



Leena Tuomiranta

Novel word learning ability in chronic post-stroke aphasia:

Variability and modality effects



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The present thesis is based on the following publications, which will be referred to in the text by their Roman numerals:

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AUTHOR'S CONTRIBUTION

I: The author had the main responsibility for background assessments, data collection, data analysis, and writing up the manuscript.

II: The author collected the entire data including background tests and the actual experiment, as well as had the main responsibility for data analysis and writing up the manuscript.

III: The author collected a major part of the data, analyzed it and had the main responsibility in writing up the manuscript.

IV: The author collected all of the behavioral data and had the main responsibility in analyzing it. Writing up the manuscript was shared between the co-authors.

SWEDISH SUMMARY - SVENSK SAMMANFATTNING

Inlärnin g av nya ord har utforskats i mycket begränsad utsträckning hos personer med afasi, även om det kunde bidra till utvecklandet av effektiva afasibehandlingsmetoder med ett relativt rent mått på inlärningspotentialen.

Huvudsyftet med avhandlingen var att undersöka vilken kapacitet personer med kronisk afasi har för associativ inlärnin g av ord-föremål -par och utforska kognitivt-lingvistiska faktorer relaterade till inlärnin gen. På en mer specifik nivå var syftet att undersöka hur personer med afasi lär sig, hur de inlärd a paren bevaras i långtidsminnet och vilken roll lexikal-semantiska förmågor har vid inlärnin gen samt jämföra inlärnin gen av fonologisk och semantisk information. Dessutom undersöktes effekten av modalitet på associativ ordinlärnin g och neurala grunder för funktionell inlärnin g.

Inlärnin gsexperimenten baserade sig på Ancient Farming Equipment (AFE) paradigmet som innehåller ritade bilder av främmande föremål och deras obekanta namn. Fallstudier med både finsk- och engelskspråkiga personer med kronisk afasi ($n = 6$) utfördes. Inlärnin gresultatet hos personerna med afasi jämfördes med motsvarande resultat hos friska kontrolldeltagare, och som mått för inlärnin g användes aktiv produktion av de nya orden och deras semantiska definitioner.

Personer med afasi lärde sig par av nya ord och bilder av föremål, men variationen mellan individer var mycket stor, från låg nivå av inlärnin g (delstudierna I-II) till resultat jämförbara med friska individers prestationer (delstudierna III-IV). Däremot lärde sig ingen av personerna med afasi oavsiktligt semantiska definitioner lika bra som de friska kontrollpersonerna. Hos några personer med afasi bevarades en del av det inlärd a i långtidsminnet upp till flera månader efter träning och en individ kunde spontant benämna alla av de nya orden korrekt sex månader efter att träningen tagit slut (delstudie IV). Välbevarade lexikal-semantiska processeringsförmågor stödde inlärnin gen hos personer med afasi (delstudierna I-II) men knappt fonologiskt korttidsminne förhindrade inte inlärnin g av nya ord. Två personer med afasi som hade bra inlärnin g och bevaring av nya ord-föremål par i långtidsminnet litade i sin inlärnin g på skriven input medan auditiv input resulterade i signifikant lägre inlärnin gresultat (delstudierna III-IV). Hos en av de här personerna kunde den tidigare oupptäckta modalitetsspecifika inlärnin gsförmågan framgångsrikt tillämpas i

träning med bekanta men otillgängliga vardagsord (delstudie IV). Funktionell magnetavbildning visade att den här personen hade en bruten dorsal talprocesseringsbana i den vänstra hjärnhalvan medan den framgångsrika inläringen genom läsning förmedlades via ett högersidigt neuralt nätverk. Slutligen antydde resultaten av delstudie III att den kognitiv-lingvistiska profilen hos en person med afasi inte alltid förutsäger den optimala inlärningskanalen. Följaktligen verkar småskaliga inläringstest användbara för att få fram de funktionella inlärningsrutterna hos personer med afasi orsakad av stroke.

Nyckelord: afasi, afasibehandling, anomi, funktionell hjärnavbildning, långtidsminne, modalitet, muntlig benämning, ordinläring, skriftlig benämning, träning, vokabulär

ABSTRACT

Novel word learning has been rarely studied in people with aphasia (PWA), although it can provide a relatively pure measure of their learning potential, and thereby contribute to the development of effective aphasia treatment methods.

The main aim of the present thesis was to explore the capacity of PWA for associative learning of word–referent pairings and cognitive-linguistic factors related to it. More specifically, the thesis examined learning and long-term maintenance of the learned pairings, the role of lexical-semantic abilities in learning as well as acquisition of phonological versus semantic information in associative novel word learning. Furthermore, the effect of modality on associative novel word learning and the neural underpinnings of successful learning were explored.

The learning experiments utilized the Ancient Farming Equipment (AFE) paradigm that employs drawings of unfamiliar referents and their unfamiliar names. Case studies of Finnish- and English-speaking people with chronic aphasia ($n = 6$) were conducted in the investigation. The learning results of PWA were compared to those of healthy control participants, and active production of the novel words and their semantic definitions was used as learning outcome measures.

PWA learned novel word–novel referent pairings, but the variation between individuals was very wide, from more modest outcomes (Studies I–II) up to levels on a par with healthy individuals (Studies III–IV). In incidental learning of semantic definitions, none of the PWA reached the performance level of the healthy control participants. Some PWA maintained part of the learning outcomes up to months post-training, and one individual showed full maintenance of the novel words at six months post-training (Study IV).

Intact lexical-semantic processing skills promoted learning in PWA (Studies I–II) but poor phonological short-term memory capacities did not rule out novel word learning. In two PWA with successful learning and long-term maintenance of novel word–novel referent pairings, learning relied on orthographic input while auditory input led to significantly inferior learning outcomes (Studies III–IV). In one of these individuals, this previously undetected modality-specific learning ability was successfully translated into training with familiar but inaccessible

everyday words (Study IV). Functional magnetic resonance imaging revealed that this individual had a disconnected dorsal speech processing pathway in the left hemisphere, but a right-hemispheric neural network mediated successful novel word learning via reading. Finally, the results of Study III suggested that the cognitive-linguistic profile may not always predict the optimal learning channel for an individual with aphasia. Small-scale learning probes seem therefore useful in revealing functional learning channels in post-stroke aphasia.

Key words: anomia, aphasia, aphasia treatment, functional neuroimaging, long-term memory, modality, spoken naming, training, vocabulary, word learning, written naming,

ABBREVIATIONS

AF	Arcuate fasciculus
AFE	Ancient Farming Equipment
AOS	Apraxia of speech
BDAE	Boston Diagnostic Aphasia Examination
BNT	Boston Naming Test
BOLD	Blood oxygen level dependent
CT	Computer tomography
dMRI	Diffusion magnetic resonance imaging
fMRI	Functional magnetic resonance imaging
ICH	Intracerebral hemorrhage
LI	Laterality index
MCA	Middle cerebral artery
MRI	Magnetic resonance imaging
PWA	People with aphasia
SAH	Sub-arachnoid hemorrhage
STM	Short-term memory
TALSA	Temple Assessment of Language and Short-term Memory In Aphasia
TMT	Trail Making Test

1 INTRODUCTION

Every year approximately 23,000 Finns suffer an ischemic or hemorrhagic stroke (National Institute for Health and Welfare in Finland) and a considerable proportion of stroke survivors are left with aphasia, i.e., acquired language impairment (LaPointe, 2005). The incidence of aphasia among acute stroke patients varies between studies from approximately 24 % to 38 % (Engelter et al., 2006; Laska, Hellblom, Murray, Kahan, & Von Arbin, 2001; Pedersen, Jørgensen, Nakayama, Raaschou, & Olsen, 1995; Wade, Hewer, David, & Enderby, 1986). Of the surviving patients with initial aphasia, around 40–50 % still have aphasia at 6 months post-stroke (Pedersen et al., 1995; Wade et al., 1986). The stroke survivors with aphasia encounter various language production and comprehension difficulties that vary greatly in type and severity.

The cardinal symptom of aphasia is anomia, i.e. difficulty in word retrieval. As practically all people with aphasia (hereafter, PWA) suffer from anomia to a varying degree (Laine & Martin, 2006), a major part of aphasia treatment research is devoted to this deficit. Anomia treatment strives at re-gaining access to the words that PWA had mastered prior to their brain lesion. However, the exact mechanisms for effective anomia treatment remain unclear. In one way or another, recovery from anomia must be based on the plasticity of the remaining brain tissue, i.e. re-organization or rebuilding the neural networks for language (Duffau, 2006). Here the learning capability of the damaged brain is presumably important. The present dissertation focuses on the functionality of the associative word learning system and cognitive-linguistic factors related to word learning. This represents a scarcely studied field despite the fact that the integrity of word learning mechanisms in PWA may be of relevance for predicting recovery from aphasia or planning therapy (Basso, 2003; Meinzer et al., 2010).

More specifically, the present thesis explores associative learning of novel words and their referents in PWA. The reason for taking this approach is that novel word learning can be argued to provide a relatively pure measure on the word learning capacity. In contrast to familiar but inaccessible words, novel words do not have pre-existing representations in the language network. Moreover, the characteristics of novel words and the type and frequency of exposure are under full experimental control.

2 REVIEW OF THE LITERATURE

2.1 Novel word learning

At the core of novel word learning lies an associative learning process where a name (phonological and/or orthographic form) is linked to a concept and/or an external referent (see Mitchell, De Houwer, & Lovibond, 2009) for models of associative learning). Novel word learning is particularly fast in childhood but this capacity is maintained throughout the life-span. Moreover, the mental lexicon is constantly updated as new words (e.g., “flash drive”, “sushi”) appear in a language and some old words gradually change their meaning (e.g., “firewall” and “tablet” as computer terms). Learning can be conscious but we learn novel words in an efficient way also incidentally, i.e. without aiming to learn (e.g. Saffran & Newport, 1997; Swanborn & de Glopper, 1999).

Acquisition of word–referent pairs is only one aspect of language learning. Natural language learning also comprises syntactic and morphological rules and semantics, as well as the pragmatic rules for how to use language. However, in this dissertation the main focus is on the associative learning of the phonological or orthographic word form and its referent. A minor part of the thesis deals with incidental learning of semantics.

The capacity to acquire new word forms is not the same across individuals but correlates with phonological short-term memory (STM) as measured with immediate serial recall and the ability to repeat pseudowords (Baddeley, Gathercole, & Papagno, 1998; Gathercole, 2006; Gupta, Martin, Abbs, Schwartz, & Lipinski, 2006). Young children expand their vocabulary with phonological input, through listening to words, but as they gain literacy, another pathway opens up for word learning. Nelson, Balass, and Perfetti (2005) studied word form learning following phonological and orthographic presentation. Their results suggest that healthy young adults learn more efficiently when words are presented in orthographic than in phonological form. The orthographic advantage in learning can emerge from the double (phonological and orthographic) coding of words presented in the written form, leading to double episodic memory traces. When words are presented auditorily, corresponding double coding into orthography does not take place. Furthermore, Nelson et al. (2005) noticed that the best recognition memory performance for novel words was gained when training and testing modalities were in line.

2.2 Neural correlates of word learning in adults

The Complementary Learning Systems model (CLS; Davis, Di Betta, Macdonald, & Gaskell, 2009; Davis & Gaskell, 2009; O'Reilly & Norman, 2002) of word learning provides a framework for understanding the memory processes of novel word learning. The model suggests that temporary associations between words and their referents are first built up rapidly in the hippocampus as episodic memory traces. After that, a slower process of memory consolidation enables long-term storage and access to the encoded contents. Memory consolidation is a cortical process where individual associations are integrated into the existing declarative memory contents. Finally, in order to use the newly learned word, the learner needs to retrieve the phonological or orthographic word form from long-term memory.

Language learning comprises of several essential phases that rely on different neurophysiological mechanisms. Rodríguez-Fornells, Cunillera, Mestres-Missé, and de Diego-Balaguer (2009) put forward an integrative functional neuroanatomical model (a simplified version of the model is shown in Fig. 1) to account for language learning in adults. The model includes three interfaces for language learning and also lists factors that can influence language learning. The first interface is the dorsal audio-motor stream (Hickok & Poeppel, 2007; Kümmerer et al., 2013; Saur et al., 2008), that connects the posterior superior temporal gyrus with the posterior inferior frontal and premotor regions in the left hemisphere via the arcuate fasciculus (AF) and the superior longitudinal fasciculus (Saur et al., 2008). This interface maps sounds onto articulation, and carries an important role in repeating heard speech and especially pseudowords. Hickok and Poeppel (2007) suggest that the dorsal interface also mediates novel language learning. The second language learning stream is the ventral meaning integration interface that connects the inferior temporal gyrus with the ventral inferior frontal gyrus. According to Rodríguez-Fornells et al. (2009), this interface includes a “self-triggered learning mechanism” for interpreting meanings. This language processing stream possibly runs via the inferior longitudinal, the inferior fronto-occipital and the uncinate fasciculus (Duffau et al., 2005; Rodríguez-Fornells et al., 2009).

The third stream of the language learning model is the episodic-lexical stream that maps the novel word form onto the referent (Rodríguez-Fornells et al., 2009) through an episodic, context-dependent memory trace. This associative process can take place very efficiently,

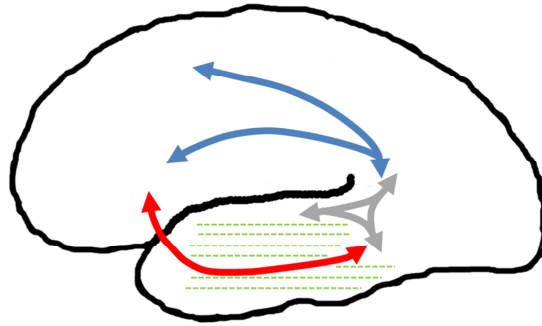


Figure 1. A simplified integrative functional neuroanatomic model of language learning in adults adapted from Rodríguez-Fornells et al. (2009). The model includes three interfaces for language learning depicted on a schematic lateral view of the left cerebral hemisphere: (a) the dorsal audio-motor interface for phonological store and rehearsal (marked with blue arrows), (b) the ventral meaning integration interface (red arrow), and the episodic-lexical interface located in the medial temporal lobe (green dashed lines). Parts of the network are shared by the dorsal and ventral interfaces (grey arrows).

after only few exposures to the novel stimuli. This mapping relies on the medial temporal lobe including the hippocampus and the parahippocampus. The newly learned word-referent associations must be integrated into the semantic memory as context-free memory traces in order to be used effortlessly in different contexts in the long-term. Memory consolidation processes (Nadel, Hupbach, Gomez, & Newman Smith, 2012) enable this cortical integration.

Of the three interfaces in the model by Rodríguez-Fornells et al. (2009), the dorsal audio-motor interface and the episodic-lexical interface in particular are of importance for the present dissertation. The dorsal audio-motor stream supports the spoken production and the initial phonological learning of novel word forms, which are essential aspects of the present word learning experiments. The episodic-lexical stream, in turn, supports the fast-mapping of the word forms onto their object referents and conceptual information. Finally, transfer of information from the medial temporal regions to the cortical “lexical storages” is needed to enable longer-term maintenance and successful retrieval of the newly learned contents. This aspect is assessed in the present dissertation through probe testing during follow-up.

Rodríguez-Fornells et al. (2009) also highlight the integrative role of the basal ganglia and the thalamus in regulating the activity of the language learning interfaces as well as controlling

important cognitive processes engaged in learning such as attention, executive functions and rehearsing the novel contents in STM. For example, in learning to name a new object from a visual presentation, the learner has to direct and maintain attention in order to perceive the new information, decode and memorize a correct visual representation of the object and the word form, and associate these two. It is suggested that the phonological loop (see e.g. Baddeley, 2012, for models of the working memory) plays the important role of storing and repeating the phonological word form until a firm phonological representation has been established. Usually, semantic features also are added to the associations, even though word learning is also possible with direct links between phonological and object representations as we can learn to name objects of which we have no semantic knowledge (Laine & Salmelin, 2010).

The CLS model (Davis et al., 2009; Davis & Gaskell, 2009; O'Reilly & Norman, 2002) and the integrative functional neuroanatomical model of language learning in adults by Rodríguez-Fornells et al. (2009) are supported by neuroimaging evidence by Breitenstein et al. (2005), James and Gauthier (2004), and Raboyeau et al. (2004). These functional neuroimaging studies with healthy individuals have linked word learning to a number of regions in the left hemisphere. Importantly, the areas discovered are the same as those that are also more generally associated with language processing. Consequently, even on the basis of these data, aphasia should in general impair novel word learning greatly. The initial phase of associative word learning has been associated with hippocampal activation (Breitenstein et al., 2005) while long-term learning has been connected to left-hemispheric neocortical activation in the traditional language areas: the temporal lobe (Raboyeau et al., 2004), inferior parietal cortex (Breitenstein et al., 2005), and inferior frontal cortex (James & Gauthier, 2004).

2.3 Novel word learning in aphasia

Common sense may tell clinicians and PWA that because even familiar, everyday words often cause so much trouble in aphasia, learning totally new words may well be beyond reach in aphasia. For example, if one struggles with words such as *banana*, learning the name of the latest exotic addition in the supermarket, *kiwano*, might feel impossible. This unarticulated assumption may be one of the reasons for the scarcity of novel word learning studies in PWA. However, the limited earlier literature reviewed below shows that PWA can hold at least restricted capacity to learn some novel vocabulary.

At first sight, the study of novel word learning in aphasia may appear even irrelevant when compared to the study of the re-acquisition of useful, everyday words. However, novel words for which the PWA do not have pre-existing lexical representations provide some advantages for this research. Firstly, word characteristics such as imageability and frequency of exposure are under experimenter's control. Secondly, one avoids the substantial intraindividual variation in naming familiar items in PWA that makes it difficult to establish a stable pre-treatment baseline. Thirdly, one can be certain that learning to name a novel object relies on acquisition of a new word-referent association. This stands in contrast to familiar items, where previously acquired lexical knowledge influences the re-acquisition process.

According to Vallila-Rohter (2014), aphasia therapy in general suffers from the lack of knowledge on how PWA learn. Due to this shortcoming, it is hard to predict aphasic individuals' treatment outcomes and to customize aphasia therapy so that it meets the special learning profiles of each individual. Vallila-Rohter (2014) compared the capacity to learn novel non-linguistic information with success in language therapy and found a positive correlation between the two. She lists feedback monitoring and hypothesis formation as common skills that play an important role both in the non-linguistic learning task and aphasia treatment. Vallila-Rohter (2014) highlights the importance of probing general learning capacity in PWA, suggesting that this factor might be the actual key factor defining how much PWA can improve in language therapy.

2.3.1 Earlier studies of word learning in aphasia

Word learning has been studied in participants with aphasia in several investigations. However, a closer look reveals that the majority of the studies are actually about relearning of previously known words or word lists (e.g. Martin & Saffran, 1999; Tikofsky, 1971) or they combine familiar and novel elements in their learning tasks (e.g. Breitenstein, Kamping, Jansen, Schomacher, & Knecht, 2004; Freedman & Martin, 2001; Marshall, Neuburger, & Phillips, 1992). The familiar elements in these studies have been real words (Marshall et al., 1992), pictures of familiar objects (Breitenstein et al., 2004), and verbal definitions (Freedman & Martin, 2001). While these investigations have added to our knowledge on aphasia and changes in language performance, they cannot be considered as "pure measures" of word learning ability (see p. 14).

2.3.2 Earlier studies of novel word learning in aphasia

Narrowing the scope to novel word learning studies where familiar elements are not present, we are left with a handful of investigations, none of which includes a longer-term follow-up of learning outcomes. Grossman and Carey (1987) taught 15 participants with aphasia a single novel name (infrequent color name “bice”) in an incidental learning task. The participants were given instructions to draw and the novel name appeared in the instructions. The aim of the study was to examine what participants with agrammatic vs. fluent aphasia could learn about the novel word. The learning measures included production of the phonological form of the word (naming and sentence production task), making grammatical judgments about the word, and comprehending the meaning of the word (object classification). A double dissociation between the aphasia groups was detected between the accuracy of grammatical judgments (the participants with fluent aphasia performing better than the agrammatic participants) and between comprehending the semantics of the novel word (the participants with agrammatic aphasia performing better than the fluent participants). During a follow-up at two weeks post training, two participants with aphasia could name the novel color.

Gupta et al. (2006) taught 12 participants with aphasia and 10 healthy controls 12 novel bisyllabic words associated with novel pictured items (“aliens from another planet”). There were two learning experiments: (a) phonological learning as measured by confrontation naming accuracy, and (b) receptive learning probed with a matching task. Both experiments included three exposure and three test blocks, as well as a final test. The time course of the study was not reported. In confrontation naming of the novel items, PWA exhibited on average 6% accuracy rate while healthy controls reached a 27% accuracy rate. A double dissociation was found between receptive recognition and phonological learning: integrity of lexical semantic processing predicted receptive learning while preserved phonological skills predicted phonological learning.

Laganaro, Di Pietro, and Schnider (2006) explored pseudoword learning in three participants with aphasia as a part of a more extensive investigation. The learning experiment focused on the effect of phonological neighborhood density on learning. They examined reasons for differential treatment-induced anomia recovery patterns, and therefore pseudoword learning per se was not the main interest of the study. The three participants with aphasia and healthy control participants were trained with 20 bisyllabic pseudowords paired with abstract drawings. There were three training sessions with a six-day interval between the second and

third session. Auditory and orthographic input was used simultaneously during training and the output modality for training was orthographic. During the written naming trials, the participants could press a help button to receive orthographic cues. Learning was measured as a function of the use of the help button. All three participants with aphasia acquired at least 50% of the novel words.

To date, the neural correlates for novel word learning in PWA have been targeted only in one investigation. This functional magnetic resonance imaging (fMRI) study by Morrow (2006) included six people with aphasia and ten healthy control participants. The participants were scanned during administration of a word learning task that consisted of judging the accuracy of given novel picture–pseudoword pairs. Participants with aphasia had three picture–pseudoword pairs to learn while the healthy controls learned eight pairs. The pictures depicted “objects unfamiliar to general public”. Feedback was given after each response. No actual baseline condition was employed in the study but both intra-participant analyses as well as comparisons of the aphasic participants’ activation patterns to their matched controls’ activations were utilized. Morrow (2006) used response accuracy and response time as measures for learning. The pilot data collected from two healthy participants suggested a change of cortical activation patterns as novel words were learned. The initial learning phase was associated with stronger hippocampal and anterior cingulate activation than the later phases. In the actual experiment, similar cortical areas were activated by the task in the healthy controls and the PWA. However, the left-hemispheric activation was significantly reduced in the latter group. Importantly, PWA performed at chance level during the receptive task while the healthy controls exhibited effective learning. The severity or nature of the language processing deficits was not found to predict the learning outcomes of the participants with aphasia. Morrow (2006) emphasized the impact of not only the language impairment but also possible impairments of attentional skills and working memory in explaining the poor learning results of the participants with aphasia. In a strict sense, the results of Morrow (2006) do not reveal activation patterns related to novel word learning in aphasia as there was no behavioral evidence of learning during the task in PWA.

Kelly and Armstrong (2009) explored novel word learning in a study of 12 participants with various aphasia syndromes. The participants were to learn names and semantic information of a set of 20 pictured “creatures”. This study took into account different learning styles, providing the participants the opportunity to choose between various learning methods and

train independently according to personal preferences. The tailor-made learning methods were employed in order to maximize learning results. The downside is that reliable cross-participant comparisons cannot be made, especially as the time used for training varied. All of the participants learned at least some (15–99%) novel creature names and their semantic content. Maintenance of the learning was followed 3–5 days post-training. At that point, the participants reached 45–83% of their initial learning results.

Martin, Schmitt, Kamen, Bunta, and Gruberg (2012) studied receptive and expressive learning of novel words in 20 PWA. In the experiment, the PWA participated in learning tasks where they learned pairs of (a) novel tools and their novel names, and (b) novel aliens and their novel proper names. Half of the items were trained first with a receptive task, whereas the other half with an expressive task. The aims of the study were to explore the impact of language processing impairments on novel word learning, measure the effect of successful receptive learning on later expressive learning of novel words, as well as to compare learning of object (tool) names and proper (alien) names. Lexical-semantic processing skills were found to correlate with both receptive and expressive novel word learning, but only when trained first with the receptive task and then continued in the expressive modality. Expressive learning of novel words was aided by previous receptive learning of the material. Learning of object names was superior to learning of proper names, but only in the receptive learning condition.

2.4 Ancient Farming Equipment (AFE) Paradigm

The present series of novel word learning experiments in PWA utilizes the Ancient Farming Equipment (AFE) paradigm (Laine & Salmelin, 2010). The paradigm is thus described in more detail. It has been employed in a number of word learning studies in healthy adults (e.g. Hultén, Vihla, Laine, & Salmelin, 2009; Hultén, Laaksonen, Vihla, Laine, & Salmelin, 2010; Meinzer et al., 2014; Whiting, Chenery, Chalk, Darnell, & Copland, 2007; Whiting, Chenery, Chalk, Darnell, & Copland, 2008), and also in memory-impaired participants (Grönholm-Nyman, Rinne, & Laine, 2010). The AFE items are black-and-white line drawings of real but unfamiliar objects that have been utilized in various tasks related to farming, hunting and fishing. The objects have therefore real use and semantics that are unknown to modern people.

Vocabulary learning with the AFE paradigm does not equal native language acquisition in naturalistic situations but, nonetheless, these two share several attributes. The language learner needs to acquire new referents and novel word forms and establish associative links between them during the learning process. The new referents and word forms are presented in pairs over several sessions during separate days, between which the learner also has time to consolidate the learning. This leads to a gradual acquisition and memory consolidation, in line with the CLS model of learning (Davis et al., 2009).

So far, the investigations with the AFE paradigm have concentrated on active phonological word learning as measured by visual confrontation naming. The maintenance of vocabulary learning with the AFE paradigm has been followed up to several months post-training. Hultén et al. (2010) demonstrated that healthy young adults can maintain novel vocabulary up to 10 months without any further training. The results of Grönholm-Nyman et al. (2010) indicated that, although participants with the amnesic type of Mild Cognitive Impairment learned fewer novel words than healthy individuals, the slope of forgetting was still comparable to that of healthy, elderly controls. Grönholm-Nyman et al. (2010) related the impaired word acquisition to the patients' deficient episodic memory system, that in turn suggests dysfunction in medial temporal lobe structures needed for successful binding of the novel words with their novel referents (Davis et al., 2009). The comparable slopes of forgetting, on the other hand, were accounted for by the patients' better preserved left-hemispheric cortical networks which are essential for long-term maintenance of newly learned lexical information.

3 AIMS

The principal aim of the present multiple-case study was to explore the functionality of the associative word learning system and cognitive-linguistic factors related to it in participants with chronic aphasia. The more specific aims were to study:

- learning vs. long-term maintenance of associative word learning (Studies I–IV)
- the role of lexical-semantic abilities in associative word learning (Studies I–II)
- acquisition of phonological (object name) vs. semantic (object definition) information in associative word learning (Studies I–IV)
- modality-specific effects on associative word learning (Studies III–IV) and their neural underpinnings (Study IV)

Study I explored explicit learning of pseudoword–novel referent pairs in two English-speaking participants with chronic fluent aphasia and matched healthy control participants. In addition, incidental learning of semantic definitions was probed. The maintenance of the learning outcomes was tested up to 6 months post-training.

Study II replicated and extended upon Study I by testing participants that were Finnish-speaking and had nonfluent aphasia. Moreover, the to-be-learned vocabulary consisted of existing words in Finnish that no longer are in common usage, whereas in Study I they were legal English pseudowords with lower phonotactic probability than words used in Study II.

Study III extended upon Studies I–II by focusing at modality effects on novel word learning in one Finnish-speaking participant with chronic nonfluent aphasia and a control group. The aphasic participant was administered a pseudoword learning task that systematically varied input and output modalities (auditory and orthographic) in a factorial setup.

Study IV explored verbal learning and its neural underpinnings in one Finnish-speaking participant with chronic fluent aphasia and healthy control participants. The aphasic participant’s learning ability was studied with a novel word learning experiment focusing at input modality (auditory vs. orthographic) during learning and also a familiar word relearning experiment administered as home-training. Moreover, the neural basis for her well-functioning word learning was investigated with learning and reading tasks in the MRI scanner.

4 METHODS

4.1 Participants

The participants included six individuals with aphasia and 15 healthy control participants. In addition, one English-speaking individual with aphasia was recruited as a pilot participant. One Finnish-speaking individual with aphasia withdrew from the study at one week post-training and his data are therefore not reported. All individuals with aphasia fulfilled the following inclusion criteria: normal hearing, no developmental learning disorders or dyslexia, no psychiatric disorders, no obvious disorders of visual processing, and aphasia type and severity that enable word repetition that was an integral part of the learning task. Basic background information of the participants with aphasia is given in Table 1 and information

on their cognitive-linguistic status in Tables 2 and 3 as well as on pp. 28–30. The cognitive-linguistic analyses are based on assessments described on pp. 30–31.

Table 1

Background information on the participants with aphasia. Post-onset time refers to the time point when the core AFE novel word learning experiment was initiated with the participant. The participants are listed in a descending rank order of learning and maintenance outcome in the AFE core experiment.

Participant	Post-onset time	Etiology of aphasia	Age in years	Gender	Education level or years	Mother tongue	Study
AA	2 years 9 months	SAH & infarct	60	female	15	Finnish	IV
TS	7 years	MCA infarct	49	female	14	Finnish	III
LL	4 years 6 months	MCA infarct	62	female	10	Finnish	II
QH	1 year 10 months	sinus venous thrombosis; left ICH	59	male	university degree	English	I
AR	15 years	SAH & infarct	59	female	9	Finnish	II
IU	2 years 8 months	multiple left infarcts	67	male	university degree	English	I

AOS, Apraxia of Speech; ICH, intracerebral hemorrhage; MCA, middle cerebral artery; SAH, sub-arachnoid hemorrhage

The healthy control participants of Study I (a 59-year-old and a 71-year-old male) and Study II (a 63-year-old and a 64-year-old female) were matched with the corresponding participants with aphasia with regard to age, gender, education, and ethnic background. For Study III, we recruited a control group consisting of six healthy individuals (50 to 64-year-old, one male, comparable education level), two of which were those that participated in Study II. In Study IV, separate control groups were used in the behavioral part and the neuroimaging part of the study. The behavioral control group (59 to 64-year-old, one male, comparable education level) included the same individuals as in Study III without the youngest, 50-year-old control participant. The neuroimaging control group consisted of seven healthy females (56 to 64-year-old, wide range of educational levels). Recruiting a new control group for the

Table 2.

Information on the aphasic participants' performances on selected language measures. Composite measures are presented either as (a) mean percentiles (%ile, obtained from the standardized Finnish version of the Boston Diagnostic Aphasia Examination) or as (b) aphasia quotients (AQ, obtained from Western Aphasia Battery). The distribution of errors in confrontation naming has been calculated either from the Boston Naming Test or the Philadelphia Naming Test.

Participant	Aphasia type, severity	Auditory comprehension (composite measure)	Naming (composite measure)	Accuracy in confrontation naming	Confrontation naming error distribution (% of all errors)	Repetition (composite measure)	APE learning outcome at term maintenance at 8 weeks post	Study
AA	fluent, 2	30%ile	47%ile	BNT, 19/60 (32%)	sem 27%, phon 46%, other 27%	23%ile	a) normal learning, b) normal maintenance	IV
TS	nonfluent, 3	70%ile	67%ile	BNT, 18/60 (30%)	sem 14%, phon 34%, other 52%	30%ile	a) normal learning, b) good maintenance but variation by modality	III
LL	nonfluent, 3	83%ile	50%ile	PNT, 24/60 (40%)	sem 3%, phon 72%, other 25%	30%ile	a) good learning, needs cueing b) moderate maintenance, needs cueing	II
QH	fluent, 4	9.9 (AQ)	7.4 (AQ)	PNT 160/175 (91.4%)	sem 59%, phon 7%, other 34%	8.2 (AQ)	a) moderate learning, b) poor maintenance	I
AR	nonfluent, 2	45%ile	37%ile	PNT 25/60 (41.7%)	sem 29%, phon 11%, other 60%	27%ile	a) moderate learning, needs cueing b) poor maintenance	II
IU	fluent, 4	8.6 (AQ)	7.3 (AQ)	PNT, 146/175 (83.4%)	sem 45%, phon 3%, other 52%	9.1 (AQ)	a) moderate learning, b) poor maintenance	I

%ile, percentile; APE, Ancient Farming Equipment; AQ, aphasia quotient; BNT, Boston Naming Test; phon, phonological; PNT, Philadelphia Naming Test; sem, semantic

Table 3

The cognitive neuropsychological impairment profile of the aphasic participants and assessments utilized in measuring their lexical-semantic and phonological skills. The performance has been labelled as follows: +, performance within normal limits; -, impaired performance at 2 SD below normal mean or lower. For the experimental tests, the comparison has been made to normal range. Some assessments were not administered to all participants due to missing test version in English/Finnish.

	Participants					
	AA	TS	LL	QH	AR	IU
<u>Lexical-semantic processing</u>						
Pyramids and Palm Trees (written)				+		+
Peabody Picture Vocabulary Test				+		+
Lexical comprehension (TALSA)	-	+	+	+	-	-
Sentence comprehension (TALSA)				+		-
Synonym judgements (TALSA)	-	-	-	+	-	-
Category judgements (TALSA)	-	+	+	+	-	+
Semantic probe (TALSA)				+		-
Odd-one-out (pictures, experimental)	+	+	+		-	
Odd-one-out (words, experimental)	-	-	-		-	
50-picture classification (experimental)	+	-	+		-	
<u>Phonological processing</u>						
Rhyme judgements (TALSA)	+	+	+	+	-	-
Word repetition (TALSA)	-	+	-	+	-	-
Nonword repetition (TALSA)	-	+	-	+	-	-
Phonological probe (TALSA)				+		-

TALSA, Temple Assessment of Language and Short-Term Memory In Aphasia.

neuroimaging study, planned after recruiting the original control group, was necessary as several of the original behavioral control participants were either unavailable or their eyesight without glasses was too poor for viewing the visual material of the experiments.

The English-speaking participants (PWA and healthy control participants) were recruited from the participant register of the Eleanor M. Saffran Center for Cognitive Neuroscience at Temple University, Philadelphia, U.S.A. The Finnish-speaking participants were found through the local stroke association and local speech and language therapists. The healthy controls were recruited from various sources. All participants were given information on the study in written and spoken form, and they signed a written informed consent. The studies were approved by the Ethics Committee of the Hospital District of Southwest Finland (studies

conducted in Finland) and the Ethics Committee of Temple University (the study conducted in the U.S.A).

4.1.1 The aphasic participants of Study I

Participant QH had suffered a sinus venous thrombosis and a left intracerebral hemorrhage (ICH) with significant temporal bleed. His aphasia was classified as mild (see Tables 2 and 3 for the cognitive-linguistic profile). In lexical retrieval, QH demonstrated difficulty in accessing the phonological forms of words. There were no effects of word frequency or length on word retrieval. He often reported tip-of-the-tongue state, produced semantic errors and series of retrieval attempts with repeated approximations to the target. QH's lexical-semantic abilities were spared and he excelled in verbal span tasks. He could repeat words and nonwords accurately and did well in other tasks measuring phonological processing.

Participant IU had multiple post-stroke ischemic left hemisphere lesions that had left him with mild aphasia. IU had impaired lexical-semantic and phonological language processing (see Tables 2 and 3 for details). His naming error profile with very few phonological errors indicated difficulties in accessing phonological word forms. IU was impaired in all tests measuring phonological processing. His repetition of nonwords was compromised with approximately 27 % accurate responses. Overall, participant IU demonstrated a more severe and extensive language processing impairment than participant QH. Also most of his verbal span measures were lower than those of QH.

4.1.2 The aphasic participants of Study II

Participant LL had suffered a left MCA infarction with a mainly frontal lesion including Broca's area, precentral gyrus and insular cortex. Basal ganglia and hippocampus were spared but dorsal parts of the left medial temporal lobe were possibly affected. LL demonstrated symptoms of Broca's aphasia with a severity rating of 3 in the standardized Finnish version of the Boston Diagnostic Aphasia Examination (BDAE; Laine, Niemi, Koivuselkä-Sallinen, & Tuomainen, 1997). However, she produced longer phrases and a wider range of grammatical structures than is typical of Broca's aphasia. In summary, the background assessment data suggested that LL suffered from post-semantic output impairments that led to mainly phonological errors in all production tasks including repetition, as well as articulation problems due to apraxia of speech (AOS). Her ability to maintain phonological representations in verbal STM and encode phonological word forms was clearly deficient.

However, her lexical-semantic abilities were relatively well preserved with good comprehension.

Participant AR had suffered a sub-arachnoid hemorrhage (SAH) caused by an aneurysm of the left internal artery. The hemorrhage had led to a vasospasm resulting in an extensive, post-surgery infarction of the left hemisphere, with subsequent aphasia and hemiparesis of the right side of the body. The latest computer tomography (CT) scan (10 years post-onset) showed an extensive left-sided fronto-parieto-temporal damage. A scattered lesion was observed throughout most of the temporal lobe and the inferior frontal gyrus. There was a more uniform hypodensity in the parietal lobe, extending anteriorly up to the precentral gyrus. The left temporal pole and possibly all of the left hippocampus were abolished. Moreover, the left basal ganglia and especially the left thalamus were affected. AR's aphasia type corresponded to the "mixed non-fluent" type with a severity rating of 2. AR's auditory comprehension was more impaired than is typically observed in Broca's aphasia. Taken together, AR had multiple deficits in language processing, including impaired phonological abilities and a milder lexical-semantic processing impairment. The activation and maintenance of both semantic and phonological representations was affected, resulting in language comprehension and production impairments. AR's naming error profile with vague descriptions and semantic errors indicated impairment in lexical-semantics and phonological output lexicon. Programming of phonemic sequences seemed to be better preserved. Although her oral repetition was much compromised even at single word level, there was no effect of word length on accuracy.

4.1.3 The aphasic participant of Study III

Participant TS had suffered a left MCA infarct leading to a massive lesion encompassing the entire temporal cortex and parts of the parietal cortex with somatosensory regions, extending to motor areas, insular cortex, and the inferior frontal gyrus. The lesion included both Broca's and Wernicke's areas. Subcortically, her ischemic lesion reached the left nucleus lentiformis and the left hippocampal region. TS had been initially globally aphasic. At the time of this study, TS's language profile corresponded to Broca's aphasia (severity rating 3) with more severe impairment in language production and relatively better preserved language comprehension. Her spontaneous speech was non-fluent and consisted of relatively short utterances with restricted syntax. She exhibited mild symptoms of AOS. TS's profile of spared and impaired abilities could be attributed mainly to a post-semantic impairment, which

may have involved both the phonological output lexicon (indicated by her error profile and effect of word frequency on accuracy in production) and the programming of phonemic sequences (nonword errors in all output tasks, length effect in repetition). Moreover, TS had a post-semantic impairment in writing including the programming of grapheme sequences.

4.1.4 The aphasic participant of Study IV

Participant AA had suffered a sub-archnoid hemorrhage caused by a large, ruptured aneurysm located in the first bifurcation of the left middle cerebral artery (MCA). The hemorrhage and subsequent infarction had left her with an extensive lesion encompassing the left superior and middle temporal gyri, severely damaging the temporo-parietal and temporo-frontal white-matter fibers of the AF, but sparing the left inferior and medial temporal areas including the hippocampus and the parahippocampal gyrus. The language deficits in AA were in line with her lesion locus. AA had initially been globally aphasic but at the time of testing exhibited moderate aphasia with fluent speech, morpho-syntactic errors in language production, severe anomia, very poor word repetition with some semantic errors, and an inability to repeat pseudowords. Her symptoms were in line with the criteria for deep dysphasia. In contrast, she could read quite well single words and pseudowords, attesting to functional orthography-to-phonology conversion. In summary, participant AA's lexical semantic processing was slightly impaired with compromised auditory comprehension. In tasks including both auditory and written test versions, her performance tended to be better in the orthographic than auditory modality. Phonologically based impairment in output was suggested by her naming error profile and the observed word length effect in repetition.

4.2 Materials

4.2.1 Cognitive-linguistic background tests

A number of background tests were administered to determine the cognitive-linguistic status of the participants with aphasia. For English-speaking participants with aphasia (Study I), these included the Western Aphasia Battery (Kertesz, 1982), the Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 2001), the Temple Assessment of Language and Short-term Memory In Aphasia (TALSA; Martin, Kohen, & Kalinyak-Fliszar, 2010), the Philadelphia Naming Test (Roach, Schwartz, Martin, Grewal, & Brecher, 1996), the Pyramids and Palm Trees Test (Howard & Patterson, 1992), the Peabody Picture Vocabulary Test (Dunn & Dunn, 1997), and the Comprehensive Trail Making Test (Reynolds, 2002). The Finnish-speaking participants with aphasia (Studies II-IV) were administered the standardized Finnish version

of the Boston Diagnostic Aphasia Examination (BDAE; Laine, Niemi et al., 1997), the Finnish adaptation (Tuomiranta, Laine, & Martin, 2009) of the TALSA (Martin et al., 2010), the Corsi Block Tapping Task (De Renzi & Nichelli, 1975), and the Trail Making Test (TMT; Poutiainen, Kalska, Laasonen, Närhi, & Räsänen, 2010). Also the standardized Finnish version of the BNT (Laine, Koivuselkä-Sallinen, Hänninen, & Niemi, 1997) was administered to participants AA and TS. In addition, experimental tasks were used to further assess the participants' lexical-semantic abilities. These included two odd-one-out judgment tasks using pictures and words (Laine, Kujala, Niemi, & Uusipaikka, 1992; Renvall, Laine, Laakso, & Martin, 2003) and a 50-picture classification task (Laine et al., 1992). AA and TS were probed in reading and repeating 90 words and pseudowords of varying length and frequency (Renvall et al., 2003). AA was administered supplementary tasks in word-picture matching (Laine et al., 1992), category-specific word-picture matching (Laine, Schmied, & Trefzer, 1998), lexical decision both auditorily and orthographically (Karttunen & Renvall, 2005), repeating words varied for length and imageability (Renvall & Tuomiranta, 2010), as well as the 36-item Token Test (Klippi, 1978). Furthermore, participant LL was administered additional speech motor tasks to confirm her AOS as defined by Duffy (2005). Cognitive-linguistic background tests were not re-administered after the learning experiments.

The healthy control participants were first interviewed to exclude difficulties in language development, learning, reading or writing. They were also tested with selected language and verbal span measures to ensure their language processing abilities were unimpaired. For the English-speaking control participants these tests included the BNT (Kaplan et al., 2001), phonological and semantic fluency tasks, narration, as well as semantic and phonological probe span tests of the TALSA (Martin et al., 2010). The Finnish-speaking healthy control participants were administered the BNT (Laine, Koivuselkä-Sallinen, et al., 1997), phonological and semantic fluency tasks, narration, the semantic odd-one-out task using pictures and words (Laine et al., 1992), and verbal span tasks of the Finnish version of the TALSA (Tuomiranta et al., 2009).

4.2.2 Training stimuli

All of the studies (I–IV) employed the same core set of 20 training stimuli. The core training set consisted of black-and-white drawings of AFE items (Laine & Salmelin, 2010) paired with their unfamiliar but real Finnish names (Studies II–IV). In study I, the original Finnish names were modified to follow English phonotactics. The training set was divided into two subsets

of ten referent–name pairs to be used in two different learning conditions: the *Name* condition where the participants were presented only with a name, and the *NameDef* condition where the name was coupled with a short definition of the referent. Sample items of both learning conditions are provided in Figure 2. The two subsets were comparable in terms of complexity of the drawings (based on Grönholm-Nyman et al., 2010) as well as grapheme/phoneme length of the names (range 4–8), syllabic length of the names (range 2–3), bigram frequency of the names (derived from a large unpublished corpus of written Finnish by the WordMill lexical search program of Laine and Virtanen (1999), and number of orthographical/phonological neighbors of the names (items one grapheme/phoneme away from the name). The definition given for the *NameDef* items was a single sentence describing the object or its use. In Study I carried out in the U.S.A, some changes were made to the definitions in order to make the use of the equipment more familiar in the different culture.

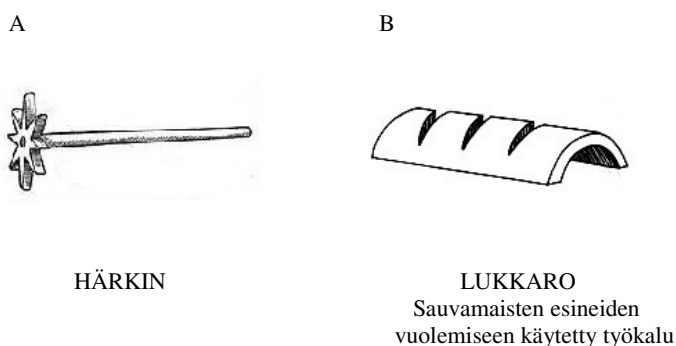


Figure 2. Sample AFE items of *Name* (A) and *NameDef* (B) learning conditions (Studies II–IV). The corresponding names used with English-speaking participants (Study I) were *varkin* (A) and *lungkero* (B), and the definition for (B) a tool used for carving objects with a cylinder shape.

Additional stimuli were introduced in studies III–IV. Bisyllabic pseudowords (4–6 phonemes/graphemes) were paired with additional AFE items to provide supplemental material to different learning conditions in studies III–IV. The training sets were balanced across the conditions in terms of image complexity and average bigram frequency of the pseudowords. For all participants, a given selection of items was administered only in a single task.

Furthermore, relearning of familiar item–word pairs was probed in study III. The materials consisted of color photographs of plants, animals, household objects, needlework items and music instruments, either as simple object pictures (naming task) or as in the context of an action (sentence production task). The target words of this experiment were 2–6 syllables and 5–14 phonemes/graphemes long, and 69% of them were compounds.

For the functional neuroimaging performed in Study IV, additional stimuli were needed. Two different tasks were introduced to study the neural underpinnings of novel word learning and reading in one participant with aphasia (AA) and seven healthy control participants. The novel word learning task performed in the scanner included ten pairs of a novel AFE drawing and a bi- or trisyllabic pseudoword, as well as ten pairs of matched familiar item–word pairs. For the reading task performed in the scanner, three sets of 48 stimuli were used: familiar written words, written pseudowords following Finnish orthotactics, and words written with an artificial, unreadable font. The three sets were comparable in terms of the amount of visual information in the words.

4.3 Study design

4.3.1 Studies I-II

A pretest was administered to all Finnish-speaking participants prior to the experiment with the core set of AFE items in order to confirm that the items and their names were in fact unfamiliar to the participants. During the pretest, the participants were asked to recall the names or any other information they might have of the objects. Knowing one of the items by name was accepted, however, and in that case that item was left out in the results of the participant.

The first two studies had an identical design (see Figure 3 for the study outline). After the pretest and the cognitive-linguistic background assessment were completed, the participants were trained to learn 20 novel words (in Finnish unfamiliar real words and in English pseudowords) paired with unfamiliar, pictured AFE items. Four training sessions of 45–60 minutes were administered on separate days, during a time period of 9–13 days (Study I) or 8–12 days (Study II).

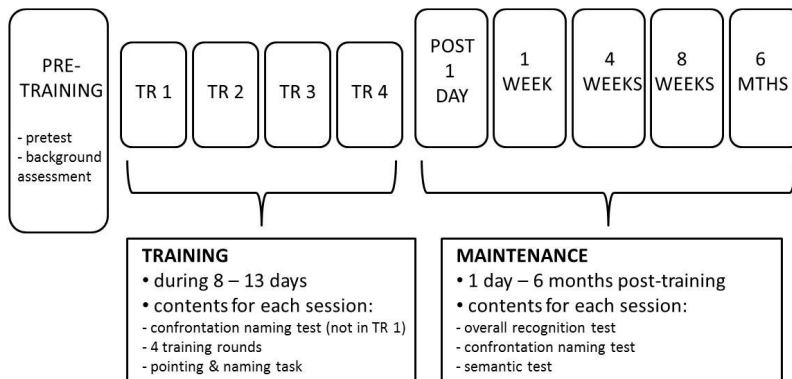


Figure 3. Study outline of the core AFE novel word learning experiment (Studies I–IV)

During the training sessions, the participant was always presented with five training cycles with the to-be-learned material with the instruction to learn the names. The first four training cycles presented the material one item at a time in a pseudo-randomized order. The participant was to look at a drawing of an item and its written name appearing on the computer screen for 12 seconds. The name was spoken aloud once by the administrator and the participant was asked to repeat the name. For the *NameDef* condition items, the administrator read aloud both the name and the semantic definition, but the participant was only asked to repeat the name. In case of an error in repetition, the participant was given feedback and another chance to repeat. After the four training rounds were completed, the participant was presented with a naming task. All of the trained items were shown to the participants simultaneously on the same test sheet. The test administrator pointed to the items one after other and asked the participant to name the items. When needed, the word-initial syllable was provided as a cue. In case of incorrect or no response, the participant was provided with the correct response. Therefore, this naming task served as a fifth training round for the participant. The participant trained each item altogether 20 times.

Learning to name was measured with confrontation naming tasks in the beginning of training sessions 2–4. The items were presented in pseudorandomized order one at a time. A similar naming task was presented at the post-training test session one day after the last training sessions, and further follow-ups 1, 4, and 8 weeks as well as 6 months post-training. A syllable cue was provided in case of incorrect or no response. Learning success was measured

by naming accuracy using a liberal criterion where responses differing from the target by one phoneme/ grapheme were also counted as correct.

In addition to confrontation naming, overall recognition of the trained items and recall of the semantic information that had been provided for half of the items were probed in the post-training sessions and all further follow-ups. The overall recognition task started each follow-up test session. During the task, the participant saw the 20 trained item drawings with 20 comparable drawings not presented during the training. The items were presented one at a time in pseudorandomized order, and the participant was to decide whether the item was a trained one or not. The distracter items were kept the same across the follow-up. After this task, the naming probe was administered. As the last task during each follow-up, the trained items were shown once more with a question “was there a definition for this item?” If the participant responded “yes”, he/she was prompted to recall the definition as well as possible. This task was designed to measure incidental learning of semantic content as the instruction given during training was to learn the names.

The participants were instructed not to try to memorize the trained names at home, for example, by writing the names down or trying to find information about the targets from books.

4.3.2 Study III

Participant TS was administered a modality-specific learning task after the initial learning experiment with the 20 AFE items (see Table 4 for the different experiments administered in Studies I–IV). The stimuli in this second task were pictured AFE items (not used in the previous experiment) paired with bisyllabic pseudowords. During the task, TS went through training with four different modality combinations, learning 15 referent–pseudoword pairs in each. Auditory (AUD) and orthographic (ORT) input, and spoken (SPO) and written (WRI) output were factorially combined to create the modality combinations: AUD–SPO, ORT–WRI, ORT–SPO, and AUD–WRI (administered in this order).

There were two training sessions per learning condition, always administered on two consecutive days. The four learning conditions were spaced one week apart from each other. During each learning condition, TS was presented with a new set of 15 novel to-be-learned

Table 4.

The different experiments administered in Studies I-IV

Task	Training targets	Study I	Study II	Study III	Study IV
Long-term novel learning	20 AFE items + 20 unfamiliar words (in Study I, pseudowords)	all participants	all participants	all participants	all participants
Short-term novel learning by input and output modality	60 AFE items + 60 pseudowords	-	-	Participant TS	-
Short-term novel learning by input modality (auditory or orthographic)	20 AFE items + 20 pseudowords	-	-	-	Participant AA
Long-term word relearning at home	42 familiar items + 42 real words	-	-	-	Participant AA

referent–pseudoword pairs. The set was trained over two sessions that both included four training cycles. During auditory input, TS heard the pseudoword spoken by the administrator as she looked at the picture on the computer screen. For orthographic input, TS looked at the written pseudoword, shown under the picture for one second to match the presentation time of auditory input. In spoken output TS was to repeat or read aloud the pseudoword, and during orthographic output, the task was to silently write the pseudoword. No feedback was provided.

Learning was probed after the second and the final fourth training cycle of each session. Either a spoken or a written confrontation naming task was utilized, according to which of these output modalities was used during learning. An additional retention test was administered in the beginning of the second training session of each learning condition. One phoneme/grapheme distortion or substitution was accepted in otherwise accurate responses.

4.3.3 Study IV

Behavioral experiments

Participant AA with aphasia and the five healthy control participants took part in a similar AFE learning experiment as in studies I–II. However, after completing the first learning experiment with the 6-month follow-up, AA was also administered a short-term learning task where she was to learn to name 20 new unfamiliar AFE items that carried bisyllabic pseudoword names. This new learning task was administered to explore modality effects in

novel word learning. The 20 items were divided into four subsets of five items, and each subset was trained over two consecutive days. New subsets were introduced on separate weeks. This task was presented with an ABBA design, where A experiments utilized only auditory and B experiments only orthographic input during the training. During the A experiments, participant AA saw an item, heard the name, and tried to repeat it. During the B experiments, the item was presented with the written name and AA was prompted to read the name aloud. AA was not given feedback on her production accuracy or corrected during the tasks. There were ten training cycles during all training sessions, and participant AA's ability to name the items was probed after each training cycle. In addition, an extra retention test always started the second training session of each subset. Learning success was measured by naming accuracy using the liberal criterion.

The final word relearning experiment for AA was a self-administered home-training program. She selected herself the semantic categories from which the training targets were chosen, according to her own interests and needs. Altogether 63 items and their names were divided into 42 trained items, and 21 control items that would not be trained (item groups comparable in terms of word frequency, length, and the semantic categories employed). Three baseline naming probes and two baseline sentence production probes ensured that AA had no access to the word forms, albeit she could give semantic information of the items (in form of circumlocutions and descriptions). AA practiced at home with a computer program that proceeded automatically and presented the items for 12 seconds together with the written name. AA was to look at the image, read the name aloud, and keep a training diary. She went through 36 training cycles during 18 days, after which she was confident about having learned to produce the names. Post-training tests were administered for both confrontation naming (the images used during pre-training tests and during training) and sentence production with the same target words (the images introduced during pre-training tests). Maintenance of the learned words was probed at 1, 4, and 9 weeks post-training. Learning success was measured by accuracy using the liberal criterion.

Neuroimaging experiments

Participant AA and seven healthy control participants took part in two MRI sessions. In addition to anatomical scans, diffusion magnetic resonance imaging (dMRI), and resting-state fMRI, the participants were to perform a novel word learning task and a reading task during fMRI. The novel word learning task resembled closely the one performed as the first

experiment in each study (I–IV). The participants saw a line drawing of an AFE item and a pseudonym shown underneath the drawing. They were to read the name silently and try to memorize it. In addition to the AFE blocks (experimental condition), the participants were presented with two control conditions: blocks of familiar pictured items paired with their real names and rest with a fixation point. The familiar items were selected such that they were consistently able to be named by participant AA and the healthy control participants. The other control condition was rest with a fixation point. Ten novel referent-name pairs were trained six times during the experiment, and learning was measured after the session with a spoken confrontation naming task. Another task performed in the MRI scanner measured blood oxygen level dependent (BOLD) responses during a reading task. The participants were shown real words and pseudowords (the experimental conditions). As for the control conditions, the participants were shown strings written with a meaningless false font and a fixation point. The task was to try to read the words silently. Reading accuracy was probed after the session.

4.4 MRI imaging methods

The neuroimaging part was performed with a Siemens Magnetom Verio 3T MRI-scanner at the Turku University Hospital. Structural images comprised a conventional high-resolution T1 image and a dMRI data set. Structural images were followed by functional BOLD images obtained with an echo planar T2-weighted gradient echo sequence. The MRI data were collected in two sessions. The first one included a T1-weighted structural sequence and a resting-state fMRI registration. The second one comprised structural (T1 and dMRI) sequences and the two fMRI tasks.

4.5 Data analysis

4.5.1 Behavioral data

All linguistic background assessments and training probe tests were transcribed from audio files. The phonological proximity of the responses was determined on the basis of the last response given by the participant. The responses were categorized into fully accurate responses (stringent criterion), responses differing from the target with one phoneme/grapheme (liberal criterion), and accurate responses given after a syllable cue (liberal criterion + cue). For analysis of incidental learning of semantic definitions (Studies I–II), we calculated the percentage of target content words from the definition or synonyms of these content words that were accurately recalled by the participant.

In the learning experiments, the McNemar test or the exact binomial test was utilized in comparing the participants' naming results to the initial zero-level naming performance (Siegel & Castellan, 1988). The aphasic participants' naming performance and recall of semantic definitions were compared to their matched controls' performances with the Mann-Whitney test (Studies I–II). The range of naming performance in a small group of healthy control participants was used as the reference value in studies III–IV. A modified *t*-test (Crawford & Garthwaite, 2002) was utilized in Study IV for comparing the aphasic individual to a small group of healthy control participants, and in Study III for comparing the performance of the control participant performing at the lowest level to the other control participants. In studies III–IV that included different learning conditions, the Kruskal-Wallis test, the Mann-Whitney test, and the chi-square test were used within participant in comparing the results achieved in the learning conditions. In analyzing possible effects of word frequency and word length on performance in the background tests, chi-square tests were utilized. In Study III, the Wilcoxon Signed-Rank test was performed in order to compare spoken and written naming in participant TS. The statistical methods applied are summarized in Table 5.

4.5.2 Neuroimaging data

The neuroimaging data consisted of dMRI data as well as the fMRI data collected during reading and word learning tasks using methods described in detail in Tuomiranta et al. (2014). After the preprocessing phase of the dMRI data, whole-brain deterministic tractography was performed. The right-sided AF could be reconstructed while the lesion inhibited the virtual dissection of the left-sided AF using deterministic tractography. The analysis continued with probabilistic tractography where statistically significant activation clusters from the fMRI analysis were used as seed regions.

The fMRI data were first preprocessed. Bilateral hippocampal and parahippocampal regions were chosen as regions of interest (ROIs) for the novel learning task where the contrast of interest was novel word–picture pairs vs. familiar word–picture pairs. Reading pathways were explored via the main contrast (words + pseudowords) vs. false-font. The statistical analysis of the imaging data is explained in detail in Tuomiranta et al. (2014).

Table 5.

Statistical tests administered in Studies I-IV

Specific study aim	Within participant (study)	Across participants (study)
Acquisition and maintenance of phonological (object name) and semantic (object definition) information in associative word learning	McNemar test (I-IV) or Exact binomial test (in case of small n , I-IV)	Mann-Whitney test for pairwise comparisons during follow-up (I-II) Modified independent samples t -test for comparing individual against a group at certain time point (III-IV) Chi-square test or Fisher's exact test for comparing individual against a group at several time points (IV)
Modality-specific effects on short-term associative word learning	Kruskall-Wallis test (4 modality conditions, III) Chi-square test (2 conditions at certain time point, III-IV) Mann-Whitney test (2 conditions at several time points, III-IV)	
Neural underpinnings of modality-specific learning	Voxel-based t -statistics (IV)	Modified independent samples t -test for comparing individual against a group (IV)

5 RESULTS**5.1 Study I**

The participants, QH, IU and their healthy controls, showed learning of active new vocabulary as measured by spontaneous, accurate confrontation naming of the novel items. Figure 4 depicts the spontaneous naming results and Figure 5 the phonologically cued naming results of all aphasic participants across the four studies, including QH and IU. Similarly, the spontaneous naming results of all healthy control participants are depicted in Figure 6 and all phonologically cued results by the control participants in Figure 7. The learning reached statistical significance (i.e. recall of at least 5/20 names) at the beginning of the fourth training session in QH and their matched control participants, and at one day post-training in IU. None of the participants learned to name all of the novel items. Additional results showed an effect of word length on learning to name novel referents, with the aphasic participants learning better shorter than longer novel words. This length effect did not emerge among the healthy control participants. The long-term maintenance of the newly learned vocabulary showed variation in the healthy control participants but stayed at statistically significant levels (i.e.

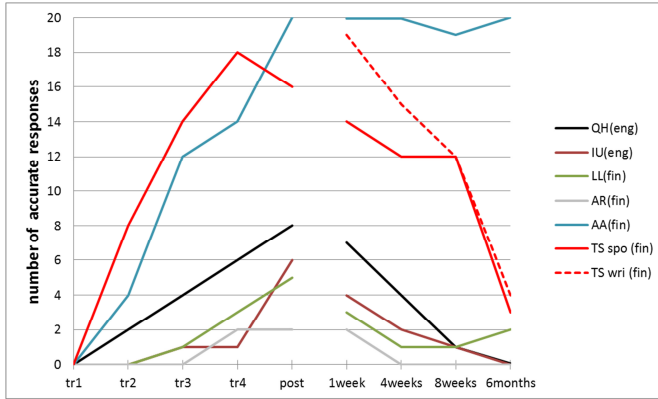


Figure 4. Naming of 20 novel AFE items in all aphasic participants across Studies I–IV. The number of spontaneously produced accurate responses (one phoneme deviance to the target accepted) during the training period and the follow-up. Participant TS has two separate lines during the follow-up as she was tested for both spoken and written naming. Eng, English-speaking; fin, Finnish-speaking; post, post-training session; spo, spoken naming; tr, training session; wri, written naming.

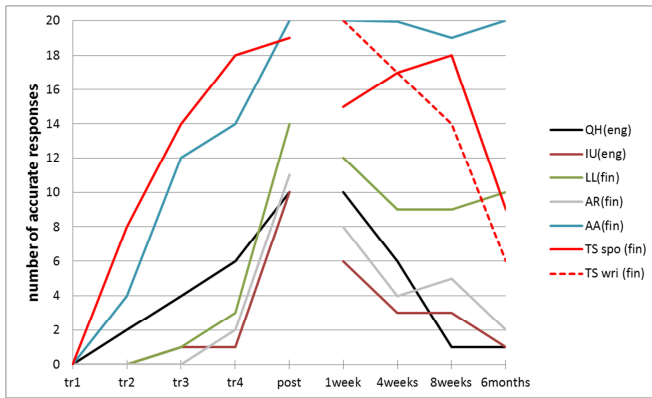


Figure 5. Naming of 20 novel AFE items in all aphasic participants across Studies I–IV. The number of spontaneously produced accurate responses (one phoneme deviance to the target accepted) during the training period and the follow-up, including also accurate responses given after phonological cueing (cueing provided from the post-training session onwards). Participant TS has two separate lines during the follow-up as she was tested for both spoken and written naming. Eng, English-speaking; fin, Finnish-speaking; post, post-training session; spo, spoken naming; tr, training session; wri, written naming.

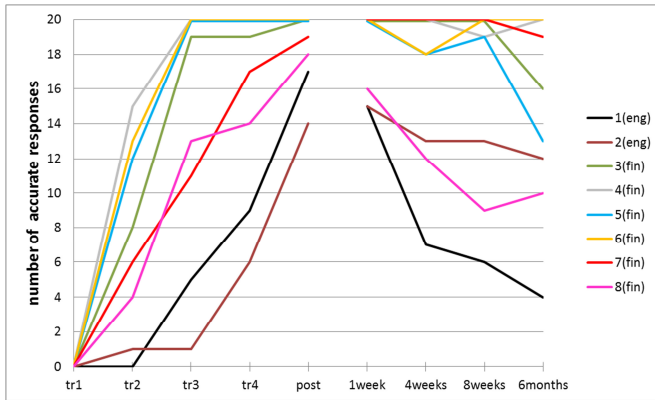


Figure 6. Naming of 20 novel AFE items in all healthy control participants across Studies I–IV. The number of spontaneously produced accurate responses (one phoneme deviance to the target accepted) during the training period and the follow-up. Control participants 1-4 are matched to aphasic participants QH (control participant 1), IU (control participant 2), LL (control participant 3), and AR (control participant 4) according to mother tongue, age, gender, education and ethnic background. Eng, English-speaking; fin, Finnish-speaking; post, post-training session; spo, spoken naming; tr, training session; wri, written naming.

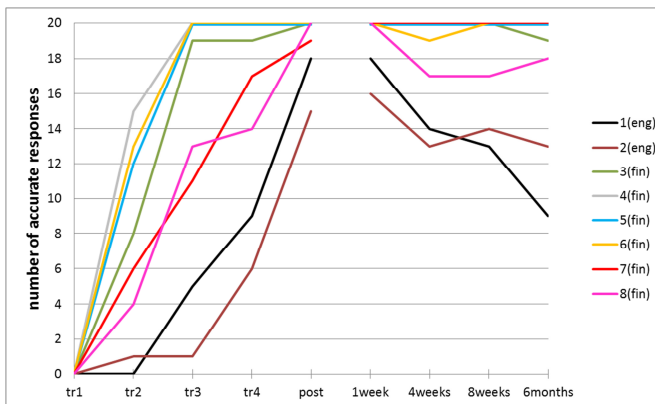


Figure 7. Naming of 20 novel AFE items in all healthy control participants across Studies I–IV. The number of spontaneously produced accurate responses (one phoneme deviance to the target accepted) during the training period and the follow-up, including also accurate responses given after phonological cueing (cueing provided from the post-training session onwards). Eng, English-speaking; fin, Finnish-speaking; post, post-training session; spo, spoken naming; tr, training session; wri, written naming.

recall of at least 5/20 names) across the 6-month follow-up. However, one control participant needed cueing at 6 months post-training to reach statistically significant maintenance. In QH and IU, the ability to recall the names either spontaneously or with cueing dissipated by 8 weeks (QH) or 4 weeks (IU) post-training. The overall recognition memory for trained vs. untrained items was good in all participants (100% for all at post-training and at 1 week post, 95%–100% during the later follow-ups). The incidental learning of semantic descriptions as measured by recall of content words of the target definitions across the follow-up was superior in QH (accuracy varied between 52% and 34%) as compared to IU (variation between 32% and 14%). The healthy control participants recalled incidentally learned semantic information significantly better than the PWA.

5.2 Study II

The aphasic participants LL and AR showed rather low levels of acquisition of the novel vocabulary as measured by spontaneous confrontation naming. Only LL's one-day post-training naming result reached statistical significance. However, when taking into account phonologically cued responses, AR's results were well above chance at 1 day and 1 week post-training, and LL maintained the newly acquired vocabulary throughout the 6-month-long follow-up by being able to name accurately 9–14 out of the 20 targets. Additional results showed that both aphasic participants learned more easily novel words of the *Name* than the *NameDef* condition. However, the long-term maintenance did not differ between the conditions. The healthy control participants learned all of the novel referent–word pairs and also maintained them at a high level throughout the follow-up. The overall recognition memory for trained vs. untrained items was accurate in all participants at 1 day post-training. After that, only AR showed decline in overall recognition memory with 65%–73% accuracy rate. Free recall of semantic definitions given for half of the novel items was a very demanding task for both AR and LL (accuracy 0–22%), while the healthy control participants could recall 59–74% of the content words in the definitions across the follow-up period.

5.3 Study III

In the first AFE experiment with 20 novel referent–word pairs, the participant with aphasia, TS, performed within the range of the healthy participants during the learning phase. During the follow-up, her maintenance of the novel referent–word pairs differed to a great extent between the two output test modalities. According to the stringent criterion, TS's maintenance

in spoken naming was clearly weaker than in the healthy control participants, and dropped to nonsignificant levels at 8 weeks post-training. In written naming, however, TS performed within the range of the healthy control group up to 8 weeks post-training. According to the liberal + cue criterion, both spoken and written naming stayed above chance level up to 6 months post-training. TS's overall recognition memory for trained vs. untrained items was accurate, but her recall of semantic content was minimal, even when she was given a probe test in written form which she herself requested. At one day post-training, TS recalled 6% of the semantic content in the spoken test (variation in the control group at post-training 53–81%) and 11% in the written one (not administered to the control group).

In the second experiment, TS showed some acquisition of novel referent–pseudoword pairs in all of the four different input–output modality combinations. However, she was statistically significantly better in her learning performance in the modality combinations that utilized orthographic input than in the ones that employed auditory input. Output modality during learning did not have a statistically significant effect on the learning outcomes. Of the four different input–output modality combinations, the one employing orthography as both the input and output channel led to the best learning results. An intriguing inconsistency between TS's linguistic profile and her learning profile emerged: TS showed more accurate repetition than reading aloud in the cognitive-linguistic background tests as well as during the actual training rounds of the learning experiment. Nonetheless, she benefited more from written than auditory input when learning novel words.

5.4 Study IV

Participant AA acquired novel referent–word pairs somewhat slower than the healthy control group in the first AFE novel word learning task, even though not differing statistically significantly from the slowest learning healthy participant. Interestingly, AA acquired all of the novel referent–word pairs and recalled them spontaneously throughout the 6-month-long follow-up, outperforming four of the five healthy controls in the recall task. AA's overall recognition memory for the trained items was accurate, but she was often unsure whether the items had been accompanied with a definition. At one day post-training, she recognized 70% of the *NameDef* items as ones having been accompanied with definitions, while the corresponding results were 80% at 1 week post, 40% at 4 weeks post, and 30% at 6 months post. In healthy Finnish-speaking control participants, the variation for success in recognizing *NameDef* items as ones having been accompanied with definitions was 80–100% at one day

post-training, 85–100% at 1 week post, 75–100% at 4 weeks post and 85–95% at 6 months post. At one day post-training, AA's semantic recall accuracy (i.e. correct content words of the definitions) was merely 14%.

Based on AA's own comments on her learning process, the written word form seemed important for her to successfully learn the novel words. The effects of input modality were studied in the second, short-term AFE learning task where AA learned novel referent–pseudoword pairs either with auditory or orthographic input. Learning from orthographic input was clearly superior to learning from auditory input (Mann-Whitney Test $U = 33.50$, $Z = 4.69$, $p < .0001$). During the orthographic training rounds of the learning task, AA read aloud at 94% mean accuracy. Her mean repetition accuracy during auditory training was significantly lower, 13%. AA did not receive feedback on the accuracy of performance but showed awareness of her errors in repetition. She tried to correct herself which led to a wide variation of erroneous forms of the pseudowords, rather than stabilized, recurrent errors.

The third learning experiment called AA to re-learn familiar but inaccessible words through a self-administered, computer-assisted training program. Learning success was measured by word retrieval in a confrontation naming task but also with a sentence production task using action pictures as prompts. From a zero baseline naming performance, AA showed full acquisition of the trained target words in both word retrieval contexts but no generalization to matched, untrained words. During the 9-week-long follow-up, her word retrieval accuracy declined to some extent, but in most instances the lower score could be explained by minor phonological errors in production rather than as a full loss of the learned item. The relearned words remained available to AA in confrontation naming and sentence production tasks.

In the neuroimaging study administered to AA and seven healthy control participants, the aim was twofold: to examine brain activity patterns and connectivity during a novel word learning task resembling the ones administered to AA earlier, and during word reading, as the orthographic input channel had been found to be the key to successful word learning for AA. The dMRI analysis confirmed that the direct segment and the posterior indirect segment of AF were disconnected in AA's left hemisphere, while the anterior indirect segment of AF could be reconstructed using probabilistic tractography. In the right hemisphere, an intact AF could be visualized.

AA showed certain differences in brain activity patterns in relation to the healthy control group. In the reading task, AA activated significantly more the right middle temporal and angular gyri than the healthy control group did (see Fig. 8 for the fMRI results for reading in AA vs. the healthy control group). On the other hand, the controls activated significantly more the left middle temporal and lingual gyri during reading. Moreover, AA showed left-sided reading-related activation in the medial-inferior occipital region, fusiform gyrus, and the middle as well as the superior frontal gyri, but tractography indicated that these posterior and frontal activation sites were disconnected from each other. A laterality index (LI) was calculated for each participant for a region of interest (ROI) comprising of the superior, middle and inferior temporal gyri. This was done in order to obtain further information on the functional hemispheric differences between AA and the control participants during reading. A statistically significant difference was detected between AA's and the control group's LIs. At least 90% of AA's reading-related temporal lobe activation took place in the right hemisphere while the control group showed left-lateralized activations except for one participant with bilateral activation.

In the novel word learning task performed in the MRI scanner, AA and the control group showed extensive activation including the middle occipital regions, fusiform gyrus, hippocampus, middle and precentral frontal gyri, as well as the superior temporal lobe. Compared to the control group, AA showed more activation in the right middle temporal gyrus, the right inferior temporal region/fusiform gyrus, and the left posterior hippocampal gyrus. On the other hand, the healthy control group activated more the left superior temporal gyrus, the right medial temporal region, and the frontal areas.

As the tasks were performed covertly in the scanner, the participants' performance was examined behaviorally after the fMRI experiments. The healthy control participants performed flawlessly in the overt reading tasks. AA's accuracy rate was 100% for the words and somewhat lower for the pseudowords (90% according to the liberal criterion and 65% according to the stringent criterion). The novel word learning task was particularly demanding with few, very short exposures. AA did not show any overt learning in this task while the healthy control participants learned to name 1–5 out of 10 novel referents.

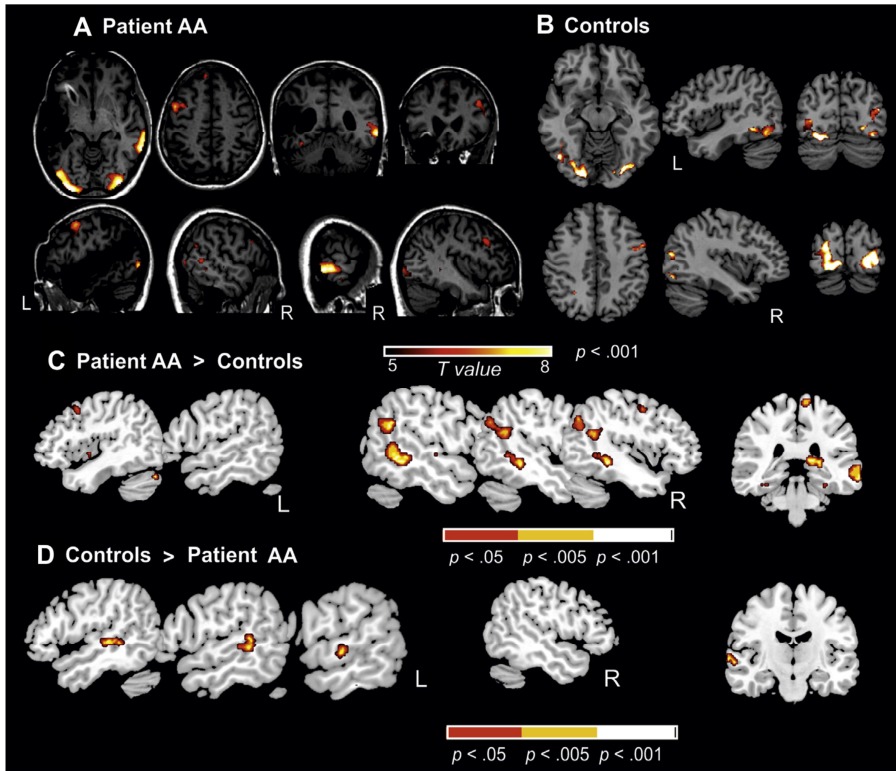


Figure 8. The fMRI results for the reading task performed in the scanner by the participant AA and a group of seven healthy control participants. (A) depicts reading-related activation in AA, and (B) in the control group. The cortical regions activated statistically significantly to a higher degree in AA than in the control group are visualized in (C) and regions activated less in AA than in the control group are shown in (D).

6 DISCUSSION

The main aims of this dissertation were to (a) explore associative learning and long-term maintenance of novel word–novel referent pairs in PWA and matched healthy controls, (b) compare the novel word learning and maintenance performance of participants with aphasia in relation to their lexical-semantic abilities and other language processing and verbal STM impairment profiles, (c) study the effects of learning modality on novel word acquisition, (d) examine the neural underpinnings of successful novel word learning in one aphasic individual, and (e) explore learning and long-term maintenance of semantic definitions in PWA and matched healthy controls.

The key findings were the following:

- (a) PWA showed a very wide variation in their associative learning ability and maintenance of novel vocabulary, from very limited capacity up to levels comparable to the performance of healthy control participants.
- (b) PWA with relatively intact lexical-semantic processing showed superior novel word learning and incidental learning of semantic definition compared to PWA with lexical-semantic impairments. Two aphasic individuals learned novel words very efficiently in spite of poor phonological STM that has been suggested to carry a central role in word learning.
- (c) Different input modalities utilized during novel word learning led to different learning results. For the two aphasic participants with the best novel word learning results, written input resulted in stronger learning than auditory input.
- (d) An aphasic individual showed normal novel word learning capacity through reading in spite of a disconnection of the left dorsal speech processing route that has been suggested to play a central role in language learning. In this individual, functional brain imaging revealed that the right dorsal route most probably provided a functional link between the posterior and anterior left-hemispheric regions activated during language tasks. Moreover, the well-preserved word learning ability in this individual could be translated directly into the treatment of her anomia.
- (e) PWA were able to learn semantic definitions incidentally. The variation in incidental semantic learning was wide but did not reach to the level of the healthy individuals.

6.1 Associative learning of novel words and their definitions in aphasia (Studies I–IV)

The focus of the present dissertation was on associative lexical-phonological learning of novel word–novel referent pairs. The novel word learning procedure used with all participants required explicit learning, and the outcomes were measured by an active production task, i.e. confrontation naming, up to 6 months post-training. In addition, the participants heard and saw semantic definitions for half of the novel referents. Incidental learning and the maintenance of these definitions were also probed throughout the follow-up period.

6.1.1 Novel word learning is possible in aphasia but the variation is great

The general learning results of the four studies are in line with previous investigations in showing that chronic aphasia does not render learning novel vocabulary impossible (Grossman & Carey, 1987; Gupta et al., 2006; Kelly & Armstrong, 2009). All of the participants in Studies I–IV showed statistically significant acquisition of novel word–novel referent pairs, at least in the short-term. Also in line with the previous studies, the variation in learning outcomes was very wide. Two participants with aphasia (AA of Study IV, and TS of Study III) reached particularly high levels of learning. Interestingly enough, they performed on a par with their healthy control participants. Comparable levels of novel word learning have not been reported previously in PWA. There was also variability within the learning of the healthy control participants. The observed variation is nonetheless in line with earlier evidence from healthy younger adults (Hultén et al., 2009; Hultén et al., 2010).

Earlier aphasia investigations have not probed long-term maintenance of novel words beyond 3–5 days post-learning except for a single case whose maintenance of novel word–familiar referent pairs¹ was probed with a recognition test at 10 months post-learning (Breitenstein et al., 2004). The present investigations that employed maintenance probes with active production tasks up to 6 months post-learning provided therefore novel information on the learning outcomes of PWA in the long-term. The wide variation of performance detected in learning applied also to the long-term maintenance. While all other PWA declined in their retrieval of the novel words during the maintenance period, the same two cases with the best initial learning results (AA and TS), also maintained the learned vocabulary on a par with healthy controls. While in TS's case this only applied to written responses, AA's spontaneous

¹ This investigation by Breitenstein et al. (2004) is not fully comparable to the present studies, as half of the to-be-learned contents, i.e. all of the referents, were familiar every-day objects.

spoken naming performance was, astonishingly enough, still fully accurate at 6 months post-learning, and she outperformed most of the healthy control participants in spite of her extensive brain lesion and moderate aphasia.

With regard to the neurocognitive mechanisms underlying the wide variation of novel word learning in PWA, lesion localization and extent must play a central role. The integrity of brain structures supporting learning in the short- and long-term (see the CLS model, Davis & Gaskell, 2009; O'Reilly & Norman, 2002) varied also in the present PWA. Lesions in the left-sided cortical language areas can be assumed to affect both the initial encoding of the novel words and the consolidation of the word–referent associations in the mental lexicon. The functionality of the associative learning process, in turn, would hinge upon the integrity of the medial temporal lobe and hippocampal structures (compare to Meinzer et al., 2010). Concerning the status of the medial–inferior structures subserving associative learning and the episodic-lexical interphase of the language learning model of Rodríguez-Fornells et al. (2009), one would have predicted superior learning in participants AA and possibly LL, whereas learning would have been more impaired in AR and TS due to their more extensive left-hemispheric lesions that also reached the medial regions of the brain. The outcomes of word learning in AA and AR followed this prediction. Also LL performed more or less in line with this prediction and learned relatively well the names, albeit she needed a lot of phonological cueing in order to be able to retrieve them. However, TS learned novel words better than one might predict on the basis of her lesion extent. In TS's case, the reason may lie in the lack of structural MRI scans from the chronic stage. In other words, the MRI scan obtained 6 days post-onset may not have given an accurate view of her lesion extent. Similarly, detailed information on the lesions of the two PWA of Study I is unfortunately unavailable. Detailed information on the lesion of participant QH would have been especially interesting, as he learned relatively well while maintenance was relatively poor. Due to the lack of up-to-date MRI data, further conclusions on the lesion–learning relationships cannot be made here, except for Study IV that included neuroimaging of an aphasic individual. As comparable neuroimaging investigations with reported learning in PWA are to date nonexistent (the participants of Morrow, 2006, did not show learning), research is needed to explore the exact relationships between lesion characteristics and encoding, learning, and maintenance of novel words in PWA.

6.1.2 People with aphasia can learn semantic definitions incidentally

In Studies I–IV, incidental learning of semantic definitions was measured with a free recall task at every follow-up probe. All six participants with aphasia showed some ability to learn semantic content incidentally and could recall some content words of the definitions, at least one day post-training. However, the semantic learning outcomes were quite low for most participants with aphasia.

Three aphasic participants with a fluent type of aphasia took part in the learning experiments: QH and IU of Study I, and AA of Study IV. With a declining accuracy curve, QH and IU managed the semantic recall task throughout the follow-up. In contrast, participant AA was often unsure whether an item had been accompanied with a definition. Her recall of the target words of the definitions was clearly inferior to that of QH and IU. The participants with nonfluent spoken output (AR and LL of Study II, and TS of Study III) exhibited low accuracy rates. While LL showed the best performance in this group, AR had difficulty in recognizing which items had been accompanied with definitions, especially from 8 weeks post-training on. TS's recall of definitions was minimal. Possible explanations for the variation of outcomes in the incidental semantic learning task will be discussed further in section 6.1.3.

6.1.3 The relationship between cognitive-linguistic profile and verbal learning

The present aphasic participants differed from each other concerning their cognitive-linguistic profiles. Earlier studies have associated phonological STM capacity (as measured by immediate serial recall) and pseudoword repetition ability with success in learning novel phonological word forms (Baddeley et al., 1998; Gathercole, 2006; Gupta, 2003). All of these performances have been suggested to rely on the functionality of the phonological loop of working memory (for a review, see Baddeley, 2012). The present results illustrate that aphasic individuals with low phonological memory spans (AA and TS) and severe impairment in repeating pseudowords (AA) can acquire novel vocabulary in a very efficient fashion. However, participant AR of Study II who had equally impaired phonological span and pseudoword repetition as AA showed the poorest learning result in the data. The most plausible explanation for this discrepancy lies in the different learning modalities available to these participants. This topic will be taken up more thoroughly in the next section 6.2. Only one of the phonological background measures, rhyme judgements, seems to be related to novel word learning in a consistent manner (see Table 3). Participants AR and IU performed significantly worse than healthy population in this assessment, and they were also the

participants with the weakest novel word learning results. It seems plausible that functional rhyming skills can promote associations to existing words that resemble the novel words and through that benefit novel word learning. However, as the present data encompass merely six PWA, it is difficult to draw a conclusion on this issue. Moreover, Martin et al. (2012) did not find this effect in their study. The PWA of the present study (especially AA, TS, and QH), however, commented on using this kind of strategy to learn.

Furthermore, the integrity of lexical-semantic processing has been found to predict benefit of aphasia treatment such as naming therapy (e.g. Martin, Fink, Renvall, & Laine, 2006; Renvall, Laine, & Martin, 2005). While lexical-semantic skills seem to play a role in re-accessing/relearning of language, it is well motivated to consider their role in novel word learning as well. In terms of the Interactive Two-step Model of Lexical Access (Dell, Martin, & Schwartz, 2007; Foygel & Dell, 2000), activation of the lexical-semantic layer of the hierarchical lexical network results in activation spreading in the lexical network. The optimal activation spreading, in turn, supports the selection of correct word forms (Dell, Schwartz, Martin, Saffran, & Gagnon, 1997). As soon as a new lexical-semantic representation begins to take shape, it can start supporting phonological STM for the novel word through activation flow between the lexical-semantic representation and the novel word candidate. This support for the phonological STM can, in turn, lead to better storage of the word. Theoretically, treating lexical-semantic processing abilities in PWA could therefore have a positive effect on word learning.

Studies I and II both included data of (a) one participant with superior lexical-semantic processing (QH and LL) and (b) one with impaired lexical-semantics (IU and AR). These participant pairs performed in line with the assumption described above. QH and LL were superior to IU and AR, respectively, both in relation to novel word learning and incidental learning of semantic definitions. The most successful novel word learners, AA of Study IV and TS of Study III, both had relatively well preserved lexical-semantic processing (even though both also performed outside the range of healthy controls in some lexical-semantic background tasks). The only participant with flawless performance in lexical-semantic tasks, QH of Study I, did, however, not learn novel words as successfully as participants AA and TS. Recall of semantic definitions was poor in all Finnish-speaking participants: LL, AR, AA, and TS. Their ranking in the semantic recall task was not predicted by the degree of preservation of lexical-semantic processing skills.

It seems evident that several factors simultaneously affect lexical learning, making it difficult to draw any definite conclusions on the specific role of lexical-semantic processing on verbal learning outcomes here. Such possible intervening factors include differential degrees of speech output problems, attentional capabilities and strategies, executive skills, and overall aphasia severity. When struggling with output, a nonfluent speaker needs to maintain contents in STM longer than usual in order to not forget what he/she wants to say. When speaking is particularly effortful, the speaker may also give up more easily. In addition, a nonfluent speaker may be more prone to lose scores due to pronunciation errors. The results are in line with the fluency–nonfluency explanation, except for participant LL (nonfluent) whose performance in semantic recall was superior to that of participant AA (fluent). In terms of overall aphasia severity, the results do not suggest that the learning outcomes correlate with severity. The participants with the best initial novel word learning and maintenance results (AA and TS) did not present with mild aphasia symptoms. Another possible intervening factor, particularly relevant for semantic recall, is poor comprehension of the definitions, and the degree of attention the participants paid to the definitions as they only were told to learn the names and also. Low attention to the definitions might explain the very poor semantic recall in participants AA and TS who, nonetheless, learned the novel names on a par with healthy control participants. The opposite cases (the lowest learning of names while showing the best recall of semantics) would be QH and IU. The background assessment of the present participants focused on their linguistic abilities, which unfortunately precludes any analysis of general cognitive functioning/executive functions vs. learning outcomes. Interestingly, Geranmayeh, Brownsett, & Wise (2014) have recently called for more comprehensive interpretations of recovery after aphasia. According to them, domain-general cognitive control systems are being largely ignored in functional neuroimaging studies of aphasia even though the domain-general systems are just as important treatment targets as the language-specific processes.

One methodological factor that hampers comparisons across the present studies is the use of different task versions. A comparison of the control data of Study I with the data of Studies II–IV reveals that the language-specific novel vocabulary learning task most likely placed higher demands on the English-speaking (Study I) than on the Finnish-speaking participants (Studies II–IV). This could be related to the fact that the Finnish names had in general more other real words closely related to the target novel word than what was the case in the English

material. After all, in the Finnish core experiment, real but unfamiliar words were utilized while in the English experiment the targets were pseudowords modified from the original Finnish names. The English-speaking control participants did not acquire all of the novel vocabulary while all of the Finnish participants managed to do it. Therefore, the results of Study I are not directly comparable with the results of the rest of the studies.

6.2 Learning modality can play an important role in aphasia (Studies III–IV)

The learning procedure of the core experiment (Studies I–IV) included simultaneous spoken and written input. Therefore, depending on the preserved/impaired language skills of a participant, there might have been two (auditory and orthographic), one (auditory or orthographic), or none of the functional input channels available for learning. A likely explanation for the great difference in the learning outcomes of AA and AR who both suffered from substantial auditory comprehension problems (see 6.1.3) is their strikingly dissimilar reading ability. While AA could read words and pseudowords quite accurately, AR struggled even with short high-frequency words. AA also described the written input as the key for her learning outcomes while AR claimed that she could not read.

The additional short-term learning tasks administered in Studies III and IV were designed to tap into possible modality effects in learning novel words. In Study IV, the focus was on input modality during learning, and in Study III, on both input and output modalities. Only the two aphasic participants with the best learning results in the core experiment, AA and TS, took part in these experiments. The results confirmed what AA and TS had already tried to describe: they relied on the orthographic form in order to learn novel words. Both of them learned significantly better from orthographic than auditory input. AA repeated very poorly during the auditory learning task and produced a large variation of erroneous forms of the pseudowords. The lack of stabilized, recurrent errors suggests that AA could not establish stable phonological representations during the training, which in turn complicated the binding process necessary for associative learning. The effect of input modality on learning observed in AA and TS is in line with the learning results of healthy young adults who also show superior learning with orthographic to auditory input (Nelson et al., 2005). Participant TS was also tested for the effect of output modality during learning (i.e., oral or written response). She did not show significantly different learning outcomes in relation to the output modality, but her most efficient learning modality combination was written input with written output. She

acquired all of the novel words in this modality combination very fast and could retrieve them in fully accurate form.

Interestingly, participant TS's learning modality effects were in conflict with her linguistic profile. She was significantly more accurate in repeating than reading aloud pseudowords. Nevertheless, she learned better from written than auditory input. The difference between TS's repetition vs. oral reading abilities was confirmed in the cognitive-linguistic background tests as well as during the initial training trials of the modality-specific novel word learning experiment. TS's learning was almost errorless (see e.g. Fillingham, Sage, & Ralph, 2006, for discussion on the errorful–errorless continuum in treatment) in the learning condition that corresponded to oral repetition (AUD–SPO), and errorful in the condition including oral reading (WRI–SPO). A possible, although speculative, explanation for the seemingly conflicting learning outcomes and performance in language processing tasks lies in differently affected connections from orthography and phonology to the medial temporal lobe. This kind of difference could bring about dissimilar learning outcomes for the two modalities while not affecting immediate performances of reading aloud and repetition. The superior novel word learning outcomes acquired with orthographic vs. auditory input are, in turn, in line with learning results from healthy adults and the dual coding hypothesis (Nelson et al., 2005).

Following the present discovery of a modality-based dissociation in word learning, one could ask whether the opposite dissociation (oral input facilitating learning more than written input) could be found in PWA. This remains to be seen, but if the present modality-specific pattern is based on dual coding, as has been shown in healthy adults (Nelson et al., 2005), the opposite pattern should not be found. Another reason for the absence of the opposite dissociation would be the fact that the diagnosis of aphasia relies to a great deal on the existence of phonological problems and difficulties with spoken input. While reading and writing are often as impaired as spoken language skills in aphasia, they are not equally crucial in the clinical diagnosis of aphasia and can thus vary considerably between patients.

6.3 Neural underpinnings of successful novel word learning via orthography (Study IV)

The results of Study IV provide novel information on the neural underpinnings of successful new word learning and reading in an aphasic individual, AA, and a group of seven control participants. Remarkably, AA learned on a par with healthy control participants despite a large lesion in regions that had been suggested as playing a crucial role in language learning

(Hickok & Poeppel, 2007; Rodríguez-Fornells et al., 2009). The dMRI analysis confirmed that AA's dorsal speech processing route of the left hemisphere had been disconnected. However, an intact dorsal pathway could be reconstructed in her right hemisphere. AA showed activation of the hippocampus/parahippocampus during a novel word learning task, indicating that she had access to the medial temporal memory system via written input. Reading-related brain activations were also probed in a separate task. Interestingly, right-hemispheric temporal regions were found to be significantly more activated in AA than in the control group. The activated regions were connected via the right AF, suggesting that the right-hemispheric dorsal route was engaged in her oral reading performance. This alternative route could apparently mediate between orthographic input processing and speech output that relies on left anterior structures. AA's right-hemispheric engagement in reading raises the issue of premorbid functional laterality in her brain. AA was, however, strongly right-handed and her severe aphasia that had followed a left-sided lesion also supported the language dominance of the left hemisphere. The language assessments administered to AA at different time points during her recovery from the stroke showed that her ability to read had recovered slowly from very poor performance to the present level. This fact suggests that slow plastic changes had taken place instead of a sudden switch to another available but latent parallel neural route/processing system (see also Duffau, 2009). Furthermore, LI analyses revealed that AA's right AF did not structurally differ from the right-sided AFs of the control group.

As long as AA remains the only aphasic individual with good learning that has undergone functional neuroimaging tasks of novel word learning, it is impossible to know how unique AA actually is in her ability to learn novel vocabulary via recruitment of a right-hemispheric neural network. An earlier neuroimaging investigation by Morrow (2006) did measure novel word learning but did not find evidence on learning in the aphasic participants. Another open question concerns the timeline for AA's plastic changes. Nevertheless, the neuroimaging results of AA challenge the present neurocognitive models on language learning in suggesting that through neural plasticity the right hemisphere can start to mediate the acquisition of active novel vocabulary.

6.4 Implications for aphasia assessment and treatment (Studies I–IV)

The present thesis work is not a treatment study, but it was conducted in the hope that its results could bear relevance to the development of effective treatment methods for PWA. Success in aphasia treatment necessarily requires some kind of modification of behavior

through for instance associative learning (see Baddeley, 1993, for discussion on learning and memory in rehabilitation, and Whitworth, Webster, & Howard, 2014, for the principles of the cognitive neuropsychological approach in treatment). Nevertheless, knowledge on how PWA learn has been scarce and the foundations for treatment in that respect incomplete. Caramazza and Hillis (1993) and Baddeley (1993) raised the issue of the importance of a theory for aphasia treatment, and ten years later, Basso (2003) claimed that knowledge about aphasia treatment unfortunately is “scattered, disconnected and dispersed” as a common basis for aphasia therapy is missing (p. 186). Her suggestion towards a theory of aphasia therapy was as follows:

A theory of aphasia rehabilitation should at least incorporate (1) a model of the cognitive processes to be treated and specific hypotheses about the functional damage(s) present in any given patient; (2) knowledge of which types of functional damage are amenable to amelioration, and which are not; (3) specific hypothesis about how neural mechanisms relate to recovery; (4) whether and which other factors, besides the damage itself, have an effect on recovery; (5) a theory of learning in brain-damaged patients; (6) and, last but not least, how to remediate each functional damage, namely, which tasks are to be utilized and how to implement them...” (p. 186)

The attention given to the different components of this “core theory” (Basso, 2003) in aphasia research is far from being in balance. Overall, Basso (2003) sees the accumulated knowledge as very insufficient. More is known of the first two of the components: there are (1) functional models of several cognitive-linguistic processes and (2) data from case studies showing which functional lesions it is possible to remediate. The rest of the components remain more or less underdeveloped in aphasia research. What is known about learning in brain-damaged persons is one of the least developed areas. In this sense, the present investigation can offer important original data, and thus fill some gaps in understanding the possibilities in recovery from aphasia. In addition, McNeil and Copland (2011), and Cahana Amitay and Albert (2015) have recently called for more complete models of aphasia rehabilitation which would also take into account knowledge on learning and memory.

The targeting of aphasia treatment in an optimal fashion has been discussed by, for instance, Basso (2003), Byng (1993), Howard and Hatfield (1987), McNeil and Copland (2011), Martin, Laine, and Harley (2002), and Whitworth et al. (2014). At issue is to which extent the

cognitive-linguistic profile of an individual with aphasia predicts the best possible cognitive-linguistic route for the treatment. The learning outcomes of TS in Study III suggest that the cognitive-linguistic test profile and the language learning profile of the same individual do not necessarily align as predicted. TS repeated words better than she could read them aloud both in tests and during the actual training trials. Still, in learning she showed the opposite profile by benefiting more from written than spoken cues. The relative strengths in the test profile may suggest choosing a learning modality that, in fact, does not lead to the strongest learning effects in the individual. Albeit this discovery in participant TS involves only a single individual, it suggests that it could be useful to probe the learning capacity of an aphasic individual with small-scale modality-specific language learning tests instead of merely focusing on the more traditional assessment. On the basis of the present results, this kind of probing could be especially recommended prior to starting anomia treatment. Of course, clinicians aiming at effective treatment may already apply this idea during treatment periods, either intuitively or on purpose.

Vallila-Rohter (2014) recently found that nonlinguistic learning capacity correlates with the benefit of aphasia treatment in a group of PWA. She suggests that probing of novel learning capacity prior to aphasia treatment can be used to predict therapy outcomes. In the present thesis work, the relationship between novel word learning capacity and language treatment success was examined only in participant AA of Study IV. The results showed that the previously undetected word learning route through orthography functioned also in her learning of familiar but inaccessible words. Furthermore, she could also maintain the acquired vocabulary with success. While further research is required to address this question, earlier neuroimaging studies suggest that processing of newly learned and familiar words recruit the same cortical regions and should therefore correlate (Hultén et al., 2009; Hultén et al., 2010).

6.5 Methodological considerations and future directions

The present investigation dealt with language acquisition from a narrow perspective which naturally restricts the generalizability of the obtained results. The focus was on the learning of unfamiliar single words or pseudowords that, moreover, were all nouns. Language is, of course, much more than just nouns, although this same emphasis on nouns is a frequent phenomenon in aphasia therapy, too. An explicit, simple paired associate learning task was chosen as the medium for the learning. This was a very different starting point than what, for example, Grossman and Carey (1987) had in their investigation. Their study measured the

learning of one single word in a more natural and implicit learning situation where the participants were not even told the objective of the activity, but merely observed a new word being used in sentences. This kind of natural learning capacity is genuinely interesting when it comes to the everyday life situations where PWA communicate and have a possibility to strengthen their language abilities and use. However, the more explicit, systematic and repetitive approach, such as the paired associate task utilized in the present investigation, is by no means unusual or irrelevant for aphasia treatment and can inform the choices that clinicians have to make.

Another difference between the present investigation and more natural language learning conditions relates to the opportunities to use the newly learned words in communication situations. Due to the nature of the to-be-learned material, the participants had no need to access the words during the long follow-up period. While evidence from a study by Friedman, Lacey, and Nitzberg Lott (2003) suggests that frequent access to words is of importance for maintenance in PWA, some of the present aphasic participants (AA, TS and also LL) could still retain novel words very successfully without further access to them.

The present dissertation is based on case methodology. While the number of participants is low and the material thereby small, the strength of the methodology lies in the depth of the assessment. In terms of Evidence-Based Practice (EBP; Morgan & Morgan, 2009), the data is modest and the selection of participants not randomized. These facts are, however, not in conflict with the idea of cognitive neuropsychology that acknowledges the need to look at individual patients in depth in order to present the individual differences (see Basso, 2003, and Whitworth et al., 2014, for the value of case studies and the cognitive neuropsychological approach in aphasia). Moreover, the idea of the present investigation is not to be representative but to show the possible variation in PWA. In connection to this, the PWA of this dissertation form a heterogenic group with variation in e.g. age, educational background, the etiology of aphasia, and time post-onset. Naturally, a larger number of participants might have revealed even more variation in learning and allowed for more elegant analyses on the correlation of various background factors on learning ability than is within the scope here. Thus, large groups of participants coupled with systematic neuroimaging would be called for in future studies.

The stimulus set of the core AFE learning experiment utilized in all of the present studies may not be optimal for displaying all the phenomena possibly affecting novel word learning. For example, use of a larger stimulus sets would have provided data for analyses of the learning condition (*Name* vs. *NameDef*) on learning to produce novel names. The previous AFE experiments administered to memory-impaired participants (e.g. Grönholm-Nyman et al., 2010) have utilized a stimulus set double the size of the current one. While the aphasic participants AA and TS might have managed to learn to produce more than the present 20 novel words, the participants performing at lower levels might have been faced with a too demanding task if the size of the stimulus sets have been increased. An alternative for the present study design would have been to measure novel word learning with receptive rather than production tasks. Receptive tasks may have been more sensitive and revealed learning even in larger stimulus sets. However, active production is the ultimate aim in anomia treatment, therefore production can be considered the most appropriate measure of learning outcomes.

Due to the nature of the data, the statistical methods utilized in this dissertation are simple and the general statistical power is poor. However, the choice and interpretation of the statistical tests has been done with caution. To take one example in the measurement of word learning, a result of learning fewer than five of twenty novel names was labelled as “no learning”, in line with the result of the binomial test. Still, the probability for producing even a single novel name accurately just by chance seems minimal indeed.

To date, the accumulated knowledge on novel word learning in PWA is still quite limited. The need for additional comprehensive, controlled case studies of individuals with varying lesions and cognitive-linguistic profiles is clear. In particular, additional case studies that systematically compare learning outcomes as the effect of different learning modalities are motivated because striking divergences were discovered in Studies III and IV. Functional neuroimaging methodology could be utilized in mapping the neural underpinnings of different aspects of novel linguistic learning in PWA. Importantly, novel language learning experiments could be administered parallel with language re-acquisition tasks (i.e., resembling aphasia treatment with familiar but inaccessible words), to examine the relationship between these capacities in PWA. Study IV is to date the only investigation that has tapped into this issue.

While anomia is a frequent, visible, persistent and disabling symptom in PWA, aphasia rehabilitation is of course much more than just anomia therapy. The numerous methods of aphasia rehabilitation can be categorized into so-called impairment-based and consequence-based approaches (Thompson & Worrall, 2008). The present investigation has its roots in the impairment-based approach where the goal for the treatment is the better functionality of the language processes themselves. Several studies have shown that this approach, aiming to restore verbal communication, is also what PWA themselves constantly aim at (e.g. Blom Johansson, Carlsson, & Sonnander, 2012). The consequence-based approaches focus at the functionality of communication, looking at the aphasic individual as a part of the community where the responsibility for functional communication is shared. Both types of approaches self-evidently have an important place in aphasia therapy, in particular in treatment of PWA with more severe language disability.

While stroke incidence and mortality are decreasing (Meretoja et al., 2011), the number of stroke patients, at least in Finland, is not declining as the average life expectancy is at the same time increasing (Lehtonen et al., 2005). Therefore, research on aphasia and aphasia treatment continues to be of importance. Basic research on how PWA learn, in turn, can be seen as one of the elements that form the basis for aphasia treatment. Effective aphasia treatment can strengthen language functions, reduce disability, promote greater life participation and better quality of life (Simmons-Mackie & Kagan, 2007). Recovery of aphasia is of importance not only to the PWA and their significant others but also to the community. Successful recovery can mean access to work and more independent life.

CONCLUSIONS

The present dissertation consisted of four original case studies that all focused on associative novel lexical-phonological learning in individuals with aphasia. The main findings were as follows:

- PWA showed a wide variation in their ability to learn novel vocabulary and maintain it in the long-term, from very limited capacity up to levels on a par with healthy control participants. PWA were also able to learn semantic definitions incidentally, but did not reach the learning and maintenance levels of the healthy controls.
- Intact lexical-semantic processing skills seemed to promote novel learning while poor phonological STM did not rule out efficient word learning.
- Written input resulted in much more efficient learning than auditory input in two aphasic individuals who showed novel word learning on a par with healthy control participants
- An aphasic individual showed normal novel word learning capacity through reading in spite of disconnection of the left dorsal speech processing route that has been suggested to play an important role in language learning. Functional brain imaging revealed a language processing network where the right dorsal route provided a functional link between the left hemisphere regions activated during language tasks.
- Functional novel word learning ability could be translated directly into anomia treatment where an aphasic individual gained access to familiar but accessible words
- Small-scale learning tasks may turn out to be useful for revealing general word learning capacity and the best modality for learning. They could thus be a valuable addition to the present cognitive-linguistic background tests.

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