investigates the effect of iconic gestures on pseudoword-learning in patients with residual aphasia. Whereas some clinical studies reported facilitating effects of gesture-based trainings on lexical retrieval for aphasia patients (for a review see Rose 2006), the effect of iconic gestures in pseudoword-acquisition has not been addressed so far. In the Behavioral Study we showed that in healthy participants iconic gestures are in particular helpful for those participants with little overall learning (Krönke, Friederici & Obrig, *Poster at GAB*, 2010b). We suggested that low performers lack efficient verbal learning strategies and therefore benefit from gesture-based pseudoword-learning, which is an elaborated learning strategy supporting memory consolidation of pseudowords. Without doubt pseudoword-learning is in particular difficult for aphasic patients whose language capabilities are limited due to their brain damage. Thus it seems plausible to view patients with residual aphasia as a particular group of low performers with regard to pseudoword-learning. Based on the results of the Behavioral Study (see section 3.1.2), the goal of this clinical study is to investigate whether iconic gestures also facilitate pseudoword-acquisition in patients with residual aphasia.

An adapted version of the previously described learning paradigm was used (see section 3.1.1.1.3). In a within-subject design, patients learned half of the pseudowords with iconic gestures and half of the pseudowords in a purely verbal-only learning condition without gestures. The previously described grooming-condition was cancelled because the Pilot Study and the Behavioral Study showed unequivocally, that learning is impaired with grooming gestures (cf. sections 3.1.1, 3.1.2). The factor phonological complexity (simple, medium, complex) was maintained to investigate whether iconic gestures are in particular helpful to learn phonologically complex pseudowords. In contrast to many other studies this study is not restricted to single case reports and includes 14 patients with mild residual aphasia who were selected according to their patholinguistic profile. To identify factors that might influence the success of gesture-based pseudoword-learning, an extensive neuropsychological and neurolinguistical test battery was applied.

Based on the results of the Behavioral Study it was expected that learning performance would be higher with iconic gestures compared to the verbal-only condition. However, aphasia is a very heterogeneous syndrome, encompassing patients with deficits in language comprehension as well as production and impairments of language processing can occur at the segmental-phonological level and at the lexico-semantic level. Thus it comes as no surprise that therapy-studies reported positive effects of gesture-training on lexical retrieval not only for aphasia patients with phonological speech deficits (e.g. noun retrieval deficits: Rose et al., 2002; verb retrieval deficits: Rodriguez et al., 2006; Rose and Sussmilch, 2008; natural setting: Lanyon and Rose, 2009; action observation and execution: Marangolo et al., 2010), but also for patients with apraxia of speech (Rose & Douglas, 2006) and even mild semantic impairment (Rose & Douglas, 2007). Therefore an alternative hypothesis of the present study is that a differential effect of gesture-based pseudoword-learning in aphasia patients might depend on the level of language impairment. It is assumed that impaired lexico-semantic processing will interfere with the multimodal integration of gesture and pseudoword. Therefore patients with lexico-semantic based deficits should not benefit from pseudowordlearning with iconic gestures. On the other hand, it is hypothesized that aphasia patients with segmental-phonologically based speech impairments will benefit most from gesture-based word learning, because in a phonologically demanding word-learning task, speech deficits at the segmental-phonological level could be compensated by additional semantic meaningful information, such as iconic gestures.

In order to investigate the implications of brain-lesions for gesture-based word-learning, brain-lesions were analyzed using the technique *voxel-based lesion-symptom mapping* (*VLSM*). Identifying critical brain lesions for gesture-based word-learning might support the clinical decision whether gesture-based word-learning is an appropriate therapeutic approach for a patient or not. On the lesion-level it is hypothesized that a prerequisite for successful gesture-based word-learning is an intact ATL, as the ATL is crucially involved in semantic processing (for a review see Patterson et al. 2007) and might contribute to the semantic integration of gestures and pseudowords.

3.2.1 Methods

3.2.1.1 Patients

Fourteen stroke patients (6 females, 37-71 years) with residual aphasia were recruited from the database of the Dayclinic for Cognitive Neurology, Universityhospital Leipzig, Germany (for an overview see Table 3). All patients were German native speakers. Patients were selected according to their patholinguistic profile. The main criteria for study inclusion were a diagnosis of mild residual aphasia combined with the ability to perform the demanding word-learning paradigm which involved reading, speaking and the use of both upper extremities in the iconic-gesture condition. Therefore no patients were included who suffered from dyslexia or severe hemiparesis. None of these patients had a premorbid history of neurologic, psychiatric or neurodegenerative disorders. At the time of testing all patients were at least 23 months post-infarction. All patients were right-handed except in one case (Patient BR). None of the patients suffered from apraxia of speech, except in one case (Patient LF).

MRI-scans and medical reports were available for 12 patients (excluding patients SF and BR). Nine patients showed a left middle cerebral artery infarction and in two patients additional lesions also involved the basalganglia (Patient WI) and the region around the posterior cerebral artery (Patient SS). One patient showed a left posterior cerebral artery infarction (Patient SG). Three patients showed hemorrhages in the left temporal lobe (Patients PA, HS) and right occipito-temporal region (Patient DJ). Patients were financially compensated and provided written informed consent according to the protocol of the local ethics committee (University of Leipzig).

Table 3 - Patient history

Patient	Sex	Age (years)	Months since last	Pre-morbid	Aetiology
			infarction	handedness	
LF	М	54	102	Right	Ischemia in left MCA
CU	F	54	94	Right	Ischemia in left MCA
WI	F	37	61	Right	Ischemia in left MCA + basalganglia
PA	F	51	52	Right	Hemorrhage in left temporal lobe
SS	F	49	49	Right	Ischemia in left MCA + PCA
MS	М	71	55	Right	Ischemia in left MCA
SF	М	55	47	Right	Ischemia in left MCA
SG	М	60	23	Right	Ischemia in left PCA
BS	F	40	34	Right	Ischemia in left MCA
DJ	М	40	63 ¹ , 216 ²	Right	Gliom ¹ , Head trauma ²
BJ	М	63	47	Right	Ischemia in left MCA
HS	F	53	78	Right	Hemorrhage in left MTG
RT	М	57	42	Right	Ischemia in left MCA
BR	М	58	46	Left	Ischemia in left MCA

Note. F = female, M = male, MCA = middle cerebral artery, PCA = posterior cerebral artery, SFG = superior frontal gyrus, MTG = middle temporal gyrus

Prior to the beginning of the word-learning paradigm an extensive test battery was administered (for an overview of the results see Appendix C). Neuropsychological diagnostics comprised: (a) Trail Making Test A/B (TMT A/B, Reitan, 1958), (b) California Verbal Sturm, Learning Test (CVLT, Niemann, Thöne-Otto & Willmes, Leistungsprüfsystem (LPS, subtest 3, (Horn, 1983)), (d) Wechsler-Memory Scale Revised (WMS-R: digit spans forward + backward, (Härting, et al., 2000)), (e) Wortschatztest (WST, Schmidt and Metzler, 1992), (f) Regensburger Wortflüssigkeits-Test (RWT, Aschenbrenner, Tucha & Lange, 2000), (g) Mini-Mental-Status Test (MMST, Folstein, Folstein & McHugh 1975) and (h) Beck's depression inventory (BDI, Hautzinger, Bailer, Worall & Keller, 1994). Neurolinguistic diagnostics comprised: (a) Token Test (TT, Orgass, De Renzi & Vignoli, 1982), (b) Aachener Aphasietest, (i.e. AAT: subtest spontaneous speech, Huber, Poeck, Weniger & Willmes, 1983), (c) LeMo – Lexikon modellorientiert, subtests: 5, 8, 9, 11, 14, 16, 25, 30 (de Bleser, Cholewa & Stadie, 2004).

¹diffuse isomorph parasagittal gliom left frontal, WHO-level 2: g. front. sup., s. cinguli, g. cinguli ant., dissection of callosal radiation ²head trauma level 2: contusions in left fronto-temporal/parietal regions, hemorrhages in s. occipitotemporalis lateralis right, left parietal, symptomatic epilepsy

3.2.1.2 Stimulus material

Stimulus-material comprised 30 sound files of pseudowords (M = 0.83 s; SD = 0.06 s) 30 written German words and 30 videos of meaningful iconic gestures (M = 3.68 s; SD = 0.86 s) (for a detailed description of stimulus-generation see sections 3.1.1.1.2 and 3.1.2.1.2). The same stimuli were used as in the Behavioral Study, except for a different rootword-pseudoword pairing on three occasions (see Table 4). In contrast to the Behavioral Study, word-pairs were reduced from 45 to 30, to adapt to the demands of the patients.

Table 4 - Stimuli of Clinical Study

No	Rootword	PW - Simple	No	Rootword	PW - Medium	No	Rootword	PW - Complex
1	Angel [fishing rod]	/voba/	11	Bürste [brush]	/vrego/	21	Bogen [bow]	/kmifa/
2	Besen [broom]	/kedu/	12	Cello [<i>cello</i>]	/blire/	22	Gabel [fork]	/bdaki/
3	Flöte [<i>flute</i>]	/beki/	13	Frisbee [frisbee]	/brake/	23	Hammer [hammer]	/bzope/
4	Gewehr [gun]	/vime/	14	Geige [violine]	/trodu/	24	Harfe [harp]	/tkedi/
5	Gürtel [<i>belt</i>]	/tume/	15	Mantel [coat]	/kruti/	25	Hose [trouser]	/tkela/
6	Löffel [spoon]	/tubi/	16	Mütze [cap]	/krulo/	26	Klavier [piano]	/tkase/
7	Pinsel [paintbrush]	/tulo/	17	Pumpe [pump]	/blefo/	27	Nadel [needle]	/kmoda/
8	Schere [scissors]	/vigu/	18	Schaufel [shovel]	/vrema/	28	Säge [saw]	/kmope/
9	Schraube [screw]	/kafu/	19	Schlüssel [key]	/vrine/	29	Socke [sock]	/bduro/
10	Tasse [cup]	/bafo/	20	Spritze [syringe]	/bregi/	30	Trommel [drum]	/bdufa/

Note. Same material as in the Behavioral Study, except for word-pairs No. 3, 11, 30. Word-pairs were reduced from 45 to 30 to adapt to the demands of the patients. Pseudowords (PW) were only presented as a sound file, as indicated by //. English translation of rootwords is provided in [*italics*].

3.2.1.3 Experimental design and training conditions

As in both behavioral studies the experimental design consisted of two factors: training-condition and phonological complexity (see section 3.1.1.1.3 for details). In contrast to the previously described behavioral studies the grooming-condition was cancelled in this study because it was already shown that learning performance is decreased in this condition (see Pilot Study and Behavioral Study). The factor phonological complexity was maintained to investigate whether iconic gestures are in particular helpful when learning complex pseudowords (see Figure 14).

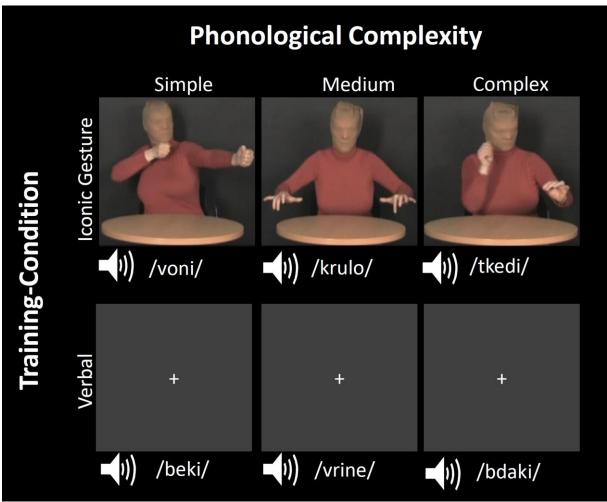


Figure 14 - Experimental design of Clinical Study. The same conditions were used as in the Pilot Study and in the Behavioral Study, except that the grooming-condition was cancelled. Pseudowords (PW) were trained with iconic gestures (first row) or without gestures (second row). PW differed in terms of phonological complexity: simple, medium, complex.

Although previous results did not support this assumption in healthy participants (see Pilot Study, Behavioral Study), a clinical sample provides a different situation. Due to impairments on the segmental-phonological level, aphasia patients should be more sensitive to phonologically manipulated stimuli and therefore the statistical power should be increased to find a possible interaction between training-condition and phonological complexity.

3.2.1.4 Training procedure and learning assessment

Whereas a single training-trial was identical with the trials in the Pilot Study and in the Behavioral Study (see section 3.1.1.1.4), the amount of learning-sessions was increased to 28 blocks, equally distributed over four consecutive days (7 blocks per day, see Figure 15). One block comprised the presentation of all 30 pseudoword-rootword pairs and lasted approximately 5 minutes. Thus overall training duration was 2 hrs. 20 min.

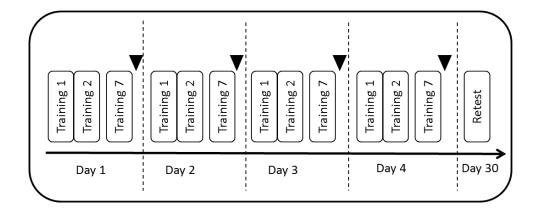


Figure 15 – Training schedule of Clinical Study. 28 training sessions were distributed over 4 consecutive days. The behavioral assessments reported here are indicate by triangles.

To assess patient's learning performance, four different memory tests were performed: (a) free recall: patients were asked to name all word-pairs they could remember, (b) cued recall to pseudoword: patients were given the German rootword and should produce the learned pseudoword, (c), cued recall to rootword: patients received the pseudoword and were requested to produce the rootword (d) decision-task: patients received the rootword and had to select the correct pseudoword out of 2, which were presented via headphones. Answers were registered by paper and pencil and additionally recorded digitally (MicroTrackII Professional 2-Channel Mobile Digital Recorder). Then responses were classified according to one of the following categories: a) correct (errorless), b) almost correct (answers include substitution, addition, elision or metathesis), c) wrong (more than one error), d) no answer. Subsequent analyses are performed for memory-assessment (b): cued recall to pseudoword. This assessment is of high ecological validity because it mirrors the demands of initial second language (L2) learning when a speaker searches the L2-word for a known German word. To enlarge the amount of data, answers from category a) correct and b) almost correct were summed up and commonly analyzed.

3.2.2 Results

3.2.2.1 Behavioral data analysis and results

A 4 x 2 x 3 repeated measurement ANOVA with the factors time (day 1, day 2, day 3, day 4), learning-condition (iconic gesture, verbal-only) and phonological complexity (simple, medium, complex) was used to investigate (a) whether lexical learning in the gesture condition is superior to learning in the verbal condition, (b) whether simple words were learned better than medium or complex words and (c) whether gesture-training is in particular helpful to learn complex pseudowords. Greenhouse-Geisser corrected degrees of freedom were used if the assumption of spherecity was violated. A significant main effect was further investigated with pairwise comparisons using Bonferroni corrections. To explore the effects of gesture-based training on the individual level the variable *individual gesture-benefit* was calculated. Individual gesture-benefit was defined as the average difference of all words learned with iconic gestures minus all words learned in the verbal condition for each patient after each training session. To investigate which variables influence gesture-benefit, correlational analyses and a hierarchical multiple regression analysis were performed.

Behavioral results

This section begins with the description of the learning performance at the group level. Then the variable individual gesture benefit is introduced which shows superior learning with iconic gestures for some patients. Based on this finding two scores are presented which describe the language capabilities of the patients at the lexico-semantic level and at the segmental-phonological level. Finally correlational analyses are used to describe the relation of these scores with individual gesture benefit.

Learning performance according to training-condition and phonological complexity

Behavioral learning performance was analyzed with a 4 x 2 x 3 repeated-measurements ANOVA including the factors time (day 1, day 2, day 3, day 4), learning-condition (iconic gesture, verbal) and phonological complexity (simple, medium, complex). There was no main effect of learning-condition (F(1, 13) = 0.23, ns), and none of the interactions reached significance (see Figure 16).

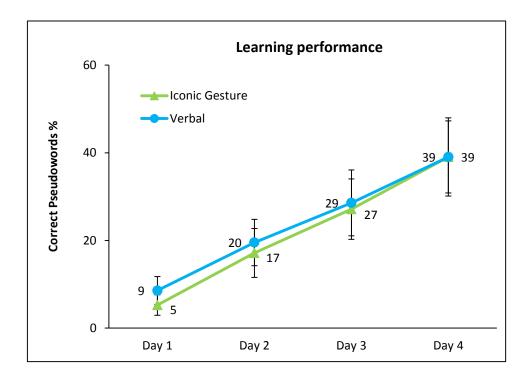


Figure 16 - Learning performance in Clinical Study. On the group-level (N=14), mean learning performance was similar with iconic gestures and in the verbal-only condition.

There was a main effect of phonological complexity (F(2, 26) = 5,77; p < .05) which was further investigated with pairwise comparisons revealing that simple words were better learned than complex words (p < .05), but learning was not different for medium and complex words.

Individual gesture-benefit

As there was no significant effect of learning-condition on the group level, the variable *individual gesture-benefit* was generated to explore the effects of gesture-based training on the individual level. Individual gesture-benefit was computed as the average difference of all words learned with iconic gestures minus all words learned in the verbal-only condition for each patient after each training session. Interestingly, several patients showed substantially better learning with iconic gestures, whereas other patients showed the reverse pattern (see Figure 17 and Figure 18).

Furthermore, after consulting the neurolinguistic test results it was revealed that the two patients with the strongest (Patient LF) and weakest gesture-benefit (Patient BR) differed in terms of their patholinguistic profiles: whereas Patient LF was mainly impaired on the segmental-phonological level Patient BR was mainly impaired on the lexico-semantic level.

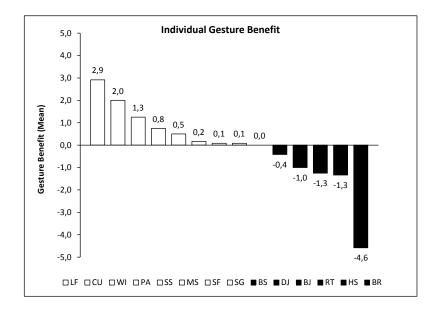


Figure 17 - Individual gesture benefit. Displayed is the average difference of all words learned in the gesture-condition minus all words learned in the verbal-condition for each patient after each training session. Patient LF learned on average 2.0 words more with iconic gestures compared to the verbal condition. Patient BR learned on average -4.6 words less with iconic gestures, compared to the verbal condition.

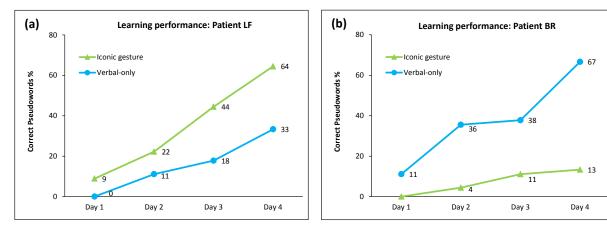


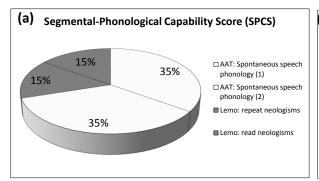
Figure 18 - Individual learning performance. Displayed is the average learning performance per day per patient for learning with iconic gestures and learning in the verbal-only condition. **(a)** Patient LF shows high gesture-benefit. **(b)** Patient BR shows no gesture-benefit.

Computation of two scores describing phonologic and lexico-semantic capabilities of patients

To investigate whether the finding that gesture-benefit depends on the patholinguistic profile is also valid on the group level, patholinguistic test results were consulted and two scores were computed for each patient: the *segmental-phonological capability score* (*SPCS*) and the *lexico-semantic capability-score* (*LSCS*) (see Figure 19). The SPCS is a composite score, which is computed as the weighted average of two AAT spontaneous speech assessments (phonologic structure) and two LEMO-subsets (No. 8 repeat neologisms, No. 14 read neologisms). Lower values on the SPCS indicate deficits at the segmental-phonological level (see Table 5a).

Analogously, the LSCS is the weighted average of two further AAT spontaneous speech assessments (semantic structure) and two further LEMO-subtests (No. 25 picture-naming, No. 30 synonymy: same/different). Lower values on the LSCS indicate speech deficits at the lexico-semantic level (see Table 5b).

For both scores spontaneous speech assessments were stronger weighted (each 35%) than LEMO-subtests (each 15%), because an expert judgment of spontaneous speech by a clinical linguist was considered to be more reliable than single test-results.



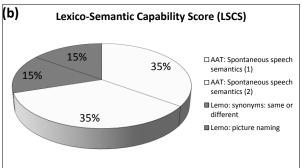


Figure 19 – Composite scores. (a) The Phonologic Capability Score (PCS) is a composite score, computed as the weighted average of two spontaneous speech assessments (phonology) and two LEMO-subtests (8 and 14), see also Table 5a. (b) Analogously, the lexico-semantic capability score (LSCS) is the weighted average of two spontaneous speech assessments (lexico-semantics) and two different LEMO-subtests (25 and 30), see also Table 5b.

Table 5 - Composite scores

Α	Segme	ntal-pho	onologica	l deficits		В	L	exico-ser	mantic de	eficits	
Patient	Spontaneous Speech Phonology (Mean)	Repeat Neologisms	Read Neologisms	Segmental- Phonological score	Gesture-Benefit	Patient	Spontaneous Speech Semantics (Mean)	Synonyms: same or different	Picture Naming	Lexico-Semantic score (weighted)	Gesture-Benefit
LF	4.5	37	34	76	35	BR	3.5	34	18	75	-55
SF	4.0	36	22	78	1	נס	4.0	28	19	81	-5
RT	4.0	37	28	80	-16	SF	4.0	30	19	82	1
WI	4.5	36	39	84	15	RT	4.0	34	19	83	-16
SS	5.0	36	39	84	6	BJ	4.0	39	17	83	-12
PA	4.5	40	38	85	9	HS	4.0	38	20	85	-15
MS	5.0	27	33	86	2	BS	4.0	39	20	86	0
CU	4.5	38	35	90	24	WI	4.5	33	20	90	15
BR	3.5	27	33	93	-55	LF	4.5	37	19	91	35
SG	5.0	38	31	96	0	PA	4.5	37	19	91	9
BS	4.0	40	38	99	0	CU	4.5	39	20	93	24
DJ	4.0	40	38	99	-5	MS	5.0	27	17	93	2
BJ	4.0	38	39	99	-12	SG	5.0	39	17	97	0
HS	4.0	40	40	100	-15	SS	5.0	37	20	99	6

Note. (A) For each patient those test-scores are displayed which were used to compute the weighted composite segmental-phonological capability score (SPCS). Patients are displayed according to their SPCS in ascending order. Patient LF showed the lowest SPCS (76) and a high gesture-benefit (35). (B) For each patient those test-scores are displayed which were used to compute the weighted composite lexico-semantic capability score (LSCS). Patients are displayed according to their LSCS in ascending order. Patient BR showed the lowest LSCS (75) and a low gesture-benefit (-55).

Correlational analyses

Correlational analyses were used to investigate the relation of gesture-benefit with the individual patholinguistic profiles of the patients. The scatterplots (see Figure 20) illustrate correlations of gesture-benefit with the SPCS and with the LSCS. There is a strong positive correlation between the LCSC and gesture benefit (r = .681, p < .05), explaining 46% of its variance. This indicates that patients whose lexico-semantic capabilities are intact benefit most from gesture-training. On the other hand, the PCSC is weakly negatively correlated with gesture benefit (r = .416, p = .069, one-sided, trend), explaining 17% of its variance. This indicates that patients with speech deficits mainly at the segmental-phonological level benefit from gesture-training. It is important to note that gesture benefit is not correlated with overall learning performance (r = .041, p = .88). Thus we suggest that the LSCS is a specific predictor for gesture-benefit, independent of general learning-performance.

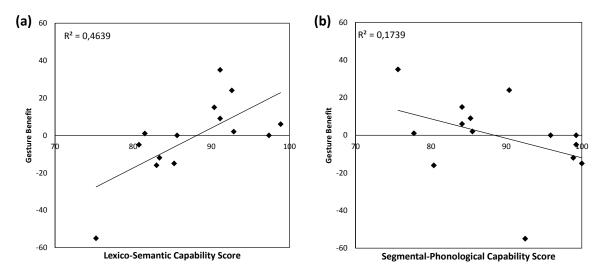


Figure 20 - Scatterplots. (a) The left scatterplot shows a strong positive correlation between LSCS and gesture-benefit (r = .68, p < .05). **(b)** The scatterplot on the right side illustrates a weak negative correlation between SPCS and gesture-benefit (r = .-416, p = .069, one-sided, trend).

Based on correlations with gesture-benefit (see Table 6), a hierarchical multiple regression analysis was performed and revealed that the amount of explained variance can be further increased from 46% to 76% if the variable *digit-span backwards* is additionally included besides the LSCS (see Table 7). None of the other variables increased the prediction significantly. Therefore we conclude that the best prediction for aphasia patients regarding gesture-benefit in pseudoword-learning is a patholinguistic profile combining high lexicosemantic capabilities with impairments in verbal working memory. Furthermore gesture-benefit is associated with deficits at the segmental-phonological level.

Table 6 - Correlations

	GB*	LSCS*	MSL*	TMT A*	DS B*	SPCS*
Gesture Benefit (GB)	1	.681**	.505	461	45	417
Sig (2-tailed)		.007	.066	<i>.097</i>	.106	.138

Note. Variables most strongly correlated with gesture-benefit.

*GB = gesture benefit, LSCS = lexico-semantic capability score, MSL = Months since lesion, TMT = Trail-Making Test, DS B: digit span backwards, SPCS = segmental-phonological capability score

Table 7 - Multiple hierarchical regression

Model	R-Square	b	SE b	ß
Model 1	.464			
Constant		-188.023	58.25	
Lexico-Semantic Score		.021	.007	.681*
Model 2	.758			
Constant		-195.79	40.91	
Lexico-Semantic-Score		.024	.005	.752*
Digit-Span backwards		527	.144	547*

Note. A stepwise method initially including all variables mentioned in the correlations-table above (Table 6) reveals that the amount of explained variance in the dependent measure gesture-benefit can be increased from 46% to 75% if the variable digit-span backwards is additionally included, besides the lexico-semantic score. The variables MSL, TMT A and SPCS do not contribute significantly to increase the amount of explainable variance and are therefore automatically excluded.

3.2.2.2 Analysis and results of lesion data:

Due to technical problems MRI-scans of two patients (BR, SF) were not available for lesion-analyses; therefore subsequent analyses were performed on MRI-scans of the remaining 12 patients.

Voxel-Based Lesion-Symptom Mapping (VLSM)

Preprocessing, segmentation and normalization of imaging data

For each patient brain-lesions were delineated manually by a neurologist and saved as a mask using MRIcroN. Preprocessing was performed with SPM 8 and included data-conversion into NIFTI-files for the T1-scan and for the lesion-mask. It was ensured that image orientation and fit between T1-scan and lesion-mask were correct. The segmentation of grey matter, white matter and CSF for the T1-scan was performed without specifying a mask. Resulting normalization parameters (voxel-size 1 x 1 x 1 mm) were then applied to the T1-scan and to the lesion-mask. Quality assurance included to check the normalization result by comparing the normalized files (T1-scan and lesion) with the corresponding originals and with a T1-template (MNI-152).

Statistical analyses

Statistical analyses for lesion-data were conducted with NPM (non-parametric mapping software developed by Chris Rorden). Analyzed voxels were restricted to those being damaged in at least 20% of all patients. As the assumption of normally distributed test-scores was not given, non-parametric Bruner-Munzel-tests were applied (Rorden, Karnath & Bonilha, 2007). Bruner-Munzel-tests were conducted for each voxel (1000 permutations) regarding the question whether behavioral test-scores differed between the lesion-group and the non-lesion group. Resulting positive Z-scores indicate that lesions in these regions predict poor performance. However, as we were not only interested in lesions predicting poor gesture-benefit, also negative Z-scores were computed to investigate which lesions predict high gesture-benefit.

Subtraction analyses

Patients were divided into two groups according to their individual gesture-benefit. The first group included lesion-data of six patients with high gesture-benefit (HGB), whereas the second group included lesion data of six patients with low gesture-benefit (LGB). To describe which lesions correlate with gesture-benefit, the overlap of the LGB-group was subtracted

from the overlap of the HGB-group (HGB minus LGB). To describe which lesions correlate with low gesture-benefit, the opposite subtraction was conducted (LGB minus HGB).

Results of lesions data

Overlapping lesions

The overlap of all lesions (see Figure 21) shows that left frontal regions (IFG, insula) were most frequently lesioned, but lesions also extended into temporal (Heschl's gyrus, MTG, ITG) and parietal regions (postcentral gyrus, supramarginal gyrus (SMG)).

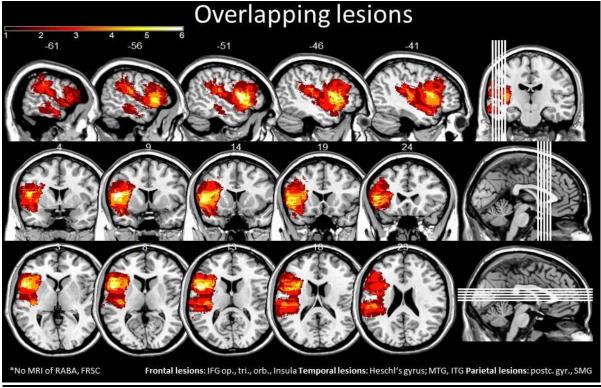


Figure 21 - Overlapping lesions. This overlap (N = 12) shows that frontal regions (IFG, insula) were most frequently lesioned (yellow color). Less frequently, lesions also extended into temporal (Heschl's gyrus, MTG, ITG) and parietal regions (postcentral gyrus, SMG) (orange/red colors).

VLSM and subtraction analyses

To answer the question whether gesture-benefit can be predicted by specific brain lesions VSLM was performed. The VLSM-result may help to improve the appropriate selection of patients for gesture-based lexical learning approaches. The VLSM-analysis revealed that lesions in the IFG orbitalis and insula predict high gesture-benefit (see Figure 22 A, B). However, as this result was not statistically significant a subtraction analysis was conducted (HGB minus LGB), confirming that IFG orbitalis and insula-lesions are around 50% more frequently damaged in the group with high gesture benefit (see Figure 22 C).

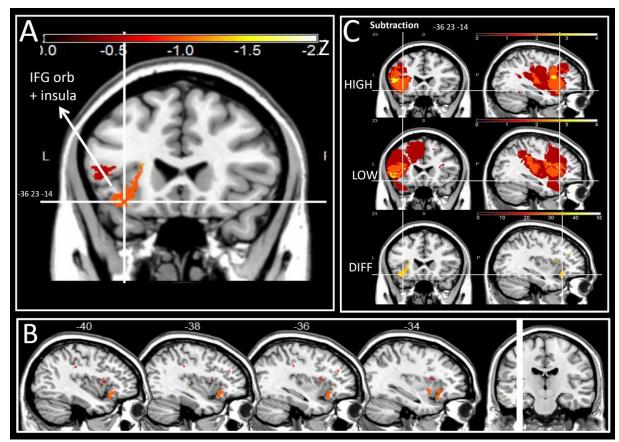


Figure 22 – VLSM high gesture benefit (HGB)*. (A+B) VLSM-results show that lesions in IFG orbitalis and insula are correlated with high gesture benefit. **(C)** A subtraction analysis confirmed that IFG orbitalis and insula are around 50% more frequently damaged in group HGB. *VLSM-analysis is restricted to voxels damaged in at least 20% of patients; 1000 permutations; range of Z-values: [-2.17, 1.9]; critical z-value (Bruner Munzel, FWE-corrected) =-2.84, n.s.

On the other hand, lesions in the IFG triangularis and temporal pole (STG) were correlated with poor gesture-benefit (see Figure 23, A, B). However, as this result was not statistically significant a subtraction analysis was conducted (LGB minus HGB), confirming that IFG triangularis and anterior STG-lesions are around 50% more frequently damaged in the group with low gesture benefit (see Figure 23 C).

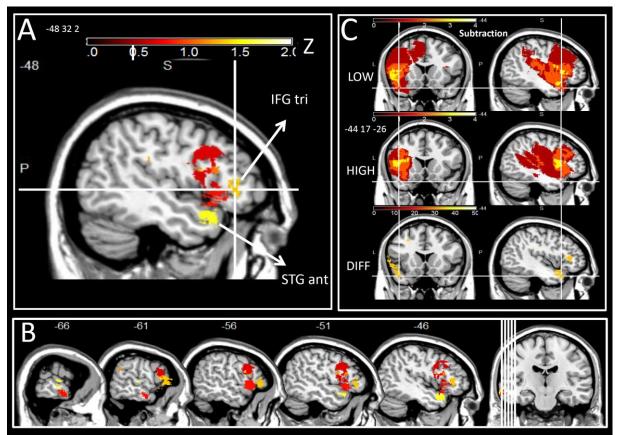


Figure 23 - VLSM low gesture benefit (LGB)*. (A+B) VLSM-results show that lesions in IFG triangularis and anterior STG are correlated with low gesture benefit. **(C)** A subtraction analysis confirmed that IFG triangularis and anterior STG are around 50% more frequently damaged in group LGB. *restricted to voxels damaged in at least 20% of patients; 1000 permutations; range of Z-values: [-2.17, 1.9]; critical z-value (Bruner Munzel, FWE-corrected) =-2.79, n.s.

To summarize: (a) gesture-benefit can be predicted by specific brain lesions, (b) lesions of IFG orbitalis and insula are associated with high gesture-benefit, (c) lesions of IFG triangularis and temporal pole (STG) are associated with low gesture-benefit.

3.2.3 Discussion

This study was conducted to investigate the effects of iconic gestures on pseudoword-learning in patients with residual aphasia. Based on the Behavioral Study (see section 3.1.2) it was hypothesized that all aphasic patients benefit from gesture-based word-learning. In a second hypothesis a differential effect among aphasia patients was considered, expecting gesture-based pseudoword-learning to be most efficient in aphasia patients with intact lexico-semantic capabilities. It was assumed that impairments at the lexico-semantic level of language processing could disturb the semantic integration of gesture and pseudoword and thus decrease the learning performance in the multimodal iconic-gesture condition.

In contrast to our first hypothesis, there was no facilitating effect of iconic gestures on the group-level. However, correlational analyses confirmed our second hypothesis and showed that gesture-benefit was associated with the patholinguistic profile of the patients. Gesture-benefit was highest for aphasia patients with intact lexico-semantic capabilities. Furthermore, a multiple regression analyses revealed that the amount of explained variance can be increased from 46% to 75% if the digit-span (backwards) is included as an additional variable. Consistent with our second hypothesis, gesture-benefit was low for patients with impairments at the lexico-semantic level. Further, in line with previous studies (Rose et al. 2002; Rodriguez et al. 2006; Rose and Sussmilch, 2008; Lanyon and Rose, 2009; Marangolo et al. 2010), there was a weak negative correlation between gesture-benefit and the segmental-phonological capabilities of the patients (r = -.416, p = .069, one-sided, trend).

Taken together these results suggest that a prerequisite for efficient gesture-based pseudoword-learning is an intact lexico-semantic processing system which enables the patient to successfully integrate additional semantic meaningful information, delivered as iconic gestures, with the pseudoword. The results suggest that even minor deficits at the lexico-semantic level of speech processing are sufficient to reduce gesture-benefit, because the prerequisites for multimodal semantic integration of gesture and pseudoword are limited. Furthermore, as revealed by the multiple hierarchical regression analysis, taking into account additional deficits in phonological working memory improves the prediction for gesture-benefit. This result suggests that, in a phonologically demanding word-learning task, deficits in phonological working memory might be compensated using additional non-phonological information during learning, such as videos of iconic gestures. Converging evidence, supporting the facilitating role of iconic gestures during word-learning for patients with phonological deficits, comes from the weak negative correlation (i.e. trend) of gesture-benefit

with the segmental phonological capability score (SPCS). In contrast to the digit-span (backwards), the SPCS is based on patholinguistic measures and describes in particular linguistic deficits on the segmental-phonological level.

One possible confound relates to the severity of speech impairments. Gesture-based learning is multimodal and involves the integration of audio-visual input with gesture-production. Due to its complexity one might expect that only the least impaired patients with highly intact cognitive capacities and high motivation would benefit from gesture-based pseudoword-learning. However, the correlation between gesture-benefit and overall learning performance was not significant (r = .041, p = .88, ns). Thus, being independent of the overall learning performance, the correlation of gesture-benefit with the LSCS is even more interesting. It underlines the unique and crucial role of the lexico-semantic capabilities in gesture-based word learning.

A second possible confound refers to the generation of the two composite scores. The motivation to generate composite scores stems from the variability of speech deficits observed among aphasia patients. Describing the patient's speech deficits on two levels (lexicosemantic, segmental-phonological) might be a good compromise between the classical broad syndromal classification on the one hand (i.e. Wernicke' aphasia, Broca's aphasia) and very specific single test results on the other hand (i.e. LEMO-subtests). However, it is difficult to decide how to measure lexico-semantic or segmental-phonological capabilities and there is little consensus in the scientific community on this issue. In this clinical study it was suggested, for both scores separately, to compute a weighted average of spontaneous speech assessments (i.e. semantics, phonology) and specific LEMO-subtests (i.e. synonyms, naming, repeat neologisms, read neologisms). The spontaneous speech assessments by a clinical linguist seemed to be highly valid and reliable and thus they were stronger weighted than single LEMO-subtests (AAT: 70% - LEMO: 30%). Being aware of potentially different opinions on the computation of those composite scores, both scores were also computed without weighting, and although diminished, the positive correlation between the LSCS and gesture-benefit remained statistically significant (r = .581, p < .05). Thus there seems to be a stable positive relationship between the intact lexico-semantic capabilities of aphasia patients and the successful use of iconic gesture for lexical learning. On the other hand, the data also suggest that patients with speech deficits at the lexico-semantic level should not be treated with gesture-methods, but rather with conventional approaches.

Using VLSM to analyze the lesions of the patients revealed that gesture-benefit is associated with specific brain lesions. Gesture-benefit was seen for patients with lesions mainly restricted to the left IFG but no gesture-benefit was seen for patients with combined left inferior frontal and left anterior temporal brain lesions. This result is very interesting with regard to the crucial role of the ATL for semantic processing (for a review see Patterson et al. 2007). The result suggests that in combination with a lesion in the left IFG a second lesion in the left ATL might prevent successful gesture-based word-learning, because the semantic integration of gesture and pseudoword is impaired. Further it was revealed that patients with brain regions restricted to left inferior frontal brain regions benefit from gestures. We suggest that these patients benefit from gestures because their temporal brain regions were mainly intact, therefore enabling rather normal lexico-semantic processing, which is necessary for the semantic integration of gesture and pseudoword.

In sum, the behavioral results of this clinical study suggest that gesture-based lexical learning is in particular helpful for patients with intact lexico-semantic capabilities and deficits in phonological working memory. Furthermore gesture-benefit was higher in patients who showed impairments at the segmental-phonological level which suggests that, in a phonologically demanding word-learning task, deficits at the segmental-phonological level of language processing might have been compensated by gestures. Analyzing the lesion-data revealed that gesture-based lexical learning was high if lesions were mainly restricted to left inferior frontal brain regions. On the other hand, patients with lesions combining the left IFG and the left ATL were not successful in gesture-based lexical learning, probably due to an impairment of the semantic integration between gesture and pseudoword. However, due to the small sample size (N = 12) the lesion-results should be considered as preliminary and future research aiming to confirm these results should include larger samples.

3.3 fMRI-Study:

Neural Correlates of Gesture-Based Word-Learning

This fMRI-study investigates the neural correlates of gesture-based word-learning (see also Krönke, Müller, Friederici & Obrig, in revision). Previously described studies suggested that gesture-based word-learning might be an efficient alternative learning strategy for healthy participants with little developed learning strategies (Behavioral Study, see section 3.1.2) and for aphasic patients with intact lexico-semantic processing capabilities (Clinical Study, see section 3.2, see also Krönke, Kraft, Domahs, Regenbrecht, Friederici & Obrig, *Poster at GAB*, 2011). Identifying its neural substrates will help us to understand the brain mechanisms which are involved in gesture-based word-learning. Furthermore if gesture-based word-learning is a unique way of learning, its neural substrate should be different from the neural substrate of classical verbal learning-strategies. Thus, the goal of this fMRI-study is to localize the neural basis of gesture-based word-learning.

The present study involves a behavioral part in which pseudowords were learned in different conditions and a neuroimaging part in which fMRI was used to measure brain activity while participants listened to those pseudowords which were previously learned in different conditions. Consistent with previously described studies (see Pilot Study, Behavioral Study) pseudowords were learned with iconic gestures, with grooming-gestures or in a verbal-only condition without any gestures. To address the importance of self-involvement both gesture types (i.e. iconic / grooming) were either passively observed or actively repeated during the learning phase. The factor phonological complexity was cancelled because in all previously described studies it was not possible to discover a differential learning effect for iconic gestures depending on the phonological complexity of the pseudoword (see Pilot Study, Behavioral Study, Clinical Study). Following the behavioral learning of pseudowords, fMRI was used to measure brain activity while participants listened to (a) pseudowords which were previously learned in different conditions and (b) pseudowords which were not previously trained.

Based on the Pilot Study and the Behavioral Study, we predict at the behavioral level higher learning performances with iconic gestures compared to learning with grooming-gestures. Additionally if enactment is an essential factor for gesture-enhanced learning we expect to find a double dissociation: active performance should enhance the facilitation effect for the iconic gestures but it should also enhance interference for the grooming gesture. However, as

learning performances between conditions should be equal before brain activity is scanned with fMRI, pseudowords were learned until a similar level was reached. Thus different learning performances are only expected at an early stage of pseudoword-learning and final learning performance before fMRI-scanning should be similar across all conditions.

On the neuroimaging level we expect differential activation for trained versus untrained pseudowords in the hippocampus, signaling episodic memorization of pseudowords. Further we expect activation of a distributed neocortical network to reflect lexico-semantic processing depending on the training condition. In particular we predict that implicit lexico-semantic retrieval shows differences in left temporal and inferior frontal regions depending on differentially successful semantic gesture-speech integration during the prior learning phase.

3.3.1 Methods

3.3.1.1 Participants

Fourteen healthy volunteers participated in the experiment. They were financially compensated and provided written informed consent according to the protocol of the local ethics committee (University of Leipzig). All participants were right-handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). The monolingual native German speakers had some knowledge in 2-5 foreign languages (median: 3). Due to extremely poor task-performance during scanning and uncorrectable head-motion three participants were excluded. Thus all analyses reported below were performed on 11 participants (7 females, 23-28 years).

Neuropsychological testing was performed in all volunteers. This comprised (a) reading-span, (b) processing speed and cognitive flexibility (*Trail Making Tests A/B*), (c) word list learning (German version of the *California Verbal Learning Test*), (d) phonemic and semantic word fluency (subtests of the German version of the *Controlled Oral Word Association Test*), (e) digit and Corsi block spans (forward and backwards, respectively), (f) verbal intelligence (vocabulary, *Wortschatztest*) and (g) nonverbal intelligence (subtest of *Leistungs-Prüfsystem*). The results of the neuropsychological tests were not used for further analyses. For mean scores of the participants see Appendix D.

3.3.1.2 Stimulus material

The stimulus material for the training over three days consisted of 42 sound files of pseudowords, 42 written German words, 42 videos of meaningful iconic gestures and 14 videos of meaningless grooming-gestures. For the fMRI-session 24 additional sound files were used: 10 German words and 14 untrained pseudowords (for all items see Table 8).

The pseudowords were bisyllabic, meaningless and had no strong resemblance with any existing German word. In contrast to previously described studies (Pilot Study, Behavioral Study), the phonological complexity of pseudowords was not manipulated. All pseudowords had the same CCVCV structure, starting with a consonant cluster according to German phonotactic rules (e.g. /bl-/) (see Rossi et al., 2011). As the number of existing pseudowords was not sufficient additional pseudowords were created. Compared to previous studies the set

was improved by better balancing of stimulus-features (e.g. same amount of words with each onset-cluster, balanced word-endings). Of all pseudowords 42 were used for training and during scanning, and 14 were presented only in the fMRI experiment (untrained pseudowords). All pseudowords were spoken by a female speaker and digitally recorded with 16 bits at a sampling rate of 44 kHz. Mean duration of pseudowords was 1.28 s [SD = 0.2 s].

The 42 bisyllabic German words used during learning referred to manipulable objects and were chosen from the previously described set of rootwords (see section 3.1.1.1.2). The three rootwords *Hose*, *Socke* and *Gürtel* were excluded, because in contrast to the other rootwords their corresponding gestures involved to move the whole body. Pseudowords and rootwords were paired excluding that vowel structure and initial phonemes of any word pair were identical. Additional 10 bisyllabic German words were used during the fMRI experiment and served as targets for the lexical decision task. They were recorded with the same speaker as the pseudowords and shared initial consonant-clusters with the pseudowords. The brain response to the German words was not analyzed and they entered the GLM as a variable of no interest. Videos of 42 meaningful iconic gestures were identical with the videos used for previous studies (for details see section 3.1.1.1.2).

3.3.1.3 Experimental design and training conditions

In a within subject design five different training conditions were tested (see Figure 24). Pairs of pseudoword-rootword were pseudorandomly assigned to these five different learning-conditions, balanced for word frequency and gestureability. Consistent with previous behavioral studies (see Pilot Study, Behavioral Study) a word-pair was either presented without any gesture (14 pairs, VERB) with a meaningful iconic gesture (14 pairs, ICON^{act/pass}), or with a meaningless grooming-gesture (14 pairs, GROO^{act/pass}). In contrast to previous studies the factor phonological complexity was cancelled because no interactions with training condition were found (see Pilot Study, Behavioral Study, Clinical Study). Moreover, to investigate the role of self-involvement, in the present study gestures were either actively repeated (7 pairs each, ICON^{act}/GROO^{act}) or passively viewed by the participants (7 pairs each, ICON^{pas}/GROO^{pas}). In sum five conditions were used to address two main research questions: (a) the effect of the two gesture conditions and the verbal-only condition (3-way comparison): ICON^{act}/GROO^{act}/VERB; (b) the interaction between self-involvement and gesture-type (2 x 2 comparison): [ICON / GROO] X [act,pas]. Assignment of word-pairs to the five different learning conditions varied across subjects to attenuate item-specific effects.

Table 8 – Stimuli of fMRI-Study

	Trained Pseudowords							
No	Rootword	Pseudoword	No	Rootword		Pseudoword		
1	Angel [fishing rod]	/bluga/	22	Messer [knife]		/klawe/		
2	Besen[broom]	/kwose/	23	Mixer [mixer]	Mixer [<i>mixer</i>]			
3	Bogen[bow]	/schlaso/	24	Mütze [cap]		/klira/		
4	Bürste [brush]	/schnari/	25	Nadel [needle]		/klupe/		
5	Cello [<i>cello</i>]	/blide/	26	Peitsche [whip]		/schtafo/		
6	Diskus [discus]	/schroge/	27	Pfanne [pan]	Pfanne [pan]			
7	Flöte [<i>flute</i>]	/braso/	28	Pinsel [paintbrush]		/knafi/		
8	Frisbee [frisbee]	/schpofe/	29	Pumpe [pump]	Pumpe [pump]			
9	Gabel [fork]	/brime/	30	Rechen [rake]		/schtoge/		
10	Geige [violine]	/bruwi/	31	Säge [saw]		/schrawi/		
11	Gewehr [gun]	/fliwa/	32	Schaufel [shovel]		/trale/		
12	Glocke [bell]	/schpali/	33	Schere [scissors]		/fruma/		
13	Hacke [<i>pick</i>]	/schwosa/	34	Schlüssel [key]		/krafi/		
14	Hammer [hammer]	/flore/	35	Schnorchel [snorkel]		/krilo/		
15	Harfe [harp]	/fluda/	36	Schraube [screw]		/trofa/		
16	Jacke [<i>jacket</i>]	/schtiwa/	37	Spaten [spade]		/krupe/		
17	Kanne [pot]	/blori/	38	Spritze [syringe]		/trumi/		
18	Klavier [piano]	/schlife/	39	Tasse [cup]		/schniwo/		
19	Löffel [spoon]	/frade/	40	Trommel [drum]		/kwipe/		
20	Lupe [magnifier]	/fropi/	41	Waage [scale]		/knoli/		
21	Mantel [coat]	/schwume/	42	Zange [pliers]		/kwoga/		
		Untraine	d Pseu	ıdowords				
1	blafe	5 klogi	9	schlodi	13	schwido		
2	brola	6 knuse	10	schnofe	14	triwa		
3	flapo	7 kroda	11 schpire					
4	frilo	8 kwuri	12	schruma				
		German W	/ords (fMRI-task)				
1	/Blume/ [flower]		6	/Krake/ [octopus]				
2	/Brise/ [breeze]		7	/Schnake/ [gnat]				
3	/Fliege/ [fly]		8	/Schwiele/ [weal]				
4	/Frage/ [question]		9	/Trage/ [stretcher]				
5	/Klage/ [complaint]		10	/Knete/ [modeling clay]				

Note. 42 German rootwords and 42 pseudowords used for training. An additional 14 pseudowords (untrained) and 10 German words were only used for the fMRI experiment. English translation is provided in [*italics*]. All pseudowords and the German words were only presented as a sound file, as indicated by //.

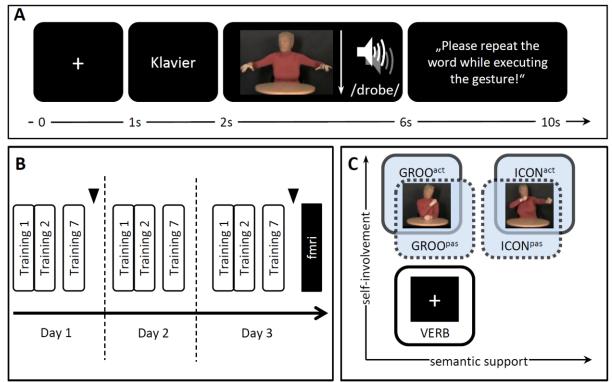


Figure 24 - Training conditions and schedule of fMRI-Study. (A) Example for the German root word *Klavier* [piano] in the ICON^{act} condition, in which the volunteer had to perform a meaningful iconic gesture while repeating the pseudoword */drobe/* to be acquired for the rootword *piano*. (B) Twenty-one training session were distributed over 3 consecutive days. fMRI was performed after the full training program. The behavioral assessments reported here are indicated by triangles. (C) Four conditions vary along two dimensions: semantic support by the gesture: iconic vs. grooming gesture (ICON/GROO); and self-involvement: active performance vs. passive observation of the gesture (act/pas). These were compared to the purely verbal condition in which no gesture was observed/performed.

3.3.1.4 Training procedure and learning assessment

The general training procedure was the same as described in previous behavioral studies (for details see section 3.1.1.1.4). In the verbal-only condition (VERB) the participant simply had to repeat the novel word aloud. Besides the active conditions (ICON^{act}, GROO^{act}), in which participants were instructed to perform the respective gesture while repeating the novel word aloud, there were two passive conditions (ICON^{pas}, GROO^{pas}) in which participants watched the gesture-videos without performing these gestures while repeating the novel word aloud (see Figure 24).

The training program consisted of 21 blocks, equally distributed over three consecutive days (7 blocks per day, see Figure 24 B). One block comprised the presentation of all 42

pseudoword-rootword pairs and lasted approximately eight minutes. Thus, overall training duration was 2 hrs. 48 min. Active and passive conditions alternated within each block: half of the participants began with the active task (21 items), followed by the passive task (21 items) and vice versa in the other half of the volunteers. The order of items was pseudorandomized, to ensure that the same training condition was not presented more than twice in a row. In addition, to exclude primacy/recency effects, the stimulus-sequence changed between blocks on the same day.

To assess participants' learning performance, three different memory tests were performed: (a) free recall: participants were asked to name all word-pairs, they could remember, (b) cued recall to pseudoword: participants were given the German rootword and should produce the learned pseudoword, (c) cued recall to rootwords: participants received the pseudoword and were requested to produce the corresponding rootword. For both cued-recall tasks the order of items changed between assessments on the same day. Responses of subjects were recorded digitally and classified according to four categories: a) correct answer, b) no answer, c) wrong answer and d) almost correct answer. Only completely correct answers (category a) of the free-recall task were considered for further analyses.

Behavioral data were analyzed using repeated measures ANOVAs and paired-samples *t*-tests. Greenhouse-Geisser corrected degrees of freedom were used if the assumption of spherecity was violated. A significant main effect was further investigated with pairwise comparisons using Bonferroni corrections.

3.3.1.5 Experimental design and procedure for fMRI

The fMRI-data reported here were acquired after the full training program had been completed (end of day 3). Notably at this stage the free recall performance was 84% correct (SE = 5%) and there was no difference between the different learning conditions. Apart from the 42 trained pseudoword another 14 untrained pseudoword and 10 German words were presented. To encourage lexical access to all the material presented in the scanner, a lexical decision task was introduced, in which participants had to press a response button (right index finger), whenever they heard a German word. The brain response to these German words was not analyzed and entered the GLM as a variable of no interest. Seven nullevents were included to allow the HDR to return to baseline. All stimuli were repeated four times resulting in a total of 292 trials (168 trained pseudowords, 56 untrained pseudowords, 40 German

words, 28 nullevents). Average trial length of 9 s yielded a total duration of 44 min. Presentation-sequence was pseudo-randomized and balanced for training-condition, cluster-frequency, target- and nullevent-distribution (see Figure 25).

The auditory stimuli (mean duration: 1.28 s) were presented in an event-related fMRI-design (jittered inter-stimulus interval of 4-8 s) via a MRI-compatible headphone-system (MR confon, Magdeburg, Germany).

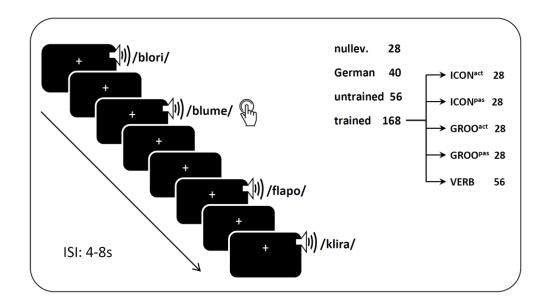


Figure 25 – fMRI-design. After the full training program participants were scanned while listening to auditory stimuli, presented in a single-trial design with a jittered interstimulus interval (ISI) of 4-8 s. The stimuli comprised 42 trained and 14 untrained pseudowords and 10 German words. Response to German words by a button press of the right index finger was required to encourage lexical processing of all the material, but the German words trials entered the analysis as a variable of no interest. The trained pseudowords had been trained in 5 different conditions. All stimuli occurred 4 times and were presented in a pseudo-randomized order including 28 nullevents, to allow for a better modeling of the HDR.

3.3.1.6 fMRI data acquisition and analysis

Functional images were acquired using a $T2^*$ -weighted gradient-echo echo planar imaging (EPI) sequence (TE = 30 ms, TR = 2 s, flip angle 90°, slice-thickness 3 mm, with 1 mm interslice gaps, matrix 64 x 64, FOV 19.2 cm, in-plane resolution 3 x 3 mm) on a Siemens MAGNETOM Verio 3T scanner with a 12-channel head-coil. Thirty axial slices oriented parallel to the AC-PC line covering the whole brain were acquired. In addition, high-resolution anatomical images were acquired (TE = 3.5 ms, TR = 1300 ms, flip angle 10° ,

matrix 256 x 256, FOV 25.6 cm, 176 saggital slices, slice thickness 1 mm) and co-registered with the functional images.

SPM 8 was used for preprocessing and statistical analyses of fMRI-data. After realignment and slice-time correction, data were normalized using the unified segmentation approach, which is based on the separation of grey matter, white matter and CSF (voxel size 3 mm). Data were spatially smoothed using an 8 mm FWHM Gaussian filter. For baseline correction data were highpass-filtered with a cut-off period of 100 s. In first-level analyses contrasts of interest were computed for each subject. These contrast images were then entered into second-level analyses. Clusters were obtained using a voxel-threshold of p < .001 with a minimum cluster-size of 56 mm³. For display reasons those clusters are shown in the figures with a voxel threshold of p < .01. The SPM anatomy-toolbox was used to identify anatomical brain structures corresponding to MNI-coordinates. The SPM rfxplot-toolbox was used to place an individual 3 mm sphere within a general 5 mm sphere around the peak voxel. Then, beta-values for each condition were extracted, plotted as percent signal change and analyzed statistically with paired samples t-tests.

3.3.2 Results

3.3.2.1 Behavioral results

The results reported here refer to the performance in the Free Recall Tests performed at the end of the *day 1* (after 7 training blocks) and after the full training program at the end of *day 3* (after 2 overnight consolidations and a total of 21 training blocks). Only pseudowords which were exactly reproduced were counted as correct. The other behavioral assessments (cued recall in both directions) yielded similar results.

Influence of gestures

To test the influence of gestures, performance on pseudowords learned under different conditions was compared. At the end of the *day 1* pseudowords actively trained with an iconic gesture (ICON^{act}) and those trained without gesture (VERB) were recalled better than pseudowords actively trained with a meaningless grooming-gesture (GROO^{act}). However, there was no advantage of the iconic-gesture condition over the verbal-only condition (i.e. ICON^{act} = VERB > GROO^{act}). At the end of the full training program on *day 3* there was an overall increase in performance (*day 3 > day 1*) but no difference between any of the three learning conditions (Figure 26 A). These results were confirmed by an ANOVA comparing the three conditions and the early vs. late recall performance ([ICON^{act} / VERB / GROO^{act}] x [*day1/day3*]; ANOVA: main effect time, F(1,10)=84.52, p < .001; main effect condition, F(2, 20) = 3.73, p < .05; interaction Time X Condition: F(2, 20) = 2.91, p = 0.078, ns; post-hoc t-tests: VERB > GROO^{act} (p < .05), all other comparisons: ns).

Influence of self-involvement

To investigate the influence of self-involvement the four gesture conditions were compared. Apart from the overall increase in performance for all conditions on *day 3* and the lower performance for the grooming-gesture condition at the end of *day 1*, Figure 26 B illustrates a small advantage for the passive over the active conditions, which is not present at the end of the full training program on *day3*. However, a 2 x 2 x 2 ANOVA ([Gesture-type: GROO/ICON] x [Self-involvement: act / pas] x [Time: *day1 /day3*]) did not show a main effect or an interaction for the factor self-involvement. The factors gesture-type and time were significant confirming previous results (Figure 26 A) in that there was a general improvement over time for all conditions and an early advantage for the iconic over the grooming-gesture

condition (ANOVA: F(1, 10) = 10.1, p < .05; pairwise comparisons: ICON > GROO, p < .05 and time (F(1, 10) = 123.46, p < .001, all other comparisons: ns).

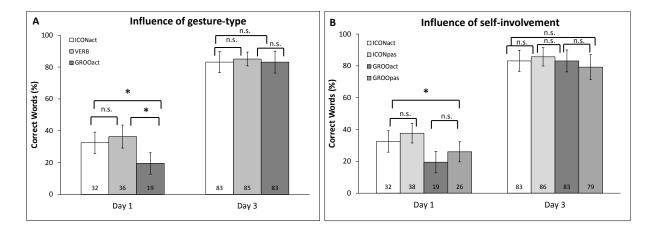


Figure 26 - Behavioral results of fMRI-Study. (A) Influence of gesture type: At the end of day 1 pseudowords learned with grooming-gestures were recalled worse that those learned with iconic gestures or without any gesture (ICON^{act} = VERB > GROO^{act}). After the full training program on day3 performance for all three conditions increased significantly but showed no advantage for any of the training conditions (ICON^{act} = VERB = GROO^{act}). (B) Influence of self-involvement: At the end of $day\ 1$ pseudowords learned with passive viewing of the gestures show a tendency for slightly better learning performance ([ICON^{pas}+GROO^{pas}] \geq [ICON^{act}+GROO^{act}]). This effect was non-significant and was not seen at the end of the full training program. The general learning effect over time (day3 > day1) and the early difference between iconic and grooming gestures on day1 (ICON > GROO) is confirmed (compare (A)).

3.3.2.2 Neuroimaging results

The fMRI-responses reported here represent the activation elicited by the pseudowords after training when memory performance did not differ between the learning-conditions (see Figure 26). Note that participants did not explicitly retrieve the meaning of the pseudowords but that the lexical decision task required a response only for the German words. BOLD contrast changes for the trained versus untrained pseudowords thus represent differentially successful implicit lexico-semantic access. Different patterns of brain activation between the training conditions indicate the different networks affording the latter task.

Effect of training

The contrast between trained versus untrained pseudowords showed that trained pseudowords elicited a larger activation in the left medial temporal lobe when compared to untrained pseudowords. The cluster includes one peak in the posterior hippocampus (MNI: -27 -40 -2, p < .001, cornu ammonis) and a second peak slightly superior to it (MNI -33, -34, 1, p < .001). Both local maxima are part of the same cluster at a less conservative threshold (p < .01, Figure 27 A and Table 9). This effect was driven by a BOLD-increase for trained but no change for untrained pseudowords. The opposite contrast (untrained > trained) yielded no statistically significant clusters.

Differential activations for learning with and without gestures

Behavioral data showed no advantage in memory performance for pseudowords trained by purely verbal repetition (VERB) over those pseudowords which were 'enacted' during training (ICON^{act}) at any time (also see Appendix E). To find out whether this equal performance is afforded by different neural networks we compared brain activation elicited by pseudowords trained in either condition. Indeed pseudowords trained with actively performed iconic gestures (ICON^{act}) compared to pseudowords trained in the purely verbal condition (VERB) elicited a larger activation in a left-hemispheric network comprising inferior frontal, inferior temporal and SMG (IFG: MNI [-39 / 47 / -14] p < .001; ITG MNI: [-57 / -31 / -23] p < .001; SMG: MNI [-60 / -55 / 25] p < .001. Figure 27 B & Table 9). This resulted from an increase in BOLD contrast only for the ICON^{act} condition. The opposite contrast VERB > ICON^{act} yielded a statistically significant difference in the left fusiform gyrus (FG, MNI [-33 / -49 / -5] p < .001, Figure 27 C & Table 9). This resulted from a deactivation for the words trained in the ICON^{act} condition.

Table 9 - Local peak activations

(i)* Trained > Untrained									
Brain region	Voxe X	I (MNI) Y	Z	Т	K	SPM Anatomy-Toolbox			
Medial Temporal Lobe	-33	-34	1	4.85	3	Not defined; left MTL			
Medial Temporal Lobe	-27	-40	-2	4.2	2	Left post. Hippoc. (cornu ammonis)			
(ii)* ICON ^{act} > ICON ^{pas}									
Brain region	Voxe X	I (MNI) Y	Z	Т	K	SPM Anatomy-Toolbox			
Temporal Lobe	-51	-31	-23	4.85	5	Left inferior temporal gyrus			
Temporal Lobe	51	-19	-29	4.58	5	Right inferior temporal gyrus			
Temporal Lobe	60	-19	-23	4.55	2	Right inferior temporal gyrus			
Cerebellum	18	-25	-29	4.69	4	Right cerebellum 21%-30% (lobules 1-4)			
(iii)* VERB > ICONact									
Brain region	Voxe X	I (MNI) Y	Z	Т	K	SPM Anatomy-Toolbox			
Medial Temporal Lobe	-33	-49	-5	4.83	7	Left posterior fusiform gyrus			
			(iv)* I	CON ^{act}	> VEF	RB			
Brain region	Voxe X	I (MNI) Y	Z	Т	K	SPM Anatomy-Toolbox			
Temporal	-57	-31	-23	7.15	11	Left inferior temporal gyrus			
Parietal	-60	-55	25	5.51	9	Left supramarginal gyrus, inferior			
						parietal Cortex, PFm			
Frontal	-39	47	-14	4.72	5	Left inferior frontal gyrus (orbital)			
		((iv)* IC	ON ^{act} >	GRO	O ^{act}			
Brain region	Voxe X	I (MNI) Y	Z	Т	K	SPM Anatomy-Toolbox			
Temporal	-54	-34	-23	4.41	3	Left Inferior Temporal Gyrus			
Cerebellum	-15	-34	-29	4.33	2	unknown, cerebellum			
Parietal	-54	-67	28	4.29	2	Inferior Parietal Cortex			

Note. Contrasts (a) trained versus untrained, (b) ICON active versus ICON passive, (c) VERB versus ICON active, (d) ICON active versus VERB (threshold p = 0.001; minimum cluster size 56mm³). The reverse contrasts untrained > trained; ICON^{pas} > ICON^{act} and GROO^{act} > ICON^{act} did not yield significant results.

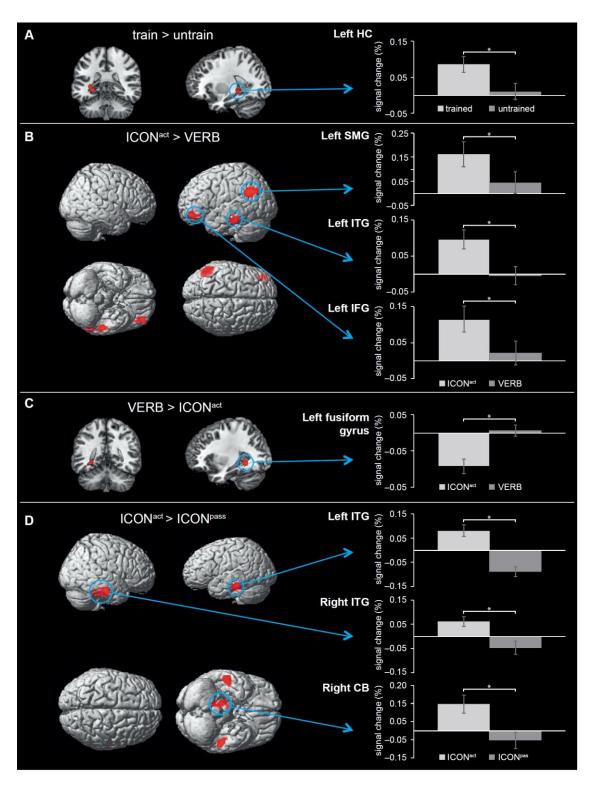


Figure 27 – Neuroimaging results. (A) Effect of training. Contrasting trained versus untrained pseudowords revealed an activation in the left medial temporal lobe, including the hippocampus. This effect was driven by a significant increase in % signal change (p < .001) for trained versus untrained pseudowords **(B)** Contrasting conditions ICON^{act} versus VERB revealed activity in left-hemispheric ITG, SMG and IFG, resulting from an increase in BOLD contrast for the ICON^{act} condition only. **(C)** The opposite comparison (VERB>ICON^{act}) showed a significant difference in the left fusiform gyrus. This difference resulted from deactivation for pseudowords trained in the ICON^{act} condition. **(D) Effect of self-involvement on iconic gestures.** The contrast elicited an activation for pseudowords trained in the active condition and a deactivation for the passive condition in a network including bilateral ITG and a right hemispheric cerebellar region.

Effect of self-involvement on iconic gestures

To investigate whether active involvement in the iconic gesture during training will lead to a stronger recruitment of a semantic network during lexico-semantic retrieval we compared BOLD contrast changes for pseudowords trained in the active versus passive condition. ICON^{act} > ICON^{pas} revealed significant differences in bilateral inferior temporal gyri (left ITG: MNI [-51 / -31 / -23] p < .001; right ITG: MNI [51 / -19 / -29] p < 0.001. Figure 27 D & Table 9) and an additional cluster in the right cerebellum (lobules I-IV; MNI [18 / -25 / -29] p < .001; probability given by SPM anatomy toolbox: 21%-30%). These differences resulted from an activation for the active and deactivation for the passive condition. The reverse contrast (ICON^{pas} > ICON^{act}) did not yield any significant clusters.

Effect of gesture type

The contrast between active performance of iconic versus grooming gestures (ICON^{act} > GROO^{act}) resulted in a cluster in the left ITG (MNI: [-54 / -34 / -23]) thus very close to the ITG clusters seen in the previous comparisons (ICON^{act} > ICON^{pas} and ICON^{act} > VERB). Additionally a small cluster projected to the left inferior parietal cortex (see Table 9). The opposite contrast (GROO^{act} > ICON^{act}) did not yield any significant clusters.

Interaction between Gesture-Type and Self-Involvement

The 'enactment' effect predicts that only for meaningful gestures active performance will enhance learning performance compared to passive viewing of the gesture. For a meaningless gesture no difference or an inverse effect is expected. Although no interaction was found for the behavioral data assessing free recall after training, it was tested whether brain activation during implicit lexico-semantic retrieval might indicate the predicted double dissociation between self-involvement and gesture-type. The analysis modeled the interaction [GROO / ICON] x [act/pas] by the contrasts: [ICONact > ICONpas] + [GROOpas > GROOact] and the inverse comparison [ICONact < ICONpas] + [GROOpas < GROOact]. The first contrast is in line with the 'enactment' prediction and yielded a distributed left lateralized network as shown in Figure 28 (clusters are listed in Table 10). Additionally to large clusters in the areas seen in the contrasts reported above (bilateral ITG, left IFG; also compare with Table 9) smaller clusters were seen in right IPC, right temporal pole, left cerebellum and notably in the left superior frontal gyrus adjacent to BA 6. The inverse contrast yielded no significant clusters.

Table 10 - Local peaks for interaction

Interaction								
Brain region	Voxe X	l (MNI) Y	Z	Т	K	SPM Anatomy-Toolbox		
left Temporal	-54	-31	-23	4.42	21	left ITG		
	-57	-43	-8	3.77	5	left MTG		
left Frontal	-33	17	-17	4.09	29	left IFG		
	-12	23	52	3.52	2	left SFG		
	-33	-1	-8	3.47	2	left frontal / unknwon		
right Temporal	51	-22	-23	3.98	15	right ITG		
	45	20	-14	3.80	8	right temporal pole		
right Parietal	60	-52	31	3.85	12	right IPC (SMG)		
left Cerebellum	-15	-34	-29	4.16	8	left cerebellum (lob I-IV)		

Note. Displayed are clusters showing an interaction between *Gesture-type* [ICON/GROO], and *Self-involvement* [act/pas]. A larger response for active over passive performance was seen for the iconic gestures while a smaller response for active over passive was seen for the grooming gestures ([ICON^{act} > ICON^{pas}] x [GROO^{act} < GROO^{pas}]). For a visualization please refer to Figure 28. The opposite contrast ([ICON^{act} < ICON^{pas}] x [GROO^{act} > GROO^{pas}]) yielded no significant clusters.

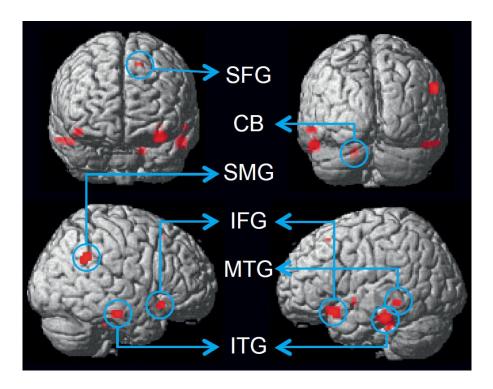


Figure 28 - Interaction. Cortical areas showing an interaction between Gesture-type [ICON/GROO], and self-involvement [act/pas], for MNI coordinates please refer to Table 10. SFG = superior frontal gyrus; CB = cerebellum.

3.3.3 Discussion

This fMRI-study was conducted to explore neural correlates of pseudowords which were learned in different conditions over three subsequent days (Krönke et al., in revision). Whereas final behavioral results showed only minor differences between learning conditions, the imaging data revealed activity for recently learned pseudowords in different cortical networks, reflecting the different learning conditions. The learning performance assessed after the training program neither supports a facilitative function of iconic gestures compared to classical purely verbal learning, nor does it confirm the view that active self-involvement in the meaningful gesture condition ('enactment') enhances memorization of pseudowords. Despite similar behavioral learning performance, the imaging data confirm that depending on the learning condition, different neural networks are involved in the representation of recently learned pseudowords. The similar behavioral learning performance suggests a high degree of flexibility with regard to learning strategies in healthy adults with intact language and memory functions. The observed differences in neural processing depending on the learning condition might be relevant when the network is challenged by a lesion or under adverse learning conditions. Behavioral and imaging data will be discussed separately.

Behavioral results

In line with a previous study (Macedonia et al., 2010a) early learning performance with iconic gestures was higher than learning with grooming-gestures. However, learning performance in the verbal-only condition was similar high as learning with iconic gestures. The effect of self-involvement was not significant and behavioral results are only partly in line with our hypothesis. Whereas, consistent with our hypothesis, learning performance is lower in the active grooming condition compared to the passive grooming condition, it was higher in the passive iconic gesture condition compared to the active iconic gesture condition. Taken together the behavioral results suggest that early learning performance with iconic gestures is higher compared to learning with grooming gestures because grooming gestures interfere with pseudoword-learning. As learning in the verbal-only condition is similar high compared to learning with iconic gestures, a facilitation effect of iconic gestures for healthy adults is not supported. Further, the learning performance was higher in both passive learning conditions compared to their respective active conditions, thus not supporting a facilitating role of self-involvement in pseudoword-learning.

Interference of semantically unrelated gestures with words, as opposed to a facilitation effect of meaningful gestures, has been proposed previously (e.g. Bernardis, Salillas & Caramelli, 2008). Furthermore, it was shown that verbal recall is reduced if gestures are meaningless (Feyereisen, 2006; Macedonia et al., 2010a) or incongruent (Kelly et al., 2009) with the verbal material. However, Kelly et al. (2009) reported a significant advantage for a speech-gesture condition over a speech-only and a repeated-speech condition. Although at odds with the results presented in this study, Kelly et al. (2009) could not investigate the additional demands generated by execution of the gesture (i.e. self-involvement) since their participants neither repeated the pseudoword nor the corresponding gesture.

One reason potentially explaining the lack of a facilitation effect of iconic gestures in this study might be different types of verbal material: studies which described the enactment effect used phrases and not words (e.g. Feyereisen, 2009; Allen 1995). As gestures and phrases were semantically related, gestures could facilitate the speech process by activating the whole common concept (cf. Sketch-model, de Ruiter, 2000), without facilitating access to single word forms. However, in the present study, iconic gestures represented unambiguously manipulable concrete objects with strong motor properties (e.g. hammer, flute, paintbrush). Thus, the written presentation of these rootwords might have been sufficient to activate motor images (cf. Hauk, Johnsrude & Pulvermuller, 2004), irrespective of whether the congruent gestures are actually performed or implicitly evoked in the purely verbal condition. Another issue refers to the language skills of the participants. In a design, similar to the present study, it was shown that high performers only benefitted from iconic gestures in a more difficult translation task (German → pseudoword), while low performers benefitted also from iconic gestures in the easier translation task (pseudoword \rightarrow German) (Macedonia et al., 2010b). Lacking efficient learning strategies, low performers might use gesture-based pseudowordlearning as an elaborative learning strategy to support memory consolidation of pseudowords. It can be assumed that gestures are in particular helpful in incompletely developed or impaired linguistic systems. In support of this notion Tellier (2008) demonstrated that recall of foreign words was higher in 5 year old children if these were learned with iconic gestures compared to foreign words learned with pictures. For acquired language impairments Rose and Douglas (2001) demonstrated that lexical retrieval was facilitated after the production of iconic gestures but not after pointing, cued articulation or visualization in some aphasic patients.

To summarize, the behavioral results show that verbal memory of pseudowords is superior if they are learned with iconic gestures or in a verbal-only condition compared to learning pseudowords with grooming-gestures. It is suggested that reduced learning with grooming gestures can be explained by an interference effect of grooming gestures which impose additional processing demands.

Neuroimaging results

Since the lexical decision task which was used during fMRI implied to identify German words, the activations obtained for the pseudowords localize cortical areas involved in implicit lexico-semantic retrieval after training. The comparison between trained and untrained (similar) pseudowords revealed increased activity in the left posterior hippocampus. While this indicates a general (episodic) memory trace for all trained pseudowords, different neocortical networks were obtained comparing pseudowords of different training conditions.

General effect of training

It is well known that the hippocampus plays a prominent role in memory formation though its general versus specific contribution to episodic, semantic and spatial memory has led to partially opposing models (Moscovitch, Nadel, Winocur, Gilboa & Rosenbaum, 2006; Tulving and Markowitsch, 1998). Based on the complementary learning system model (McClelland, McNaughton & O'Reilly, 1995), Davis and Gaskell (2009) suggested a model of word learning with two stages, emphasizing the different roles of hippocampal and neocortical structures. The hippocampus is assumed to support the first stage of rapid initial familiarization in which novel words are encoded like other novel experiences as episodic memories. In the second stage of slow lexical consolidation, knowledge of words becomes independent of the hippocampus and dependent on neocortical temporal and temporoparietal brain regions. The model assumes that the process of slow consolidation from episodic memory towards long term memory requires sleep. The assumed role of the hippocampus in word-learning was supported by a study which used an associated learning paradigm (Breitenstein et al., 2005). Decreasing hippocampal activity was correlated with increasing correct responses over the course of associative learning during fMRI-scanning. Interestingly Breitenstein et al. (2005) reported that less decline of hippocampus activity across learning predicted both verbal semantic fluency and successful acquisition of lexical knowledge in the novel vocabulary. In another study familiarization of pseudowords without an explicit meaning association was examined over two days. Again it was shown that initial hippocampus-activation correlated with recognition memory (Davis, Di Betta, Macdonald & Gaskell, 2009). In a recent PET-study a decrease in hippocampal activation was found during repetitive associative word-pseudoword pairing when compared to the memorization of words and pseudowords in isolation (Paulesu et al., 2009). Whereas these studies investigated encoding and report changes in more anterior parts of the left hippocampus (e.g. y = -30 in Breitenstein et al., 2005), the present study revealed a more posterior cluster (y = -40) for the comparison between trained and untrained pseudowords. This is in line with a suggested gradient between anterior and posterior hippocampus, respectively corresponding to encoding and retrieval of semantic associations (Prince, Daselaar & Cabeza, 2005; Mestres-Missé, Càmara, Rodriguez-Fornells, Rotte & Münte, 2008; Lepage and Habib, 1998). It is important to note that there was no differential activation in hippocampus when comparing the different training conditions. The present study suggests that activity in the left posterior hippocampus is a general neural correlate of pseudoword-learning, independent of the training condition.

Furthermore the results suggest that differential neocortical networks support implicit semantic retrieval strategies, depending on the learning condition. In the following, the relevant contrasts are discussed, comparing BOLD-responses of pseudowords learned in different conditions.

Effect of training conditions

Overall the comparisons between single conditions yielded clusters in left/bilateral inferior temporal, left inferior frontal, left SMG, left FG and the right cerebellum. Most consistently the left (bilateral) ITG was more activated for pseudowords trained with actively performed iconic gestures (ICON^{act} > VERB, ICON^{act} > GROO^{act}, and bilaterally ICON^{act} > ICON^{pas}). An early PET-study showed that both left ITG and left IFG (see below) are part of a 'common semantic system' (Vandenberghe, Price, Wise, Josephs & Frackowiak, 1996). Similarly a recent review assigns semantic functions to both areas (Price, 2010).

The left ITG is part of the ventral stream which was suggested to map sound to meaning (Hickok & Poeppel, 2007). According to the dual-stream model the left ITG serves as a lexical interface linking phonologic with semantic information. Recently its role in semantic

retrieval (rather than selection) was emphasized in a study eliciting multiple meaning of homonyms by double priming with little semantic competition (e.g. primes: /dance/&/play/target: /ball/) (Whitney, Jefferies & Kircher, 2011).

Enhanced brain activity was also found in the left IFG (pars orbitalis) when pseudowords trained with iconic gestures were compared with pseudowords trained in the verbal-only condition. The left IFG was proposed to play a crucial role in the neural integration of semantic information conveyed by speech and gestures (Willems et al., 2007). Moreover, it was shown that the left IFG is not only involved in explicit but also in implicit lexical retrieval tasks (Ruff, Blumstein, Myers & Hutchison, 2008). However, it is crucial to consider the functional differentiation within IFG between anterior/rostral (BA 47, pars orbitalis) and more posterior portions (BA 45, BA 44). While BA 45 / BA 44 are involved in syntactic operations (Friederici, 2011) and more general executive processes, the rostral IFG (BA 47) supports assessment of lexicality in verbal material (Kotz et al., 2010; Gough, Nobre & Devlin, 2005; Sharp et al., 2009). A recent meta-analysis contrasting words versus nonwords confirmed the relevance of BA 47 in semantic processes (Davis and Gaskell, 2009; Price, 2010). In addition, a dissociation between the pars orbitalis (BA 47) controlling semantic access and pars triangularis (BA 45) dealing with selection of competing retrieved representations has been proposed (Badre and Wagner, 2007). To summarize, contrasting brain activity for pseudowords learned with iconic gestures versus pseudowords learned in the verbal-only condition (ICON^{act} > VERB) revealed activity in ITG and left anterior IFG (BA 47), supporting the notion that the semantic representation is stronger evoked for pseudowords learned with iconic gestures. This is most notable since the lexical decision task in the scanner did not require the active retrieval of the meaning of the pseudowords and the final behavioral learning performance was similar across all conditions.

The significance of the left SMG (for ICON^{act} > VERB) and the right cerebellar cluster (for ICON^{act} > ICON^{pas}) in the respective comparisons is less clear. The left SMG has been suggested to support the phonological store of verbal short-term memory (Paulesu, Frith & Frackowiak, 1993, Henson, Burgess & Frith, 2000), while a recent review posits that a more ventral part of SMG (bordering posterior planunm temporale) affords subvocal articulation during challenging speech comprehension conditions (Price, 2010). For the acquisition of novel words the SMG is proposed to be part of a *phonological word form learning device* (Paulesu et al., 2009), however it remains speculative why any of these functions should be

more taxed by implicit retrieval of pseudowords learned in the ICON^{act} -condition, when compared to the verbal-only condition.

Activations of the cerebellum have been reported for various cognitive tasks regarding working memory, implicit and explicit learning, memory and language (for reviews see Desmond and Fiez, 1998; Murdoch, 2010). For the right cerebellum (ICON^{act} > ICON^{pas}) the most quoted function regarding language is verb generation (e.g. Petersen, Fox, Posner, Mintun & Raichle, 1989). Similarly, our results show enhanced right-cerebellar activity for pseudowords which were learned while actively executing congruent gestures compared to pseudowords learned while passively observing gestures. However, the lack of a cluster in (pre-)motor areas does not support this view. Alternativeley, Desmond and Fiez (1998) suggested that activations of the right cerebellum reflect the search for valid responses from semantic memory. With regard to the lexical decision task during our fMRI-study the rightcerebellar activation might reflect the increased demand to decide whether a pseudoword is German or not. Here, it is suggested that this increased demand applies in particular for pseudowords learned in condition ICON^{act}, because the higher semantic salience may render these pseudowords a stronger semantic competitor for the German words which required a response. This idea is in line with another study, reporting right-hemispheric activations of the cerebellum in a semantic discrimination task, being stronger for more difficult semantic tasks (Xiang, et al., 2003).

The only cluster of greater activation for purely verbally trained pseudowords (VERB > ICON^{act}) projected to the left posterior FG. The specific function of this region is not clear. A review of studies on semantic processing identifies the left FG as one of the seven key areas (Binder, Desai, Graves & Conant, 2009). While according to Binder its role is considered heteromodal and its posterior portion may relate to visual (non-verbal) attributes of objects, other studies have considered the left mid-fusiform gyrus to house a *visual word form area* (Ma et al., 2011). Following the above considerations regarding the SMG cluster for the opposite contrast, it is speculated that pseudowords paired only with the orthographic representation of the rootword may have been partially stored in a corresponding orthographic representation.

Modeling the interaction between Gesture-Type x Self-Involvement, a large bilateral network showed greater activation for the interaction predicted by the 'enactment' effect. The largest clusters were seen in bilateral ITG and left IFG supporting the above view that 'enactment' during learning strengthens the semantic association of the novel words during implicit

retrieval. Additionally the analysis highlights the relevance of iconicity of the gesture since grooming-gestures showed an inverse relationship in that active performance compared to passive viewing led to a lesser activation in these areas. This parallels the early inhibitory effect seen in our behavioral assessment. One very small cluster projected to the left superior frontal gyrus, adjacent to the premotor cortex (BA 6). The latter area has previously been reported as the main locus where iconic gesture training resulted in larger activation when compared to training with meaningless gestures (Macedonia et al., 2010a). Macedonia and coworkers employed a training largely identical with two of our conditions (ICON^{act}, GROO^{act}), however, during the fMRI assessment participants performed a trained/unknown forced choice task only on pseudowords simultaneously presented in a written and auditory form. Such a recognition task may enhance the reactivation of the motor memory trace for meaningful gestures, which were always paired to the same pseudoword during training. Interestingly the study did not report stronger activations in other key areas of the lexicosemantic network. Thus beyond the apparent problems of reproducibility and sensitivity in small sample imaging experiments, the different tasks during the fMRI assessment may have highlighted different aspects (recognition vs. semantic salience) of the trained novel wordform.

The role of motor representations in language processing

Interestingly, our imaging-results did not reveal (pre-)motor cortex activity, when contrasting trained versus untrained pseudowords or contrasting pseudowords learned in the active iconic gesture condition versus pseudowords learned in the passive iconic gesture condition.

At first, this might be surprising, bearing in mind that the learned words referred to manipulable objects such as *cup*, *scissors* or *piano*. Based on the study by Hauk et al. (2004), who showed a somatotopic activation of the motor cortex, when listening to action words, one could have expected similar motor activations in our study for recently learned novel words with motor content. Similarly, one could have speculated that words trained in the active iconic gesture conditions would have reflected their motor-based training in (pre-)motor cortex activation. Furthermore, Macedonia et al. (2010a) reported increased premotor-cortex activity for novel words learned with iconic gestures in contrast to novel words learned with grooming-gestures, suggesting that premotor cortex activity was elicited by internal motor simulation processes. The crucial role of internal motor simulation was also emphasized in a

fMRI-study by Tomasino, Werner, Weiss & Fink (2007), who reported activity in the primary motor cortex (M1) during reading of short action phrases in an explicit imagery task, in contrast to a letter detection task which prevented any simulation strategies.

However, although there is no doubt that the (pre-)motor cortex can be activated by motor imagery, it is a matter of debate whether motor imagery is a necessary aspect of action word comprehension. Does motor imagery occur automatically during action word comprehension, or is motor imagery rather task-specific and occurs only sometimes as a corollary phenomenon or as a side effect? This question was investigated in a study using transcranial magnetic stimulation (TMS). Tomasino, Fink, Sparking, Dafotakis and Weiss (2008) showed a facilitation effect of TMS applied to M1 in an imagery task, but no facilitation effect of TMS during silent reading and frequency judgements. The authors concluded:

These results suggest that the relation between action word comprehension and internal motor simulation is not automatic: in order to understand language, subjects do not need to run a mental simulation of the word content. Rather, the modulation of M1 activation during action-related word understanding depends on whether or not, during reading, subjects simulate the movements the words are referring to (Tomasino et al., 2008, p.1924).

In another TMS-study Papeo, Vallesio, Isaja & Ida Rumiati (2009) investigated whether motor activation occurs automatically, even if the task barely requires explicit retrieval of the motor content of action verbs. It was shown that TMS did not enhance activity in M1 when applied during early stages of lexico-semantic processing (170ms, 350ms post-stimulus), but M1 activity was increased when TMS was applied 500ms post-stimulus. Papeo et al. (2009) concluded:

This study demonstrates that the motor activation related to action language is not strictly necessary to its understanding in a narrow sense (i.e., lexical-semantic encoding). This phenomenon is more likely to reflect post-conceptual operations resulting from the explicit retrieval of the motor information associated with action language, when this is critical to solve a task (Papeo et al., 2009, pp. 8-9).

In a subsequent lesion-study action performance and action-word understanding was investigated in 12 patients with left-hemispheric brain lesions (Papeo, Negri, Zadini & Ida Rumiati, 2010). Papeo et al. (2010) found a double dissociation and concluded "[...] that

motor representations underlying action performance are not a necessary component of word representations" (p.454).

To sum up, motor activity during action word comprehension might be explained by internal motor simulation processes. However, consistent with the lack of (pre-)motor cortex activity in our study, several other studies have shown that internal motor simulation processes are neither automatic nor necessary for word comprehension, but may be triggered in explicit tasks (e.g. Tomasino et al., 2008; Papeo et al., 2009). Further, we propose that, compared with the study of Macedonia et al. 2010a, the lack of (pre-)motor cortex activity in our study might be explained by using different fMRI-tasks. Whereas in the study of Macedonia et al. (2010a) explicit motor imagery might have been triggered by asking participants whether they had learned a word or not, participants of our fMRI-study had to distinguish German words from pseudowords, and BOLD-activity was measured during implicit retrieval of the pseudowords. Thus the lack of (pre-)motor cortex activity in our study might be explained by the fact that our fMRI-task did not encourage internal motor simulation. Our results support the view, that an explicit task emphasizing motor imagery is necessary to elicit motor activity during listening of recently learned novel words with motor content (Tomasino et al., 2008; Papeo et al., 2009).

In sum, our fMRI-study showed that novel words learned with actively performed iconic gestures (relative to the verbal-only condition) increased activity in a left-hemispheric semantic network consisting of left IFG, ITG and SMG. Activation of this network suggests that learning with meaningful gestures strengthens the lexico-semantic encoding of novel words, whereas in our study there was no evidence of (pre-)motor cortex contribution for gesture-based pseudoword-learning.

Conclusion

Whereas the behavioral data of this study do not support the view that iconic gestures facilitate lexical learning, neuroimaging results revealed different cortical networks reflecting the different learning conditions of pseudowords. Based on the observed differences in neural processing for lexical learning with gestures and without gestures future research should investigate whether patients with specific lesions to the language network might benefit from a respectively tailored gesture-based therapy.

4 General Discussion

Speech is often accompanied by gestures. But gestures also affect verbal learning and memory. In this dissertation the idea of gesture-based word-learning was investigated on three levels: On a behavioral level different gesture-types were compared with a verbal-only condition revealing that a facilitating effect of iconic gestures was most prominent in healthy participants with little general learning success. Clinical data showed that iconic gestures were most helpful in aphasic patients with intact lexico-semantic speech capabilities but impairments in phonological working memory. Converging evidence for the relevance of lexico-semantic processing comes from the lesion-data, which revealed that temporal brain regions, which are involved in lexico-semantic processing, were mainly spared in patients who benefitted from iconic gestures. Finally, fMRI was used in healthy participants to localize neural correlates of gestures-based word-learning. A left-hemispheric network was identified, comprising inferior frontal, inferior temporal and inferior parietal brain regions. This result suggests that learning with iconic gestures strengthened the lexico-semantic properties of recently acquired novel words.

4.1 A differentiated view on the efficiency of gesture-based word-learning

Before discussing the fMRI- and lesion-data, similarities and differences in the behavioral results across all studies are considered. On the one hand, behavioral results described how different gestures affect word-learning in the healthy uncompromised language network. On the other hand, the effect of gestures in word-learning was also investigated in the impaired language network of stroke patients with residual aphasia. Whereas the behavioral results of healthy participants did not unequivocally support the idea that lexical learning is facilitated by iconic gestures, the clinical results suggested an advantage of gesture-based learning over classical verbal learning for a subgroup of aphasic patients with intact lexico-semantic capabilities, but impairments in phonological working memory and on the segmental-phonological level of speech.

Examining the role of the gesture-type in lexical learning, the behavioral results clearly showed that gestures only facilitate word-learning if they are meaningful and semantically congruent with the concept of the new word (see Pilot Study, Behavioral Study in section 3.1;

early behavioral results of fMRI-Study, in section 3.3). Learning with grooming-gestures was always worse than learning with iconic gestures. This is in line with our hypothesis and with previous studies, which emphasized the crucial role of semantic congruence between gesture and verbal material (Feyereisen, 2006; Kelly et al., 2009; Macedonia et al. 2010a). However, this result does not answer the question whether iconic gestures facilitate word-learning or whether word-learning is impaired by grooming-gestures. Comparing learning success with iconic gestures and learning in the verbal-only condition allowed a more differentiated view. The Pilot Study and the early behavioral data of the fMRI-study showed similar learning in both conditions (i.e. VERB ~ ICON), whereas at the same time learning was superior with iconic gestures compared to learning with grooming gestures (i.e. ICON > GROOM). These results speak for an interference effect of grooming-gestures, which might impose increased processing demands and therefore impair the cognitive demanding learning process (see also Bernardis et al., 2008). On the other hand an advantage for learning with iconic gestures over learning in the verbal-only condition (ICON > VERB) was found in the Behavioral Study, which used the same design but increased the sample size and learning time. A similar facilitation effect of iconic gestures on verbal memory and learning has been described in many other studies before (e.g. Engelkamp and Krumnacker, 1980; Feyereisen, 2006; Tellier 2008; Kelly et al., 2009; Macedonia et al., 2010a). Interestingly, the Behavioral Study revealed that iconic gestures are especially helpful for adults with a low general learning performance (see also Macedonia et al., 2010b). This result suggests that, lacking efficient learning strategies, low performers might benefit from iconic gestures because iconic gestures provide an alternative elaborated learning strategy for lexical learning. In sum, investigating gesture-based word-learning in healthy participants confirmed that the semantic content of the gestures is crucial and furthermore that lexical learning in adults with little developed wordlearning strategies can be facilitated by iconic gestures.

The idea that gestures might be in particular helpful in adults with limited language learning capabilities was followed up in a clinical study investigating gesture-based word-learning in the impaired language networks of patients with residual aphasia. Whereas, in contrast to our first hypothesis, no general effect of gestures was found on the group-level, the results confirmed our second hypothesis and showed that iconic gestures facilitate lexical learning in a subgroup of patients with mainly intact lexico-semantic speech capabilities but impairments in phonological working-memory and at the segmental-phonological level of speech. The correlation between gesture-benefit and segmental-phonological speech deficits is consistent with previous studies (Rose and Douglas, 2001; Rose et al., 2002; Rodriguez et al., 2006;

Rose and Sussmilch, 2008; Lanyon and Rose 2009; Marangolo et al. 2010). Taken together these results suggest that a prerequisite for efficient gesture-based pseudoword-learning is an intact lexico-semantic processing system which enables the patient to successfully integrate additional semantic meaningful information, delivered as iconic gestures, with the pseudoword. Even minor deficits at the level of lexico-semantic processing decrease gesture-benefit, because the prerequisites for multimodal semantic integration of gesture and pseudoword are limited. Furthermore, as revealed by the multiple hierarchical regression analysis, taking into account additional deficits in phonological working memory improves the prediction for gesture-benefit. This result suggests that, in a phonologically demanding word-learning task, deficits in phonological working memory might be compensated using additional non-phonological information during learning, such as videos of iconic gestures.

In sum the behavioral results suggest that gesture-based word-learning might be in particular helpful if lexical learning capabilities are limited. Whereas in the uncompromised language network of healthy adults iconic gestures are in particular helpful for those adults with little developed learning strategies, aphasic patients with lesions of the language network benefit from gestures if their lexico-semantic speech capabilities are intact.

4.2 Contributions of the left IFG and left ATL in gesture-based word-learning

The neuroimaging results showed that in contrast to classical verbal learning, pseudowords learned with iconic gestures elicited activity in a left-hemispheric network comprising the ITG, the IFG and the SMG. Based on these brain activations we suggested that in contrast to learning in the verbal-only condition, word-learning with iconic gestures strengthens the lexico-semantic properties of the novel word (see discussion of fMRI-data, section 3.3.3). The lesion data showed that gesture-benefit was high in patients whose lesions were mainly restricted to left-hemispheric inferior frontal brain regions but whose temporal brain regions were spared. Integrating the lesion data with the clinical behavioral finding, that intact lexico-semantic capabilities are crucial for successful gesture-based word-learning, we suggested that due to their function regarding lexico-semantic processing, intact temporal brain regions are a prerequisite for successful gesture-based word-learning (see discussion of clinical data, section 3.2.3). The contributions of frontal and temporal brain regions to gesture-based word-learning are discussed in turn.

The left inferior frontal gyrus / Broca's area

Whereas Broca's area was initially described as the core center for language production, recent imaging studies revealed additional functions of Broca's area, such as action observation, sequencing or semantic selection (Koechlin and Jubault, 2006; Molnar-Szakacs, Iacoboni, Koski & Mazziotta, 2005; Thompson-Schill, D'Esposito, Aguirre & Farah, 1997). With regard to semantic processing, Broca's area was described to be involved in the selection of competing semantic meanings (Thompson-Schill et al., 1997; Fletcher, Shallice & Dolan, 2000; Moss et al., 2005), controlled semantic retrieval (Wagner, Paré-Blagoev, Clark & Poldrack, 2001; Gold and Buckner 2002; Poldrack et al., 1999) or both processes (Badre and Wagner, 2007). On a sentence level it was shown that anterior portions of the left IFG are involved in lexical processes under strategic control (Rodd, Davis & Johnsrude, 2005; Newman, Ikuta and Burns, 2010). Considering the different functions ascribed to Broca's area it is important to take into account that the left inferior frontal cortex is divided cyto- and receptoarchitectonically into different subregions (Amunts et al., 1999, 2010). On a functional level it was often shown that the posterior part of the left IFG (pars opercularis, BA 44) is involved in syntactic processing, whereas more anterior parts of the left IFG (pars triangularis, BA 45 and pars orbitalis, BA 47) are involved in semantic processing (Friederici, 2011; Vigneau et al., 2006).

In the fMRI-study of this dissertation the anterior left IFG (pars orbitalis, BA 47) was part of a network which was activated for pseudowords learned with iconic gestures. As was described above we suggest that this activation reflects strengthening of the lexico-semantic properties of the previously learned novel words following gesture-training.

Cortical integration of language and gesture: IFG or STS?

The IFG also plays a key role in the semantic integration of language and gesture (Willems et al., 2007; Skipper et al., 2007; Dick, Goldin-Meadow, Hasson, Skipper & Small, 2009; Straube et al., 2009). Willems et al. (2007) concluded that the left IFG is not restricted to language processing but also involved in the semantic integration of gesture and language. Furthermore, Dick et al. (2009) showed that in particular anterior parts of the IFG are sensitive to co-speech gestures accompanied by speech. This is in line with the finding that anterior IFG is active during observation but not imitation of hand actions (Molnar-Szackacs et al., 2005).

Interestingly, Holle et al. (2008) did not find activation in the left IFG when contrasting meaningful gestures with grooming gestures. Instead they reported activity in a distributed cortical network consisting of the left posterior STS (pSTS), the inferior parietal lobe bilaterally and the ventral precentral sulcus bilaterally. According to Holle et al. (2008), who emphasize the role of the STS in audiovisual integration, the activity observed in the left pSTS might reflect the interaction between a meaningful gesture and an ambiguous sentence at a local level, whereas the IFG activation reported by Willems et al. (2007) might be explained by a subsequent integration stage at a global level. The involvement of the STS during integration of gesture and speech was replicated in a subsequent study in which Holle, Obleser, Rueschemeyer & Gunter (2010) showed bimodal enhancement for gesture-supported sentences in the pSTS and adjacent STG.

In order to clarify the contributions of pSTS and left IFG during integration of gesture and speech, Willems, Özyürek & Hagoort (2009) used a mismatch paradigm in which speech was either presented with pantomimes or with co-speech gestures. Whereas bilateral pSTS/MTG were involved in semantic integration of speech and pantomimes, the left IFG was involved in the integration of speech and co-speech gestures as well as of speech and pantomime. Willems et al. (2009) concluded that there are different roles for the pSTS/MTG and the left IFG during multimodal integration of gesture and speech. In contrast to local integration of gesture and speech in the pSTS/MTG, they suggested that higher-order integration of gesture and speech in the left IFG is characterized as an online construction of a new and unified representation of both input streams. This view is consistent with other studies reporting left IFG involvement in the integration of novel combinations (Hein et al. 2007; Naumer et al., 2009). The left IFG activation found in our fMRI-study further supports the view that the left IFG is involved in the semantic integration of novel combinations, because previously unknown novel words acquired lexico-semantic meanings following training with iconic gestures. On the other hand, Holle et al. (2010) suggested that activity in the pSTS reflects initial conceptual matching between both input streams and that in contrast to semantic integration in the LIFG, integration in the pSTS is more data-driven and more sensitive to the concrete physical form of the stimulus (see also Willems et al., 2009).

In contrast to the previously described studies (Willems et al., 2007, 2009; Holle et al., 2008, 2010) our fMRI study examined the interaction of gesture and speech in a more subtle way. Whereas Willems et al. (2007, 2009) and Holle et al. (2008, 2010) examined neural correlates for the effects of gestures during sentence comprehension, we investigated the effect of

different gestures on learning of novel words and subsequently measured BOLD-activity for single pseudowords, which were previously learned either with iconic gestures or in a verbal-only condition. As pseudowords were only presented auditorily, there was no need for audio-visual integration, potentially explaining the lack of activation in the pSTS.

In sum we suggest that activation of the anterior IFG in our fMRI-Study reflects a strengthening of the lexico-semantic properties of those novel words which were previously learned with iconic gestures. On the other hand, activity in the pSTS, which was found in other studies (Holle et al., 2008, 2010), might reflect audiovisual integration of simultaneously presented gesture and speech, which was not measured in our fMRI-study.

Changing roles of Broca's area

Faced by the growing amount of task-involvements, more general functions were ascribed to Broca's area such as 'regulation of mental activity' (Thompson-Schill, Bedny & Goldberg, 2005). However, searching for the 'superfunction' of Broca's area according to the 'one area one function rule' might be misleading (Willems and Hagoort, 2007) and it is important to emphasize connectivity and cortical networks in the brain (Mesulam, 1990, 1998). In line with a network approach, Broca's area could be imagined to be a node of multiple different networks and the function of Broca's area being determined by the specific network of which Broca's area is part at a given time. Task-dependent different functions of Broca's area have already been described by Friederici (2002), who reviewed studies with an involvement of Broca's area and concluded that Broca's area is not only involved in language comprehension and production but also in the processing of musical sequences, the perception of the rhythm of motion and the imagery of motion.

In the fMRI-study of this dissertation the left anterior IFG (BA 47) was part of a distributed left-hemispheric network, comprising speech-relevant inferior frontal, inferior temporal and inferior parietal brain regions. Being part of such a network suggests a prominent role for the anterior left IFG (BA 47) in lexico-semantic processing of recently learned novel words.

The left anterior temporal lobe

The relevance of middle and inferior temporal brain regions for lexico-semantic processing during language comprehension is widely acknowledged (e.g. Hickok and Poppel, 2007; Price, 2010). In our fMRI-study the left ITG was part of the same network which was activated while contrasting words learned with iconic gestures versus words learned in the verbal-only condition. Thus, our imaging results in healthy participants supported the role of the left ITG in lexico-semantic processing.

Analyzing the lesion data of our Clinical Study revealed another brain region in the left temporal lobe that might be critical for gesture-based word-learning: patients with residual aphasia did not benefit from gestures if in addition to a lesion in the left IFG there was another lesion in the left ATL. The crucial role of the ATL in processing word meanings is known from *semantic dementia*, a syndrome in which reduced semantic processing is associated with degeneration in the ATL (Hodges et al., 1992; Patterson et al. 2007). Furthermore, a functional division within the ATL was suggested by Humphries, Binder, Medler & Liebenthal (2006), who suggested a stronger sensitivity of the most anterior portion of the STS for syntactic structure and an involvement of the region directly posterior to it in processing of semantic information. Recently Friederici (2012) suggested an anterior running gradient from the primary auditory cortex to the anterior STG / STS, moving from phonemes to words and phrases (see also meta-analysis by DeWitt and Rauschecker, 2011). Furthermore the involvement of the ATL in semantic processing is supported by Friederici (2012), who suggested that back-projections from BA 45 to anterior STG and MTG via ventral connections support top-down processes in the semantic domain.

In sum, the left ATL is likely to be involved in lexico-semantic and syntactic processes. However, the contribution of the left ATL in gesture-based word-learning is complex, because a lesion in this region reduces gesture-benefit for aphasia patients, but on the other hand the left ATL was not part of the gesture-associated network activated in healthy participants (cf. fMRI-Study in section 3.3.2.2, contrast ICON^{act} > VERB). Furthermore, patients with combined lesions in the left IFG and left ATL showed preserved word-learning skills in the verbal-only condition, thus excluding a deep semantic disorder. Humphries et al. (2006) speculated that the ATL is composed of polymodal and heteromodal cortex and they highlighted the strong connections between the ATL and other temporal and frontal regions. Thus it might be possible that the left ATL in the healthy language network is not sensitive to gesture-based word-learning, while at the same time a lesion in the left ATL impairs the

multimodal semantic integration of gesture and novel wordform, possibly explaining the lacking effect of gesture-benefit in patients with combined lesions in left IFG and left ATL. This view is consistent with the role of the left ATL in the healthy language networking regarding lexico-semantic processing and word-recognition (Friederici, 2012; DeWitt and Rauschecker, 2011).

Cortical networks

Furthermore the relevance of cortical networks should be emphasized. Whereas the consequences of isolated lesions might be easy to describe, a completely different and much more complex picture emerges if several brain regions are simultaneously lesioned. As lesions often extend into the white matter, crucial connections between functionally different brain regions might be destroyed. Thus it is difficult to ascribe behaviorally observed deficits solely to a single lesion in the brain.

According to the *cortical language circuit* (Friederici, 2012) auditory speech comprehension begins in the primary auditory cortex, proceeding to the anterior STG and via ventral connections to the inferior frontal cortex. Whereas ventral back-projections from BA 45 to anterior STG/MTG are assumed to support semantic top-down processes, dorsal back-projections from BA 44 to posterior STG/STS are assumed to subserve syntactic top-down processes. A dorsal pathway from the primary auditory cortex via posterior STG/STS to the premotor cortex is assumed to support auditory-to-motor mapping. Furthermore, the inferior and middle longitudinal fasciculi are connecting anterior and posterior regions within the temporal cortex.

Thus combined lesions in the left anterior IFG plus ATL (see Clinical Study) might reduce successful gesture-based word-learning because relevant brain regions for lexico-semantic processing are directly impaired (BA 45, ATL), or alternatively because white matter fiber tracts might be damaged, limiting access to important lexico-semantic areas in middle and inferior temporal brain regions. Furthermore the results also suggest that the effects of isolated IFG- lesions on multimodal semantic integration can be compensated, whereas the effects of multiple extensive lesions including left IFG and ATL and perhaps even white matter fibres, cannot be compensated.

However, due to the *small sample size* (N = 12) these results should be considered as preliminary and future research aiming to confirm these results should include larger samples. Furthermore, in order to better understand the effect of brain lesions, future lesion-studies should also examine possible damage of white matter fibre tracts.

4.3 General conclusion

The behavioral results of this dissertation have shown that gesture-based pseudoword-learning is a promising alternative word-learning strategy for healthy adults with little efficient learning strategies. Furthermore the clinical results suggest that aphasia patients with intact lexico-semantic speech capabilities could benefit from gesture-based lexical learning. However, it was also shown that there is no general advantage of lexical learning with iconic gestures compared to classical verbal learning. Thus the practical use of gesture-based word-learning depends on the individual needs and motivation.

Furthermore, gesture-based word-learning is an interesting research topic because it enables to directly investigate the interaction of the motor system with the language system. Clarifying the role of inferior frontal and inferior/middle temporal brain regions in gesture-based pseudoword-learning could lead to clinically useful hypotheses concerning the indication of gesture-based therapy for aphasia patients depending on the location of the brain lesions.

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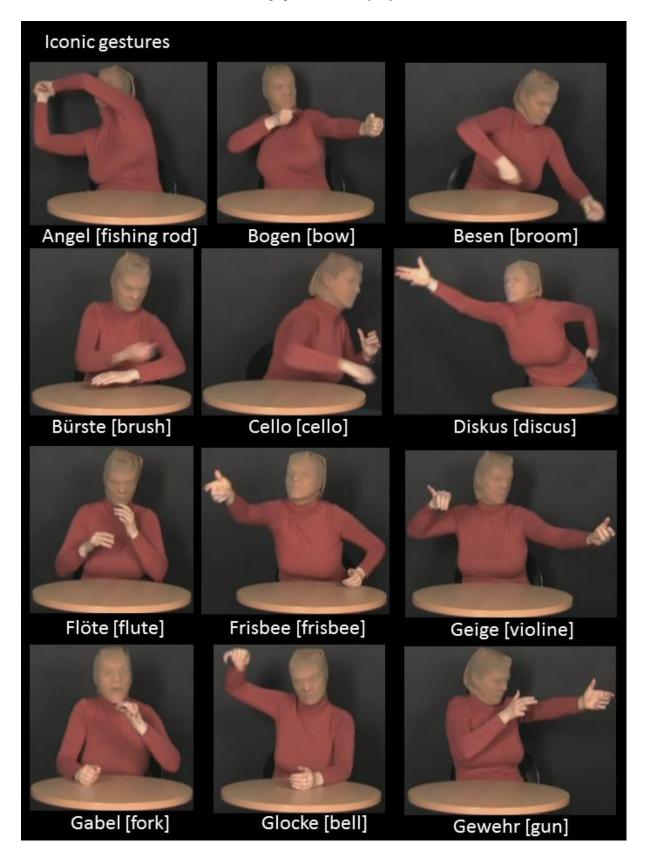
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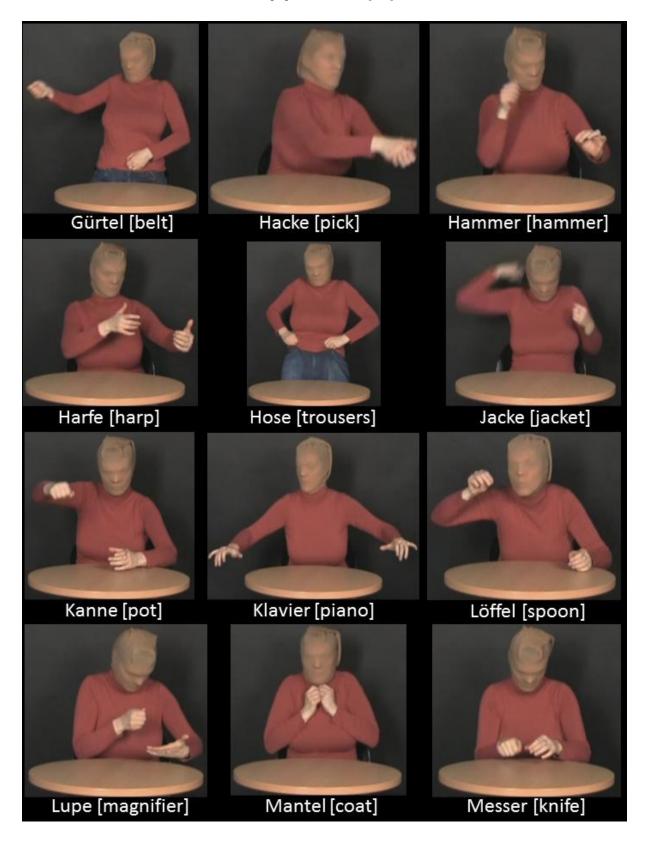
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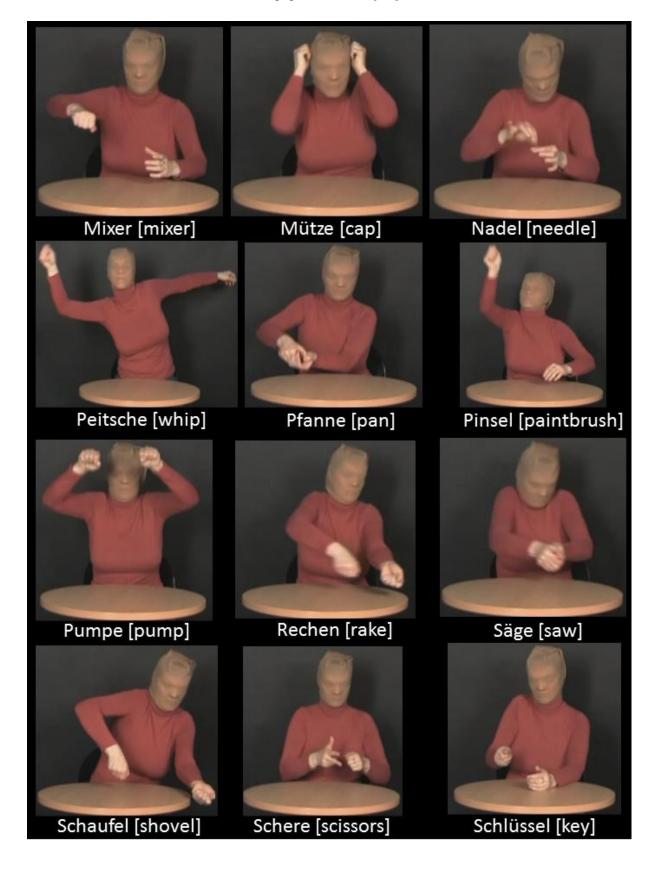
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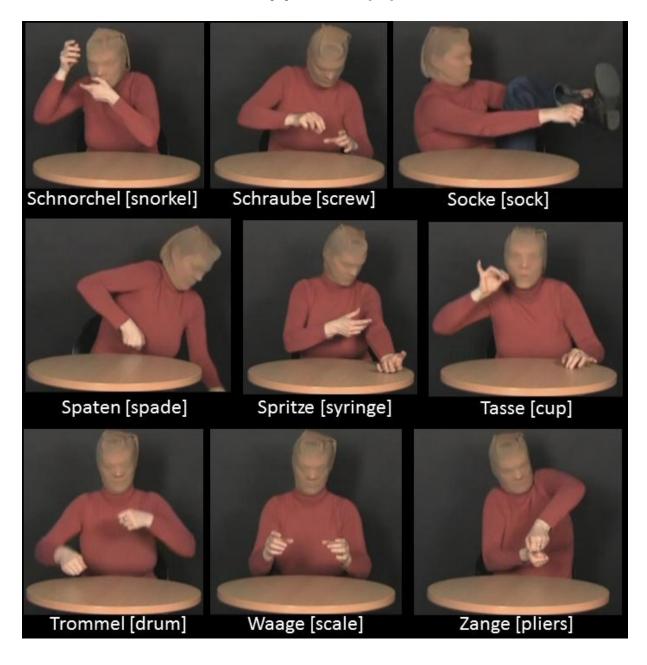
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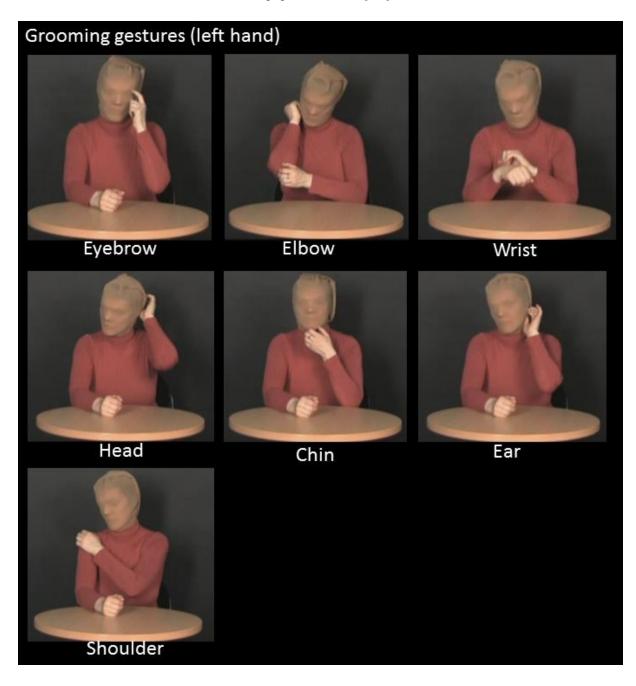
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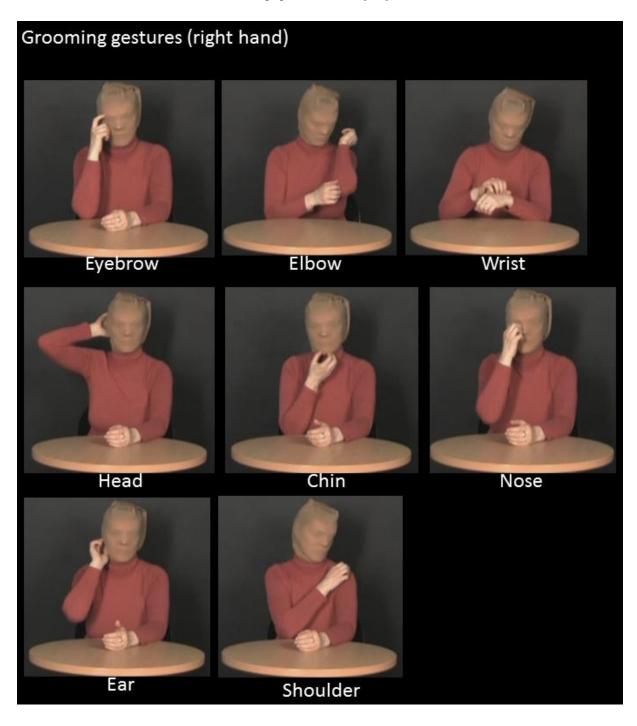












Appendix (B) – Behavioral Study

Neuropsychological diagnostics.

Note. Displayed are raw test values.

ΛÞ	Geschlecht	Alter	Reading Span	DS_fwd	DS_bwd	RWT_B	RWT_Tiere	RWT_Wechsel	CVLT_DG1	CVLT_DG5	CVLT_LIS	CVLT_VFWZ
BJST	ε	24	4.5	10	6	17	34	20	6	16	71	16
LAMU	%	21	5.5	6	9	21	31	29	6	15	89	15
SABE	W	21	5.5	10	6	28	48	25	12	14	72	15
FRWI	Ε	28	3.5	10	6	16	42	22	12	16	73	16
YVPE	*	56	3.0	10	11	19	29	19	10	16	73	16
ROSC	*	56	3.5	00	9	26	29	24	16	16	8	16
JEPE	*	32	3.5	12	11	16	37	22	2	15	28	13
TOHI	Ε	27	2.0	00	6	26	39	21	7	16	89	16
SIGU	*	27	2.5	7	4	20	35	19	2	15	27	16
YVSC	*	28	2.5	10	2	14	56	16	11	16	74	15
STKA	Ε	27	5.5	10	12	34	45	23	00	16	71	16
CHNA	Ε	27	6.0	6	10	18	29	31	10	16	71	16
LYGO	%	56	3.0	00		26	54	32	12	15	29	15
RULA	Ε	25	5.5	10	10	32	64	27	11	16	74	16
NOKU	*	24	2.0	9	2	18	33	20	7	16	65	16
TIWE	*	23	2.5	10	7	27	20	26	6	16	70	15
ANGO	Ε	30	2.5	7	œ	21	45	25	_∞	15	49	16
MAZE	%	22	3.0	6	10	21	35	24	7	16	69	16
STNE	Ε	56	2.0	11	10	27	46	25	10	16	70	13
MAHO	Ε	27	5.5	11	11	24	39	24	_∞	14	63	13
MABA	ш	30	2.5	10	12	26	99	28	10	16	70	16

Appendix (C) – Clinical Study (1)

Neuropsychological diagnostics.

Note: Displayed are raw test values and in brackets percentage ranking except for LPS UT3 (T-values) and WST (IQ-values).

Patient	T.	5	M	PΑ	SS	MS	SF	SG	BS	70	8	HS	RT	88
						Ph	Phonologic Digit Span (PDS)	git Span (PD	(S)					
PDS forwards	5(2)	2(<2)	5(8)	8(53)	8(53)	5(15)	3(2)	8(67)	5(8)	7(35)	5(2)	7(34)	4(2)	5(<20)
PDS backwards	4(2)	2(<2)	4(5)	5(13)	6(34)	4(13)	2(2)	8(80)	4(5)	6[30]	5(12)	6 (34)	6(38)	6(38)
							Visual Digit Span (VDS)	Span (VDS)						
VDSforwards	9(71)	9(71)	8(32)	8(50)	8(50)	9(77)	8(58)	9(85)	8(32)	7(13)	8(58)	9(71)	8(58)	11(98)
VDS backwards	9(79)	6(11)	10(92)	7(31)	6(11)	8(67)	8(70)	7(45)	10(92)	8(40)	9(85)	9 (79)	9(85)	10(92)
						Californ	California Verbal Learning Test (CVLT)	earning Test	(CVLT)					
CVLT 1	8(64)	10(85)	7(34)	9(81)	9(81)	3(3)	5(13)	5(13)	8(64)	4(4)	6(25)	8(57)	9(81)	7(43)
CVLT 5	16(88)	13(14)	15(47)	15(63)	15(63)	5(<1)	8(2)	6(1)	15(63)	10(2)	11(5)	15(47)	16(88)	16(88)
CVLT LS	65(94)	61(59)	64(58)	67(91)	61(63)	20(<1)	30(1)	31(1)	64(72)	44(7)	44(13)	64(70)	67 (99)	61(86)
CVLT VFW2	16(92)	13(34)	16(85)	14(76)	13(62)	4(<1)	7(8)	0(<1)	13(48)	9(8)	10(33)	16(85)	16(92)	13(76)
						Regenst	Regensburg Word Fluency Test (RWT)	Fluency Test	(RWT)					
RWT phon (B)	4(<1)	19(40)	16(12)	15(12)	13(6)	3(<1)	5(<2)	9(2)	8(1)	5(<1)	3(<2)	18(23)	12(8)	12(8)
RWT sem (animals)	29(24)	43(90)	30(9)	32(31)	30(24)	4(<1)	19(3)	15(2)	25(3)	14(<1)	16(<2)	40(61)	22(8)	27(21)
RWT exec (change)	22(59)	23(63)	21(31)	21(39)	15(<1)	4(<1)	17(<1)	13(4)	18(9)	15(2)	12[3]	15(4)	24 (70)	22(59)
						TrailMai	Trail Making Test (executive functions)	xecutivefur	nctions)					
TMTA	37(20)	38(20)	25(50)	37(20)	44(10)	75(10)	56(10)	56(10)	28(40)	53 (10)	103(10)	36(36)	32 (40)	26(60)
TMT B	154(10)	130(10)	105(10)	63(50)	203(10)	300(10)	300(10)	122(10)	58(50)	132(10)	300(10)	49(68)	70 (40)	123(10)
							Intellig	igence						
Nonverb. (LPS UT3)	6(55T)	7(60T)	6(55T)	5 (50T)	4(47T)	4(45T)	5 (50T)	6(55T)	6(55T)	6(55T)	6(55T)	5(50T)	7(60T)	7(60T)
Verbal (WST), IQ	32(104)	37(122)	25(90)	32(104)	30(99)	30(99)	23(88)	23(88)	20(84)	19(83)	35(114)	32(104)	27 (93)	31(101)
					Screen	ings for Alz	Screenings for Alzheimer's disease and Major Depression	Sease and N	Aajor Depre	Ssion				
MMST (>25)	29/30	29/30	29/30	29/30	27/30	27/30	27/30	26/30	28/30	30/30	28/30	30/30	30/30	29/30
BD1 (>20)	0/63	8/63	2/63	0/63	14/63	4/63	8/63	8/63	17/63	14/63	14/63	14/63	24/63	6/63
ומסטונתם	70./0	n la	2014	co./o	en int	70/4	ca./o	ro.le	colit	70./47	70./67	10/14		

Appendix (C) – Clinical Study (2)

Neurolinguistic diagnostics

Note. Raw values are displayed. Assessment of spontaneous speech varies between 1=bad performance to 5=good performance. '-' indicates no data.

Patient	J.	no	IM	PA	SS	MS	SF	9.0	BS	70	88	와	RT	BR
						achener Ap	Aachener Aphasie Test (AAT) – spontaneous speech	AT) – sponta	an eo us speed	£				
Phonologic early	m	4	4	4		4		2	2			2		2
Phonologic late	4	2	4	4	4	2	4	2	2	2	2	2	4	5
Semantic early	4	4	4	4		2		2	4			en		en
Semantic late	2	2	2	2	2	2	4	2	4	4	4	2	4	4
;						;	!						,	
Token Test (>7)	0	4	2	0	0	10	17	0	0	m	m	0		0
							3	LEMO						
Lexical Decision	08/62	08/9/	74/80	78/80	74/80	08/29	73/80	08/92	74/80	08/29	78/80	08/22	75/80	74/80
Repeat Neo	37/40	38/40	36/40	40/40	36/40	27/40	38/40	38/40	40/40	40/40	38/40	40/40	37/40	27/40
Repeat Word	39/40	40/40	40/40	40/40	40/40	37/40	40/40	39/40	40/40	39/40	40/40	40/40	38/40	38/40
Repeat backw	19/40	27/40	28/40	28/40	31/40	17/40	11/40	25/40	16/40	30/40	39/40	37/40	16/40	26/40
Read Neo	34/40	35/40	39/40	38/40	39/40	33/40	22/40	31/40	38/40	38/40	25/40	40/40	28/40	33/40
Read reg./irreg.	54/60	09/65	09/95	25/60	09/95	25/60	09/05	23/60	28/60	25/60	21/60	23/60	54/60	52/60
Synonymy	37/40	39/40	33/40	37/40	37/40	27/40	30/40	39/40	39/40	28/40	39/40	38/40	34/40	34/40
Naming	19/20	20/20	20/20	19/20	20/20	17/20	19/20	17/20	20/20	19/20	17/20	20/20	19/20	18/20

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Appendix (D) - Imaging Study

Neuropsychological test results

VP	Gender	Age	FR	CR_P	CR_G	All	Abitur	German	For_lang	RS
R5	F	23	42	42	42	126	1.4	2	3	3.5
N3	M	23	41	42	42	125	2.3	2	2	3.5
V2	M	27	41	42	41	124	2.6	2	4	4.0
KA	F	25	39	42	42	123	1.4	1	4	2.0
B1	F	28	40	40	42	122	2.8	2	3	3.0
L5	F	23	40	41	41	122	1.3	2	4	3.0
J3	M	28	32	40	42	114	2.2	2	2	3.0
K4	F	26	34	38	40	112	2.4	2	2	2.5
D5	F	28	32	41	39	112	1.9	1	5	3.0
HC	F	25	28	33	35	96	2.0	2	4	3.0
B4	M	26	17	22	27	66	-	-	3	3.0

Note: Learning performance after training measured as the amount of correct words (total = 42 words). FR=Free Recall, CR_P=Cued Recall to Pseudo, CR_G=Cued Recall to German, For_lang=foreign languages, RS=Reading Span. In italics: Performance below Median.

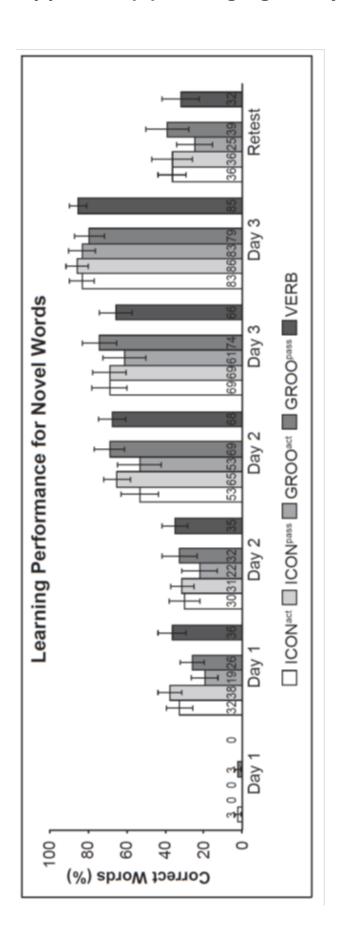
Neuropsychological test results

WMS-R (digit-spans)				CVLT			RWT			TMS		LPS*	WST**		
VP	aud	litory	vis	sual	DG1	DG5	LS	VFW2	В	Animals	Change	Α	В	UT3	
	forw	back	forw	back											
R5	84	53	95	75	85	27	58	85	78	31	37	70	K. A.	65	107
И3	84	53	50	0	74	47	55	62	50	88	30	60	80	60	107
V2	97	98	90	13	74	79	82	85	63	44	61	60	90	60	107
KA	71	88	76	93	100	79	82	85	60	35	67	80	90	65	105
В1	97	98	97	88	100	79	100	85	70	49	88	90	80	70	103
L5	93	95	95	93	85	79	74	85	42	86	67	60	90	70	95
J3	12	12	5	32	34	79	64	85	55	75	49	40	60	50	109
K4	25	56	65	55	74	79	74	62	31	59	22	40	40	60	112
D5	68	98	90	93	17	47	34	62	50	88	56	60	90	65	105
нс	97	98	97	78	74	79	70	85	31	53	49	30	90	65	112
В4	87	92	65	32	74	6	6	8	1	9	22	70	50	70	107

Note. All values given: percent ranking, except for *LPS=T-values and **WST=Z-values. WMS = Wechsler Memory Scale Revised, CVLT = California Verbal Learning Test, RWT = Regensburger Wortflüssigkeitstest, TMS = Trail Making Test, LPS = Leistungsprüfsystem, WST = Wortschatztest. In italics: 16% and/or less of population reach this value (84 % reach better values).

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Appendix (E) – Imaging Study



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List of abbreviations

AAT Aachener Aphasie Test

ANOVA Analysis of variance

ATL Anterior temporal lobe

BA Brodman area

BOLD Blood-oxygen-level-dependent

CSF Cerebrospinal fluid

deoxyHb Deoxygenated hemoglobin

EEG Electroencephalography

FG Fusiform gyrus

fMRI Functional magnetic resonance imaging

FOV Field of view

FWHM Full-width-half-maximum

GB Gesture-benefit

GLM General linear model

GROOM Experimental learning condition: grooming gestures

HDR Hemodynamic response

HGB High gesture benefit

ICON Experimental learning condition: iconic gestures

IFG Inferior frontal gyrus

ITG Inferior temporal gyrus

L2 Second language

LEMO Lexikon modell-orientiert

LGB Low gesture benefit

LSCS Lexico-semantic capability score

M1 Primary motor cortex

MEG Magnetoencephalography

MNI Montreal Neurological Institute

MTG Middle temporal gyrus

oxyHb Oxygenated hemoglobin

pSTS Posterior superior temporal sulcus

SMG Supramarginal gyrus

SNR Signal to noise ratio

SPCS Segmental-phonological capability score

SPM Statistical parametric mapping

STG Superior temporal gyrus

STS Superior temporal sulcus

TMS Transcranial magnetic stimulation

TR Repetition time

VERB Experimental learning condition without gestures, verbal-only

VLSM Voxel-based lesion-symptom mapping

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In Revision

Krönke, K.-M., Mueller, K., Friederici, A. & Obrig, H. (in Revision). Learning by Doing? The Effect of Gestures on Implicit Retrieval of Newly Acquired Words. *Cortex*.

In Vorbereitung

Krönke, K.-M., Kraft, ... & Obrig, H. (in Vorbereitung). Differential efficiency of gesture-based word-learning in patients with residual aphasia.

Vortrag

Learning by doing? Die differentielle Wirksamkeit Gesten-unterstützten Wort-Lernens bei Aphasie-Patienten (2012). *Gesellschaft für Neuropsychologie (GNP)*, Marburg

Poster

Krönke, K.-M., Mueller, K., Friederici, A. & Obrig, H. (2012). Learning by Doing? The Effect of Gestures on Newly Acquired Words. *Human Brain Mapping (HBM)*, Beijing, China

Krönke, K.-M., Kraft, I., Domahs, F., Regenbrecht, F., Friederici. A. & Obrig, H. (2011). Gestenunterstütztes Phonologisches Lernen bei Restaphasie. *Gesellschaft für Aphasieforschung und - behandlung (GAB)*, Konstanz.

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Bibliographische Darstellung

Klaus-Martin Krönke

"Learning by doing? Gesture-based word-learning and its neural correlates in healthy volunteers and patients with residual aphasia"

Fakultät für Biowissenschaften, Pharmazie und Psychologie Universität Leipzig Dissertation

154 Seiten, 159 Literaturangaben, 28 Abbildungen, 10 Tabellen

Speech is often accompanied by gestures. Gestures in turn also affect verbal learning and memory. However, the specific roles of different gestures in word-learning remain unclear. In the behavioral part of this dissertation a word-learning study was conducted, comparing the efficiency of different gesture-training conditions with a classical verbal-only learning condition. Gestures also have a long tradition in aphasia therapy. Whereas some studies reported facilitating effects of gesture-based therapy on lexical retrieval, the role of gestures in word-learning remains unclear. Thus in the clinical part of this dissertation it was investigated whether gestures help patients with residual aphasia to learn novel words. Moreover, the technique *voxel-based lesion-symptom mapping* was used to investigate the implications of brain lesions for gesture-based word-learning. In the neuroimaging part of this dissertation functional magnetic resonance imaging was used to localize neural correlates of gesture-based word-learning in order to improve our understanding of the underlying brain mechanism.

Taken together, the behavioral results of this dissertation have shown that gesture-based word-learning is a promising alternative word-learning strategy for healthy adults with little efficient learning strategies. However, it was also shown that there is no general advantage of lexical learning with iconic gestures compared to classical verbal learning. Thus the practical use of gesture-based word-learning depends on the individual needs and motivation. The involvement of a left-hemispheric brain network, comprising the anterior inferior frontal gyrus, inferior temporal gyrus and supramarginal gyrus suggests a deeper lexico-semantic encoding for novel words learned with iconic gestures. Finally, the clinical results showed that gesture-based word-learning is helpful for aphasia patients with intact lexico-semantic processing capabilities but impairments in phonological working memory and at the segmental-phonological level of language processing. Clarifying the role of inferior frontal and temporal brain regions in gesture-based word-learning could lead to clinically useful hypotheses concerning the indication of gesture-based therapy for aphasia patients.

Summary of dissertation

Speech is often accompanied by gestures. Gestures in turn also affect verbal learning and verbal memory. The role of gestures in verbal learning and memory received an increased amount of attention in the early 1980s when Engelkamp and Krumnacker (1980) discovered that memory is improved for verbal phrases which were learned with gestures. Recently the same principle was applied to word-learning (e.g. to learn the pseudoword *krulo* for the rootword *piano*). Macedonia, Müller and Friederici (2010a) revealed that more novel words were learned with iconic gestures compared to learning with grooming-gestures (i.e. body-focused movements such as scratching). This finding is fascinating because it provides the basis for a promising alternative to classical vocabulary-learning, which is regularly cumbersome. However, the specific roles of different gestures in word-learning remain unclear. Whereas, on the one hand, iconic gestures could facilitate word-learning, an alternative explanation for some findings could be that grooming-gestures interfere with word-learning.

In the behavioral part of this dissertation this problem was investigated in a word-learning study, comparing the efficiency of different gesture-training conditions with a classical verbal-only learning condition. If iconic gestures facilitated pseudoword-learning, more pseudowords should be learned with iconic gestures compared to learning with grooming-gestures and learning in the verbal-only condition. On the other hand, if grooming gestures interfered with pseudoword-learning, the learning performance should be better with iconic gestures than learning with grooming gestures but not different from learning in the verbal-only condition.

Gestures also have a long tradition in aphasia therapy. They can be used instead of verbal communication (i.e. for compensation) but also to improve verbal communication (i.e. for restoration). Whereas some studies reported facilitating effects of gesture-based therapy on lexical retrieval, the role of gestures in word-learning remains unclear. Thus in the clinical part of this dissertation it was investigated whether gestures help patients with residual aphasia to learn novel words (i.e. pseudowords such as *krulo*). Moreover, *voxel-based lesion-symptom mapping (VLSM)* was used to investigate the implications of brain lesions for gesture-based word-learning.

Neuroimaging techniques such as *functional magnetic resonance imaging (fMRI)* are used to investigate the neural basis of cognitive processes. Models describing the brain basis of speech comprehension emphasize the role of both auditory cortices for spectrotemporal analysis, the posterior part of the superior temporal sulcus (STS) for phonological processing, the middle and inferior portions of the temporal lobe for lexico-semantic processing, and a left parieto-temporal region as a sensorimotor interface. However, different accounts exist regarding the brain basis of gesture and speech. A relevant brain region for gesture-speech integration might be the left inferior frontal gyrus (IFG) but also an involvement of the left STS is currently discussed. In terms of word-learning it is

known that the hippocampus plays an important role for the initial acquisition of novel word forms. However, only very little is known about the neural correlates of novel words, which were recently trained in different conditions. In the neuroimaging part of this dissertation fMRI was used to localize neural correlates of gesture-based word-learning, in order to improve our understanding of the underlying brain mechanism.

Results

Behavioral results showed that learning performance is higher with iconic gestures, compared to learning with grooming-gestures. Whereas the Pilot Study did not reveal superior learning performance with iconic gestures compared to purely verbal learning, the results of the Behavioral Study supported the hypothesis of a facilitating effect of iconic gestures in word-learning. Interestingly this effect was driven by those participants who showed little overall learning (i.e. low performers). It seems to be likely that low performers benefit from iconic gestures because, lacking efficient learning strategies, they might use gesture-based pseudoword-learning as an elaborative learning strategy to support memory consolidation of pseudowords.

Investigating stroke patients with residual aphasia, no facilitating effect of iconic gestures was found on the group level. However, correlational analyses revealed that gesture-benefit was associated with the patholinguistic profile of patients. Gesture-based word-learning was more helpful for patients with intact lexico-semantic capabilities. Furthermore, there was a weak negative correlation between gesture-benefit and the segmental-phonological capabilities of the patients. As was revealed by a hierarchical multiple regression analysis, the amount of explained variance in gesture-based pseudoword-learning can be further increased from 46% to 75% if the variable digit span (backwards) is also included, in addition to the lexico-semantic capabilities of the patients. Taken together these results suggest that a prerequisite for efficient gesture-based word-learning is an intact lexico-semantic processing system, which enables the patient to successfully integrate additional semantic meaningful information, delivered as iconic gestures, with the pseudoword. Furthermore, as revealed by the multiple hierarchical regression analysis, taking into account additional deficits in phonological working memory significantly improves the prediction for gesture-benefit. This result suggests that, in a phonologically demanding word-learning task, deficits in phonological working memory might be compensated using additional non-phonological information during learning, such as videos of iconic gestures. Converging evidence, supporting the facilitating role of iconic gestures during word-learning for patients with phonological deficits, results from the weak negative correlation of gesture-benefit with the segmental phonological capability score (SPCS). In contrast to the digit-span (backwards), the SPCS is based on patholinguistic measures and describes in particular linguistic deficits on the segmental-phonological level.

The relevance of intact lexico-semantic capabilities for successful gesture-based pseudoword-learning was further supported by the lesion data. As revealed by VLSM, patients with high gesture-benefit showed lesions mainly restricted to the left IFG, but no lesions in temporal brain regions which are known to be involved in lexico-semantic processing. On the other hand no gesture-benefit was seen for patients with combined left inferior frontal and anterior temporal brain lesions. As both regions are involved in lexico-semantic processing, lesions to these regions might prevent gesture-benefit, because the semantic integration between gesture and pseudoword is impaired.

Finally, in the neuroimaging-study fMRI was used to investigate the neural correlates of gesture-based pseudoword-learning in healthy participants. The comparison between trained and untrained pseudowords revealed increased activity in the left posterior hippocampus, indicating a general (episodic) memory trace for all trained words, independent of the learning-condition. Furthermore pseudowords elicited activity in different cortical networks reflecting the different learning conditions. Contrasting brain activity for pseudowords learned with iconic gestures versus pseudowords learned in the verbal-only condition revealed a stronger activation of left-hemispheric inferior frontal and temporal brain regions, which are involved in lexico-semantic processing, and also stronger activation of the left supramarginal gyrus (SMG) which has been related to phonological wordform-learning. On the other hand, pseudowords learned in the verbal-only condition elicited more activity in the left fusiform gyrus, a brain region associated with the orthographic representation of word-forms. Thus the neuroimaging data suggest, that in contrast to classical verbal learning, there is deeper lexico-semantic encoding for pseudowords learned with iconic gestures.

General conclusion

Taken together, the behavioral results of this dissertation have shown that gesture-based word-learning is a promising alternative word-learning strategy for healthy adults with little efficient learning strategies. However, it was also shown that there is no general advantage of lexical learning with iconic gestures compared to classical verbal learning. Thus the practical use of gesture-based word-learning depends on the individual needs and motivation. The involvement of a left-hemispheric brain network, comprising the anterior IFG, ITG and SMG in gesture-based word-learning suggests a deeper lexico-semantic encoding for novel words learned with iconic gestures. Finally, the clinical results showed that gesture-based word-learning is helpful for aphasia patients with intact lexico-semantic processing capabilities but impairments in phonological working memory and at the segmental-phonological level of language processing. Clarifying the role of inferior frontal and inferior/middle temporal brain regions in gesture-based word-learning could lead to clinically useful hypotheses concerning the indication of gesture-based therapy for aphasia patients depending on the location of the brain lesions.

Zusammenfassung der Dissertation

Sprache wird oft von Gesten begleitet. Gesten wiederum beeinflussen verbales Lernen und verbales Gedächtnis. Die Rolle von Gesten für verbales Lernen und Gedächtnis erlangte ein erhöhtes Maß an Aufmerksamkeit in den frühen 1980er Jahren als Engelkamp und Krumnacker (1980) entdeckten, dass die Gedächtnisleistung für verbale Phrasen erhöht ist, wenn diese mit Gesten gelernt wurden. Kürzlich wurde dasselbe Prinzip auf Wort-Lernen angewandt (z.B. das Pseudowort *krulo* zu lernen für das Stammwort *Klavier*). Macedonia, Müller und Friederici (2010a) zeigten, dass mehr neue Wörter gelernt wurde mit ikonischen Gesten im Vergleich zu Lernen mit Grooming-Gesten (d.h. körperbezogene Bewegungen wie z.B. kratzen). Dieses Ergebnis ist faszinierend, weil es die Basis bereitet für eine vielversprechende Alternative zu klassischem Vokabellernen, was häufig mühsam ist. Jedoch bleiben die spezifischen Rollen von verschiedenen Gesten-Typen beim Wort-Lernen unklar. Während auf der einen Seite denkbar wäre dass ikonische Gesten Wort-Lernen erleichtern, so könnten einige Ergebnisse alternativ auch durch einen interferierenden Effekt von Grooming-Gesten auf Wort-Lernen erklärt werden.

Im behavioralen Teil dieser Dissertation wurde dieses Problem in einer Wort-Lernstudie untersucht, in der die Wirksamkeit verschiedener Gestentrainings-Bedingungen mit einer klassischen rein verbalen Lernbedingung verglichen wurde. Falls ikonische Gesten Pseudowort-Lernen erleichtern sollten, müssten mehr Pseudowörter mit ikonischen Gesten gelernt werden im Vergleich zu Lernen mit Grooming-Gesten und Lernen in der rein verbalen Bedingung. Auf der anderen Seite, falls Grooming-Gesten mit Pseudowort-Lernen interferieren sollten, sollte die Lernleistung mit ikonischen Gesten besser sein als Lernen mit Grooming-Gesten aber nicht unterschiedlich zu Lernen in der rein verbalen Bedingung.

Gesten haben auch eine lange Tradition in der Aphasie-Therapie. Sie können eingesetzt werden an Stelle von verbaler Kommunikation (d.h. zur Kompensation), aber auch um verbale Kommunikation zu verbessern (d.h. zur Wiederherstellung). Während einige Studien Erleichterungseffekte berichteten für gesten-basierte Therapie i.B. auf lexikalischen Abruf, so bleibt die Rolle von Gesten für Wort-Lernen unklar. Daher wurde im klinischen Teil dieser Dissertation untersucht, ob Gesten Patienten mit Restaphasie helfen neue Wörter zu lernen (d.h. Pseudowörter wie z.B. *krulo*). Darüber hinaus wurde die Methode *voxel-based lesion-symptom mapping (VLSM)* verwendet um die Implikationen von Hirnläsionen für Gesten-basiertes Wort-Lernen zu untersuchen.

Bildgebungstechniken wie die *funktionelle Magnetresonanztomograhphie* (*fMRT*) werden genutzt um die neuronale Basis von kognitiven Prozessen zu untersuchen. Modelle, welche die Hirnbasis von Sprachverständnis beschreiben betonen die Rolle beider auditorischer Kortizes für die spektrotemporale Analyse, den posterioren Teil des sulcus temporalis superior (STS) für die phonologische Verarbeitung, die mittleren und inferioren Bereiche des Temporallappens für die lexiko-semantische Verarbeitung und einer linken parieto-temporalen Region als eine sensomotorische Schnittstelle. Jedoch existieren verschiedene Befunde bzgl. der Hirnbasis von Gesten und Sprache. Eine relvante Hirnregion für die Integration von Gesten und Sprache könnte der linke gyrus frontalis inferior (IFG) sein, aber eine Beteiligung des linken STS wird zur Zeit genauso diskutiert. In Bezug auf Wort-Lernen ist bekannt, dass der Hippokampus eine wichtige Rolle spielt für den anfänglichen Erwerb von neuen Wortformen. Jedoch ist kaum etwas bekannt über neuronale Korrelate von neuen Wörtern, die erst kürzlich in verschiedenen Bedingungen trainiert wurden. Im Bildgebungsteil dieser Dissertation wurde fMRT

genutzt um neuronale Korrelate Gesten-unterstützten Wortlernens zu lokalisieren um unser Verständnis zu verbessern über den zu Grunde liegenden Hirnmechanismus.

Ergebnisse

Die behavioralen Ergebnisse zeigten, dass die Lernleistung höher ist mit ikonischen Gesten, im Vergleich zu Lernen mit Grooming-Gesten. Während die Pilot-Studie nicht zeigte, dass die Lernleistung mit ikonischen Gesten besser ist verglichen mit rein verbalem Lernen, so unterstützten die Ergebnisse der Behavioralen Studie die Hypothese eines Erleichterungseffekts von ikonischen Gesten beim Wortlernen. Interessant war, dass dieser Effekt durch diejenigen Probanden erzielt wurden, die eine geringe Gesamt-Lernleistung zeigten (d.h. low performer). Es erscheint wahrscheinlich, dass sog. low performer von ikonischen Gesten profitieren, weil sie, ohne dass sie wirksame Lernstrategien besitzen, Gesten-basiertes Pseudowortlernen als eine elaborierte Lernstrategie nutzen um die Gedächtniskonsolidierung der Pseudowörter zu unterstützen.

Die Untersuchung von Schlaganfallpatienten mit Restaphasie zeigte keinen Erleichterungseffekt von ikonischen Gesten auf der Gruppenebene. Jedoch zeigten Korrelationsanalysen, dass Gesten-Benefit mit dem patholinguistischen Profil der Patienten einhergingen. Gesten-basiertes Wortlernen war hilfreicher für Patienten mit intakten lexiko-semantischen Fähigkeiten. Weiterhin, gab es eine schwache negative Korrelation zwischen Gesten-Benefit und den segmental-phonologischen Fähigkeiten der Patienten. Wie durch eine hierarchische multiple Regressionsanalyse aufgedeckt, so konnte der Anteil erklärter Varianz in Gesten-unterstütztem Pseudowortlernen weiter erhöht werden, von 46% auf 75%, wenn die Variable Zahlenspanne (rückwärts) auch berücksichtigt wird, zusätzlich zu den lexiko-semantischen Fähigkeiten der Patienten. Zusammengefasst legen diese Ergebnisse nahe, dass eine Voraussetzung für wirksames Gesten-unterstütztes Wortlernen in einem intakten lexiko-semantisches Verarbeitungssystem liegt, welches es dem Patienten erlaubt auf erfolgreiche Weise zusätzliche semantisch bedeutungsvolle Information, in der Form von ikonischen Gesten, mit dem Pseudowort zu integrieren. Weiterhin, wie durch die multiple hierarchische Regressionsanalyse aufgedeckt wurde, kann die Vorhersage für Gesten-Benefit signifikant verbessert werden wenn zusätzliche Defizite im Bereich des phonologischen Arbeitsgedächtnis berücksichtigt werden. Dieses Ergebnis legt nahe, dass in einer phonologisch anspruchsvollen Wortlernaufgabe Defizite im phonologischen Arbeitsgedächtnis kompensiert werden könnten, durch die Nutzung zusätzlicher nicht-phonologischer Informationen während des Lernens, wie z.B. Videos von ikonischen Gesten. Ein konvergierender Befund, der den Erleichterungseffekt ikonischer Gesten während des Wortlernens bei Patienten mit phonologischen Einschränkungen unterstützt, resultiert aus der schwachen negativen Korrelation von Gesten-Benefit mit den segmental-phonologischen Fähigkeits-Score (SPCS). Im Gegensatz zur Zahlenspanne (rückwärts), basiert der SPCS auf patholinguistischen Messungen und beschreibt besonders linguistische Einschränkungen im segmental-phonologischen Bereich.

Die Relevanz intakter lexiko-semantischer Fähigkeiten für erfolgreiches Gesten-basiertes Pseudowortlernen wurde weiter unterstützt durch die Läsionsdaten. Wie durch VLSM aufgedeckt wurde, so zeigten Patienten mit hohem Gesten-Benefit hauptsächlich Läsionen, die auf den linken IFG beschränkt waren, jedoch keine Läsionen in temporalen Hirnregionen, welche bekannt dafür sind in lexiko-semantischer Verarbeitung involviert zu sein. Anderderseits gab es keinen Gesten-Benefit bei Patienten mit kombinierten Läsionen im inferior frontalen und

anterior temporalen Bereich. Da beide Regionen an lexiko-semantischer Verarbeitung beteiligt sind, könnten Läsionen in diesen Regionen Gesten-Benefit verhindern, weil die semantische Integration zwischen Geste und Pseudowort gestört ist.

Schließlich wurde in der Bildgebungsstudie fMRT eingesetzt um neuronale Korrelate Gesten-basierten Pseudowortlernens in gesunden Probanden zu untersuchen. Der Vergleich zwischen trainierten und untrainiereten Pseudowörtern zeigte erhöhte Aktivität im linken posterioren Hippocampus, was eine generelle (episodische) Gedächtnisspur für alle trainierten Wörter reflektiert, unabhängig von der Lernbedingung. Weiterhin erzeugten Pseudowörter Aktivität in verschiedenen kortikalen Netzwerken, was die verschiedenen Lernbedingungen reflektiert. Der Vergleich der Hirnaktivität von Pseudowörtern, die mit ikonischen Gesten gelernt wurden versus Pseudowörter die in der rein verbalen Bedingung gelernt wurden, zeigte eine stärkere Aktivierung links-hemisphärischer inferiorer frontaler und temporalen Hirnregionen, welche in lexikosemantischer Verarbeitung involviert sind, und auch eine stärkere Aktivierung des linken gyrus supramarginalis (SMG), der mit phonologischem Wortformlernen in Verbindung gebracht wurde. Auf der anderen Seite, erzeugten Pseudowörter, die in der rein verbalen Bedingung gelernt wurden mehr Aktivität im linken gyrus fusiformis, einer Hirnregion, die mit der orthographischen Repräsentation von Wortformen assoziiert wird. Die Bildgebungsdaten zeigen also, dass im Gegensatz zu klassischem verbalen Lernen, eine tiefere lexikosemantische Enkodierung für Pseudowörter stattfindet, die mit ikonischen Gesten gelernt wurden.

Allgemeine Schlussfolgerungen

Zusammengefasst zeigten die behavioralen Ergebnisse dieser Dissertation dass Gesten-basiertes Wortlernen eine vielversprechende alternative Wortlernstrategie ist für gesunde Erwachsene mit wenig wirksamen Lernstrategien. Jedoch wurde auch gezeigt, dass es keinen generellen Vorteil lexikalischen Lernens mit ikonischen Gesten gibt im Vergleich zu klassischem verbalen Lernen. Daher ist der praktische Nutzen von Gesten-basiertem Wortlernen abhängig von den individuellen Bedürfnissen und Motivationen. Die Beteiligung eines links-hemisphärischen Netzwerks, bestehend aus dem anterioren Ifg, ITG und SMG, bei Gesten-basiertem Wortlernen legt nahe, dass es eine tiefere lexiko-semantische Enkodierung für neue Wörter gibt, die mit ikonischen Gesten gelernt wurden. Schließlich zeigten die klinischen Ergebnisse, dass Gesten-basiertes hilfreich Wortlernen besonders ist Aphasie-Patienten bei mit intakten lexiko-semantischen Verarbeitungsfähigkeiten aber Beeinträchtigungen im phonologischen Arbeitsgedächtnos und auf dem segmental-phonologischen Level der Sprachverarbeitung. Die Konkretisierung der Rolle inferior frontaler und inferior / mittlerer temporaler Hirnregionen in Gesten-basierten Wortlernen könnte zu klinisch nützlichen Hypothesen führen, bzgl. der Indikation von Gesten-basierter Therapoer für Aphasie-Patienten in Abhängigkeit von dem Ort der Hirnläsion.

Selbstständigkeitserklärung

Hiermit erkläre ich, dass die vorliegende Arbeit ohne unzulässige Hilfe und ohne Verwendung anderer als der angegebenen Hilfsmittel angefertigt wurde. Die aus fremden Quellen direkt oder indirekt übernommenen Gedanken sind als solche in dieser Arbeit gekennzeichnet. Die Arbeit ist in keinem früheren Promotionsverfahren angenommen oder abgelehnt worden.

Klaus-Martin Krönke,

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