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Novel word learning in aphasia:
a new approach to an old problem

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Abstract

Aphasia is a significant communication disorder that arises from damage to the brain's language areas, affecting comprehension, expressive language, reading, and writing. This condition severely disrupts daily communication, leading to a reduced quality of life and limited social interactions. While speech and language therapy remains the primary treatment for aphasia, the mechanisms driving its success are not fully understood. Despite advancements in language processing theories and therapeutic interventions, variability in patient outcomes remains a challenge. Factors like lesion size, location, and co-existing cognitive deficits play roles, but their collective influence on recovery remains elusive. From a cognitive perspective, the source of language recovery—whether from new neural connections, reactivation of latent linguistic information, or a blend of both—is debated. Current treatments help patients access existing language skills, but introducing new linguistic content might offer a therapeutic direction. Recent studies indicate that the ability to learn new words might be pivotal for therapy outcomes in chronic aphasia patients. This thesis delves into novel word learning, emphasizing the potential of implicit learning, an unconscious knowledge acquisition method. The research covers four studies, all designed to compare implicit and explicit learning mechanisms. Participants were introduced to pseudowords and unfamiliar objects, aiming to discern their capacity to form associations through statistical co-occurrence in the implicit condition and through direct instruction in the explicit one. Their retention was assessed after a week. In Chapter 2, the first study begins by exploring the two learning mechanisms across various age groups and educational backgrounds, recognizing that insights from neurologically healthy individuals can enhance therapeutic approaches for aphasia. Younger participants demonstrated higher learning accuracy and speed. However, age differences were less pronounced in implicit learning. While education impacted explicit learning, its influence on implicit learning was subtle. Both age groups demonstrated reduced accuracy in the immediate recognition task for the implicit condition compared to the explicit one. This disparity diminished after one week, making accuracies for both conditions comparable. Chapter 3 encompasses two experiments, engaging both aphasia patients and controls. The first experiment's results, which showed limited learning outcomes for aphasia patients, led to a second experiment with adjusted vocabulary and more repetitions. Throughout, control groups consistently surpassed the aphasia cohorts in performance. Implicit learning showcased remarkable resilience, especially evident within aphasic contexts. Notably, factors such as lesion location and severity played pivotal roles in shaping learning outcomes. Across both experiments, controls consistently outperformed the aphasia group. Implicit learning showed resilience, especially within the aphasia context. Notably, lesion location and severity emerged as significant factors influencing learning outcomes. Chapter 4 investigated the efficacy of transcranial direct current stimulation (tDCS) in augmenting implicit learning among aphasia patients. By focusing on the middle superior temporal gyrus (mSTG) - a region linked to implicit learning - the study evaluated the effects of anodal, cathodal, and sham stimulation. Notably, anodal stimulation enhanced both the recall and the overall learning trajectory. In conclusion, this work emphasizes the need for tailored therapeutic strategies that account not only for lesion location and aphasia type but also for individual learning profiles. Finally Incorporating techniques like tDCS, and principles of implicit learning for aphasia offers promising avenues. However, more research is needed to further refine and expand these insights.

Riassunto

L'afasia, un disturbo comunicativo derivante da danni nelle aree cerebrali deputate al linguaggio, altera la capacità di espressione e/o di comprensione con conseguenze sulla qualità di vita. Sebbene la terapia logopedica sia il trattamento cardine dell'afasia, i meccanismi che ne determinano il successo sono solo parzialmente compresi. Infatti, nonostante i progressi nelle teorie linguistiche e terapeutiche, la variabilità dei risultati tra i pazienti rimane una sfida significativa. Fattori come dimensione e posizione della lesione, presenza di deficit cognitivi concomitanti, influenzano il recupero, ma la loro esatta incidenza è ancora da definire. Rimane inoltre dibattuto se questo recupero sia dovuto alla formazione di nuove connessioni neurali, alla riattivazione di conoscenze linguistiche latenti o a una combinazione dei due. Benché i trattamenti attuali siano volti a facilitare l'accesso a competenze linguistiche preesistenti, l'acquisizione di nuovi contenuti linguistici potrebbe rappresentare una nuova frontiera terapeutica. In questo contesto, la tesi esplora il potenziale di apprendimento nell'afasia, con particolare attenzione all'apprendimento implicito. La ricerca si articola in quattro studi, nei quali i partecipanti sono stati esposti a non-parole e oggetti sconosciuti, con l'obiettivo di valutare la loro capacità di formare associazioni basate sulla co-occorrenza statistica, nel caso dell'apprendimento implicito, e attraverso l'istruzione diretta, nel caso di quello esplicito. La loro capacità di ritenzione è stata valutata nell'immediato e dopo una settimana.

Considerando che lo studio su soggetti neurologicamente intatti può contribuire a perfezionare le teorie sulla riabilitazione del linguaggio, il secondo capitolo analizza i due tipi di apprendimento in soggetti sani in relazione a età e livello di istruzione. I risultati evidenziano prestazioni migliori nei partecipanti più giovani e minori discrepanze nell'apprendimento implicito, suggerendo una sua maggiore stabilità rispetto alle variazioni individuali. L'istruzione influisce sull'apprendimento esplicito, ma meno su quello implicito. Nonostante una performance iniziale inferiore nell'apprendimento implicito in entrambi i gruppi di età, le prestazioni si sono allineate dopo una settimana, mostrando una comparabilità tra le due modalità. Il terzo capitolo include due esperimenti con pazienti afasici e gruppi di controllo. I risultati del primo studio, che evidenziano capacità di apprendimento limitate nei pazienti afasici, hanno portato alla realizzazione di un secondo, caratterizzato da un vocabolario ridotto e un maggior numero di ripetizioni. In entrambi gli studi, i soggetti sani hanno mostrato prestazioni superiori rispetto ai pazienti afasici. L'apprendimento implicito ha dimostrato una notevole resilienza, particolarmente evidente nel contesto afasico. Il quarto capitolo esamina il potenziale della stimolazione transcranica a corrente continua (tDCS) nell'aumentare le capacità di apprendimento implicito in afasia. Concentrandosi sul giro temporale superiore medio, lo studio ha comparato diversi tipi di stimolazione: anodica, catodica e sham. I risultati hanno rivelato un miglioramento significativo nell'apprendimento con la stimolazione anodica, sia durante la fase di apprendimento che nel successivo compito di riconoscimento. In tutti gli studi con pazienti afasici, variabili come sede della lesione e la gravità dell'afasia hanno giocato un ruolo determinante nell'influenzare l'apprendimento. In conclusione, questa tesi sottolinea l'importanza di adottare strategie terapeutiche personalizzate, tenendo conto non solo della gravità e del tipo di afasia, ma anche dei profili individuali di apprendimento. Inoltre, l'integrazione di tecniche come la tDCS e principi di apprendimento implicito potrebbe aprire nuove prospettive nella riabilitazione del linguaggio. Ulteriori ricerche sono necessarie per approfondire la comprensione in questo ambito.

CHAPTER 1: Introduction

Aphasia is an acquired neurogenic communication disorder that may affect the main critical components of the language network: comprehension, expressive language, reading, and writing. It hampers individuals' overall everyday communication skills, affecting their quality of life and social participation (Bullier et al., 2020; Rohde et al., 2013). The primary treatment for persons with aphasia (PWA) that begins with evaluation is speech and language therapy (SLT), applicable at all stages of recovery, including the chronic stage (Basso & Macis, 2011; Brady et al., 2016; Elsner et al., 2019). Even though its efficiency is well-documented, the fundamental neurophysiological and theoretical foundations of speech-language therapy remain ambiguous (Kelly & Armstrong, 2009).

Despite decades of progress in theories and models of language processing and impairment (A. Gupta & Padma Srivastava, 2020; Hickok, 2022; Howard & Hatfield, 2018; Matchin et al., 2022; Nasios et al., 2019; Vogelzang et al., 2020) and in developing evidence-based assessments and therapies (Brady et al., 2016, 2016; REhabilitation and recovery of peopLE with Aphasia after StrokE (RELEASE) Collaborators, 2022; Sheppard & Sebastian, 2021), we are still far from fully understanding the mechanisms upon which SLT exerts its effects and even further from being able to prescribe the most appropriate treatments based on individual language deficits and cognitive profiles (Best & Nickels, 2000; Kelly & Armstrong, 2009; Vallila, 2017).

A critical open question remains why some patients derive greater benefits from therapies compared to others (Coran et al., 2020; Kelly & Armstrong, 2009; Nickels & Best, 1996; Peñaloza et al., 2022). Although predictors of long-term recovery have been identified to be initial aphasia severity, lesion location, and size (Benghanem et al., 2019; Hillis et al., 2018; Kristinsson et al., 2022), along with poststroke depression and social isolation after aphasia onset (C. Baker et al., 2018; Vickers, 2010), it is not entirely clear why patients with similar linguistic profiles may have differing recovery trajectories (Fillingham et al., 2003; Laganaro et al., 2006; Lambon Ralph et al., 2010; Peñaloza et al., 2022).

The reasons for these variations in therapeutic responses are unknown but could be due differences in lesion size and location, to the co-occurrence of other cognitive deficits and abilities (Fridriksson et al., 2006; Gonzalez et al., 2020; Leśniak et al., 2008) and the brain's capacity to deploy different mechanisms such as partially restoring the damaged neural pathways or recruiting redundant neural pathways that are not normally utilized (Hopper & Holland, 2005; Kelly & Armstrong, 2009; Peñaloza et al., 2022).

At the cognitive level, it remains undetermined whether language recovery in rehabilitation results from new learning and the formation of new neural connections, the reactivation of previously stored verbal information, or a mix of both (Kelly & Armstrong, 2009; Laganaro et al., 2006; L. Tuomiranta et al., 2014). Another question is whether aphasia primarily impacts the ability to remember words (storage) or retrieve words (access) (Shallice, 1988).

Current therapies primarily aim to assist PWA in accessing their pre-existing linguistic skills, but learning new content may offer an alternative therapeutic method. Recent research links the ability to learn new words with responses to therapy in chronically aphasic individuals (Dignam et al., 2016). This indicates that exploring the remaining learning capabilities might be key to understanding language recovery mechanisms in aphasia (L. Tuomiranta et al., 2014) and provide valuable insights for diagnosis and treatment approaches (Peñaloza et al., 2016).

This thesis will focus on a specific form of learning, termed implicit. Unlike explicit learning, which involves conscious, intentional, and declarative processes, implicit learning is a form of unconscious, incidental, and procedural knowledge acquisition, which has been shown to be significantly different (Wang, 2020).

Implicit learning in PWA, despite being less explored compared to explicit learning, it may offer a supplementary and alternative approach to reduce the overall cognitive load and effort, both typically impaired in aphasia - thereby maximizing learning within this population (Breitenstein et al., 2004).

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1. 1. Post-stroke aphasia

Aphasia is an acquired communication impairment that hinders the ability to comprehend or articulate language. Frequently, it is a consequence of brain injury due to a stroke, tumor, infection, or a decline in cognitive abilities. Statistics reveal that aphasia is a potential outcome for 25%–50% of all stroke victims (Flowers et al., 2016; Grönberg et al., 2022).

The symptoms and severity of post-stroke aphasia can significantly vary among patients, making it a heterogeneous group. To streamline diagnosis, treatment, and language research, various classification systems have been developed. The most common of these is based on the Broca-Wernicke-Lichtheim-Geschwind model of language, which asserts that speech production is associated with left hemisphere inferior frontal regions (Broca, 1861), and comprehension is tied to left posterior temporal regions (Wernicke, 1874), with the arcuate fasciculus facilitates communication between these regions (Catani & Mesulam, 2008; Geschwind, 1965).

Starting from this model, aphasiologists developed various methods to categorize different types of aphasia. The most widely used system is the Boston classification system, which was created in the 1960s by Norman Geschwind, Frank Benson, Harold Goodglass, and Edith Kaplan, who updated traditional descriptions of aphasia subtypes. The Boston neoclassical classification system consists of eight subtypes: Broca's, Transcortical Motor, Global, Mixed Transcortical, Wernicke's, Transcortical Sensory, Conduction, and Anomic. These subtypes are differentiated by three binary criteria: fluency, comprehension, and repetition (Sheppard & Sebastian, 2021) and are thought to be associated with damage to particular cortical regions, with potential extension into subcortical areas. Based on this classification, one of the most commonly used diagnostic tools is the Aachen Aphasia Test (AAT). The Aachen Aphasia Test (AAT), developed in the 1970s by Wolfgang Huber, Klaus Poeck, and Klaus Willmes at the University of Aachen in Germany, is a pivotal tool for assessing language in those with aphasia. It encompasses subtests such as the Token Test (understanding spoken instructions), evaluations of spontaneous speech, auditory comprehension, written language, and naming abilities. Using the AAT, clinicians can pinpoint the type of aphasia an individual has, aligning it with the Boston classification system's subtypes like Broca's, Wernicke's, Conduction, and Anomic, among others. Beyond its diagnostic capabilities, the AAT is instrumental in tracking therapeutic progress and has versions tailored for diverse languages and cultures globally (Huber et al., 1984).

Nevertheless, the accuracy of predicting lesion locations based on these subtypes are debated in the literature, with some studies finding a correlation between predicted lesion location and aphasia syndrome while others showing discrepancies between predicted and actual lesion locations (Kasselimis et al., 2017; Yourganov et al., 2015). In addition to this, it is relatively common for a patient’s language impairment profile to be unclassifiable because it does not fit neatly within any of the well-defined neoclassical aphasia syndromes. This may be due to the fact that, potentially, deficits do not results from an all or nothing loss of the different language sub-processes, and that traditional models do not account for the involvement of "non-traditional" regions, such as subcortical regions and the right hemisphere, in language disturbance (Fridriksson et al., 2015, 2018). Functional imaging studies have shown that language systems involve multiple regions working together in a distributed network rather than functioning independently (O’Sullivan et al., 2019).

Even when patients fit within a specific profile, they may differ significantly from other patients with the same syndrome classification due to individual differences and non-linguistic concomitant deficits. These variations among individuals sharing the same aphasic profile highlight the complexity of aphasia.

While the Boston classification system takes a neuroanatomical approach, emphasizing the location and nature of brain damage, other models, such as the psychological model, offer a more comprehensive exploration into the cognitive underpinnings of aphasia. This psychological model suggests that the linguistic challenges faced by individuals with aphasia are intricately linked to disruptions in various cognitive processes. These disruptions encompass functions ranging from memory and attention to executive functions and foundational linguistic processing, providing a richer understanding of the condition.

The Psycholinguistic Assessments of Language Processing in Aphasia (PALPA, Kay, Lesser and l, 1996) test stands as a testament to the principles of the psychological model. The PALPA offers a thorough assessment that probes both the preserved and disrupted language-processing abilities in adults who have developed aphasia from various events, like strokes or traumatic brain injuries. Comprising 60 sub-tests, the PALPA is categorized into four primary areas: Auditory Processing, Reading and Spelling, Word and Picture Semantics, and Sentence Processing. These sub-tests serve as valuable tools for researchers and clinicians, enabling them to devise and confirm theories about the exact nature of language deficits in affected individuals. Moreover, the findings from these sub-tests serves in guiding subsequent assessments and crafting therapeutic plans. Furthermore, the psychological model's emphasis on cognitive processes highlights the interconnectedness of language with other cognitive domains. It suggests that effective therapeutic interventions for aphasia might benefit from strategies that also target cognitive functions, ensuring a more holistic approach to rehabilitation (Bate et al., 2010).

1.2. Concomitant non-linguistic cognitive deficits

A growing body of research has highlighted the presence of concomitant cognitive deficits in patients with aphasia (Gonzalez et al., 2020; Helm-Estabrooks, 2002; L. L. Murray, 2012; Nicholas & Connor, 2017; Schumacher et al., 2022).

Impaired areas include attention (Erickson et al., 1996; Hula & McNeil, 2008; L. Murray et al., 2018; L. L. Murray, 2012), memory (Salis et al., 2015), executive functions (Coelho et al., 2005; Fridriksson, 2010a; L. L. Murray & Heather Ray, 2001), visuospatial skills (Hwang et al., 2022) and learning (Vallila-Rohter & Kiran, 2013).

A study conducted by Van de Sandt-Koenderman et al. (2008) explored the factors contributing to treatment outcomes in 58 individuals with aphasia and found that attention, concentration, verbal and nonverbal memory, and executive functions were the most significant variables in predicting treatment response. El Hachioui et al., (2013) reported that in a sample of 147 adults with aphasia, 88% of individuals showed impairment in at least one cognitive domain at 3 months after stroke onset and 80% of individuals continued to demonstrate cognitive deterioration(s) at 12 months after stroke. In their review involving 47 studies and a total of 1710 PWA, Fonseca et al., (2016) found that in around 60% of the studies, individuals with aphasia tended to achieve lower scores on nonverbal cognitive tests compared to healthy individuals. Dignam et al., (2017) found that verbal short-term memory ability significantly predicted naming gains for treated items immediately after therapy and for untreated items immediately after therapy and at a 1-month follow-up testing. In 2018, Fonseca and colleagues discovered that individuals with non-fluent aphasia performed poorly in areas of memory, executive functions, and attention. Conversely, those with fluent aphasia were observed to have deficiencies only in memory tests. More recently, a study by Yao and collaborators (2020) aimed to assess the non-linguistic cognitive impairments in 86 stroke survivors with and without aphasia. The results showed that PWA had more extensive and severe non-linguistic cognitive impairments compared to stroke patients without aphasia and control groups.

Even without taking therapy into account, the presence of cognitive impairments has been found to influence spontaneous recovery in the first 12 months post-onset and is significantly related to poorer functional outcomes (El Hachioui et al., 2013).

Neuroimaging studies have provided support for the role of general cognitive functions in aphasia rehabilitation, with evidence suggesting that areas known to modulate memory, attention, and cross-modal integration may be integral to the rehabilitation process (Fridriksson et al., 2007; Geranmayeh et al., 2014; Meinzer & Breitenstein, 2008).

Among the cognitive deficits likely to affect rehabilitation outcomes, this thesis focuses on learning ability. This skill has only recently begun to receive attention in the field of aphasia (Peñaloza et al., 2022). Several scholars have recognized learning ability as a crucial factor in rehabilitation, whose foundation relies precisely on intact learning mechanisms.

Indeed, even if therapy does not contemplate new words or grammar learning, it involves teaching, practice, and accumulated experience over time(Helm-Estabrooks, 2002; Vallila, 2017).

Recent neuroimaging research on aphasia has delved into the link between treatment-induced changes and brain structures and activity. Menke et al., (2009) identified a connection between short-term therapeutic progress and bilateral activity in the hippocampus, a vital region for memory. Following this, Meinzer et al., (2011) used diffusion tensor imaging to reveal an association between successful language treatment and the structural health of the hippocampus and its adjacent fiber pathways. Research on new word, meaning, and sentence structure learning in healthy subjects has highlighted the involvement of similar brain regions (Breitenstein et al., 2005; Opitz & Friederici, 2003). This indicates that similar mechanisms might be at play in both language recovery and new learning in healthy people (Menke et al., 2009).

Nevertheless, despite the increasing recognition of the role of learning in aphasia therapy, a few studies have yet to be devoted to comprehending this process. Shifting the focus of aphasia research towards exploring the interactions between language and learning systems could help clinicians and researchers to address important unanswered questions and improve rehabilitation (Peñaloza et al., 2022; Vallila,

2017) after all, as Baddeley (1993) stated, “A theory of rehabilitation without a model of learning is a vehicle without an engine.”

1.3. Aphasia rehabilitation

Language therapy is the main treatment for aphasia, with a growing body of research underscoring its effectiveness, even in the chronic stages of the disorder (Basso & Macis, 2011; Brady et al., 2016; Duncan et al., 2020; Shah-Basak et al., 2015). Although there is some understanding of how post-stroke aphasia patients regain language, why therapy is successful for some but not for others remains unresolved(Best & Nickels, 2000; Kelly & Armstrong, 2009) However, the precise therapeutic mechanisms remain elusive (Ferguson, 1999), and there is still a gap in tailoring treatments to individual language deficits and cognitive profiles (Best & Nickels, 2000; Kelly & Armstrong, 2009).

Functional neuroimaging studies investigating aphasia recovery typically interpret their findings within the context of three overarching mechanisms. The first, known as the 'perilesional' hypothesis, posits that recovery results from the reconstitution of domain-specific language systems in the tissue surrounding the lesion (W. D. Heiss et al., 1999; Meinzer & Breitenstein, 2008; Rosen et al., 2000; Warburton et al., 1999). This hypothesis aligns with previous findings that recovery is dependent on the reconstitution of language systems in undamaged tissue around the lesion (Fridriksson, 2010; Hillis et al., 2006; Meinzer & Breitenstein, 2008; Saur et al., 2006; van Oers et al., 2010).

The second mechanism, the 'laterality-shift' hypothesis, suggests that recovery can be attributed to a 'shift' of language function to the homotopic cortex in the contralateral hemisphere (Blasi et al., 2002; Turkeltaub et al., 2012; Winhuisen et al., 2005). This hypothesis has been supported by studies such as Tuomiranta et al., (2014), which reported a patient with extensive left-hemispheric damage responding to therapy with improved behavioral performance associated with right hemispheric regions. Nonetheless, a more successful recovery rate in the chronic phase is likely to be associated with the involvement of structurally unimpaired areas surrounding the lesion (Saur et al., 2006; Vitali et al., 2007, 2011). To elaborate, according to Saur et al. (2006), the brain undergoes a reorganization process during the recovery of language abilities that unfolds in three separate stages. Initially, there is a marked decrease in the activation of structurally sound language regions during the acute phase. This is followed by an increase in activity, with the engagement of corresponding language areas in the non-dominant hemisphere, a change that is linked with improvements in language capabilities. The process culminates with a phase where the activation levels stabilize, potentially indicating the completion of the reorganization within the language system. Nevertheless, numerous researchers have viewed the changes in right hemisphere activation during aphasia recovery as a result of transcallosal disinhibition, which might not necessarily indicate genuine recovery. This perspective aligns with the 'disinhibition' hypothesis, a third mechanism derived from functional neuroimaging studies. This hypothesis suggests that the activity on the right side arises due to the diminished transcallosal inhibition and could potentially impede recovery by reciprocally inhibiting any surviving undamaged tissue in the left hemisphere (Naeser et al., 2005; Price & Crinion, 2005; Thiel et al., 2006).

A hierarchy for aphasia recovery has been proposed by Heiss and Thiel (2006) that attempts to integrate these diverse findings. The synthesis suggests that the best recovery is achieved by restoring the original activation patterns within the dominant hemisphere's network, which becomes less likely after large lesions. Compensation may also involve secondary centers of the ipsilateral network, a less efficient reorganization. If most of the ipsilateral perisylvian cortex is infarcted, the least efficient compensation is mediated by homotopic contralesional regions.

More recently, the research conducted by Stockert et al., (2020) significantly built upon the hierarchical model by Heiss and Thiel (2006) by proposing an expanded model, which provided a more detailed understanding of the neural mechanisms underlying language recovery after stroke. In their study Stockert and collaborators examined patients with circumscribed lesions in either the left frontal or temporo-parietal cortex. By comparing these two patient groups, the researchers were able to directly compare the contributions of distinct lesion-dependent network components to language reorganization. They found that the global network disturbance in the acute phase, characterized by reduced functional MRI language activation, and subsequent subacute network reactivation were driven by temporo-parietal lesions, suggesting that the site of the lesion influences the initial disruption and subsequent recovery of language networks.

Furthermore, they found that regardless of lesion location, early compensation in the subacute phase was accompanied by increased activation of bilateral domain-general networks and reactivation of perilesional cortex. In the later chronic phase, reorganization was mainly conveyed by left hemisphere language areas in the anterior temporal lobe and posterior temporal lobe. This indicates that while undamaged left hemisphere language networks are crucial for recovery, other regions, such as domain-general networks and perilesional cortex, also play a role in compensatory mechanisms.

These three mechanisms were initially perceived within the confines of the "classical model", which asserted that aphasia manifests exclusively due to lesions in the fronto-temporo-parietal cortical areas, a viewpoint that dramatically underestimated the expansive network of brain regions now known to be instrumental in language comprehension (Price, 2012) and production (Indefrey, 2011). In contrast, contemporary research unequivocally acknowledges that aphasia can also emerge as a consequence of damage to white matter tracts (Corbetta et al., 2015; Forkel & Catani, 2018; Marebwa et al., 2017; Yourganov et al., 2015) and subcortical areas (Cappa et al., 1986; Fritsch et al., 2022; Papagno & Guidotti, 1983; Radanovic & Almeida, 2021; Stockert et al., 2020). Despite this expanded understanding, the significant role that subcortical areas play in the recovery process remains underappreciated in the existing literature, necessitating further exploration and acknowledgment (s et al., 2023; Poeppel et al., 2012).

1.4. Language learning in patients with aphasia

1.4.1. What is learning?

Within the scope of cognitive neuroscience, learning is commonly understood as the process by which knowledge or abilities are gained, synthesized, and adjusted through lived experiences, prompting changes in neural structures and functions. This comprehensive process incorporates the encoding, consolidating, and recalling of information within the brain (Magill, 2016; Schilling et al., 2013; Squire & Wixted, 2011). Existing research (Ashby et al., 2002; Ashby & O'Brien, 2005; M. H. Davis & Gaskell, 2009) posits that there are several learning systems at play, with alterations in stimuli, tasks, and feedback potentially leading to the deployment of diverse behavioral and neural strategies.

Regarding language, language learning unfolds across various layers of the intricate language system encompassing the phonological structure of speech, the grammatical rules directing the combination of lexical and sublexical units, their orthographic representation, and the arbitrary associations between words and their meanings. This thesis primarily delves into the latter aspect: the process of learning new words and in particular, how language impairment, resulting from brain damage, affects this word learning capabilities and the role memory and learning systems play in language rehabilitation.

1.4.2. Memory, language and learning systems

Research has shown that learning mechanisms are influenced by various elements, including the presence and timing of feedback, the diversity of stimuli, and repetition (Vallila-Rohter & Kiran, 2013). This complements the widely accepted notion that we possess multiple learning systems. These systems are generally divided into two main categories: explicit and implicit learning (N. C. Ellis, 2001). Explicit learning is often linked to our declarative memory system, whereas implicit learning corresponds to the non-declarative system.

Many theoretical models posit that the process of word acquisition utilizes both the declarative and procedural memory systems, though certain facets of word learning may be more reliant on one system than the other.

A predominant model is the Declarative/Procedural (DP)(Ullman, 2001, 2004). This framework proposes that language hinges on two pivotal capabilities:

1. A mental lexicon, which holds specific word-related data, including word sounds, meanings, and classifications. This storage also encompasses unpredictable word forms and even idiomatic expressions.
2. A mental grammar, which contains the rules dictating the arrangement of language representations, enabling the understanding and creation of intricate linguistic constructs.

This framework differentiates between memory systems in relation to language facets. The mental storage relies on declarative memory, while the mental syntax is underpinned by procedural memory. The declarative memory system supports the learning and use of semantic and episodic knowledge and it's anchored primarily in the medial temporal lobe (MTL), including structures like the hippocampus, perirhinal, entorhinal, and parahippocampal cortex.

These MTL structures establish extensive connections with neocortical regions, including the temporal and parietal areas. Additionally, other cortical regions, such as the prefrontal cortex and temporal and parietal lobes, are particularly important for processing semantic knowledge (Scoville & Milner, 1957; Squire et al., 2004). Declarative memory facilitates the swift acquisition of new memories and the formation of arbitrary associations that can be consciously recalled. Over time, these memories gradually become more dependent on neocortical regions, especially within the temporal lobes (Hodges & Patterson, 1997; Squire et al., 2001).

Conversely, the procedural memory system encompasses a distinct brain network that involves the basal ganglia (especially striatum with its caudate and putamen), cerebellum, frontal cortex, in particular Broca’s area and pre-motor regions, parietal cortex, particularly the supramarginal gyrus and possibly the superior parietal lobule (BA 7); superior temporal cortex (Batterink et al., 2019; R. Ellis, 2008; P. J. Reber, 2013; Squire, 1994). This system aids in acquiring sensory-motor skills, sequences, and general regularities in both linguistic and non-linguistic contexts. While the acquisition of grammar is instinctive and not consciously accessible in one's native language, it might be less accessible for late-language learners of a second language. However, with sustained practice, there might be an increase in grammatical proficiency and a shift towards relying on the procedural system.

The DP framework also highlights that while the two memory systems operate largely independently, they can interact in both competitive and collaborative manners. Damage to one system might enhance the other's learning capabilities, potentially offering a compensatory mechanism for language acquisition in certain neurological conditions. Individual differences might exist in the reliance on these memory systems, and not all language facets depend on them. However, some might partially depend on these systems when language functions are compromised. It's essential to note that research involving patients with Parkinson’s disease (PD) and Alzheimer’s disease (AD)indicates that modifications in task structure and method of administration can either support or impede learning (Ashby et al., 2003; Koenig et al., 2007; Shohamy et al., 2004). For instance, patients with PD, who have the degeneration of dopamine-producing neurons, resulting in a deficiency of dopamine and consequent deficits in striatal regions, often show impairments in procedural-based learning and may benefit from explicit methodologies. In contrast, patients with AD face challenges primarily with episodic memory and there is evidence indicating relatively retained capacity for implicit learning (Grafman et al., 1990; Mahendra et al., 2007) Hence, while people without neurological impairments adapt across multiple task variations using diverse learning techniques, many patient groups are especially affected by changes in tasks that favor the use of explicit or implicit processes. In this light, persons with aphasia stemming from neurological injuries might possess intact learning systems that are not exploited in current rehabilitation approaches, which mainly focuses on explicit learning.

Another relevant model is the Complementary Learning Systems model (CLS) of word learning, proposed by (M. H. Davis & Gaskell, 2009; O'Reilly & Norman, 2002). This model posits that initial rapid knowledge acquisition is facilitated by sparse and highly plastic representations within the medial temporal lobes and other parts of the episodic memory network. These regions support the encoding of novel words as context-specific episodic memories, initially relying on the hippocampus (Breitenstein et al., 2005). As learning progresses and multiple exposures to novel words occur, these memories transition into more stable lexical representations through slow learning and offline consolidation processes within neocortical structures. This transition involves complementary learning operations between the hippocampal system and the neocortex, with consolidation processes mediating the shift from rapid hippocampus-dependent learning to slower neocortex-dependent learning. This consolidation also enables newly learned words to compete with existing lexicon entries.

Finally, Rodríguez-Fornells, Cunillera, Mestres-Missé, and de Diego-Balaguer (2009)proposed an integrative functional neuroanatomical model to explain language learning in adults, emphasizing three interfaces for language learning and identifying factors influencing language acquisition. The first interface, the dorsal audio-motor stream, connects the posterior superior temporal gyrus to the posterior inferior frontal and premotor regions in the left hemisphere via the arcuate fasciculus and the superior longitudinal fasciculus. This interface plays a crucial role in mapping sounds to articulation and is involved in repeating heard speech and pseudowords. It may also mediate novel language learning. The second interface, the ventral meaning integration interface, connects the inferior temporal gyrus with the ventral inferior frontal gyrus and includes a self-triggered learning mechanism for interpreting meanings. The third interface, the episodic-lexical stream, maps novel word forms to their referents through episodic, context-dependent memory traces. This mapping process is highly efficient and relies on the medial temporal lobe, including the hippocampus and the parahippocampus.

To enable the effortless use of newly learned words in different contexts over the long term, the word-referent associations must be integrated into semantic memory as context-free memory traces, a process facilitated by memory consolidation. The dorsal audio-motor interface and the episodic-lexical interface are particularly relevant to this dissertation. The dorsal audio-motor stream supports spoken production and the initial phonological learning of novel word forms, critical aspects of the word learning experiments in this study. The episodic-lexical stream, on the other hand, enables rapid mapping of word forms to object referents and conceptual information. Successful transfer of information from the medial temporal regions to cortical "lexical- semantic storages" is essential for long-term retention and retrieval of newly learned content. This aspect will be assessed through probe testing during follow-up.

Additionally, Rodríguez-Fornells et al. (2009) highlight the integrative roles of the basal ganglia and thalamus in regulating language learning interfaces and controlling cognitive processes such as attention, executive functions, and rehearsal of novel contents in short-term memory. These cognitive processes are essential for language learning, involving tasks such as perceiving new information, decoding and memorizing visual representations, associating word forms with objects, and maintaining attention. The phonological loop, a component of working memory, plays a pivotal role in storing and repeating phonological word forms until a robust phonological representation is established. Often, semantic features are incorporated into these associations, although word learning can occur with direct links between phonological and object representations, even when there is no semantic knowledge about the objects.

The CLS model and the integrative functional neuroanatomical model of language learning by Rodríguez-Fornells et al. (2009) are supported by neuroimaging studies (Breitenstein et al., 2005; James

& Gauthier, 2006; Raboyeau et al., 2010) in healthy individuals. These studies have identified brain regions in the left hemisphere associated with word learning, which overlap with regions involved in language processing. Hippocampal activation has been linked to the initial phase of associative word learning, while long-term learning has been associated with activation in left-hemispheric neocortical regions, including the temporal lobe, inferior parietal cortex, and inferior frontal cortex. Consequently, individuals with aphasia are expected to face significant challenges in novel word learning, given the involvement of these regions in the initial and long-term phases of associative word learning.

1.4.3. Learning and relearning

The primary focus of current language therapy strategies is to enhance the efficiency of an impaired language system, rather than introducing new concepts. However, therapy might involve a process of novel learning, where new neuronal connections and pathways are formed (Kelly & Armstrong, 2009). Understanding the processes underlying Speech and Language Therapy (SLT) could provide insights into whether rehabilitation taps into previously known but now inaccessible information due to stroke damage, facilitates new learning, or both. If new learning is integral to aphasia rehabilitation, it would be beneficial to delve into theories and methodologies of learning to better comprehend therapy.

Recent studies have evaluated adults with chronic post-stroke aphasia on their ability to learn new vocabulary and participate in therapy to ameliorate their word-finding difficulties (Dignam et al., 2016). The study discovered a significant correlation between the participants' capacity to learn new words and their improvement in naming ability post-therapy. This implies that the mechanisms involved in learning new words are akin to those involved in relearning words during therapy for anomia. It is worth noting that, in this context, the studied learning mechanism pertains exclusively to language; therefore, it consistently utilizes the same mechanisms. However, the evidence supporting the occurrence of new learning during the therapeutic process remains insufficient.

To effectively address this issue, it is imperative to conduct further research on the extent to which individuals with aphasia can exhibit new learning despite their language difficulties. Kelly and Armstrong (2009) suggest that once a clearer understanding is obtained, the tools and techniques used in language therapy sessions should be adjusted accordingly. If people with aphasia acquire new knowledge, this could lead to integrating innovative approaches to facilitate this newfound learning.

Although research in this field is still mixed and limited, it has shown that individuals with aphasia can successfully learn new words and their meanings after receiving training (Peñaloza et al., 2022) and that the retention of this newly acquired vocabulary can last for days (Kelly & Armstrong, 2009) or even months (Tuomiranta et al., 2014; Tuomiranta et al., 2012). As for grammar, research findings suggest that artificial grammar learning (AGL) may be preserved, to some extent, in PWA without syntactic impairments. These individuals exhibit performance patterns closer to healthy controls, indicating a lesser degree of impairment in AGL capabilities compared to other PWA subgroups. However, the exact location of brain lesions doesn't consistently determine AGL ability, with impairments observed across various lesion sites (Cope et al., 2017; Dominey et al., 2003; Schuchard & Thompson, 2017; Vadinova et al., 2020; Zimmerer et al., 2014).

1.4.4. Stimuli

As highlighted in the recent review by Peñaloza and colleagues (2022), various strategies have been adopted in this field of research, encompassing different types of stimuli and goals. Traditionally, the focus has predominantly been on helping aphasic individuals reacquire words that have become inaccessible due to their condition, predominantly leveraging stimuli such as known words paired with new referents or novel words paired with familiar referents (Freedman & Martin, 2001; R. C. Marshall et al., 2001). This conventional strategy offers a realistic, naturalistic approach to word learning, resembling the process that occurs when acquiring vocabulary in one's native language (Gupta et al., 2003).

Despite the prominence of this approach, a shift has been noted with some researchers pursued an innovative strategy by introducing completely novel materials. Here, unfamiliar referents are associated with entirely new names (P. Gupta et al., 2006; Laganaro et al., 2006; McGrane, 2006; Morrow & Fridriksson, 2006; L. M. Tuomiranta et al., 2011, 2012, 2014).

This novel pathway not only maintains the clinical necessity of reteaching known but inaccessible words to aphasic persons but potentially presents a more unadulterated measure of learning capability (Tuomiranta et al., 2012). This approach essentially minimizes the impact of prior vocabulary exposure and dependence on existing representations for learning (J. C. Marshall & Halligan, 1992). It permits valid individual comparisons among aphasic individuals and group comparisons between aphasic and non-aphasic speakers, given that the materials used are equally unfamiliar to all participants.

Furthermore, this method bypasses potential issues related to psycholinguistic properties that could affect the retrieval of known words. These could otherwise complicate the assessment of the integrity of learning in aphasia (Peñaloza et al., 2022). Hence, for these reasons, the experiments proposed in this thesis have decided to utilize only new materials.

1.5. Learning and language therapy

A number of investigations have delved into both the acquisition of new words and the response to language therapy among individuals with aphasia. A noteworthy single-case study conducted by Tuomiranta et al. (2014) highlighted the close correspondence between effective word learning skills and successful reacquisition of vocabulary. In this case, both processes were underpinned by preserved cognitive functions and the associated brain region. The individual examined in this study exhibited an exceptional aptitude for learning new words, demonstrated flawless verbal recall comparable to that of healthy controls, maintained this newly acquired vocabulary for an impressive six months, and successfully relearned the vocabulary used during therapy, with sustained improvements for nine weeks. These findings provide support for the link between word learning ability and the outcomes of anomia therapy. Moreover, they align with previous research that has shown that the utilization of learning strategies conducive to expressive language acquisition in healthy individuals can translate into effective treatment results for individuals with aphasia (Basso et al., 2001). Another study, this time a case series by Laganaro et al. (2006), showcased the success of computerized anomia therapy based on written naming and feedback in three individuals with aphasia. These participants demonstrated significant improvements in treated items, with two of them also exhibiting generalization to untrained items and sustained gains for a month. Impressively, all three participants displayed an ability to learn new words, albeit performing below the level of healthy controls. Notably, phonological similarities among words influenced both treatment outcomes in one patient and new word learning in all healthy controls and one additional individual with aphasia. This observation suggests that shared sub-lexical units may play a role in facilitating both treatment-related improvements and the acquisition of novel lexical representations, either by forging new connections or reinstating pre-existing ones. A more recent large group study conducted by Dignam et al. (2016) delved into this association by involving thirty individuals with aphasia who received therapy consisting of semantic feature analysis, phonological component analysis, and computerized exercises focused on repetition, picture naming, and cueing, administered in either a concentrated three-week program or a distributed eight-week schedule. Both groups demonstrated significant therapy-related enhancements in naming for both treated and untreated items, which were sustained at the one-month follow-up. Additionally, participants exhibited substantial progress in a novel word learning task, with more robust receptive recognition relative to expressive recall. Notably, the study identified a significant link between immediate therapy gains on treated items and receptive word learning, although this connection was not statistically significant at the one-month mark. As previously noted, individuals with aphasia characterized predominantly by lexical-semantic deficits displayed impaired word learning abilities, underscoring the influence of the site of language impairment. Both the capacity to learn new words and treatment outcomes were modulated by the severity of aphasia and lexical-semantic processing capabilities.

Only one study by Schuchard et al. (2017), investigated the correlation between implicit learning in individuals with aphasia and the response to implicit language treatment focused on passive sentence comprehension. Firstly, the authors explored implicit learning using the Serial Reaction Time Task and found out that individuals with aphasia displayed a significant increase in reaction time between sequenced and random blocks of the SRTT, indicating successful implicit sequence learning. However, while the participants with aphasia in the study exhibited implicit learning abilities in the SRTT, they didn't demonstrate substantial benefits from an implicit sentence comprehension training program focused on exposure to grammatically correct passive sentences. Nevertheless, it's worth noting that the results of the implicit treatment protocols should be interpreted cautiously due to methodological limitations. The study involved a relatively small number of participants and focused on training only one sentence structure (passive sentences) over a limited number of sessions. Variability in performance during baseline assessments and the small number of baseline probes complicated the interpretation of changes during training and potentially underestimated treatment effects. Additionally, the study's limitations prevented a comprehensive examination of the relationship between implicit learning abilities and the response to implicit sentence comprehension treatment. As the implicit treatment was not effective, the study couldn't explore potential associations between improvements in linguistic skills and performance in the implicit learning task. Moreover, the study relied on a single non-linguistic task to assess implicit learning abilities. Ideally, assessments of implicit learning should encompass multiple tasks assessing learning for different structures and in different domains. Additionally, the authors conclude that to assess the efficacy of implicit language treatment more thoroughly, research should directly compare the effects of implicit and explicit training methods. This comparison was done just by one study by Silagi et al. (2020), who examined the impact of two different therapeutic methods, Mapping Therapy and Oral Reading for Language in Aphasia (ORLA), on the oral and written production of individuals with agrammatism, specifically those with Broca's aphasia. Mapping Therapy, although primarily focused on oral production, includes an explicit learning protocol engaging conscious analysis and directed attention to grammatical aspects. On the other hand, ORLA, which relies on reading training without explicitly teaching syntactic rules, tends to promote more implicit learning, facilitated by the repetition of the same stimulus during reading. The study included six participants in the chronic stage of aphasia, where spontaneous language improvement tends to be minimal, making the therapeutic effects more noticeable. It's important to note that the participants displayed variability in lesion location, primarily in frontal and posterior perisylvian regions, including subcortical areas. The severity of aphasia among the participants was predominantly in the more severe range, and some also presented with comorbidities like apraxia of speech. Results indicated that Mapping Therapy led to improvements in written production, including the number of words, nouns, verbs, closed-class words, and complete sentences. In contrast, ORLA resulted in improvements in agrammatism in oral language, including the number of words, verbs, and speech rate. The study's findings align with previous research that suggested the effectiveness of Mapping Therapy for individuals with less severe agrammatism, while ORLA appeared more effective for individuals with more severe agrammatism and comorbidities. This discrepancy in results might be attributed to the different profiles of participants in various studies. Additionally, the study highlighted the potential for cross-model transfer of competence, where improvements in one language modality (e.g., reading) can have positive effects on another modality (e.g., oral production). Some studies have shown that reading-based therapies can enhance verbal skills, and vice versa. The study demonstrated that individuals with agrammatism in Broca's aphasia can benefit from both implicit and explicit learning methods in language therapy. Mapping Therapy showed promise in improving written production, while ORLA was effective in addressing agrammatism in oral language. These findings highlight the importance of considering different learning models and tailoring therapy to individual profiles in aphasia rehabilitation.

1.6. Explicit learning in patients with aphasia

The study of explicit learning in PWA has been primarily conducted through associative learning paradigms (Peñaloza et al., 2022). These paradigms, which involve the association of individual words with conceptual referents through systematic mappings, typically include a learning phase where participants are taught word-picture pairings presented visually, auditorily, or both, followed by a test phase that assesses the success of word learning through recall and recognition measures.

Research in this area, though limited, has demonstrated that PWA can learn new vocabulary (Freedman & Martin, 2001; Kelly & Armstrong, 2009; J. C. Marshall & Halligan, 1992; L. M. Tuomiranta et al., 2011). Most studies suggest that the newly acquired linguistic information can be effectively retained for up to a week post-training. However, compared to healthy individuals, PWA generally exhibit a lower learning capacity, and this ability varies significantly among individuals.

Marshall et al. (1992) conducted a study involving 23 PWA and eight healthy controls to determine the effectiveness of different facilitation and cueing tasks on word-symbol pairings. The study employed four facilitation tasks: visual matching, auditory matching, combined visual and auditory matching, and a non-rehearsal condition. They also used four cueing tasks: repetition, self-cueing, determinate sentence completion, and indeterminate sentence completion. The results indicated that PWA had lower accuracy compared to healthy controls but showed improvement in all training conditions, with the repetition condition resulting in the highest improvement. Although naming ability decreased one week after training in all conditions, some learning still occurred.

In a similar vein, Marshall et al. (2001) carried out a study with 30 individuals who had aphasia. The study focused on unfamiliar word-picture pairings of different dog breeds. The researchers used two conditions in their study: associative learning through self-cueing using semantic and visual features and phonological cueing using the first phoneme and number of syllables. Accuracy during training was measured, and naming probes without cueing were conducted one week, one month, and six months after training. Both conditions showed learning after training, but the self-cueing condition demonstrated better naming accuracy and maintenance at the 6-month mark.

Research has shown that the use of semantic and phonological cues can help PWA maintain the learning material for extended periods of time, typically ranging from 1 month (Freed & Marshall, 1995; Tuomiranta et al., 2011) to 6 months (Tuomiranta et al., 2012, 2014). Freed and Marshall (1995) conducted a study involving 10 PWA and 10 individuals without any impairments to assess associative learning using self-cueing. Both semantic and visual features were utilized in the study. Participants were taught 20 word-picture pairs related to dog breeds, while another set of 20 pairs served as control stimuli featuring dogs and birds. The results indicated that the participants with aphasia performed worse than the control group in all three sets of stimuli. However, they showed better naming abilities for the trained items than the untrained ones. Additionally, the learning effects were found to be long-lasting as they persisted during testing at both one-week and one-month intervals.

Freed et al. (1995) conducted a study on associative learning involving 30 individuals with aphasia. The participants were presented with 30 pairings of real words and abstract symbols, with 20 pairings used for training and 10 for control purposes. The study aimed to compare self-cueing, where participants generated their own associations based on semantic and visual features, with provided cueing, where associations were created by the participants but given by the examiner. Both cueing procedures resulted in similar accuracy levels during mid-training, post-training, and follow-up naming probes, indicating that the skills were maintained equally well thirty days after testing. Additionally, both groups showed similar improvements on control items during training. However, neither group showed significant improvements in naming accuracy on the cued naming probe compared to the final non-cued naming probe thirty days after training.

Moreover, the study conducted by Tuomiranta et al. (2014) discovered that successful word learning, and vocabulary re-learning are connected to preserved processing abilities, specifically in orthography rather than phonology and the corresponding brain regions. The patient in this study exhibited exceptional ability to learn new words with verbal recall similar to healthy individuals, as well as sustained learning maintenance for six months and vocabulary re-learning for all trained words with maintained gains for nine weeks.

In a more recent study by Dignam et al. (2016), thirty individuals with aphasia underwent therapy that included semantic feature analysis, phonological component analysis, and computerized therapy focused on repetition, picture naming, and cueing. The therapy was administered either in a 3-week intensive schedule or an 8-week distributed schedule. Both groups showed significant improvements in naming for treated and untreated items, which were maintained at one month. Participants also demonstrated significant improvement in a novel word learning task, with better receptive recognition than expressive recall. The study found a significant association between immediate therapy gains on treated items and receptive word learning, although this association was not significant at one month.

In addition to the above studies, a study by Tuomiranta et al. (2012) found that using semantic and phonological cues can help PWA maintain the learning material for extended periods, typically ranging from 1 month to 6 months. The study involved 10 PWA and 10 individuals without any impairments and aimed to assess associative learning using self-cueing. Both semantic and visual features were utilized in the study. The participants were taught 20 word-picture pairs related to dog breeds, while another set of 20 pairs served as control stimuli featuring dogs and birds. The results indicated that the participants with aphasia performed worse than the control group in all three sets of stimuli. However, they showed better naming abilities for the trained items compared to the untrained ones. Additionally, the learning effects were found to be long-lasting as they persisted during testing at both one-week and one-month intervals.

In summary, explicit learning in PWA has been shown to be possible, albeit at a lower capacity compared to healthy individuals. This learning is facilitated through semantic and phonological cues. Importantly, learned material can be retained for extended periods, ranging from one month to six months post-training. However, there is considerable variability among individuals, emphasizing the need for personalized intervention strategies. Preserved processing abilities, particularly in orthography play a pivotal role in word learning. In conclusion, while explicit learning in PWA has its challenges it is achievable with the right strategies. Further research will likely uncover more effective ways to enhance learning in this population.

1.7. Implicit learning in patients with aphasia

The central focus of this thesis is the exploration of implicit learning in the context of aphasia, a topic that has not been as thoroughly investigated as explicit learning. The potential role and significance of implicit learning in language rehabilitation remain largely uncharted territories (Peñaloza et al., 2022).

Before examining the studies on implicit learning in aphasia, it's useful to better understand the concept of implicit learning, its paradigms, and its neural correlates. This understanding is pivotal in grasping the clinical implications and the rationale for selecting this type of learning as a focus for the thesis.

Implicit learning is a foundational process described as the capacity to learn without awareness of the products of learning (Frensch & Rünger, 2003). This crucial capability is deeply intertwined with human cognition's inherent ability to discern patterns in the environment, a skill paramount in various aspects, from perception and language to decision-making and even the appreciation of avant-garde music. While "implicit learning" has been a core research area since the works of Reber in 1967, another distinct research trajectory has revolved around "statistical learning", which pertains to the extraction of statistical properties of sensory data over time or space (Frost et al., 2015; Schapiro et al., 2016; Siegelman et al., 2017). Although these research paths utilize diverse tasks and methodologies, they share commonalities (Batternink, 2019). Implicit learning research has traditionally focused on understanding the nature of knowledge acquired during the learning process, particularly discerning whether it's conscious or unconscious (Batternink et al., 2019). On the other hand, statistical learning research has been primarily concerned with the incidental nature of learning, noting that it often occurs without explicit instructions to recognize patterns (Batterink et al., 2019; Saffran, 2003; Saffran et al., 1996, 1997). Despite these distinctions, both fields intersect in many areas, suggesting they might tap into similar foundational memory processes. This overlap is supported by scholars such as Christiansen (2019) and Perruchet & Pacton (2006). Both paradigms underscore the importance of incidentally extracting structural information from the environment, primarily through passive exposure, without a deliberate intent to learn. The behavioral outcomes of these types of learning are comparable, whether it's identifying phoneme or word boundaries, as observed in statistical learning, or reproducing learned motor sequences, characteristic of implicit sequence learning. Some recent discussions suggest the potential to unify these two areas under the term "implicit statistical learning" (ISL) (Rebuschat & Monaghan, 2019).

In the laboratory setting, various paradigms have been employed to investigate ISL, including the Artificial Grammar Learning task (AGL; Reber, 1967), the Serial Reaction Time task (SRTT; Nissen & Bullemer, 1987), the Artificial Speech Segmentation task (Saffran et al., 1996, 1996, 1997) and Cross-Situational Learning (CSL; Rebuschat et al., 2021) In the following section, I will delve into a detailed explanation of these paradigms, explore the neural correlates associated with them, and discuss studies involving healthy and aphasic individuals.

1.7.1. Artificial Grammar

In the AGL task (Reber, 1967), participants are exposed to sequences of letters formed by a specific artificial grammar. After being exposed to these sequences, participants are informed of the underlying rules and are then tasked with categorizing new sequences as either following the grammar or not. Interestingly, even without clearly articulating the rules, participants tend to correctly categorize the sequences more often than not (A. S. Reber, 1967, 1976).

Neuroimaging has unveiled the involvement of various brain regions in Artificial Grammar Learning, including the prefrontal cortex, particularly the left inferior frontal regions, parietal areas, and the basal ganglia (Forkstam et al., 2008; Petersson et al., 2012; Skosnik et al., 2002; Uddén & Bahlmann, 2012). Different researchers have emphasized different brain regions in their interpretations. For instance, the activation of the left inferior frontal gyrus, often associated with linguistic processing, has been linked to sequence processing and learning (Forkstam et al., 2006; Hagoort, 2005; Petersson et al., 2012).

Supporting this and aligning with the DP model regarding the role of the inferior frontal regions and the basal ganglia in implicit language learning (Ullman, 2001, 2004), impaired AGL for complex abstract structures was identified by Dominey and collaborators (2003) in Broca's aphasia, an aphasia subtype most commonly associated with lesions in the left frontal lobe. In their study, Dominey et al., (2003) utilized AGL to test order processing impairment in 7 patients with aphasia. Participants were trained on a specific sequence structure, where transforming the first half of the sequence (123) resulted in the second half (213). This structure was represented using letters (e.g., ABCBAC or DEFEDF). After the exposition phase, participants were asked to determine whether new sequences were correct or incorrect. Agrammatic aphasia appeared to only cause a selective impairment for non-canonical complicated letter sequences (123–213). On the other hand, participants with agrammatic aphasia performed similarly to control participants when it came to processing simple and canonical structured letter sequences (123-123), suggesting that their impairment was specific to more complex linguistic structures. Similarly, investigations focusing solely on non-linguistic implicit learning in aphasia highlighted poor or abnormal visual AGL in patients with agrammatic aphasia, whereas non-agrammatic patients performed within the normative range on the same tasks (Christiansen et al., 2010; Zimmerer et al., 2014).

Focusing on basal ganglia, putaminal lesions predicted linguistic AGL in PWA with agrammatism in a study by Cope et al. (2017) who administered an AGL task involving non-words and tones to patients with Broca's aphasia, nonfluent Primary Progressive Aphasia (PPA), and healthy controls. The participants were exposed to pseudoword and tone artificial grammars and then had to determine whether test sequences were consistent with the rules they learned during exposure. The results showed that both patient groups had impaired pseudoword sequence learning, with PWA performing worse than controls. However, all groups improved with additional exposure across all rule types. Simple linear rules were more accessible to learn than complex configurational and hierarchical rules for all groups. Nevertheless, contrary to the DP model and above-mentioned neuroimaging evidence, AGL abilities were not entirely lacking in these groups. Similar results were found in Schuchard and Thompson (2017), who conducted a study involving patients with agrammatism and healthy controls. Participants were exposed to monosyllabic pseudoword-based grammatical phrases as they watched a silent nature video, unaware of the underlying rules that determined the order of items in the language's hierarchical phrase structure grammar. In an artificial grammar judgment test, both the trained groups surpassed an untrained control group in performance, displaying comparable accuracy. However, only the control group showed significant progress over multiple testing sessions. This pattern was also found in Jarret et al., (2019) whose findings showed amodal (visual and auditory) artificial grammar learning in patients after inferior frontal lesion. Their research is of particular interest because it allows for the investigation of the pivotal role of the left IFG, which is especially significant given that studies involving aphasia often show variability in lesion sites and that the lesions in aphasic patients can also encompass subcortical regions like the basal ganglia. According to the authors, the left IFG might not have a singular role in implicit learning. It could be proposed that intact artificial grammar learning observed in left IFG patients occurs because either the right IFG compensates for the left IFG dysfunction or the left IFG is a component of a comprehensive neural network underpinning grammar learning including basal ganglia, which not only have been linked to implicit learning but also project to Broca's area.

1.7.2. Serial Reaction Time Task

In a parallel vein, Schuchard and Thompson (2014) conducted an examination on ten persons with aphasia, specifically those with syntactic impairments, utilizing a distinct experimental framework to probe into both implicit and explicit learning deficits in aphasia. The findings illuminated that implicit learning was not as severely impacted as explicit learning. The researchers posited that the explicit awareness and retention of a sequence exert undue pressure on working memory, thereby obstructing the fruitful progression of learning. The employed paradigm was the Serial Reaction Time Task (SRTT), wherein participants are tasked with responding to a series of visual cues appearing in one of four possible locations by pressing a corresponding button. The cues, unknown to the participants, follow either a repeating sequence or a random pattern. As participants unconsciously discern the concealed pattern, their response times to the recurring cues gradually diminish, beyond the general response time reduction observed with randomly ordered cues due to task practice effects. A linguistic version of the paradigm includes letters or words in place of visual cues and was used in this study.

Neuroimaging studies have associated the learning of trained sequences in the SRTT with activation in the striatum and cortical areas tied to motor planning (Daselaar et al., 2003; Doyon et al., 1996; Grafton et al., 1995). Additionally, hippocampal activation, which tends to wane over the training duration, is often observed during the initial exposure to the sequence (Albouy et al., 2008; Fletcher et al., 2005). Positive correlations have been identified between learning success and activation in the striatum

(Garraux et al., 2007; Peigneux et al., 2000), and deactivation in the Medial Temporal Lobe (Albouy et al., 2008; Rieckmann & Bäckman, 2009).

Building on the results of Schuchard and Thompson (2014), several other studies have explored the idea that aphasia patients should be able to engage in implicit learning if they have a functioning striatal projection system, as suggested by Breitenstein (2002). These studies used the SRTT method and produced varied results.

For instance, Goschke et al. (2001) in their first experiment, discovered that individuals with both Broca's and Wernicke's aphasia exhibited spatial-motor sequence learning in the SRTT on par with healthy participants. This was despite the absence of explicit learning as evidenced by a recognition test and a sequence prediction task. In their second experiment, Goschke et al. delved deeper by contrasting phoneme sequence learning between individuals with Broca's aphasia and healthy participants across two scenarios. In one, spoken phonemes were presented randomly, but their spatial locations formed a consistent pattern. In the other, the spoken phonemes followed a consistent sequence, but the motor responses were randomized. The findings indicated that while healthy participants mastered both sequences, those with Broca's aphasia only grasped the motor sequence, struggling specifically with the phoneme sequence. Notably, no group exhibited overt sequence knowledge, though one aphasic participant could replicate the entire phoneme sequence, albeit with a minor Reaction Time (RT) cost.

In a study in a similar vein, Dominey et al. (2003) utilized a visual letter SRTT to probe into the learning of serial structures (the sequence order of elements) and abstract structures (the rules governing element relationships) among two individuals with agrammatism and healthy controls. The findings highlighted that both the aphasic individuals and controls retained their ability to learn serial structures. However, when it came to abstract structures, the aphasic individuals faced challenges, whereas the healthy controls exhibited a notable ability to transfer to predictable sequences, coupled with an RT reduction when comparing predictable to unpredictable sequences.

1.7.3. Speech Segmentation

Finally, speech segmentation, a traditional statistical learning task, contributes to research aimed at understanding ISL in both healthy individuals and those with aphasia (Karuza et al., 2013; Saffran et al., 1996, 1997). In this task, participants are introduced to a continuous stream of speech comprising recurring three-syllable nonsensical "words" (e.g., bupada, babupu, tutibu create bupadababupututibu; Saffran et al., 1996, 1997). The challenge for learners is to discern the statistical regularities between adjacent syllables, which are more frequent within words than between them, to identify the embedded "word" structures. Subsequent to this exposure, adult participants' learning is typically assessed through a forced-choice recognition test, differentiating words from the exposure stream (e.g., bupada) from pseudoword distractors (e.g., pubati). Successful learning is deduced if performance surpasses random guessing. Other metrics, such as reaction times in a rapid target identification task, have also been employed to gauge the impact of learning on real-time processing (e.g., Batterink et al., 2015; Franco et al., 2015; Kim et al., 2009; Turk-Browne et al., 2010; Turk-Browne & Scholl, 2009). Analogous methodologies have been applied in the visual domain, where participants observe sequences of images or abstract forms arranged into repetitive triplets (Fiser & Aslin, 2002; Turk-Browne et al., 2005).

A select number of neuroimaging studies have delved into the neural foundations of statistical learning, juxtaposing activations triggered by speech streams with recurring words against those triggered by randomized syllable streams (Cunillera et al., 2009; Karuza et al., 2013; McNealy et al., 2006). A consistent observation from these studies is that statistical patterns amplify activations in advanced auditory networks, particularly in regions previously associated with auditory or linguistic processing, such as the left superior temporal gyrus and the left inferior frontal gyrus, extending to the premotor cortex (Cunillera et al., 2009; Karuza et al., 2013).

In this case, as well, it is noteworthy to look at the findings by Peñaloza et al. (2015), where both fluent and non-fluent PWA and controls were exposed to a continuous spoken artificial language. The results indicated that both the aphasia group and the healthy control group achieved comparable and significantly above-chance performance on a 2-alternative forced-choice test designed to assess their ability to distinguish pseudowords from the artificial language from pseudowords. Nevertheless, participants with primarily anterior lesions affecting the opercular and insular areas (regardless of potential basal ganglia damage) recorded lower outcomes on the speech segmentation test reinforcing the pivotal role of the left frontal cortex in statistical learning (Cunillera et al., 2009; Karuza et al., 2013).

1.7.4 Cross-situational Learning

Subsequent research by Peñaloza et al., (2016) delved into cross-situational learning in individuals with aphasia, with different lesion locations, and a group of healthy participants, while also exploring its connection with SL as described in their earlier work (Peñaloza et al., 2015). In the CSL experiment, each trial presents an ambiguity, featuring two spoken pseudowords paired with two unfamiliar visual objects, leading to four potential word-object associations. By observing word and object co-occurrences over multiple trials, participants could discern the correct associations. All participants exhibit significant CSL, while individuals with aphasia learned at a slower pace and achieved lower proficiency compared to the control group. Interestingly, seven of the patients showed learning in the initial recognition test, and nine displayed cumulative learning by the final test. The research also highlighted a notable correlation between CSL and SL across all participants, indicating a shared learning process for word acquisition and word-object associations in aphasia. This underscores the potential of SL as a mechanism that, for some individuals with aphasia, can facilitate the acquisition of new word phonology (Peñaloza et al., 2015) and basic lexical-semantic relationships (Peñaloza et al., 2017) through the bottom-up analysis of statistical patterns in a new language context.

1.7.5. Incidental Learning

Lastly, in order to introduce the remaining studies and the paradigm that will be used in this thesis, a preamble is necessary. Implicit learning often overlaps with incidental learning (Hulstijn, 2007; Leow, 2015). This overlap can be traced back to the common feature that both types of learning can transpire without a deliberate intention. However, implicit learning is distinct in that it operates without any awareness during the learning phase (J. Williams, 2012). In situations of incidental learning, participants might become aware, or might not, of the linguistic emphasis of the study. On the other hand, implicit learning requires that participants stay unaware of what they are assimilating throughout the study. Implicit learning is thus always incidental, but incidental learning is not always implicit (Hulstijn, 2012, 2003).

Neuroscientific studies have shown that the striatal projection, a part of the brain involved in reward and reinforcement, plays a crucial role in incidental learning. The striatum is a subcortical structure located within the basal ganglia of the brain, which are involved in procedural learning. It receives inputs from various areas of the cerebral cortex and is involved in various forms of cognitive flexibility, including the ability to shift attention between different tasks (Grahn et al., 2009). This suggests that the striatum may play a role in the ability to learn incidentally by shifting attention between different aspects of a task.

The seminal work of Grossman and Carey (1987) marked a significant contribution to the understanding of incidental learning. They investigated this form of learning in eight agrammatic Broca's PWA, seven fluent PWA, and five controls. Their study aimed to understand the extent to which PWA can learn new words and whether the aspects of the word they acquire depend on their specific language processing deficit. The researchers introduced the participants to the new word "bice," which referred to the dark green portion of the color spectrum. Participants heard the word used correctly in sentences without explicit instruction or definition during a drawing task involving pens of different colors, including some colored as bice and some that were not bice-colored. The grammatical and semantic knowledge was assessed 15 minutes later during the post exposure period. The findings of Grossman and Carey's study revealed that brain-damaged patients could engage in lexical acquisition, but Broca's PWA and fluent PWA learned different aspects of the new word. Both groups exhibited increasingly accurate hypotheses for identifying a bice-colored object when exposed to "bice" multiple times. However, agrammatic aphasics struggled with understanding the grammatical form class of "bice" in metalinguistic judgment tasks. In contrast, fluent aphasics had difficulty classifying bice-colored objects as "bice" in an object classification task.

In a subsequent study, Breitenstein et al. (2004) investigated incidental associative learning in young controls and individuals with Broca's or Wernicke's aphasia. They presented pseudoword-known object picture pairings during training. The learning principle was the higher statistical co-occurrence of "correct" pairings compared to "incorrect" pairings. Each correct pairing was presented ten times more often than each incorrect pairing. The results showed successful learning in healthy participants, with visual feedback enhancing performance, while both PWA groups demonstrated above-chance learning during training and on transfer tests without feedback. This confirms the hypothesis that propelled the study, which posits that implicit learning should be feasible in patients with aphasia given an intact striatal projection system. Nonetheless, the research examined this learning modality in merely two young patients - one with Broca's and another with Wernicke’s aphasia, both in the chronic phase, underscoring the necessity for replication with a larger participant pool. Moreover, in their study, Breteistein and collaborators utilized existing objects, not representing a pure measure of learning as previously elucidated.

Although Peñaloza et al. (2022) categorized this paradigm divergently from implicit learning, defining it as incidental learning, and defining incidental learning as a separate mechanism, the original authors, Breitenstein et al., (2005, 2002), asserted that word acquisition was accomplished implicitly, through a simple statistical association between words and objects. Methodologically, incidental learning has been operationalized as an experimental condition wherein participants are unaware of the fact that they will be tested later (Hulstijn, 2003, 2013; Williams, 2009). As already mentioned, while implicit learning further characterizes itself through the absence of awareness throughout the learning process (Williams, 2009), in incidental learning settings, participants may or may not become aware of the linguistic focus of the experiment. In this paradigm, participants are not explicitly informed about the linguistic focus, for this reason, when using it authors such as Antonenko et al. (2016) and Flöel et al., (2008) refer to it as both an incidental and implicit learning task. Additionally, the distinction between learning types is not always clear, especially when the definitions intersect or overlap. Peñaloza's concern indicates that incidental learning paradigms do not preclude the recruitment of explicit learning processes and MTL structures. However, as we observed earlier, MTL can be activated during tasks of implicit and statistical learning as well (Batterink et al., 2019; Plante et al., 2015, 2017; J. N. Williams, 2020), and an increasing number of investigations highlight the potential interplay between these two learning systems (Yang & Li, 2012). Breitenstein, during an fMRI study, investigated the neural correlates of this exact paradigm and found that the left hippocampus showed synchronized activity with other neocortical brain regions, including the left superior temporal cortex, a region pivotal not only to auditory processing but also to statistical learning (Batterink et al.,2019; Williams,2020).

As Antonenko et al. (2016) and Flöel et al., (2008) we consider this paradigm both an incidental and implicit statistical learning. For this thesis, the choice of this paradigm is driven both by the neuroanatomical hypothesis, whereby patients affected by aphasia may exploit areas typically not impacted by stroke but potentially responsible for implicit and associative learning, and a behavioral hypothesis whereby implicit incidental learning conditions should maintain cognitive strategies relatively homogeneous and keep attentional demands low (Breitenstein, 2004).

1.8. Boosting Learning: Effects of Transcranial Electrical Stimulation Techniques on language learning

Given that the capacity to learn new words may be pivotal in deciphering the mechanisms of language restoration in aphasia and that this understanding could reshape both diagnostic and therapeutic approaches (Peñaloza et al., 2016), it's valuable to explore methods that enhance this learning capability. Such methods could form the basis for targeted linguistic strategies that facilitate rehabilitation (Basso et al., 2001; Breitenstein et al., 2004; Kelly & Armstrong, 2009; Flöel et al, 2008). Among various interventions that can amplify learning, non-invasive brain stimulation, such as repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), and transcranial alternating current stimulation (tACS), and transcranial random noise stimulation (tRNS), stands out (Balboa-Bandeira et al, 2021).

In particular, considering the benefits of tDCS, such as its cost-effectiveness, ease of use, portability, and potential as an ideal supplementary treatment during stroke rehabilitation (Marangolo et al., 2018; Marangolo & Caltagirone, 2014; Marangolo & Papagno, 2020; Monti et al., 2013) , it was the selected method for experimentation in this thesis.

tDCS involves the application of a mild electric current via electrodes placed on the scalp. The electric current travels from the cathode (negative electrode) to the anode (positive electrode) interacting with the underlying cerebral cortex. While the exact mechanisms of tDCS remain to be fully understood, it's widely recognized that its effects on brain activity vary based on the current polarity, intensity, and duration (Monti et al., 2013). Typically, in healthy subjects, anodal stimulation is believed to increase neuron excitability by depolarizing them, while cathodal stimulation tends to have the inverse effect. The underlying mechanisms of tDCS can be categorized into two main types: synaptic (which involves changes in the strength of synaptic connections) and non-synaptic (which involves alterations in the resting potentials of both pre and post-synaptic neurons) (Brunoni et al., 2012; Stagg & Nitsche, 2011). The immediate effects of tDCS, which arise from adjustments to the resting membrane potential, might differ from its long-term impacts. These prolonged effects, though lasting, can be reversed and are thought to be linked to various processes, with the primary ones being the induction of Long-Term Potentiation (LTP) and Long-Term Depression (LTD) (Monti et al., 2013). Hebb (2005) outlined LTP as the enhancement of the neural link between two neurons that activate concurrently. In contrast, LTD denotes a sustained reduction in neural activity. These events signify an intensification and a diminution of synaptic links, respectively. They hold significance in the domains of learning, memory creation, and neural adaptability, and might play a role in the brain's functional recovery post-injury (Nitsche et al., 2008). Some authors like Barbati et al (2020) have emphasized nitric oxide (NO) as a novel facilitator of tDCS effects in fostering long-term potentiation. N-methyl-D-aspartate (NMDA) receptors also seem to play a part in the synaptic plasticity induced by tDCS. Nitsche et al. (2003) found that when an NMDA receptor blocker was given, tDCS offline effects disappeared. Moreover, serotonin and dopamine are believed to be instrumental, in enhancing excitatory and repressive stimulation, respectively. Their interplay with tDCS remains somewhat ambiguous, necessitating further research for clarity (Sandars et al., 2016). Ardolino et al. (2005) proposed another theory on how tDCS might induce lasting brain alterations, suggesting these changes could stem from non-synaptic mechanisms triggered by stimulation. They theorized that axonal molecules might undergo structural and functional modifications when subjected to direct current stimulation.

tDCS is increasingly acknowledged for its potential to enhance language learning in healthy individuals (Balboa-Bandeira et al., 2021) and recovery in people with aphasia (Elsner et al., 2020). In 2008, Flöel and his team studied the effects of tDCS on healthy adults and found enhancements in their ability to learn non-words (Flöel et al., 2008). Subsequent research has delved into various linguistic capabilities, such as verbal fluency (as seen in studies by Cattaneo et al., 2011, 2016; Monti et al., 2013), naming abilities (as researched by Fertonani et al., 2010; Sparing & Mottaghy, 2008), word retrieval (highlighted by Fiori et al., 2011), and vocabulary enhancement (noted in Flöel et al., 2008 and Hussey et al., 2015).

While results across studies have shown some variability, there is a consensus that transcranial electrical stimulation (tES) has the potential to augment the language learning phase. A meta-analysis by Simonsmeier et al. (2018), which analyzed 35 studies, underscored the positive role of tES in enhancing various linguistic skills including language learning. Similarly, Balboa-Bandeira et al. (2021) conducted a comprehensive meta-analysis to evaluate the impact of tES on the acquisition of a second or foreign language among healthy individuals. Their research pointed to a moderate positive effect of different types of tES techniques, such as transcranial direct current stimulation, high-definition transcranial direct current stimulation (HD-tDCS), transcranial random, noise stimulation (tRNS), and transcranial alternating current stimulation (tACS) on the overall process of language acquisition. However, the benefits did not extend to faster response times or sustained learning after a week. Importantly, the effectiveness was observed across various tES methods, especially when applied for 20-25 minutes on areas of the brain associated with language. When it comes to the study of non-word learning, several researchers have focused on specific brain regions. Flöel et al. (2008), for instance, applied anodal tDCS to Wernicke’s area and observed improvements in non-word learning. Similarly, Fiori et al. (2011) targeted both the Wernicke’s area (anodal tDCS) and the right occipitoparietal area (cathodal tDCS), finding beneficial effects on word learning, recognition, and name retrieval. Meinzer et al. (2014) shifted their focus to the left posterior temporoparietal junction and found that anodal tDCS facilitated learning, especially with multiple applications. Owusu and Burianová (2020) also targeted Wernicke’s area with anodal tDCS and observed better performance in non-word recalls. Lastly, Perceval et al. (2020) applied anodal tDCS to the left inferior frontal gyrus and found that multisession tDCS improved verbal associative learning, particularly in participants with lower baseline learning scores. In the realm of artificial grammar learning, De Vries et al. (2010) concentrated on Broca's area with anodal stimulation, though their results showed a trend in favor of the tDCS group without significant group differences. For studies focusing on foreign word learning, specifically in Swahili, Pasqualotto et al. (2015) applied transcranial random noise stimulation with bilateral high frequency(100–600Hz)to the dorsolateral prefrontal cortex and the Posterior parietal cortex. Their results suggested that posterior parietal stimulation might play a role in foreign language learning. Antonenko et al. (2016) delved into implicit language learning and applied tACS bilaterally at 6Hz to the Temporoparietal cortex and Wernicke's area. Their findings indicated that implicit language learning performance improved after receiving tACS. In the study of foreign verb learning using Italian as the language, Fiori et al. (2018) targeted the left inferior frontal gyrus and the contralateral fronto-polar region. Their results showed behavioral improvements with the anodal tDCS condition. The only study that has compared the effects of tDCS on both implicit and explicit learning is the research conducted by Perikova et al. in 2022. In this study, the researchers specifically examined the impact of anodal and cathodal tDCS on core language areas, namely Broca's and Wernicke's, in relation to primary word-learning mechanisms. They identified two main strategies crucial for natural word acquisition: explicit encoding (EE), which is based on direct instructions and repetition, and fast mapping (FM), which functions implicitly through context-based inference or deduction. Their findings revealed that anodal tDCS of Broca's area significantly enhanced both implicit and explicit acquisition of new vocabulary compared to sham tDCS. Interestingly, there was no marked difference between the EE and FM learning regimes. This study underscores the role of the left inferior-frontal neocortex in novel vocabulary learning regardless of the types of word acquisition.

1.8.1. Effects of transcranial electrical stimulation techniques in patients with aphasia

In poststroke rehabilitation, the use of tDCS in conjunction with behavioural interventions for aphasia has broadened its scope. While initially focused on addressing word-finding challenges (J. M. Baker et al., 2010; Fiori et al., 2011, 2013; Fridriksson, 2010b; Fridriksson et al., 2011), the application has expanded to aid in the recuperation from articulatory impairments (Marangolo et al., 2011, 2013). to foster enhancements in speech production capabilities (Marangolo et al., 2013, 2014) and the application's uses continue to expand.

A systematic review from Elsner and collaborators (2020), which incorporated a network meta-analysis, aimed to assess the efficacy of all active tDCS forms (anodal, cathodal, or dual) in improving post-stroke functional communication. The findings, incorporating 25 studies and 471 participants, suggested that while tDCS didn't markedly improve functional communication, anodal tDCS, particularly when targeted at the left inferior frontal gyrus, showed promise in enhancing naming performance.

Reviews from Elsner et al., 2019, 2020, Galletta et al., 2016, Monti et al., 2013, Ulanov et al., 2019, Zettin et al., 2021, indicate that the majority of the tDCS studies on aphasic patients have favored anodal stimulation on the left hemisphere's intact regions to boost cortical activity while cathodal stimulation has been applied to the right hemisphere's corresponding language areas to decrease their excitability (Fiori et al., 2019). A combination of left anodal and right cathodal stimulation has also been common (Lee et al., 2013).

Anodal stimulation, especially when combined with specific tasks, has led to improvements in areas like object naming, speech articulation, and naming precision. When combining left frontal tDCS with language tasks, participants typically exhibited significant enhancements in speech clarity (Marangolo et al., 2011), picture naming (Baker et al., 2010; Vestito et al., 2014) image narration, and constructing sentences (Campana et al., 2015). Targeting Wernicke's region also led to better speed and accuracy in naming (Fiori et al., 2011; 2013).

Pestalozzi et al. (2018) targeted the left dorsolateral prefrontal cortex (DLPFC) with A-tDCS during naming and repetition exercises, resulting in increased verbal fluency and the ability to name commonly used words.

A few scholars argue for the potential benefits of right hemisphere anodal stimulation, especially when paired with Melodic Intonation Therapies (Vines et al., 2009, 2011). On the other hand, studies with cathodal stimulation studies have primarily aimed to inhibit the right hemisphere's Broca's area counterpart, with varying outcomes based on lesion characteristics (Rosso et al., 2014).

Some studies even ventured into traditionally non-language regions, like the primary motor cortex (Branscheidt et al., 2018; Meinzer et al., 2016) and the cerebellum (Marangolo et al., 2017). Only one study by You and collaborators (2011) focused on the impact of tDCS on the superior temporal gyrus (STG), specifically in relation to auditory verbal comprehension in subacute global aphasia patients. The findings revealed that cathodal tDCS over the left superior temporal areas led to more pronounced improvements in auditory verbal comprehension than anodal or sham stimulation. This region is not only integral to auditory processing but also to statistical learning (Batterink et al.,2019; Williams,2020). Specifically, the STG has demonstrated its role in structural sequence learning across both auditory and visual modalities and in implicit procedural language. This has been supported by studies such as McNealy et al. (2006), Plante et al. (2015), Schapiro et al. (2013), Turk-Browne et al. (2009), and Ullman (2004). Moreover, assuming that neocortical regions are responsible for the extended consolidation of freshly acquired linguistic information when these areas suffer damage, it is probable that such information encounters challenges in transitioning to a hippocampus-independent state and developing into enduring representations within the language processing system. This proposition finds support in recent research by Gore et al. (2022). Their study reveals that, following the learning process, heightened activation of the left hippocampus in older healthy individuals is linked to reduced accuracy, prolonged response times, and improved long-term retention when naming newly acquired words. Conversely, heightened activation in neocortical regions responsible for established vocabulary, specifically, the left IFG and anterior superior temporal lobe, is associated with increased accuracy and shorter response times. Additionally, Yun et al. (2015) utilized a computerized neuropsychological assessment that includes evaluations such as Verbal Learning Tests to gauge auditory memory. Their findings demonstrated that applying tDCS to the left anterior temporal lobe (T3 according to the 10-20 EEG system) effectively enhanced auditory memory in patients with post-stroke cognitive impairment.

No more than two studies investigated the effect of tDCS on learning in PWA. In a study from Riley et al. (2022), researchers sought to determine the effects of anodal tDCS on the dorsolateral prefrontal cortex and cathodal tDCS on the right supraorbital region when paired with artificial grammar training in individuals with aphasia. Twelve participants with mild to moderate aphasia took part in the study and were exposed to tDCS while undergoing artificial grammar training, where they were tasked with recalling sequences of shapes following a specific grammar rule. Post-training evaluations revealed that sustained attention improved significantly in participants, as did their understanding of the artificial grammar. As for word retrieval, Fiori and colleagues studied the effects of tDCS on enhancing associative verbal learning in 10 healthy individuals and improving word retrieval deficits in three patients with stroke-induced aphasia. Healthy participants underwent three different tDCS sessions spanning three weeks: one anodal tDCS over the left Wernicke's area, one sham session over the same area, and one anodal tDCS over the right occipito-parietal area. The three aphasic patients received intensive language training with tDCS over two weeks. Each patient had five consecutive sessions of both anodal tDCS and sham stimulation over Wernicke's area while doing a picture-naming task. Results showed that by the end of each week, anodal tDCS significantly improved the patients' accuracy in naming pictures. Both healthy participants and patients named faster during anodal tDCS than during the sham condition. In two follow-ups with the aphasic patients, the benefits of the anodal condition were still evident, indicating a lasting effect on alleviating their word-retrieval issues.

Nevertheless, in this paradigm, the words that participants had to retrieve were the ones that participants consistently did not name correctly and not novel words, as in the control group. This could represent a limitation for a pure study of learning as previously explained. No study, to the best of our knowledge, has investigated the use of tDCS on learning novel words-novel referents association in persons with aphasia.

1.9. Objective and General Overview

Delving into language learning theories and their fundamental mechanics is crucial in aphasia research, providing valuable insights that may guide diagnostic methods and interventions for aphasia. Presently, research on explicit and implicit learning in people with aphasia is not only scarce but also yields a range of diverse outcomes, particularly in the realm of implicit learning (Peñaloza et al., 2022). Despite this, such a learning approach might offer an alternative to alleviate overall cognitive load and effort, as some PWA might struggle to benefit from explicit instruction when a learning task imposes significant working memory demands. The limited studies and the promising potential of implicit learning underscore the critical need for further research to determine the relevance of various forms of implicit language learning in aphasia rehabilitation and to explore their potential implications for future, individualized treatment plans.

Furthermore, the potential to enhance learning through non-invasive brain stimulation, as evidenced in healthy individuals (Balboa-bandeira et al., 2021), and its impact on word retrieval (Fiori et al., 2011) and other linguistic abilities in aphasia (Elsner et al., 2019), introduces an additional dimension that warrants exploration.

In this light, this thesis aims to investigate the learning of completely new word references in PWA, providing a reliable measure of learning; compare implicit and explicit learning in this population and its maintenance after one week; and finally, explore the potential effect of tDCS on implicit novel word learning in aphasia.

Chapter 1 sets the theoretical foundation by offering a brief general introduction to post-stroke aphasia and theories of speech production, followed by detailed sections on relevant neuroscientific and aphasiological literature that explore two broad, cross-cutting themes in this thesis: neurotypical vocabulary acquisition and vocabulary re-acquisition in PWA.

Given that a deeper comprehension of the methodologies and cognitive capabilities that underpin learning in neurologically intact individuals could offer valuable insights for enhancing anomia therapy (Basso et al., 2001), Chapter 2 involves a between-within-design study of novel word learning in young and older adults under implicit and explicit conditions and examines retention immediately and after one week. The role of education is taken into consideration.

Chapter 3 is dedicated to examining word-learning capabilities in patients with post-stroke aphasia. Through two sequential studies, this chapter seeks to understand the integrity of word learning abilities in the face of language impairments caused by brain damage. It evaluates both implicit and explicit learning conditions and tests retention after one week, aiming to discern the role of memory/learning systems in language recovery. The chapter also investigates the influence of aphasia severity and lesion locations on learning outcomes.

Chapter 4 shifts the focus to the potential of non-invasive brain stimulation, specifically tDCS, and its impact on implicit novel word learning in individuals with post-stroke aphasia. Alongside evaluating the effects of tDCS, this chapter also examines how aphasia severity and lesion locations might modulate the outcomes of this intervention. The overarching goal is to shed light on the potential therapeutic benefits of tDCS in enhancing learning capabilities in this population, considering individual variability in severity and lesion profiles.

Chapter 5, the General Discussion, synthesizes the findings and explores their implications in the broader context of aphasia research and intervention.

CHAPTER 2: Implicit vocabulary learning in the Healthy Aging Brain

Abstract

Background: The lifelong process of vocabulary acquisition is influenced by both implicit and explicit learning mechanisms. While implicit learning is incidental and subconscious, explicit learning is conscious and intentional. With a significant portion of strokes, leading to conditions like aphasia, occurring in older adults, understanding the nuances of these learning methods in this age group becomes crucial.

Method: The study engaged 44 participants, comprising 22 young adults (average age: 25.3 years) and 22 older adults (average age: 70.1 years). All participants were native Italian speakers with no neurological disorders. Using a unique set of stimuli, participants were exposed to pseudowords and unfamiliar objects in both implicit and explicit learning conditions. Their retention capabilities were then assessed after a week.

Results: Younger participants exhibited superior accuracy in both learning modalities and displayed a more pronounced learning trajectory. In contrast, older adults consistently learned but at reduced accuracy levels. Age had minimal impact on implicit learning, with performance outcomes becoming more aligned over time. While education significantly impacted explicit learning results, its effect on implicit learning was marginal.

Conclusion: The study highlights the potential of implicit learning in aphasia rehabilitation across all ages. Both young and older participants demonstrated the ability to acquire

knowledge under both conditions. The research offers valuable insights into the cognitive functions across age groups and presents promising strategies for aphasia rehabilitation, emphasizing the importance of understanding implicit memory's enduring nature.

2.1. Introduction

The acquisition of vocabulary is a continuous process that persists throughout our lives, extending beyond formal education and into adulthood. As we journey through life, we are constantly introduced to new words that mirror our evolving experiences. These new words, which often arise from technological advancements, foreign influences, and emerging professions, continue to enrich our lexicon even in adulthood (A. D. Abel et al., 2020; Hulme et al., 2019). Interestingly, most of these words are learned incidentally, without any deliberate instruction or conscious effort (A. D. Abel et al., 2020; Nagy et al., 1985; Saragi et al., 1978). In the realm of research, when learning occurs both incidentally and without awareness, it is referred to as implicit learning (Williams, 2009).

Implicit learning, as opposed to explicit learning, which involves a conscious, intentional, and declarative process, has been found to have a distinct impact on language acquisition and cognitive functioning (Ellis, 2015). Morgan-Short, Steinauer, Sanz, and Ullman discovered that explicit and implicit learning of a second language resulted in different behavioral and neural responses (Morgan-Short et al., 2011). Interestingly, their participants showed no differences in behavioral performance based on their proficiency in the second language. However, when it came to neural response to syntactic violations, there were marked difference. Implicit training at low proficiency produced an N400, but at high proficiency, it mirrored the neural activity of native speakers, showing an anterior negativity followed by a P600 and a late anterior negativity. In contrast, explicit training at low proficiency had no significant neural effects, and at high proficiency, it only showed an anterior positivity followed by a P600. Suggesting, that while the P600 response might seem native-like, the overall neural pattern from explicit training does not match that of native speakers. In essence, only implicit training led to brain activation patterns consistent with those of native speakers (Morgan-Short et al., 2011).

Research suggests that implicit learning and implicit memory are less affected by age compared to explicit learning (Hedden & Gabrieli, 2004; Ward & Shanks, 2018). The impact of aging on learning, particularly implicit learning, has been a subject of extensive debate. While some studies suggest that implicit learning and memory are not significantly affected by age, unlike explicit learning (Hedden & Gabrieli, 2004), others argue that the effects of aging on implicit learning are not uniform across all types of implicit processes and forms of implicit learning. For instance, older adults often exhibit preserved implicit learning on non-linguistic serial reaction time tasks compared to direct learning measures of the same sequence (D. V. Howard & Howard, 1992, 1997, 2013; Nissen & Bullemer, 1987). However, there is also substantial evidence indicating a decline in implicit learning ability among older adults compared to younger adults in various types of implicit/procedural tasks, such as probabilistic sequence learning for higher-order serial dependencies and non-rule-based categorization tasks (Fama et al., 2022; Howard & Howard, 1997, 2013) . In this context, the findings of Kurten et al. (Kürten et al., 2012) offer a compelling perspective. In their study young and elderly participants were exposed to letter sequences formed through an artificial grammar, followed by testing their recognition abilities. The study distinguished between "chunk-based" (specific sequences) and "rule-based" (general patterns) learning. Results indicate that age distinctly affects rule-based and chunk-based learning: while the inherent implicit nature of rule-based learning remained unaffected, chunk-based learning, possessing explicit learning elements, saw a decline among older participants.

The majority of research on implicit learning has primarily focused on motor learning (Howard & Howard, 2013; King et al., 2013), with very few studies exploring implicit language learning in older adults. In fact, despite the increasing attention to language learning in older adults, there is a significant gap in research in this specific area (Pfenninger & Singleton, 2019).

An expansion of studies centered on word learning in cognitively intact participants could be instrumental in enriching our understanding of language re-acquisition in patients with aphasia, a condition characterized by language impairments arising from brain damage (Flöel et al., 2008; Hopper & Holland, 2005; Meinzer et al., 2014). This line of reasoning is backed by various researchers who postulate that similar mechanisms may underlie language rehabilitation processes and new language learning in unimpaired individuals (Basso et al., 2001; Menke et al., 2009; Rijntjes, 2006). Compelling parallels have been drawn between usual linguistic errors observed in healthy individuals and unsuccessful word retrieval attempts in those suffering from aphasia (Basso et al., 2001; Dell et al., 1997). In fact, even typical individuals, despite their usually rapid and effortless word recall, can occasionally struggle with word retrivial, reinforcing the complexity of language processes.

Additionally, a greater focus on older adults is essential to gather more meaningful and targeted insights into aphasia learning, as this group has often been neglected in research. The need to study both implicit and explicit learning in older people is highlighted by the high occurrence of strokes within this age group (Antonenko et al., 2012). Although strokes can occur in individuals at any age, about two-thirds of all strokes happen in people who are 65 years old or older (Ellis & Urban, 2016).

This study aims to delve deeper into the process of implicit and explicit vocabulary learning in both young and older healthy adults. The experiment will also examine the retention of these learnings after one week, which has hardly been explored in this cohort, thereby exploring potential differences based on the type of learning and the age of the participants. As a secondary objective, it aims to investigate the effect of years of education not only on learning, which was found to be significant in Balboa-Bandeira's meta-analysis on learning in healthy adults, but also its impact on the type of learning, both implicit and explicit.

Furthermore, it carries implications for individuals with aphasia, a population known to potentially exhibit implicit learning capabilities as long as their striatal projection system is intact (Breitenstein et al., 2004). Since it is possible that cortical regions usually involved in explicit language learning (as the left IFG) are damaged in PWA (C. Ellis & Urban, 2016; N. C. Ellis, 2005), it may be necessary to exploit different neural pathways and mechanisms, which seem to be at least partially distinct in implicit and explicit learning. Understanding these learning processes could potentially provide alternative methods to decrease the often-impaired short-term memory load and cognitive effort in aphasia, maximizing learning in this population. This is particularly crucial as stroke patients with aphasia often exhibit coexisting nonlinguistic cognitive deficits, and their rehabilitation requires active use of all cognitive domains.

The study sets itself apart from previous research by using entirely new stimuli involving non-words and unfamiliar objects in line with recommendations from previous research (Tuomiranta et al., 2012; Peñaloza, et al., 2022) for a purer measure of learning. In doing so, this research fills a significant gap in the understanding of implicit language learning in older adults, contributing to the broader body of work examining the effects of aging on implicit learning.

2.2. Materials and methods

Participants: Forty-four participants, 22 healthy young (ten women; mean±SD age: 25.3±3.5 years, range: 18–34; years of education 16.3±2.9 years, range: 13–23) and 22 older adults (twelve women; mean±SD age: 70.1±3.9 years, range: 65–79; years of education 14.5±3 years, range: 8–18) participated in the study. All were native Italian speakers and had no history of neurological disorders Before the experiment, all older participants were assessed for their Intelligence Quotient (IQ) using Raven's Colored Progressive Matrices (Caffarra et al., 2003; cut-off: 20.72) to confirm normal cognitive functioning. Performance levels in all cognitive domains were consistent with the norms related to age and education.

Written informed consent was obtained from all participants prior to participation.

The study was approved by the ethics committee of the Università degli Studi di Milano-Bicocca and conducted in accordance with the Helsinki Declaration.

Stimuli

Participants were presented with pairings of pseudowords and images of non-existent objects in two learning conditions, implicit and explicit. The stimuli used in the learning paradigms were completely new (a new word form paired with a new referent), allowing for a relatively pure investigation of individuals' word learning capabilities.

For both paradigms, 40 bisyllabic pseudowords and 40 novel object images were selected and then randomly divided into two separate vocabularies.

A collection of 40 bisyllabic pseudowords was taken from the 60 created bisyllabic words assembled by Basso and collaborators (2001). These words were designed to exhibit minimal resemblance to Italian words, incorporate a consonant cluster, and ensure a direct correlation between each phoneme and its corresponding grapheme. They follow Italian phonotactic rules. In both paradigms, pseudowords were presented as auditory (See Appendix A). All stimuli were synthesized through the text-to-speech program Balabolka (version 2.15.0.851) and were all normalized to the same volume and length through the recording and editing software Audacity (version 3.1.3).

A collection of 40 images had been selected from the Novel Object and Unusual Name (NOUN) Database (see http://www.sussex.ac.uk/wordlab/noun), a free tool for researchers offering images of novel objects and unusual names (Horst & Hout, 2016) (See Appendix B).

Bisyllabic pseudowords and images were randomly matched.

Procedure

Participants underwent two learning conditions, implicit and explicit, in a randomized order in two separate sessions with two different sets of non-words and images. After a week, they were tested on both sets of non-words (both explicit and implicit).

Implicit Learning Paradigm. This paradigm was tailored from earlier research (refer to Antonenko et al., 2016, and Flöel et al., 2008, for an exhaustive explanation) and presented through the software OpenSesame (version 3.3.14 Lentiform Loewenfeld, accessible at https://osdoc.cogsci.nl/). Briefly, the paradigm involved presenting non-word/picture pairs. For each participant, a set of 20 pseudowords and 20 unknown images were randomly matched up to 20 "correct" pairings (Antonenko et al., 2016). Subjects learned over the course of five sessions whether an image of a non-existent object was correctly paired with a given non-word. The learning principle was the higher statistical co-occurrence of "correct" pairings compared to "incorrect" pairings. During the learning phase of the experimental session, five training blocks with 80 trials each were presented (400 trials in total). "Correct" pairings occurred ten times (twice per block); additionally, each image was presented ten times with various "incorrect" pseudowords. "Incorrect" pairings were only shown once. Thus, each correct pairing was presented ten times more often than each incorrect pairing. The order of trials was randomized for each subject and each block. In each trial, the image was presented 200 ms after the onset of the spoken non-word (all normalized to the same loudness and length).

Participants were instructed to decide whether a given pairing was "correct" or "incorrect" based solely on their intuition or what might be described as their 'gut feeling.' During the presentation of each image, subjects were required to press one of two buttons within a 1500 ms time window. . This was done to ensure that they responded quickly and without prolonged reflection on their choices. The buttons corresponded to "correct" and "incorrect" judgments. The assignment of these buttons (i.e., which button meant "correct" and which meant "incorrect") was randomized between subjects to prevent any potential biases. After each block of images, there was a short break, allowing participants to proceed to the next block at their own pace. Participants were not informed of the underlying frequency pattern. This setup ensured a condition of incidental and implicit learning for all participants.

Testing Phase: The recognition test consisted of simultaneously presenting three images with an auditory non-word. Participants had to choose the correct image. The dependent variable was the percentage of correct responses. The recognition test was presented immediately after the learning phase and after a week to verify the retention.

Explicit Learning Paradigm The paradigm was adapted from a previous paradigm (Meinzer et al., 2014) and presented through the software OpenSesame (version 3.3.14 Lentiform Loewenfeld, accessible at https://osdoc.cogsci.nl/). During the learning phase, an image was presented 200 ms from the onset of the non-word. A total of 20 images and 20 non-words were presented, with the images remaining for four seconds on the screen. The images were presented twice per block, for five blocks, for a total of 10 presentations per image. After each block, there was a short break so that participants could proceed to the next block at their own pace (Meinzer et al., 2014).

Testing Phase: As for the implicit learning paradigm, the recognition test consisted of simultaneously presenting three images with a non-word. Participants had to choose the correct image. The dependent variable was the percentage of correct responses. The recognition test was presented immediately after the learning phase and again after a week.

Q.I. assessment

Older participants' non-verbal intelligence was tested in the first session, before the learning part.

Raven’s Colored Progressive Matrices (Raven, J. C. ,1936; Domino et al., 2006). Participants are presented with a figure that misses the bottom right corner to be completed. Below this figure, six pieces are presented as options to complete the figure above. The participant is asked to choose the one that fits accurately in the space missing. The examiner records the answers given by the participant in the corresponding answer sheet.

2.3 Statistical Analysis

All analyses described in the subsequent sections were conducted using the R statistical software. However, the specific analytical approach varied depending on the dependent variable under consideration.

2.3.1. Recognition task

Preliminary descriptive statistics were computed including mean accuracies and standard error across the different age groups, conditions of learning, and time points. Additionally, the Exact Binomial Test was employed to determine if performance significantly exceeded chance levels. These analyses facilitated an overview of task performance trends and variations across the specified conditions.

Inferential statistical analysis was conducted using R lme4 package for generalized mixed modeling (Bates et al., 2015). Generalized mixed models (GLMM) were calculated for task performance with subjects and items as random intercepts. Fixed factors included group (old and young), conditions of learning (implicit and explicit), time (immediate test and after one week) and education. The random intercept for subjects and items was included to account for the variability and repeated measurements within these units. The interaction between the fixed factors was also explored to examine the nuanced differences across groups, learning conditions, and timeframes. Following this, to specifically investigate the role of education under different learning conditions, two distinct models were constructed: one for the implicit condition and another for the explicit condition.

2.3.2. Learning curve for implicit condition

For the learning curve variable for the implicit task, we employed a statistical analysis technique known as multilevel regression, specifically using growth curve analysis (GCA) based on a second-order orthogonal polynomial model to examine changes over time in learning curves (Mirman, 2014). The analysis included fixed effects for time (block) and group, as well as random effects for participants related to the different time points. Given that the outcome variable was binary (correct or incorrect response), logistic GCA was used for data analysis. Model comparisons were conducted to assess group differences in relation to specific time-related factors. In orthogonal polynomial models, the intercept represents the overall average outcome, the linear term reflects the linear slope, and the quadratic term captures the curvature.

2.4. Results

2.4.1. Recognition test - Descriptive Analysis

In the recognition tests, all groups and conditions consistently demonstrated mean accuracy rates significantly above the chance level, as determined by the Exact Binomial Test.

Specifically, older participants under the explicit condition during the immediate test exhibited a mean accuracy of 0.705 [95% CI: 0.660, 0.748], while their younger counterparts achieved a remarkable 0.923

[95% CI: 0.894, 0.946]. After one week, the older group's accuracy decreased to 0.500 [95% CI: 0.452, 0.548], whereas the younger group maintained a robust performance at 0.739 [95% CI: 0.695, 0.779].

Under the implicit condition, older participants achieved accuracies of 0.634 [95% CI: 0.587, 0.679] during the immediate test and 0.484 [95% CI: 0.437, 0.532] after one week. Meanwhile, the younger group showcased accuracies of 0.836 [95% CI: 0.798, 0.870] and 0.700 [95% CI: 0.655, 0.742] at the respective time points.

2.4.2. Recognition test - Inferential statistics

The effects of group, condition, time, and their combined interactions on ACCURACY were examined using a generalized linear mixed model (family: binomial with a logit link function). The results pointed out a significant main effect for the GROUP (comparing young and older), which had an estimate of 1.38041 SD = 0.194 , and $p < 0.001$. There was also a significant effect for CONDITION, recording an estimate of -0.20412, SD= 0.101, and $p < 0.01$, indicating a lower performance during the implicit task as compared to the explicit one. A pronounced main effect was also detected for TIME, with an estimate of -0.46146, SD = 0.072, and $p < 0.001$, being generally the performance after one week worse than the immediate one. Investigating the interactions, there was a significant relationship between the GROUP and TIME (Estimate of -0.28340, SD=0.128, $p < 0.01$), indicating that the difference between Time 1 and Time 2 is not consistent across groups. Specifically, the young group showed a bigger drop compared to the old group. Specifically, the young group showed a bigger drop compared to the old group. In fact, older adults exhibited a slightly larger drop (about 20% and 15% drops in the explicit and implicit conditions, respectively) compared to the younger group (about 19% and 13% drops)."

Likewise, a significant interaction was observed between the implicit CONDITION and GROUP (Estimate of -0.33221, SD=0.168, $p < 0.01$), meaning that within the implicit condition, scores for young group were lower than those in the explicit one, with this difference being more pronounced that that observed in the old group. However, the interaction between TIME and CONDITION (Estimate= 0.13663 , SD= 1.348, p = 0.177818) and the three-fold interaction between GROUP , learning CONDITION, and TIME did not reach statistical significance, (Estimate of 0.19820, SD= 0.168, p = 0.24).

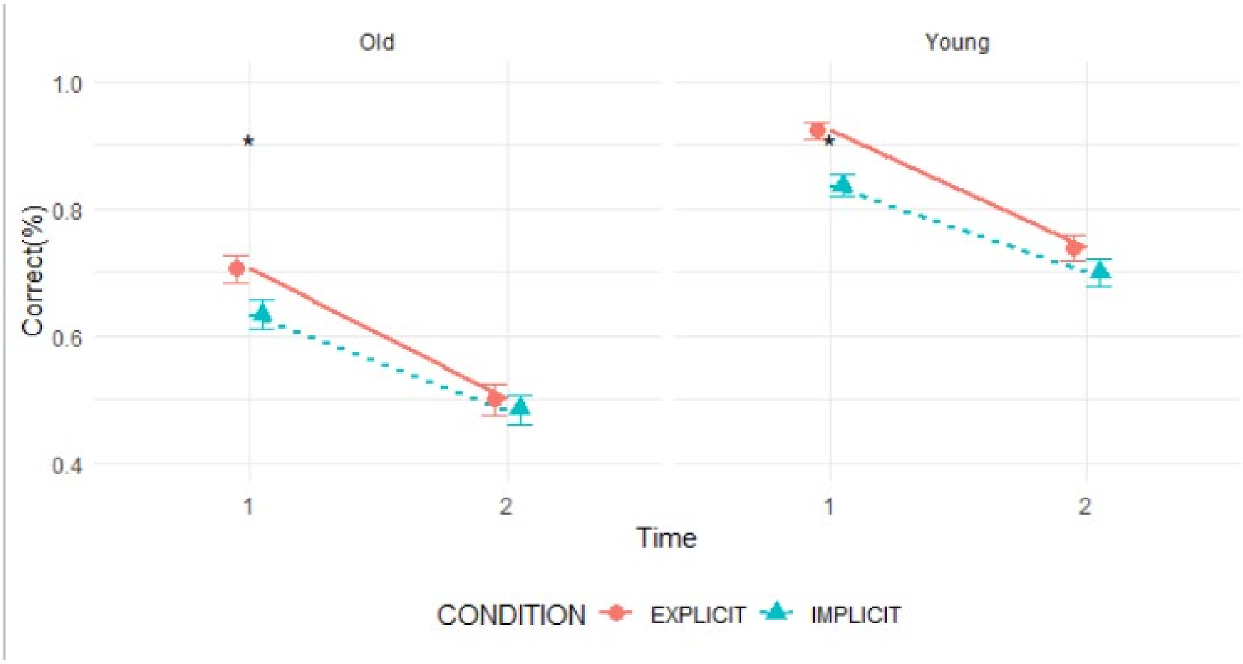


Fig. 1. Recognition task conducted with both young and older participants, both immediately and one week later.

The influence of education was examined by incorporating covariates such as EDUCATION and it. he main effect of EDUCATION (p=0.369227) was not statistically significant, suggesting that, in this generalized model, the level of EDUCATION did not significantly influence the dependent variable across different conditions.

To further delve into the specific influence of education under distinct learning conditions, two separate models were constructed for the implicit and explicit conditions. In the implicit model, the effect of education on ACCURACY was not significant (p = 0.137). , indicating that educational background did not play a significant role in influencing accuracy in the implicit condition. Conversely, in the explicit model, a significant positive relationship between education and ACCURACY (p = 0.0273) was observed. This suggests that individuals with higher levels of education tend to perform better in tasks associated with the explicit condition.

3.4.3. Learning Curve

The task performance of both the young and older groups in the implicit condition exhibited a significant improvement across the learning blocks. The GCA was employed to delve into the differences in learning trajectories between the Old and Young groups across varying blocks. The model, fit using a binomial distribution with a logit link function, is apt for dichotomous response variables. It models the response variable based on the group (either Old or Young), polynomial terms of the block (both linear and quadratic), and their interactions. Additionally, the model takes into account the random effects associated with individual participants (ID), capturing the inherent variability in intercepts and slopes across blocks. The intercept, representing the average log-odds of a positive response for the reference group (Old) at the initial block, is significant with an estimate of 0.2212, indicating a notable response at the outset. Furthermore, the Young group demonstrates a significantly elevated log-odds of a positive response in comparison to the Old group, as highlighted by the estimate of 0.6905. In terms of the learning trajectory, the linear term of the block was significant (Estimate=54.4866, $p<0.001$), suggesting a marked linear augmentation in the log-odds of a positive response as the blocks advance. The quadratic term of the block, which would typically capture any curvature in the learning trajectory, is not significant, implying that the learning trajectory remains primarily linear without any pronounced curvature (Estimate= -1.7141, p=0.336919)

Diving deeper into the group-specific learning trajectories, the interaction between the Young group and the linear term of the block stands out as significant. This underscores that the Young group's rate of linear increase in the log-odds of a positive response is distinctively steeper than that of the Old group (Estimate= 54.4866, p<0.001). The interaction between the young group and the quadratic term of the block is also significant, hinting at a difference in the curvature of the learning trajectory for the Young group, even though the overarching trajectory remains linear (Estimate=16.7133, p<0.001).

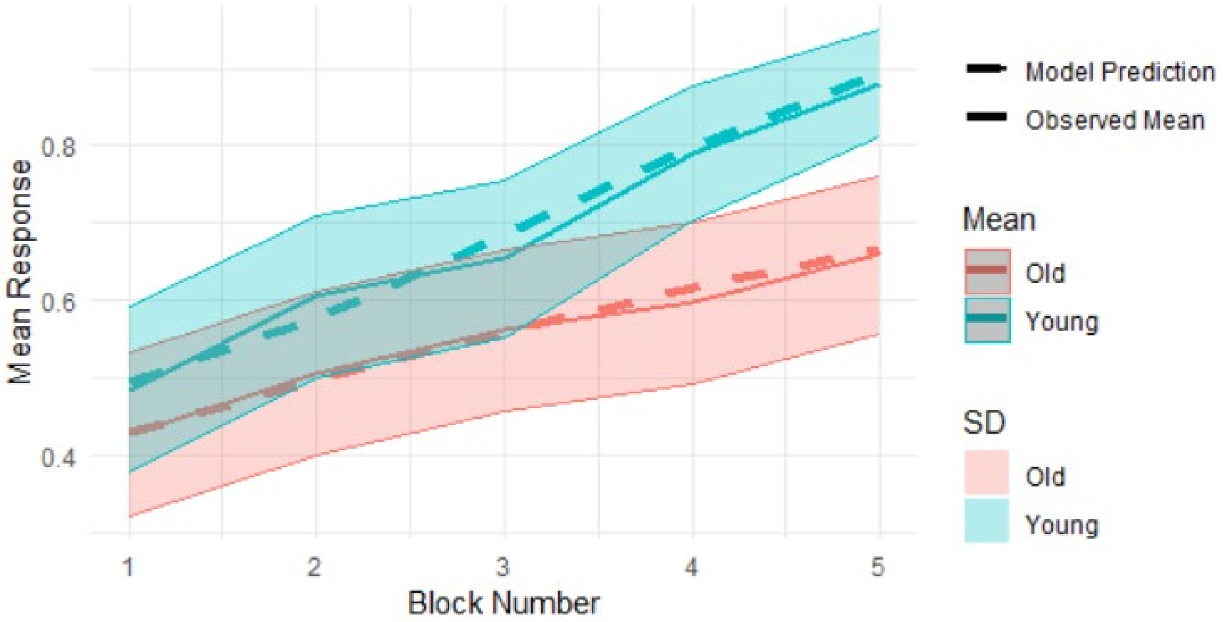


Fig.2 Comparison of learning curves for the young and old adults. The observed (dash) and logistic GCA model fit (lines) learning curves are depicted for the two groups.

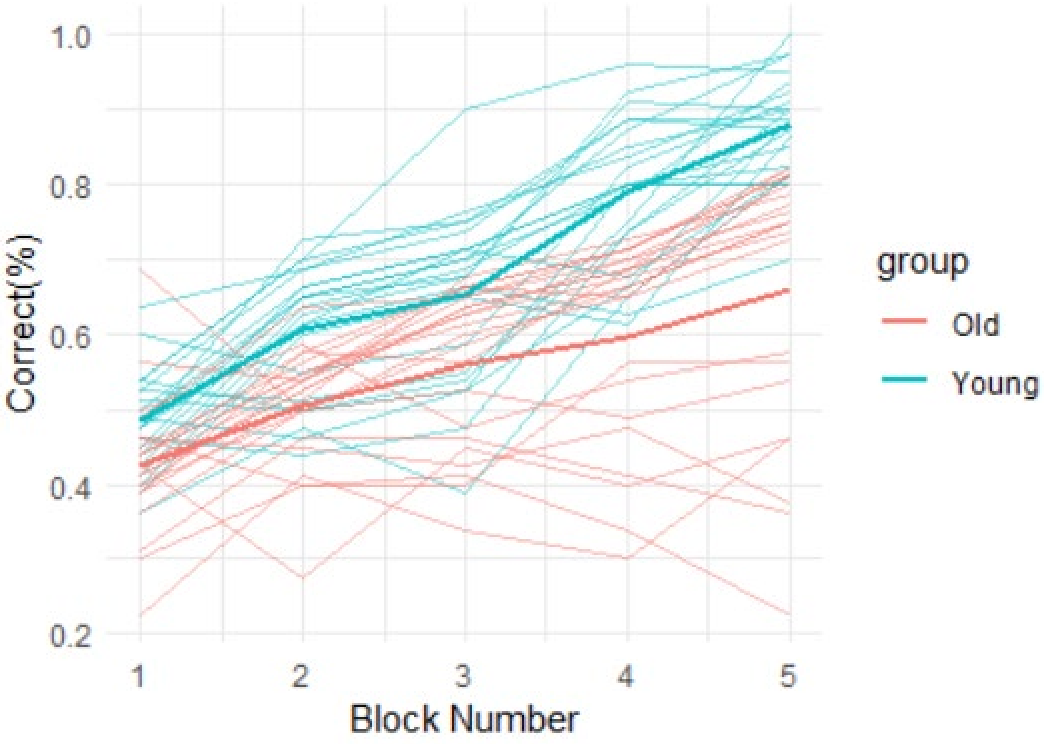


Fig. 3. Individual variability across learning blocks and groups.

To evaluate the effect of education, scholar years were added as a continuous fixed effect on each time term. The intercept, representing the average log-odds of a positive response at the initial block, was not significant, suggesting a neutral starting point (Estimate=0.08980, p=0.52149). The coefficient for EDUCATION was significant with an estimate of 0.03271, indicating that there is a difference in the likelihood of a positive response based on the level of EDUCATION (p= 0.00169). In terms of the learning trajectory, the interaction between EDUCATION and the linear term of the block was significant, indicating that the rate of linear increase in the log-odds of a positive response varies based on EDUCATION. Specifically, the positive estimate of 33.96647 for this interaction suggests that as EDUCATION increases, there is a steeper increase in the likelihood of a positive response as blocks progress ($p<0.001$). On the contrary, the interaction between EDUCATION and the quadratic term of the block was significant, hinting at a similarity in the curvature of the learning trajectory based on EDUCATION, even though the overarching trajectory remains linear (Estimate=11.503; p=0.15530).

2.5. Discussion

In this study we introduced both explicit and implicit novel word-learning tasks to young and elderly participants. Participants were tested immediately after a learning task and again after one week. The results showed distinct performance levels between groups and between learning condition.

The study of second language acquisition has traditionally centered on children and younger adults. However, recent research has expanded its focus to older adults, those in their "third age" (Kliesch et al., 2017; S. Pfenninger, 2018; S. E. Pfenninger & Kliesch, 2023; Pot et al., 2018). This shift is particularly pertinent given the increasing relevance of understanding language learning in this demographic, especially in the context of clinical settings for people with aphasia.

As individuals age, they often experience cognitive declines, such as reduced working memory, slower processing speed, and diminished attention (Pfenninger & Singleton, 2019). These cognitive changes are linked to structural alterations in the brain, like the decline of white matter integrity (Damoiseaux et al., 2008; Salat et al., 2004; Sowell et al., 2003). However, it's crucial to note that these cognitive changes don't encompass the entire learning potential of older adults. Interdisciplinary research from fields like education and neurolinguistics suggests that age is not the sole determinant of language learning outcomes (Green, 2018). Contemporary neurocognitive aging studies emphasize that the brain, even in its later stages, retains a significant degree of plasticity, suggesting its continued receptiveness to new languages (Park & Reuter-Lorenz, 2009; Peltzer-Karpf, 2006; Raz & Lindenberger, 2013; Schlegel et al., 2012). Our results align with these findings, showing that older participants consistently demonstrated some degree of learning. Older participants’ scores were significantly above chance levels under both implicit and explicit conditions. Over time, while the older group's accuracy decreased, but it remained significant, contrasting with the younger group's sustained performance. This lower accuracy in the older group compared to the young one can be attributed to the earlier mentioned neural alterations associated with aging (Burke & Barnes, 2006; Lövdén et al., 2010; Nilsson et al., 2021) and corroborates with other findings indicating the pace of verbal learning abilities, such as word acquisition, does vary between older and younger individuals. Davis et al. (2003) found that while many younger participants reached peak performance, only a smaller percentage of older participants could recall all stimuli. Similarly, in research conducted by Fiori et al. (2017), it was observed that a significant proportion of younger participants (53%) achieved a perfect score (20/20) in recalling words by the end of their training, regardless of the tDCS conditions. In contrast, only a small fraction (13%) of the elderly participants managed to recall all the stimuli. In a similar line, in our dataset under explicit conditions during the initial assessment, five younger participants achieved a 100% recall rate while only two older participants reached this total score under the same conditions. The different results between the two studies may lie in the nature of the stimuli and in the verification method presented to the participants. In Fiori et al. (2017), participants were exposed to sixty bisyllabic pseudowords paired with pictures of varying familiarity, spanning diverse semantic categories. This approach might have enabled participants to form associations based on prior knowledge or familiarity with the objects. In contrast, our study tasked participants with associating new, unfamiliar objects with pseudowords. This distinction inherently measures a different aspect of learning. The absence of familiar objects in our study introduces an added layer of complexity, as participants are required to form associations without the crutch of prior knowledge. This could potentially be a more challenging measure of learning, given the absence of any familiar anchoring points. Furthermore, the testing methodologies employed in the two studies were notably different. Fiori et al. (2017) presented participants with stimulus pairings on a computer screen, with 60% being correct pairings and the remaining 40% being incorrect. Participants had to indicate when a pairing was correct, receiving immediate feedback, which could facilitate better recall. In our study, the testing paradigm was more challenging: participants were presented with one pseudoword and had to choose the correct object association from three possibilities. This task demands a higher level of recall and cognitive engagement, as participants must discern the correct pairing among multiple options. Focusing on implicit learning, we found that both young and old participants performed above chance-level immediately and after one week. Interestingly, while both age groups demonstrated reduced accuracy in the immediate recognition task for the implicit condition compared to the explicit one, this disparity diminished after one week, rendering the accuracies for both conditions comparable. Our research outcomes align with the perspective of certain scholars who propose that implicit memory tends to remain relatively steady with age or experience only minor age-related modifications (Jacoby et al., 2001). In our study, younger adults outperformed their older counterparts in the recognition test, which was further supported by the learning curve analysis, indicating that the learning trajectory in the older group was less steep and more gradual. Similarly, when we look at how both the young and older groups learn over the course of the blocks in the implicit condition, although both groups seem to learn at a consistent pace, improving their responses as they progress through the learning sessions or blocks, the young group displayed a steeper learning curve compared to the one of the old group. These findings appear to be in contrast to several other studies that found no significant differences in implicit learning when comparing young and older individuals (Frensch & Rünger, 2003; D. V. Howard & Howard, 1989, 1992). In fact, one study by Howard et al. (2008) reported no age-related decline in performance when older participants were tasked with learning letter strings with a given letter consistently appearing at the same position. Both young and old adults demonstrated comparable implicit learning in this context. The authors of this study demonstrated that learning primarily occurred during the encoding phase. This and similar research suggest that older individuals retain the capacity to efficiently adapt to environmental regularities.

On a related note, our findings are consistent with a study by Howard et al. (1997) which highlighted age-related deficiencies in implicit learning in a complex task. In this particular investigation, which contrasted individuals categorized as young-old (aged 65-73) and old-old (aged 76-80), a decline in implicit learning performance was evident within the aging process itself. However, older adults appeared to maintain some degree of sensitivity to highly complex sequential patterns, although their learning was less robust compared to younger adults, as reported by Bennet et al. (2007). This stability aligns with research indicating that well-practiced or automatic processes generally remain unchanged throughout one's lifespan (Light et al., 2000).

Concerning implicit novel word learning, in contrast to our findings, Greve et al. (2014) did not observe implicit incidental learning in older individuals. This discrepancy in results may be attributed to their focus on fast-mapping (FM) as the mechanism under investigation. The effectiveness of FM in adult learning remains a topic of debate in the scientific community. FM is a memory encoding process that has garnered attention due to its potential to ameliorate memory deficits and has been argued to primarily depend on the neocortex, largely independent of the medial temporal lobe and hippocampal circuits (Carey & Bartlett, 1978; Kaminski et al., 2004). However, the efficacy of FM remains a contentious issue. Sharon et al. (2011) initially suggested that FM could significantly enhance memory in amnesic patients, but this claim has faced challenges in replication by multiple research groups. Importantly, there is no conclusive evidence that FM leads to faster or more robust integration of new information in explicit memory tests for healthy adults with intact hippocampi when compared to explicit encoding (EE)(Cooper et al., 2018; Shtyrov et al., 2019).

On the other hand, utilizing a similar paradigm to our present study but with a larger set of word-objects pairings (30) for learning, Antoneko and colleagues (2016) investigated the effect of transcranial alternating current stimulation (tACS) over the temporoparietal cortex on implicit language learning. They found that older individuals, even under sham conditions (without tACS), exhibited above-chance learning. However, it's worth noting that they did not assess the retention of this learning, which was a focus of our study.

Concerning explicit learning, we observed that both younger and older participants performed significantly better than chance both immediately and one week later. Nevertheless, a pronounced temporal effect was evident, with accuracy discernibly declining after the one-week duration.

When comparing the two kinds of learning, our results indicated that explicit learning initially provided a clear advantage in performance for both groups. This advantage could be linked to the conscious and declarative characteristics of explicit learning processes, which create a conducive environment for swift acquisition at the beginning (Ellis, 2015; Morgan-Short et al., 2011). However, as time passed, a convergence in the performance between the two learning protocols became apparent. This convergence might be influenced by the long-term retention capabilities of implicit memory. In fact, explicit traces usually fade faster than implicit ones (Goshen-Gottstein & Kempinsky, 2001; Graf et al., 1984; Liu et al., 2023; Rappold & Hashtroudi, 1991). Examining implicit, conceptually driven memory, Thomson, Milliken, and Smilek (2010) provided evidence of its resilience over extended periods. Through their decade-long research, they demonstrated that certain memories, formed without conscious effort, can persist and influence behavior weeks after the initial exposure. In their study, participants were exposed to a low-frequency U.S. state name during a lecture. Remarkably, even after 4 to 8 weeks, these participants were more likely to recall that specific state name, showcasing the enduring nature of conceptually driven implicit memory. Lee and Vakoch (1996)conducted a study using two tasks that tested rule learning to evaluate both implicit and explicit learning processes. In their study, a more complex task was associated mainly with implicit learning, while a simpler task was linked to explicit learning. When subjects were retested a week later, their explicit knowledge decreased, but their implicit knowledge remained stable. These findings suggest that implicit and explicit learning are governed by two distinct systems and that implicit learning may be a more stable mechanism. In our study, the same learning pattern was found both in young and older participants, these findings corroborate the idea that in typically developing learners once statistical patterns are acquired, they are preserved over an extended period (Frank et al., 2013; Perry et al., 2010). These results and our findings suggest that even if explicit learning provides an initial advantage, its immediate benefits might be leveled out in the long run due to the enduring nature of implicit memory. This underscores that especially in crucial long-term retention contexts such as clinical settings, the lasting effects of implicit learning cannot be overlooked.

Finally, in our study, we found that individual differences in new word learning were influenced by the number of years of education. This observation aligns with prior research, which has noted an interaction between age and education, particularly in episodic memory tasks (Burke & Light, 1981; de Souza-Talarico et al., 2007). Specifically, our findings suggest that a longer educational background is positively correlated with explicit learning. In fact this was not only evident in the recognition task, but also in the implicit learning curve, where model comparisons revealed education-related differences on the intercept term and the quadratic term.

These disparities seemingly reflect variations in the learning trajectories based on educational backgrounds in the initial phases of the learning curve rather than the culmination of learning. In essence, participants with higher educational levels manifested rapid learning, experiencing a pronounced upward trend as blocks progressed. In contrast, those with lower educational backgrounds, while showing a different learning pace, eventually converged to a similar trajectory by the end of the blocks. The overarching linear trend remained consistent, yet nuances in the early stages were evident based on education.

Across various studies, it's evident that higher educational attainment generally corresponds to improved cognitive function in adulthood (Albert et al., 1995; Anstey & Christensen, 2000; Atkinson et al., 2005; Yen et al., 2004). In the context of aging, factors like education can potentially mitigate or slow down the age-associated decline in memory capabilities (Angel et al., 2010; Foubert-Samier et al., 2012). Empirical evidence, particularly from episodic memory studies, has consistently shown that older adults with more education tend to outperform those with less education (Angel et al., 2010; Guerrero-Sastoque et al., 2021; Shimamura et al., 1995). However, a recent investigation by Lövdén et al., (2023), which assessed hippocampus volume and episodic memory in 708 middle-aged and older participants, found no direct relationship between education and the link between episodic memory changes and hippocampus volume changes. In this line, while several studies have found a correlation between higher education and a reduced risk of dementia (Alley et al., 2007; Andel et al., 2006; Fritsch et al., 2002; Hall et al., 2009; Le Carret et al., 2003; Ngandu et al., 2007; Sando et al., 2008), this link remains a subject of debate (Seblova et al., 2020). This divergence from the widely-held belief suggests that education, while influential, doesn't uniformly impact all cognitive abilities.

Interestingly, in our research, we did not find that education predicted implicit learning. This is consistent with prior studies suggesting that implicit memory does not necessarily correlate with factors like academic achievement, explicit learning abilities, or intelligence (Gebauer & Mackintosh, 2007; Maybery et al., 1995; A. S. Reber et al., 1991). Given these findings, it further underscores the hypothesis that implicit learning may be particularly advantageous for individuals with aphasia, especially considering that sociodemographic variables do not appear to modulate its efficacy, thereby eliminating potential confounding variables or factors that might attenuate its impact.

When interpreting the results of our research, several limitations need consideration. To begin with, our study operated with a relatively small sample size, although it is worth noting that this aligns with sample sizes utilized in previous, similar research endeavors (Peñaloza et al., 2022; Vadinova et al., 2020). Moreover, our initial choice of Raven’s Colored Progressive Matrices was due to their simplicity and applicability across a wide population, aiming to facilitate future comparisons with individuals affected by aphasia. However, this assessment provides limited insights into an individual's overall cognitive profile. Considering alternative evaluations, such as Nonword Repetition Tasks (NWRT) and the Digit Span subtests from the Wechsler Memory Scale-Revised (WMS-R), specifically designed to assess short-term (STM) and working memory (WM), alongside comprehensive assessments like the Montreal Cognitive Assessment, could have offered a more detailed and comprehensive understanding of cognitive abilities.

In fact, one notable oversight in our study was the absence of a specific assessment of participants of short-term memory and working memory, especially its phonological component.

Short-term memory denotes the ability to retain a limited set of information for a brief duration while keeping it easily accessible (Cowan, 2008). It's often seen as a facet of working memory a comprehensive concept devised to encompass various forms of temporary memory and encompass both storage and processing functions (Cowan, 1996, 2008). Investigations into STM and WM have significantly contributed to understanding language learning, with the term "WM" gaining prominence following Baddeley and Hitch's influential model, which highlighted distinct storage systems like the phonological loop and the visuospatial sketchpad controlled by a central executive (Baddeley & Hitch, 1974; Baddeley, 1986, 2003). The phonological loop, central to this model, temporarily holds language memory traces through a phonological store and keeps them accessible via articulatory subvocal rehearsal. The phonological loop is crucial for language acquisition across diverse populations (Baddeley et al., 1998; Gathercole and Baddeley, 1990; Gupta, 2003; Papagno et al., 2017). It's instrumental in storing unfamiliar word sound patterns until more stable long-term representations are formed, differentiating its role from basic word memorization, highlighting its significance in language learning (Baddeley et al., 1998; Papagno et al., 2017; Papagno, 2022). Studies on adult word learning indicate involvement of verbal WM. Papagno and Vallar's work (1992, 1995) demonstrated how phonological similarity and item length affect associative word memorization, supporting the role of verbal WM in learning new words. They showed that polyglots with higher nonword repetition scores outperformed controls in memorizing word–nonword pairs, suggesting the involvement of verbal WM in foreign vocabulary acquisition (Papagno et al., 1995). Gupta (2003) proposed a supplementary model delineating the interplay between word learning, nonword repetition, and immediate serial recall, positing that verbal STM mechanisms operate at the lexical level. In this perspective, a short-term sequence memory component encodes and temporarily sustains the sequential order of lexical and sub-lexical representations (e.g., words in immediate serial recall, novel word forms in new word learning) post speech input, facilitating accurate sequence recall. This mechanism aids in maintaining connections between lexical and sublexical levels, fostering long-term learning (Gupta, 2003).

Given the insights offered by models emphasizing the role of working memory in language learning, incorporating assessments focusing on these memory functions in our study could have significantly enriched our understanding. These measures would have provided valuable insights into the mechanisms underlying language acquisition, offering a more comprehensive perspective on the cognitive aspects involved in our research.

2.6 Conclusion

In conclusion, our study offers a nuanced understanding of the interrelationship between implicit and explicit learning across various age groups. A salient observation was the ability of both younger and older participants to acquire knowledge under both conditions, with their performances converging over time. Notably, implicit learning demonstrated an enduring nature, hinting at its potential applicability in aphasia rehabilitation across all ages. Furthermore, our findings indicated a discernible effect of years of schooling, particularly influencing the outcomes in the explicit learning condition. Recognizing the dual mechanisms of implicit and explicit learning not only deepens our grasp of cognitive functions across different age brackets but also illuminates potential strategies for aphasia rehabilitation. Such insights highlight the dual contributions of our study to both cognitive science and clinical applications.

CHAPTER 3: Implicit and explicit novel word learning in aphasia

Abstract

Background:

Aphasia, a language disorder resulting from neurological damage, often manifests as anomia, affecting daily communication. While speech and language therapies are primary interventions, their effectiveness varies among individuals. Recent research has shifted focus from language difficulties to other cognitive processes, emphasizing the role of learning mechanisms in aphasia treatment and recovery prediction. This study aimed to explore the learning capabilities of aphasia patients, particularly in implicit and explicit learning systems, given the potential of these systems in vocabulary acquisition.

Methods: Two experiments were conducted involving aphasia patients and healthy controls. In the first experiment, 38 participants (16 with aphasia and 22 healthy controls) were exposed to two vocabularies of 20 pseudo-words each, probing learning under implicit and explicit conditions and assessing their retention immediately and after a week. Observing impaired learning outcomes in aphasia patients, a second experiment was designed with 32 participants (15 with aphasia and 18 controls), reduced vocabulary sets of with 9 pseudo-words and increased repetitions. Importantly, both experiments utilized non-words and non-existent objects as a pure measure of novel learning.

Results: In the first experiment, aphasia patients performed worse than control and demonstrated learning below chance levels after a week, regardless of the learning condition. In the second experiment, with task adjustments, aphasia patients displayed above-chance learning levels both immediately and a week later. The control group consistently outperformed the aphasia group in both conditions. Implicit learning

appeared more stable than explicit learning. Furthermore, within the aphasia group, severity and lesion location significantly influenced learning trajectories.

Conclusion: The study underscores the potential of implicit learning in aphasia rehabilitation and highlights the need for tailored therapeutic approaches considering individual cognitive abilities and lesion location. While the research offers valuable insights into language learning in aphasia, further studies with larger cohorts are essential to validate and expand upon these findings.

3.1. Introduction

Aphasia, a neurologically-induced language disorder, and one of its most prevalent symptoms is anomia — the difficulty to retrieve a desired word (Laine & Salmelin, 2010; Nickels & Best, 1996, Goodglass & Wingfield, 1997). This characteristic feature of aphasia disrupts day-to-day communication activities and is prevalent across patients with aphasia (PWA), irrespective of the specific location or the overall severity of the brain injury they have suffered, although the underlying mechanism can vary depending on the specific aphasic deficit (Basso et al., 2001; Crinion & Leff, 2007; Dronkers & Ivanova, 2023; Peñaloza et al., 2022). As a primary response to this condition, speech and language therapies have been employed and are recognized for their pivotal role in evaluating and treating anomia (Brady et al., 2016). However, the efficacy of these therapeutic interventions varies significantly across individuals, even among those who present with similar profiles of anomia (Laganaro et al., 2006). Such variance emphasizes that merely identifying these impairments is not enough to create effective therapeutic interventions (Peñaloza et al., 2022). In recent years, the approach to understand aphasia has evolved. Instead of solely focusing on the apparent language difficulties that individuals with aphasia face, researchers have begun to see the bigger picture. They are now considering other cognitive processes that might be involved, recognizing that these are not only related to the manifestation of language problems but could also be key in predicting recovery after therapy (Dignam et al., 2017; Hillis, 2007; Wall et al., 2017). This shift in perspective has led to a greater emphasis on learning mechanisms, acknowledging that they play a significant role in the study and treatment of aphasia (D. Howard et al., 2006; Oppenheim et al., 2010).

Indeed, the core principle of rehabilitation, no matter what specific condition is being treated, revolves around learning. This learning process includes the ongoing gathering of new information and the creation and growth of strategies. These strategies can either help to bring back lost language abilities or develop new ways to lessen the impact of language problems (Hopper & Holland, 2005; Nickels et al., 2002). Therefore, understanding how patients with aphasia learn new words becomes an essential part of this process (Basso et al., 2001; Gupta & Tisdale, 2009; Nickels et al., 2002).

Despite the residual language impairment that characterizes aphasia, individuals with this condition still have the ability to learn new associations between words and their referents (Peñaloza et al., 2017; 2022). This potential for learning is not confined to a single method but can be observed through various facilitation procedures (Marshall et al., 2001). Moreover, the training and long-term retention of novel words, as well as some pre-existing but temporarily inaccessible vocabulary, is possible (Tuomiranta et al., 2012; 2014). However, even in this case, there is considerable inter-individual variability among PWA in their capacity to learn and store new word forms and to re-learn vocabulary affected by their condition (Kelly & Armstrong, 2009).

Zooming into the domain of word learning, it is fundamental to investigate its underlying mechanisms. Word learning is underpinned by both implicit and explicit learning systems. As we have extensively discussed in the previous chapters, implicit learning, sometimes referred to as incidental learning, unfolds naturally without a conscious effort, predominantly through passive exposure to language in diverse contexts (N. C. Ellis, 2005; Krashen, 1989; Miller & Gildea, 1987). On the other end of the spectrum, explicit learning demands active, conscious effort and is typically directed by instruction (Nation, 2001). Both these learning pathways have their roles to play in vocabulary acquisition. However, the dominance of one over the other can be influenced by various factors, including age, level of language proficiency, and the specific context in which the learning is taking place (N. C. Ellis, 2001; Hulstijn, 2003).

Though both implicit and explicit learning mechanisms are crucial, it has been observed that research mainly focused on explicit learning paradigms, especially when investigating learning paradigms in aphasia treatments. This is primarily because explicit learning strategies are heavily employed in contemporary speech therapy treatments designed for aphasia (Meinzer et al., 2014; Nickels et al., 2002). Conversely, studies exploring implicit learning remain scarce (Schuchard et al., 2016), and research pertaining to implicit learning post-stroke has mostly been confined to the motor domain, rarely addressing language implications (Schuchard & Thompson, 2014). Among these studies, most focus solely on patients with Broca's aphasia, who have medium to severe syntactic impairment (Christiansen et al., 2010; Cope et al., 2017; Dominey et al., 2003), with few exceptions, including patients without syntactic impairment (Zimmerer et al., 2014; Vadinova et al., 2020). These studies provided mixed results, indicating that understanding implicit learning mechanisms in aphasia is a complex endeavor.

For instance, Dominey et al. (2003) and Christiansen et al. (2010) found that patients performed significantly worse than control participants on an artificial grammar learning (AGL) task, suggesting that the syntactic deficits in Broca's aphasia reflect damage to domain-general implicit learning mechanisms. However, Zimmerer et al. (2014) found that grammatical impairment was associated with a more pronounced deficit in implicit learning mechanisms, but the individual pattern of performance was within the normal range in healthy controls and PWA without syntactic impairment. In contrast, Cope et al. (2017) found that patients with Broca's aphasia and nonfluent Primary Progressive Aphasia (nfvPPA) exhibited impairment on an AGL task compared to controls, but implicit-statistical learning (ISL) capacities were not completely absent in these groups. Vadinova and collaborators (2020) explored the impact of frontal versus posterior brain lesions on ISL in PWA and the correlation between ISL impairment and syntactic deficits. Participants, including aphasic individuals with different lesion locations and controls, were subjected to a visual statistical learning task. Participants with aphasia also performed various linguistic tests. The results indicated that ISL mechanisms were impaired in aphasic patients regardless of the lesion location, suggesting that ISL might extend to posterior brain regions or be susceptible to other cognitive dysfunctions. Notably, a correlation was found between ISL mechanisms and syntactic, not lexical, impairments in aphasia.

To date, only one study directly compared implicit and explicit learning in aphasia. Schuchard and colleagues (Schuchard & Thompson, 2014) explored implicit and explicit learning of an auditory word sequence in individuals with stroke-induced agrammatic aphasia using a serial reaction time task adaptation. Aphasic individuals showed significant learning under implicit, but not explicit, conditions, aligning with previous studies of post-stroke learning not related to language. Boyd and Winstein (2004) found that explicit information about sequential learning tasks assisted motor learning in healthy individuals but interfered with learning in stroke patients, indicating that explicit information could potentially overload the working memory of some stroke patients.

Moreover, as regards implicit learning, all the aforementioned studies have concentrated on learning artificial grammar, with only a few experiments having investigated implicit learning of new words in subjects with aphasia (Peñaloza et al., 2017; Breitenstein et al., 2004). Breitenstein and colleagues (2004) tested implicit word learning in healthy adults and in three subjects with aphasia, comparing it with learning through explicit feedback. Despite the promising results, the study was limited by a small sample size and the use of familiar images with new words, which could potentially influence the task outcomes due to the type of image, word frequency, and word priming effects (Tuomiranta et al., 2012). Therefore, this type of stimuli may not be suitable for a relatively pure investigation of individuals' word-learning abilities.

In this study, we conducted two related experiments to investigate the learning capabilities of participants with aphasia employing non-words and non-existent objects. Initially, we engaged the participants in a learning task involving two vocabularies, each consisting of 20 -pseudo-words. The task was designed to explore learning under two distinct conditions: implicit and explicit and its retention after one week. Nevertheless, following the observation of the learning patterns, we noted that aphasic participants demonstrated learning inferior to the chance level after a one-week interval regardless the learning condition.

Motivated by these findings, we conducted a subsequent experiment using the same type of non-existing objects and non-words but with reduced vocabulary sets containing nine words each and we also added a control group for this condition. This adjustment was made in response to the specific learning challenges faced by the aphasic participants as compared to non-aphasic individuals. By tailoring the task to the specific learning capacities of the aphasic group, we aimed to provide a more nuanced understanding of the underlying cognitive processes and to identify potential strategies for enhancing learning outcomes in this population.

3.2. Materials and methods - Experiment 1

Participants: Forty individuals, eighteen patients with aphasia (nine women; mean±SD age: 65.7±10 years, range: 45–81; years of education 12.85±3.5 years, range: 8–18) and a control group including twentytwo healhty old adults (Participants Chapter 2; twelve women; mean±SD age: 70.1±3.9 years, range: 65–79; years of education 14.5±3 years, range: 8–18) were recruited in the study. All were native Italian speakers. All healthy participants had no history of neurological disorders and underwent neuropsychological testing prior to study inclusion in order to ensure normal cognitive functioning. The eligibility criteria for individuals in the aphasia group encompassed an age range spanning from 18 to 85 years, confirmation of their first and single stroke via CT or MRI scan, enduring aphasia arising from the stroke, persisting for a minimum of 6 months from the onset of the stroke, as established through a comprehensive speech and language assessment and the capability to comprehend and execute instructions necessary for the completion of the experimental task. The diagnosis of aphasia and aphasia severity was determined using Aachen Aphasia Test (AAT) (IT-AAT: De Bleser et al., 1986; Luzzatti et al., 1987; Willmes et al., 1988; Luzzatti et al., 1994). Two participants with aphasia only participated in the first session and then dropped out due to health reasons.

Written informed consent was obtained from all participants prior to participation.

ID	Age	Sex	Years of Education	Etiology	Lesion	Severity	Type
1	47	M	8	Ischaemia	Left Temporal Occipital regions	mild	Wernicke
2	76	M	8	Hemorrhage	Left temporal Lobe	Moderate	Fluent
3	59	F	17	Ischaemia	Left Frontal-parietal-temporal regions	severe	Global
4	71	M	13	Ischaemia	Left MCA (Temporal Gyrus)	Mild	Conduction
5	73	F	11			Mild	
6	62	M	11	Hemorrhage	Left temporal and parietal region	mild	Werniclke
7	63	F	16	Hemorrhage	Left Temporal	mild	Conduction
8	61	M	8	Hemorrhage	Left Frontal-parietal region	severe	Global
9	71	M	8	Hemorrhage	Left Frontal	Moderate	Broca
10	68	F	17	Ischaemia	Left MCA(insula, frontal region)	Severe	Non fluent
11	45	F	13	Ischemiae	Insular parietal regions	Moderate	Wernicke
12	59	M	17	Ischaemia	Left Frontal and insular region	severe	Broca
13	69	F	18	Hemorrhage	Extended Parietal-Temporal region	Moderate	Wernicke
14	72	F	13	Hemorrhage	Left MCA(insula, frontal and temporal region)	Severe	Wernicke
15	75	F	13	Hemorrhage	Extensive MCA (Frontal rehions and insula)	Moderate	Broca
16	81	F	13	Ischemiae	MCA (frontal and insular region)	severe	Anomic

Table 1. Demographic and clinical data patients with chronic aphasia

Notes: M = male; F = female; MCA = middle cerebral arter

Stimuli and procedure

Procedure and stimuli are identical to the ones reported in Chapter 2 with healthy participants.

3.3. Statistical analysis

All analyses described in the subsequent sections were conducted using the R statistical software. However, the specific analytical approach varied depending on the dependent variable under consideration.

3.3.1. Recognition task

Preliminary descriptive statistics were computed including mean accuracies and standard error, across the different groups, conditions of learning, and time points. Additionally, the Exact Binomial Test was employed to determine if performance significantly exceeded chance levels. These analyses facilitated an overview of task performance trends and variations across the specified conditions.

Inferential statistical analysis were conducted using R statistical software, with the lme4 package for generalized mixed modelling (Bates et al., 2015). Generalized Mixed Models (GMM) were calculated for task performance w. Fixed factors included group (PWA and controls), conditions of learning (implicit and explicit), and time (immediate test and after one week). The random intercept for subjects and items was included to account for the variability and repeated measurements within these units. The interaction between the fixed factors was also explored to examine the nuanced differences across groups, learning conditions, and timeframes.

3.3.2. Recognition task and aphasia severity and lesion location

To examine the effect of aphasia severity and lesion location on word learning, the analyses were restricted to just the participants with aphasia, and the individual scores on the AAT severity rating scale and the location of the lesion, either anterior or posterior (see Vadinova et al., 2020; Peñaloza et al; 2016) , were added as a continuous fixed effect to the GMM including subject and item as random intercept and conditions (implicit and explicit) and time (immediate and after one week) as fixed factor.

3.3.3. Learning curve for implicit condition

For the implicit task's learning curve variable, a multilevel regression approach was adopted, specifically employing growth curve analysis (GCA) based on a second-order orthogonal polynomial model to probe temporal changes in learning curves (Mirman, 2014). The analysis incorporated fixed effects for time (block) and group, alongside random effects for participants corresponding to various time points. As the outcome variable was binary (correct or incorrect response), logistic GCA was the chosen method for data analysis. Model comparisons were undertaken to evaluate group disparities concerning specific time-related elements. In orthogonal polynomial models, the intercept denotes the overall average outcome, the linear term signifies the linear trajectory, and the quadratic term represents the curvature.

3.3.4. Learning curve and aphasia severity and lesion location

To examine the effect of aphasia severity and lesion location on word learning, the analyses were restricted to just the participants with aphasia and the individual scores on the AAT severity rating scale and the location of the lesion, either anterior or posterior, were added as a continuous fixed effect on each time term. As in the group comparisons above, the base model contained the fixed effects of each time term (intercept, linear, and quadratic) and random effects of participants for each of the time terms. The continuous fixed effect of severity and lesion location on each time term was added to successively evaluate its continuation to model fit.

3.4. Results

3.4.1. Recognition Test - Descriptive Analysis

Upon initial evaluation, both PWA and controls exhibited performances that were statistically above chance. The Binomial Exact Test for the aphasia group indicated significant performance above chance at Time 1 in the explicit condition (Estimate = 0.55, SE = 0.498, $p < .001$) and in the implicit condition (Estimate = 0.44, SE = 0.497, $p < .001$). For the control group, the Binomial Exact Test revealed above-performance under both explicit (Estimate = 0,70, SE=0.218, p <) and implicit condition (Estimate = 0.63, SE = 0.230, $p < .001$). However, a longitudinal assessment after one week revealed differential patterns between the groups, with the aphasia group performing under chance-level at Time 2. Specifically, in the explicit condition, the aphasia group showed a marked decrease in mean accuracy, transitioning from an accuracy of 0.55 at Time 1 to 0.341 at Time 2. The implicit condition also revealed a decline, with accuracy values of 0.441 at Time 1 and 0.353 at Time 2. Conversely, the control group consistently exhibited performances that were statistically above chance across both explicit (Estimate = 0.5, SE = 0.239) and implicit (Estimate = 0.484, SE = 0.239) conditions and time points, with all p-values registering below 0.001.

3.4.2. Recognition Test - Inferential Statistic

A generalized mixed model was fitted to ACCURACY of the recognition task with a binomial family and a logit link function. The predictors included the main effects and interactions of GROUP (aphasia and control), TIME (1- immediate and 2- after one week), and CONDITION (implicit and explicit), with a random intercept for ID and ITEM. GROUP was found to be significant, with the control group demonstrating a greater accuracy, with an estimate of 0.686585 ($p < 0.001$). The predictor `TIME` also showed significance, with the second time point indicating a notable decrease in accuracy, as evidenced by an estimate of -0.443485 ($p < 0.001$). For the `CONDITION` predictor, the implicit condition exhibited a worse accuracy as compared with the explicit one, with an estimate of -0.197957, though this effect was marginally significant ($p = 0.0896$). The interaction between the GROUP and TIME and GROUP and CONDITION and the three-way interaction between GROUP, TIME, and CONDITION were not statistically significant.

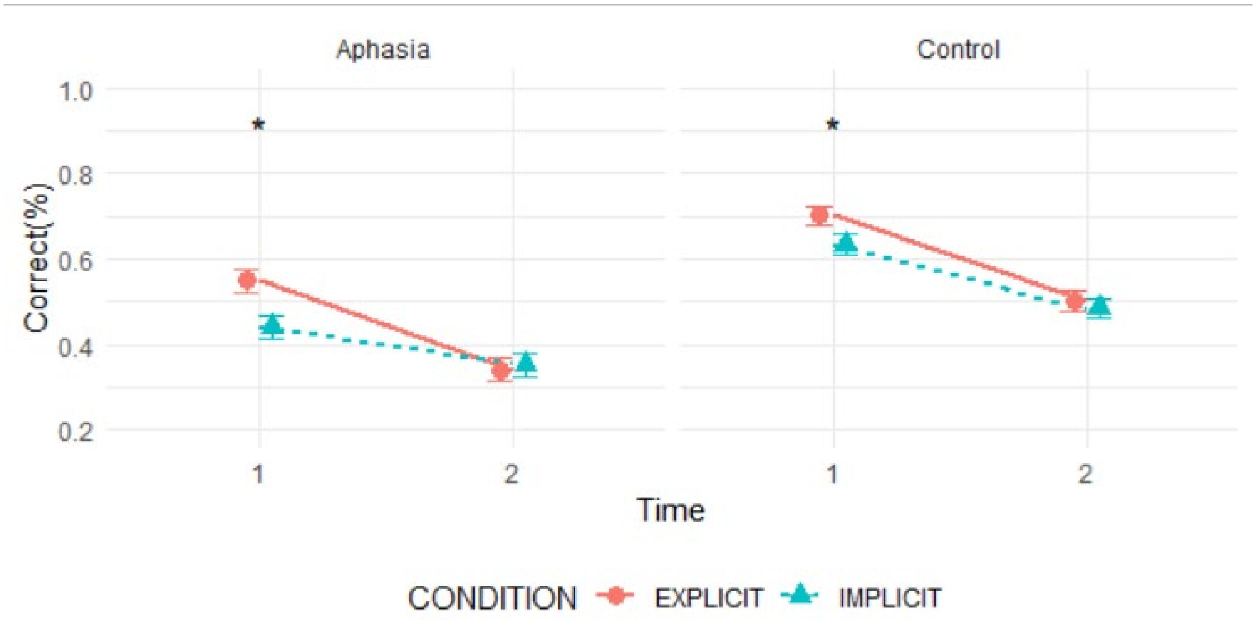


Fig.3 Recognition task carried out by both participant with aphasia and controls, both immediately and one week later.

3.4.3. Recognition task and aphasia severity and lesion location

A generalized mixed model was fitted to the data with a binomial family and a logit link function on aphasic patients' performance. The response variable was ACCURACY of the recognition task, and the predictors included main effects and interactions of SEVERITY, LESION, TIME, and CONDITION, with a random intercept for ID and ITEM. The predictor 'SEVERITY' showed varied significance across its levels. While the moderate severity did not exhibit a significant difference when compared to the mild level, with an estimate of 0.11679 ($p = 0.5831$), the severe level was notably significant with an estimate of -0.06238 ($p = 0.04661$). This signifies that patient with severe aphasia demonstrated a diminished accuracy in the recognition test compared to those with mild aphasia. The LESION predictor, specifically for the posterior lesion type, showed a trend towards increased accuracy with an estimate of 0.29592, but it did not reach statistical significance ($p = 0.0901$). The TIME predictor was highly significant, with the second time point indicating a decrease in accuracy with an estimate of -0.62916 ($p < 0.001$). The CONDITION predictor, specifically for the implicit condition, showed a trend towards decreased accuracy with an estimate of -0.20794, but it did not reach statistical significance ($p = 0.0729$). In summary, among the predictors, only the TIME variable was found to be statistically significant at the $p < 0.05$ level, indicating its strong influence on accuracy.

3.4.4. Learning Curve

To investigate the differences in growth curves, the Control group was set as the reference level for the fixed effect of Group. The logistic growth curve analysis (GCA) was conducted on the response variable response that was dichotomous, with predictors including the polynomial terms of block (both linear and quadratic) and their interactions with Group. A random intercept for ID and a random slope for block were also included. The GCA revealed that the linear term of block had a significant effect, with an estimate of 12.3732 ($p < 0.001$), indicating a significant linear increase in accuracy as blocks progressed. The quadratic term of block also showed a significant effect, with an estimate of -19.1518 ($p < 0.001$), suggesting a curvature in the learning trajectory. When comparing the Control group to the aphasia group, the Control group demonstrated a significant difference in accuracy with an estimate of 0.5070 ($p < 0.001$), reaching thus higher levels of accuracy during learning. The interaction between the linear term of block and the Control group was significant, with an estimate of 29.9886 ($p < 0.001$), indicating that the rate of linear increase in accuracy differed for the aphasia group compared to the control group, with a steeper curve for the last one. Similarly, the interaction between the quadratic term of block and the Control group was significant, with an estimate of 17.3635 ($p < 0.001$), suggesting that the curvature of the learning trajectory also was more pronounced for the Control group.

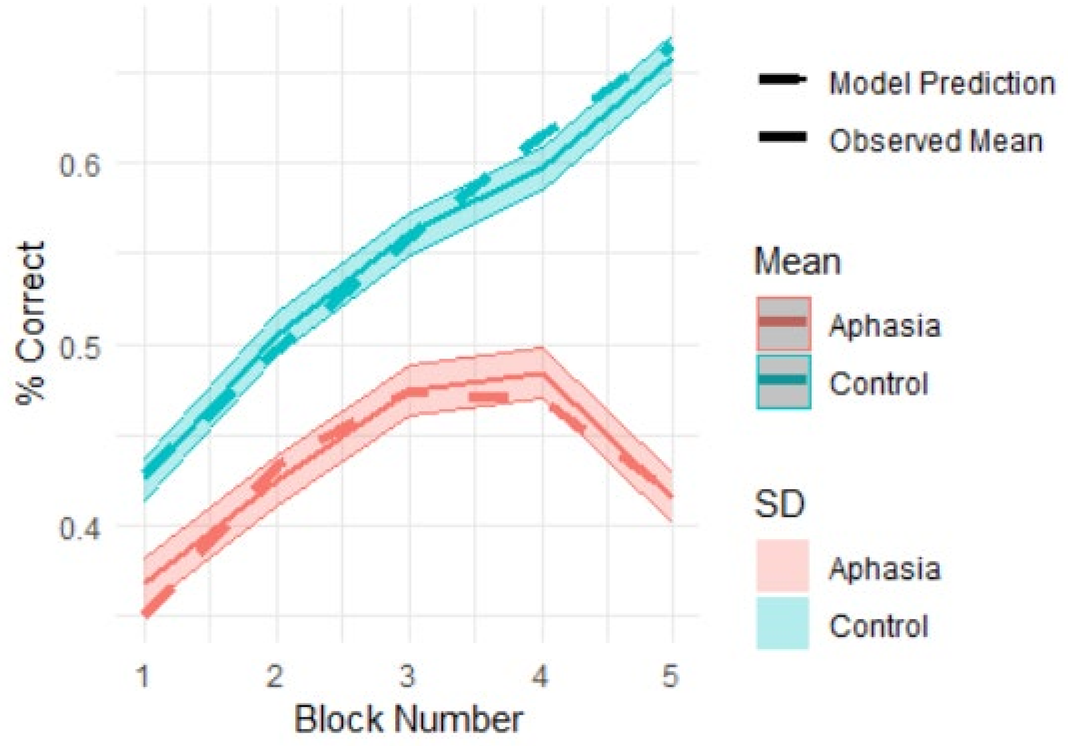


Fig.4 Comparison of learning curves for participants with aphasia (PWA) and matched control.. The observed (dash) and logistic GCA model fit (lines) learning curves are depicted for the two groups.

3.4.5. Learning curve and aphasia severity and lesion location

To investigate the influence of aphasia severity and lesion location on implicit learning, the analysis was limited to the aphasia participants, and we incorporated both 'severity' and 'lesion' as categorical fixed effects into our model. As with the group comparisons detailed earlier, the foundational model encompassed the fixed effects of each time term (intercept, linear, and quadratic) and random effects for participants linked to each time term. Our model comparisons indicated that the individuals with moderate severity don't seem to deviate significantly from the mild aphasic in their general learning response, as evidenced by an estimate of -0.1516 (p = 0.677498) Those with severe aphasia, however, might have a slightly different general learning response, with an estimate of -0.3569, although this difference is not conclusively significant (p = 0.075592). When it comes to the progression of learning over time, or the learning steepness, individuals with moderate severity don't show a marked difference from the mild aphasia group, as indicated by an estimate of 3.6861 for the interaction with the linear term of block number (p = 0.445835). In contrast, those with severe aphasia exhibit a distinct learning velocity, with a significant estimate of 10.3009, suggesting a different rate of learning as the sessions progressed (p = 0.010246). For the overall learning curve, represented by the quadratic term, individuals with moderate severity don't seem to differ notably from the mild group, with an estimate of 11.8520 (p = 0.389246). However, those with severe aphasia display a significant pattern in their overall learning performance, as shown by an estimate of 12.2533 (p = 0.029730). Regarding lesion location, individuals with post-lesion conditions might have a different learning response from the anterior group, with an estimate of 0.4954, though this is not conclusively significant (p = 0.07082). Their learning velocity, represented by the interaction with the linear term of block number, doesn't seem to differ significantly from the reference mild group, with an estimate of -4.9976 (p = 0.31492) Similarly, their overall learning performance, as indicated by the interaction with the quadratic term, doesn't show a marked difference from the reference group, with an estimate of -13.1414 (p = 0.22290).

3.4.5. Individual difference

To understand the variability in learning and recognition among individuals with aphasia, we analysed their performance across different learning performances and times. In the group with aphasia, ten participants performed significantly above chance in the immediate recognition test in the explicit condition and six in the implicit one (binomial test, p ≤ .05 in all cases). Of these, only participants four under the explicit, and two under the implicit, performed significantly above chance in the follow-up test (binomial test, p ≤ .05 in all cases). All the remaining participants were not reliably different from the chance level in both recognition tests (binomial test, p > .05 in all cases).

In terms of learning curves, a majority of the participants showed a positive learning trajectory. Specifically, twelve demonstrated a learning curve, indicating improvement over time. On the other hand, four participants did not exhibit a significant learning curve, suggesting a relatively stable performance across the blocks. The individual learning curves of the PWA are depicted in Fig.5.

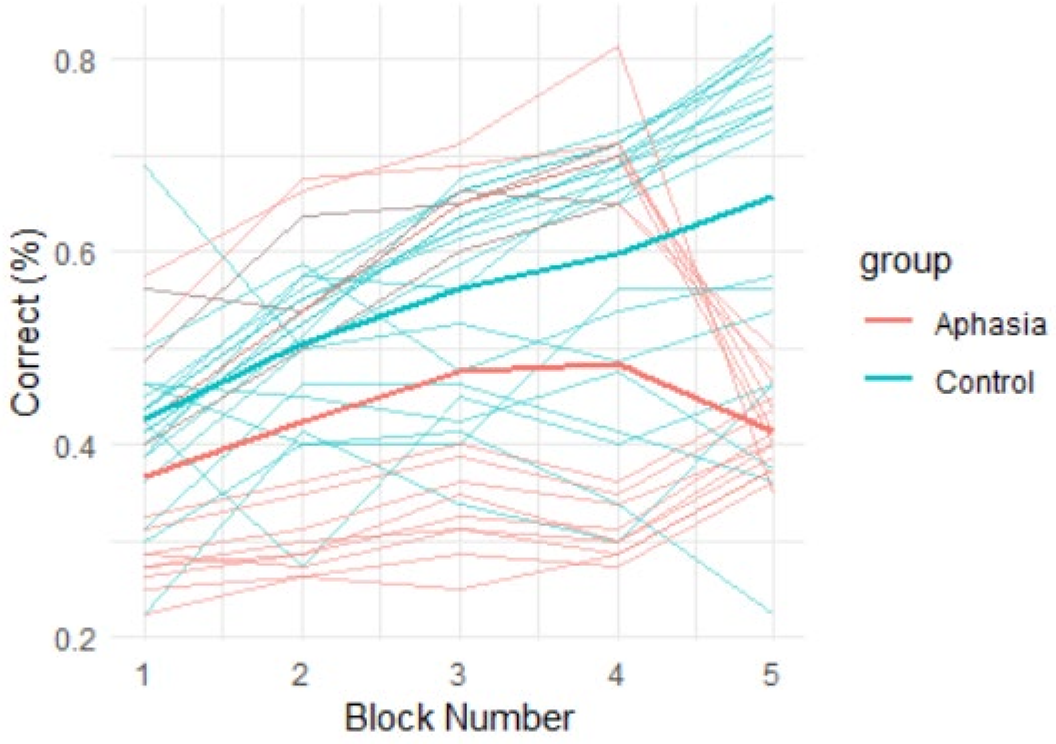


Fig 5. Individual learning curves across blocks and groups.

3.5. Discussion Experiment 1

The results of the first study provide a first insight into the learning capabilities of patients with aphasia in comparison to healthy participants. Consistent with previous research, patients with aphasia did exhibit some degree of learning in both conditions and this learning was notably inferior compared to healthy participants. A particularly salient finding was the marked decline in the group-level performance of patients with aphasia after one week, with their learning dropping to levels at chance. This was not true for all participants but for the majority (12 out of 15 or 80%). Interestingly, older participants exhibited learning patterns that were more akin to the aphasia group than to the younger participants. This observation suggests that age-related cognitive decline might share some similarities with the cognitive impairments observed in aphasia. However, it's essential to note that while older participants showed similarities to the aphasia group, they still outperformed them, highlighting the distinct and more pronounced impact of aphasia on learning.

Zooming into the implicit learning condition, only six participants performed above chance in the recognition test, while twelve showed a learning curve, meaning that half of this twelve couldn't show learning in the recognition test, although they actually had a learning behavior during the presentation of association. This aligns with research findings suggesting that individuals with aphasia frequently have the ability to implicitly process linguistic information, even though they might not be able to demonstrate this learning explicitly (Hagoort, 1993; Revonsuo, 1995; Revonsuo & Laine, 1996; Roberts et al., 2010) Looking at the effect of severity we found that only patient with severe aphasia performed worse compared to the ones with mild and moderate aphasia. When examining the lesion location of aphasia, individuals with posterior lesions, although not reaching statistical significance, demonstrated better learning capabilities, especially during implicit learning. This observation aligns with the prevailing notion that the frontal lobe, integral to executive functions, working memory, and attention, is crucial for the acquisition and retention of new information.

Motivated by the fact that patients with aphasia lost almost all their learning after just one week, a subsequent study was designed. By reducing the number of word-referent pairs but maintaining the same structure and principles of implicit learning, the aim was to create a more streamlined and potentially more effective learning paradigm. The hope was that this refined approach would have shed further light on the nuances of learning in aphasia, particularly the challenges they face in long-term retention, and provide a clearer understanding of the underlying cognitive mechanisms.

3.6. Materials and methods - Experiment 2

Participants: 18 healthy adults (11 women; mean±SD age: 55±8.3 years, range: 42–68; mean±SD years of education: 15.2±2.7 years, range: 8–17)and 15 patients (9 from the previous study) with aphasia participated in the study (seven women; mean±SD age: 56,73±12,25 years, range: 38–75; years of education 12,3±3.8 years, range: 8–16)). All were native Italian speakers. All healthy participants had no history of neurological disorders and underwent neuropsychological testing prior to study inclusion in order to ensure normal cognitive functioning. The eligibility criteria for individuals in the aphasia group encompassed an age range spanning from 18 to 85 years, confirmation of their first and single stroke via CT or MRI scan, enduring aphasia arising from the stroke, persisting for a minimum of 6 months from the onset of the stroke, as established through a comprehensive speech and language assessment and the capability to comprehend and execute instructions necessary for the completion of the experimental task. The diagnosis of aphasia and aphasia severity was determined using Aachen Aphasia Test (AAT)T (IT-AAT: De Bleser et al., 1986; Luzzatti et al., 1987; Willmes et al., 1988; Luzzatti et al., 1994). Written consent was obtained from all participants prior to participation.

ID	Age	Sex	Years of Education	Etiology	Lesion	Severity	Type
1	59	M	17	Ischaemia	Left Frontal and insular region	severe	Broca

2	62	M	11	Hemorrhage	Left temporal and parietal region	mild	Werniclke
3	59	F	17	Ischaemia	Left Frontal-parietal-temporal regions	severe	Global
4	38	F	13	Hemorrhage	Left Frontal	severe	Broca
5	47	M	8	Ischaemia	Left Temporal Occipital regions	mild	Wernicke
6	45	F	13	Ischemiae	Insular parietal regions	Moderate	Wernicke
7	44	M	16	Hemorrhage	Left MCA (Parietal)	mild	Transcortical sensorial
8	61	M	8	Hemorrhage	Left Frontal-parietal region	severe	Global
9	54	F	8	Hemorrhage	Left Frontal-temporal-parietal region	severe	Non fluent
10	54	M	8	Hemorrhage	Left MCA/intracerebral regions	severe	Wernicke
11	63	F	16	Hemorrhage	Left Temporal	mild	Conduction
12	42	M	16	Ischemiae	Left Parietal and temporal regions	mild	Fluent
13	67	M	8	Hemorrhage	Left MCA (temporal)	mild	Anomic
14	81	F	13	Ischemiae	MCA (frontal and insular region)	severe	Anomic
15	75	F	13	Hemorrhage	Extensive MCA (Frontal rehions and insula)	Moderate	Broca

Table 2. Demographic and clinical data of patients with chronic aphasia.
Notes: M = male; F = female; MCA = middle cerebral arter

Stimuli

Participants were presented with pairings of non-words and images of non-existent objects in two learning conditions, implicit and explicit. The stimuli were similar to the ones of the first experiment but not the same ones. For both paradigms, 18 bisyllabic pseudowords and 18 novel objects images were selected and then randomly divided into two separate vocabularies.

Bisyllabic pseudowords were taken from the 60 created bisyllabic words assembled by Basso and collaborators (2001), and the novel objects were taken from the Novel Object and Unusual Name (NOUN) Database (see http://www.sussex.ac.uk/wordlab/noun; (Horst & Hout, 2016)) (See Appendix C). Bisyllabic pseudowords and images were randomly matched.

Procedure

Participants underwent two learning conditions, implicit and explicit, in two separate sessions with two different sets of non-words and images. After a week, they will be tested on both sets of non-words (both explicit and implicit).

In light of the findings from Experiment 1, we have adapted the Implicit Learning Paradigm from Antonenko et al., 2014, while adhering to the rule of presenting each 'correct' pairing ten times more frequently than each 'incorrect' pairing. This foundational principle consistently guides our experimental design throughout the entire learning phase, ensuring a substantial disparity in exposure frequency between 'correct' and 'incorrect' pairings, with each 'correct' pairing presented ten times more frequently than each 'incorrect' pairing, all while we have implemented certain changes. To reiterate, we have selected 9 specific "correct" pairings as opposed to the 20 used in experiment one and the 30 used in Antonenko and Flöel's earlier experiment. This reduction in the number of "correct" pairings is one of the key differences. These 9 "correct" associations are consistently presented four times within each session over the course of five learning sessions, resulting in a total of 20 exposures for each "correct" pairing throughout the learning phase, as proposed by the original paradigm presented by Breitenstein et al., 2004. This arrangement ensures that participants are repeatedly and consistently exposed to the "correct" associations, in line with the 10-fold rule. On the other hand, "incorrect" pairings are presented in the same way as Experiment 1: Each "incorrect" pairing is featured twice within a single session, but importantly, they are not repeated across sessions. As a result, each "incorrect" pairing only receives 2 exposures throughout the five sessions. Blocks were five (as in Experiment 1), each containing 54 randomized trials, totalling 270 trials, these carefully constructed exposure frequencies come into play. The randomized order of trials for each subject and session ensures that participants encounter the pairings in an unpredictable manner, eliminating potential order effects. In each trial, a non-word is spoken, followed by the presentation of an image 200 milliseconds later. Importantly, both the non-word and image are normalized to the same loudness and length, maintaining consistency and removing any stimulus presentation variations as a confounding factor.

Explicit Learning Paradigm

The paradigm was adapted from the first Experiment according to the implicit paradigm. As before, during the learning phase, an image was presented 200 ms from the onset of the non-word. A total of 9 images and 9 pseudo-words were presented, with the images remaining for four seconds on the screen. The images were presented four times per block, for five blocks, for a total of 20 presentations per image. After each block, there was a short break so that participants could proceed to the next block at their own pace (Meinzer et al., 2014).

Testing Phase: The recognition phase was identical to experiment 1.

3.7. Statistical analysis

Thes statistical analysis were carried out as in Experiment 1.

3.8. Results

3.8.1. Recognition Test - Descriptive Analysis

In the recognition tests, participants from the aphasia and healthy groups displayed varying levels of accuracy across different conditions and time points, as assessed using the Exact Binomial Test. Under the explicit condition, the aphasia group initially exhibited a mean accuracy of 0.615 [95% CI: 0.512, 0.683], but their accuracy dropped to 0.407 [95% CI: 0.338, 0.510] after one week. Notably, the second instance of the explicit condition did not result in accuracy above chance for this group. Meanwhile, under the implicit condition, their accuracy was 0.630 [95% CI: 0.535, 0.704] during the immediate test, which decreased to 0.471 [95% CI: 0.392, 0.565] after one week, staying above the chance level.

In contrast, the control group consistently demonstrated above-the-chance high accuracy rates across conditions and time points. For the explicit condition, they achieved a mean accuracy of 0.981 [95% CI: 0.947, 0.996] during the immediate test and 0.840 [95% CI: 0.774, 0.892] after one week. Under the implicit condition, their accuracy was 0.969 [95% CI: 0.929, 0.990] during the immediate test and 0.859 [95% CI: 0.796, 0.908] after one week.

3.8.2. Recognition Test - Inferential Statistics

To thoroughly investigate these results, a generalized linear mixed model (GLMM) was employed, considering group, condition, time, and their interactions. The model revealed significant main effects: group, with the healthy group performing better than the aphasia one (Estimate=2.3625020 SD = 0.1736063, p = 0.01) and time, with a significant decrease of accuracy over time (Estimate= -1.0284, SD = 0.1562, p = 0.001). Additionally, the effect of the condition was not significant (Estimate= 0.1360, SD =0.895, p =0.371). Finally, interaction between GROUP and CONDITION, GROUP and TIME, CONDITION and TIME AND the three-way interaction involving the group, condition, and time did not yield a significant effect.

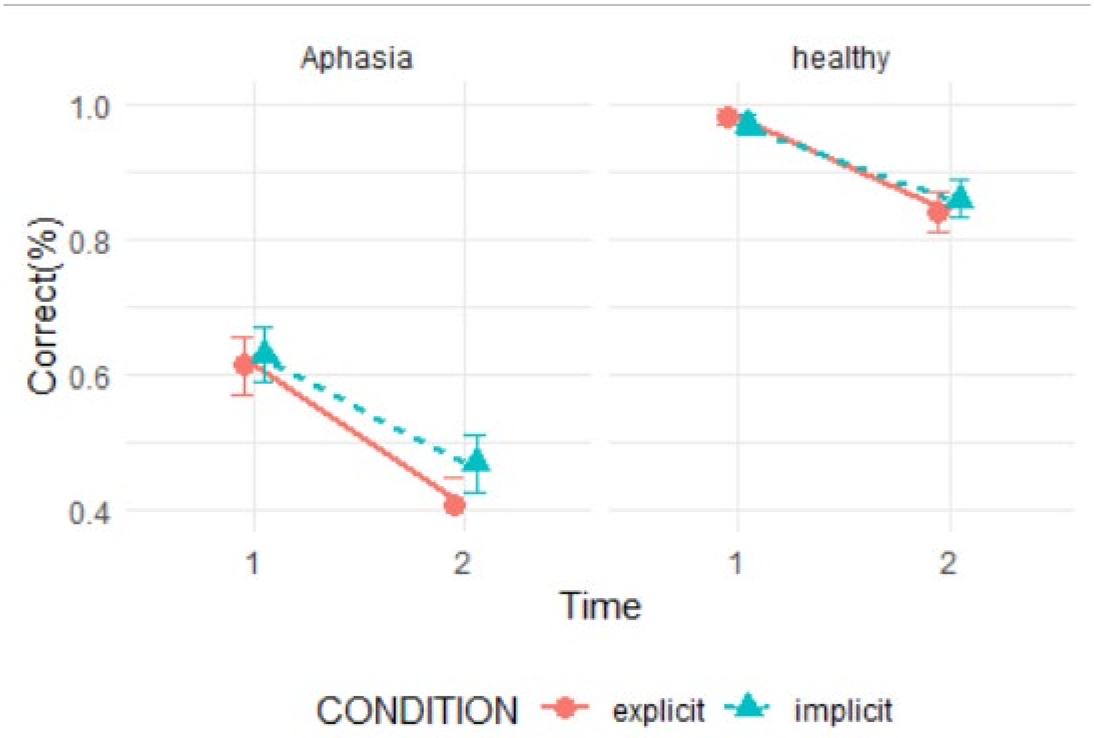


Fig.6 Comparison of recognition task for participants with aphasia and matched controls immediately and after one week.

3.8.3. Recognition task and aphasia severity and lesion location

In an effort to understand the factors influencing accuracy in aphasia patients, a generalized linear mixed models were employed, each focusing on a different predictor: severity, of aphasia, and lesion location. The model was structured to predict accuracy based on the predictors 'lesion', 'severity', 'time', and 'condition', while accounting for random effects associated with individual participants (ID) and items (ITEM). From the fixed effects, it was observed that the posterior lesion location had a positive direction of effect on accuracy compared to the anterior one, with an estimate of 0.4561, though this effect was not statistically significant ($p = 0.139531$). Moderate severity had a negative direction of effect although not significant (estimate = -0.3127, $p = 0.353682$), indicating a decrease in accuracy compared to mild severity. Similarly, severe aphasia also showed a negative effect on accuracy (estimate = -0.5751), but this effect was significant ($p = 0.043340$). This suggests that as the severity of aphasia increases, there might be a decline in accuracy, with the effect being more pronounced in individuals with severe aphasia.

3.8.4. Learning curve

To explore the differences in learning curves between groups, the aphasia group served as the reference level for the fixed effect of group. This allowed for the estimation of parameters for the control group in relation to the aphasia group. The logistic growth curve analysis (GCA) highlighted significant disparities between the groups concerning overall accuracy during the learning process. The intercept term, which signifies the average overall accuracy, was significant for the control group (Estimate = -0.27995, SE = 0.07988, $p < 0.001$). This indicates that the control group had a distinctively different response accuracy compared to the aphasia group. Specifically, the control group exhibited a notably higher accuracy, as evidenced by an estimate of 0.82828 ($p < 2e-16$). Moreover, the interaction between the polynomial term for block and the group variable was significant, indicating that the learning trajectory or the progression of the learning curve was not uniform across groups. Specifically, the control group's learning trajectory was steeper, as indicated by the positive estimates for these interactions (poly(block, 2)1:group; Control = 68.06938 and poly(block, 2)2:groupControl = 27.24333). This implies that the control group's learning pace and pattern were markedly different, and in this context, more accelerated than that of the aphasia group.

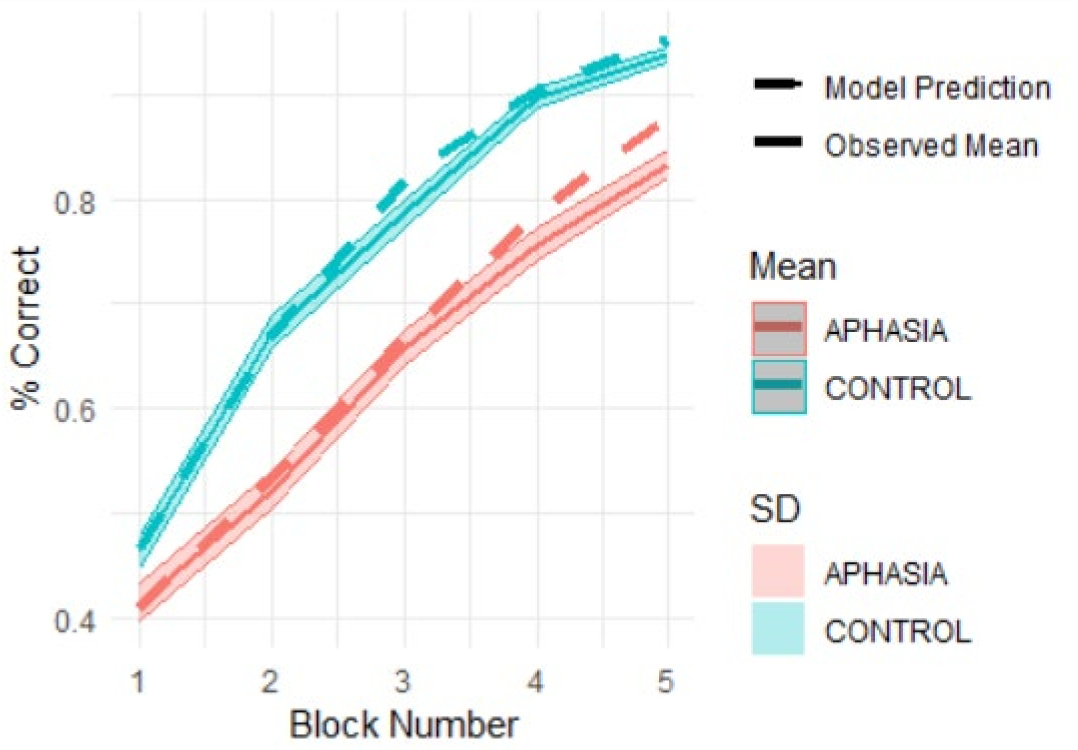


Fig.7. Comparison of learning curves for the participants with aphasia and matched controls. The observed (dash) and logistic GCA model fit (lines) learning curves are depicted for the three groups.

3.8.5. Learning curve and aphasia severity and lesion location

To investigate the trajectory of responses across different block numbers in individuals with aphasia, we employed a GCA focusing only on the aphasia group. This approach allowed us to model the influence of both `SEVERITY` and `LESION` location on the learning curve. The model incorporated polynomial terms for block number to capture the shape of the learning curve, along with the fixed effects of `SEVERITY` and `LESION`. A random intercept for individual participants (`ID`) was also included to account for individual variability in the responses. The GCA results highlighted a significant linear trend in the learning curve, as evidenced by the significant polynomial term for block number with an estimate of 47.69909 ($p < 2e-16$).

Regarding the influence of `SEVERITY`, the interaction of the quadratic term with severe aphasia produced a significant negative estimate of -9.3760($p = 0.03489$), suggesting a distinct curvature in the learning trajectory for this group as block numbers.

Regarding the influence of LESION, the data suggests that individuals with posterior lesion conditions exhibit a distinct learning trajectory compared to the anterior group. The main effect of the posterior lesion condition yielded a significant positive estimate of 0.8373 ($p = 0.00103$), indicating a greater in the baseline learning response for these individuals compared to the ones with anterior lesion. When examining the interaction between LESION and the polynomial terms for block numbers, several patterns emerged. The linear term of block number (poly(block_num, 2)1) for the overall sample had a significant positive estimate of 35.3360 ($p < 0.001$), suggesting a consistent increase in learning velocity as block numbers progressed. The interaction of this linear term with the post-lesion condition produced a significant positive estimate of 32.7231 ($p < 0.001$), indicating that individuals with anterior conditions might experience an smaller increase in learning velocity over time. On the other hand, the quadratic term (poly(block_num, 2)2), which represents the overall learning accumulation, had a significant positive estimate of 6.1722 ($p = 0.04446$) for the entire sample. This suggests a general performance of learning as the block numbers increased. However, when interacting with the lesion location, there was no statistical difference between the two groups ($p = 0.13712$).

3.8.6. Individual variability

Our analysis of recognition accuracy among participants with aphasia reveals intriguing patterns of individual variability. Among our participants, we identified cases where word-referent recognition accuracy was deemed significant (probability < 0.33) and those where it did not reach the significance threshold (probability ≥ 0.33). Almost all participants exhibit above-chance learning at TIME 1 in at least one condition of learning. Eight PWA showed above chance accuracy under both conditions at the immediate recognition task, nevertheless of the eight only two maintained the accuracy above chance after one week. One of the eight lost all the learning after one week. One participant didn't show any accuracy in any condition and time. Two participants showcased significant accuracy just under the explicit condition, and two others just under the explicit one. Interestingly in the explicit condition, of the eleven participants that reached above chance immediately, just three maintained this significance after one week. Contrary, of the twelve participants reaching significant accuracy under implicit conditions, six maintained performances above chance.

In the analysis of learning slopes, we observed varying levels of individual performance among our participants with different degrees of steepness (Fig.8) nevertheless, all the participants demonstrated positive slopes, indicating that they exhibited a noticeable improvement in their learning over time.

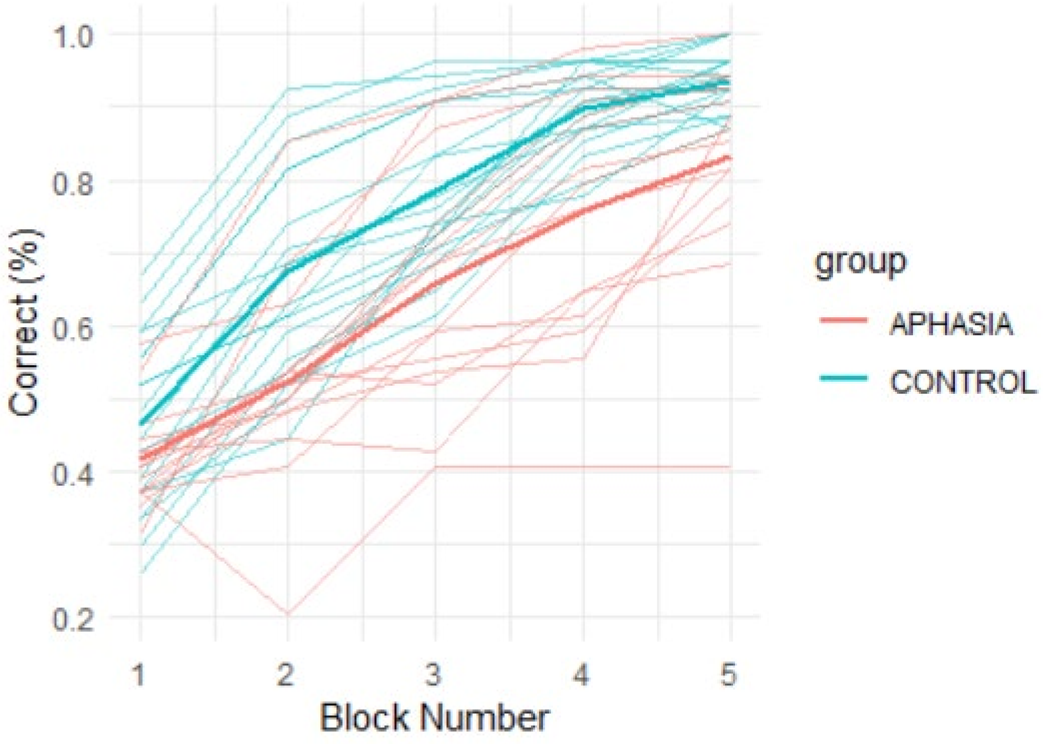


Fig.8. Comparison of learning curves in participants with aphasia and matched controls.

3.9. Discussion Experiment 2

In the recognition tests, participants with aphasia exhibited intriguing patterns of accuracy under explicit and implicit conditions over time. Initially, individuals with aphasia displayed moderate accuracy under explicit conditions, but their performance declined as time elapsed. In contrast, when subjected to implicit conditions, aphasia participants showcased better and more resilient accuracy, maintaining their performance over time. Meanwhile, healthy controls consistently demonstrated high accuracy across conditions and throughout the study. Our statistical analysis underscored the substantial impact of aphasia on recognition memory, with the healthy group consistently outperforming the aphasia group. Moreover, accuracy exhibited a universal decline over time, affecting both groups, while the type of condition did not yield a significant impact on accuracy. Also, for the learning curve during the implicit learning, it became evident that aphasia participants faced greater challenges compared to healthy controls. Their overall accuracy was lower, and their improvement over time exhibited less linearity, shedding light on the distinct learning difficulties encountered by individuals with aphasia.

Delving deeper into the aphasia group, we explored the roles of severity, and lesion location in shaping recognition outcomes. Severe aphasia emerged as a critical factor, leading to significant learning performance deviations and underscoring the unique challenges faced by individuals with severe aphasia. Interestingly, individuals with mild and moderate severity levels did not experience a substantial impact on their performance.

3.10. General discussion study 1 and 2 on implicit and explicit learning in aphasia

In this study, we conducted two experiments to investigate the learning capabilities of both persons with aphasia and healthy controls under implicit and explicit conditions. Participants were assessed immediately post-learning and then re-evaluated after a one-week span. Our findings highlighted marked differences in learning outcomes based on the time (immediate vs. one week) and the group (PWA vs. healthy controls). This exploration was necessary as, despite the longstanding importance of aphasia therapy, its intersection with learning and memory theories has been underexplored. With limited and often disparate evidence in the field, as pointed out by Peñaloza et al. (2021), our research provides a comprehensive analysis, bridging this gap and underscoring the potential for integrating learning mechanisms in aphasia rehabilitation. Moreover, our study uniquely delves into the realm of implicit learning, a domain less explored in aphasia rehabilitation compared to explicit learning. While explicit learning has traditionally been the cornerstone of rehabilitation efforts, the uncharted territory of implicit learning presents a promising avenue. Implicit learning, rooted in distinct neural mechanisms, could potentially be preserved in individuals with aphasia, offering new prospects for language rehabilitation.

The initial experiment involved two vocabularies, each consisting of twenty words, and aimed to investigate learning under two distinct conditions: implicit and explicit. However, after observing the learning patterns, we noted that participants with aphasia demonstrated learning inferior to chance levels after a one-week interval, regardless of the learning condition. This finding was consistent with previous research that indicated individuals with aphasia might face challenges in certain learning tasks compared to healthy adults. Motivated by these results, we conducted a subsequent experiment using the same type of non-existing objects and non-words but with reduced vocabulary sets containing nine words each. By tailoring the task to the specific learning capacities of the aphasic group, we aimed to provide a more nuanced understanding of the underlying cognitive processes and identify potential strategies for enhancing learning outcomes in this population.

In the second experiment, we observed that although participants still experienced some loss of learning over time, their performance was above chance levels under implicit and explicit learning in the immediate recognition test and in the follow-up. Several factors may have contributed to this difference in learning outcomes between the two experiments. Firstly, the reduced number of associations to remember in the second experiment likely eased the cognitive load on participants, making it easier for them to retain the information. Secondly, we increased the number of presentations of the material, which may have facilitated learning by allowing participants to encounter and process the information more frequently. It is worth noting that there is a trade-off between the number of items to learn and the number of repetitions, and we opted for increased repetitions to enhance learning. Our decision to use nine pairs in the second experiment was influenced by previous studies such as Peñaloza, which investigated statistical learning through cross-situational learning (2015, 2017). This paradigm involves learning associations between items by observing their co-occurrence across different contexts, and Peñaloza's study successfully demonstrated learning with only nine pairings. Given these findings and the need for a protocol that lasted at least 20 minutes to accommodate transcranial direct current stimulation (tDCS) in our sequential study, we chose to use nine pairs and increased the number of presentations to optimize learning conditions.

In the context of explicit learning, the control group consistently demonstrated accuracy levels above chance in the recognition task, both immediately after learning and one week later, across both experiments. While both the control and the PWA groups exhibited higher accuracy immediately after learning under the explicit condition, this advantage diminished over time. Notably, by the one-week mark in the second experiment, the aphasia group's recognition accuracy for vocabulary learned under the explicit condition had dropped below chance level.

Significantly, our findings, both from experiment 1 and 2, suggest that implicit learning appears to be more stable than explicit learning in individuals with aphasia, at least for reasonably easy task difficulties. This aspect of learning in people with aphasia remains largely unexplored. The sole study by Schuchard and Thompson (2014) that demonstrated substantial learning under implicit conditions, as opposed to explicit ones, did not assess the retention of the learned material over time. Existing research has predominantly focused on the long-term retention of words acquired through explicit learning, with findings indicating sustained retention up to a week post-training (Marshall et al., 1992, 2001; Tuomiranta et al., 2011). However, the maintenance of implicit learning in aphasia remains an under-researched area. Our study partly fills this gap, presenting evidence of recognition levels exceeding chance even a week later. Furthermore, no previous research has undertaken a comparative analysis of these two learning conditions in aphasia. Even in healthy individuals, implicit memory exhibits stronger long-term retention than explicit memories, which tend to diminish more quickly (see Discussion Chapter 2).

Looking at implicit learning, both experiments confirm that some individuals with aphasia frequently have the ability to implicitly process linguistic information, even though they might not be able to demonstrate this learning explicitly. This was more evident in experiment one where only six participants performed above-chance in the recognition test, while twelve showed a significant implicit learning curve. In the second experiment, thirteen participants showed above-chance learning while all participants showed a significant learning curve. This aligns with research findings suggesting that individuals with aphasia frequently have the ability to implicitly process linguistic information, even though they might not be able to demonstrate this learning explicitly (Hagoort, 1993; Mimura et al., 1996; Revonsuo, 1995; Revonsuo & Laine, 1996; Roberts et al., 2010) Regarding the learning performance, distinct patterns emerged between control and aphasia groups. Initially, both groups demonstrated above-chance performance, underscoring their ability to learn. However, as time progressed, the control group consistently outperformed the aphasia group, with a notably steeper learning curve. This suggests that while both groups were capable of learning, the control group's pace and pattern of learning were more accelerated. Diving deeper into the aphasia group, the severity of aphasia and lesion location played pivotal roles in shaping their learning trajectories. Mild aphasia individuals mirrored the learning patterns of the control group, while those with severe aphasia exhibited a unique curvature in their learning trajectory, especially as the learning sessions advanced. This nuanced difference underscores the heterogeneity within the aphasia group and the influence of severity on learning patterns. Lesion location further added layers of complexity to the learning trajectories. Individuals with posterior lesions demonstrated a different baseline learning response compared to their anterior counterparts. As the learning sessions progressed, those with posterior lesions experienced a more pronounced increase in learning velocity, suggesting that lesion location might influence the rate at which individuals adapt and learn over time.

One major drawback in both studies, as emphasized in the second chapter which involved solely healthy participants, is the absence of assessment for short-term and working memory, especially regarding their phonological aspects. This oversight is particularly relevant in individuals with PWA. In aphasia research, several studies highlight the connection between verbal short-term/working memory and explicit word learning. Kroenke et al. (2013) found links between lexical-semantic abilities and gesture-based expressive word learning, while phonological processing abilities correlated with expressive word learning via repetition without gestures. Case studies also suggest that patients with preserved nonword repetition and lexical-semantic processing tend to display better expressive new word learning and long-term retention compared to those with impaired lexical-semantic processing. Freedman and Martin (2001) conducted a case series study examining word learning in individuals with phonological or semantic STM deficits, revealing that these deficits influenced learning profiles despite performance on simple phonological and semantic tasks. Verbal STM components, such as phonological and lexical-semantic STM, independently contribute to the long-term learning of phonological and semantic material in aphasia. When it comes to implicit learning, its connection with verbal STM in aphasia exhibits diverse associations across different studies, unlike the clearer connections observed in healthy individuals

(Peñaloza et al., 2017; Arciuli and Torkildsen, 2012). Phonological processing in aphasia has been linked to cross-situational learning, yet this association becomes less pronounced when considering aphasia severity (Peñaloza et al., 2017). Due to these divergent findings, we missed an opportunity to thoroughly investigate this aspect in our study, which could have allowed for a deeper understanding of the relationship between implicit language learning and cognitive abilities in aphasia.

Finally, it is important to say that the limited size of our sample potentially restricts the robustness of our analysis, particularly when examining the differences between various severity levels of aphasia and lesion locations. The sample might not be representative of the broader population of individuals with aphasia, making it challenging to generalize our findings. Future research would benefit from a larger and more diverse cohort to validate and strengthen the observations made in the current study.

3.10. Conclusion

In conclusion, our research adds valuable insights to the field of language learning in aphasia. We conducted experiments that explored both implicit and explicit learning, providing a comprehensive view of how individuals with aphasia acquire new word-object associations. Our findings suggest that individuals with aphasia face challenges in learning tasks, but adjusting the task as lowering the number of word-referent associations and improving the repetition can yield better outcomes. Implicit learning appears to be more robust and durable than explicit learning for this population. We also observed that aphasia severity plays a significant role in word learning, particularly in cases of exceptionally severe aphasia. However, individuals with moderate to mild aphasia may not be as affected by severity. Lesion location, and thus the profile of aphasia, initially influenced learning outcomes, but compensatory mechanisms may come into play over time. Our results challenge conventional ideas about the impact of frontal lesions on learning.

Overall, our research highlights the need for tailored approaches to language rehabilitation in aphasia, considering individual variability in cognitive abilities and lesion location. This understanding holds promise for the future of aphasia therapy. Nonetheless, it is crucial to acknowledge that our study represents a single piece of the puzzle, and further research is imperative to solidify these findings.

CHAPTER 4: Effect of transcranical direct current stimulation on implicit vocabulary learning in patients with aphasia

Abstract

Background: The field of aphasia rehabilitation has undergone notable advancements, largely due to an enriched understanding of the neural and cognitive mechanisms underlying language recovery. While many therapeutic strategies aim to reactivate latent linguistic competencies, there is an emerging emphasis on enhancing the capacity to acquire new linguistic information. Within this framework, transcranial direct current stimulation (tDCS) has been spotlighted as a potential tool to enhance language learning and rehabilitation in individuals with aphasia.

Methods: Eight post-stroke aphasia patients participated in a single-blind sham-controlled crossover design study. They underwent three distinct stimulation conditions: anodal tDCS, cathodal tDCS, and sham, targeting the left middle superior temporal gyrus (mSTG), a region associated with implicit learning across auditory and visual domains. Each session was separated by a week to mitigate carryover effects. During these sessions, participants engaged in an implicit learning paradigm, specifically designed to assess their ability to assimilate novel words through a simple statistical association between words and objects without explicit instruction. Data were analyzed using recognition task analysis and growth curve analysis to assess the impact of tDCS on their learning trajectory.

Results: The anodal tDCS condition demonstrated a pronounced positive effect on recognition test and the overall learning curve. Participants under anodal stimulation outperformed those in the cathodal and sham conditions. Growth Curve Analysis indicated a consistent improvement in accuracy across the

learning blocks, with the type of tDCS condition significantly influencing this trajectory. Additionally, individual variability was observed, suggesting the potential need for personalized tDCS protocols.

Conclusion: This study underscores the potential utility of tDCS in aphasia rehabilitation. The findings advocate for a more individualized approach in therapeutic interventions, considering lesion location and the specific tDCS condition. The results hint at the possibility of optimizing aphasia rehabilitation by integrating tools like tDCS with a nuanced understanding of individual patient profiles.

4.1. Introduction

In the past few years, there has been a significant increase in research related to aphasia rehabilitation, leading to more evidence-based treatment methods. Studies on how the brain and psychology affect language have paved the way for a more advanced understanding of both clinical and linguistic approaches. This has allowed for clearer objectives aimed at enhancing patient recovery (Vallila, 2017). However, even with these strides, determining how a patient will respond to treatment remains difficult. Notably, some patients show better results with therapy compared to others (Kelly & Armstrong, 2009).

The variability in therapeutic responses may be attributed to the individual's ability to engage a spectrum of brain mechanisms, either reactivating damaged neural pathways or forging new connections. The precise nature of language recovery during rehabilitation remains a subject of debate; it is unclear whether it stems from the development of new neuronal connections, the reactivation of pre-existing verbal information, or synergy of both (Laganaro et al., 2006; Tuomiranta et al., 2014). Current therapies predominantly aim to assist individuals with aphasia in accessing their pre-existing linguistic capabilities. However, fostering the ability to learn new material presents a promising alternative therapeutic avenue. Recent studies have underscored a correlation between the capacity to acquire new words and positive responses to anomia therapy in chronic aphasic individuals (Dignam et al., 2016).

Examining the remaining ability to learn new words might play a crucial role in understanding the processes behind language recovery in aphasia, which in turn could influence diagnostic and treatment strategies (Peñaloza et al., 2016). As a result, techniques that boost this learning ability could lay the groundwork for specific linguistic interventions that aid in rehabilitation (Basso et al., 2001; Breitenstein et al., 2004; Kelly & Armstrong, 2009).

In this evolving landscape, transcranial direct current stimulation (tDCS) emerges as a promising tool. tDCS, a non-invasive brain stimulation technique, has been increasingly recognized for its potential to augment language learning and recovery processes. This technique involves the application of a low electrical current to specific areas of the brain, potentially facilitating or inhibiting neuronal activity, thereby influencing learning and memory processes.(Nitsche et al., 2008; 2000)

Recent research has illuminated the potential of tDCS in enhancing language learning and rehabilitation in aphasia. Studies have demonstrated that anodal tDCS over areas such as the Wernicke and Broca regions can significantly enhance various linguistic performances, including semantic and phonemic fluency, verb acquisition, and the speed of naming tasks (Cattaneo et al., 2011; Fiori et al., 2013; Marangolo et al., 2018; Meinzer et al., 2014). Moreover, a comprehensive meta-review by Balboa-Bandeira et al. (2021) identified a moderate influence of transcranial electrical stimulation techniques, including tDCS, on the overall learning process in terms of accuracy, albeit without significant advantages regarding response speeds or enduring outcomes. Nevertheless, to our knowledge, no studies have investigated the effect of tDCS on word learning in PWA.

Building upon these findings, the present study aims to investigate the potential effects of anodal and cathodal tDCS over the middle superior temporal gyrus (mSTG) in enhancing implicit learning in post-stroke aphasia patients. We have selected this area because middle STG is often preserved in aphasia and it linked to implicit learning across both auditory and visual modalities and also to implicit statistical learning (M. H. Davis & Gaskell, 2009; McNealy et al., 2006; Plante et al., 2015; Schapiro et al., 2013; Turk-Browne et al., 2009; Ullman, 2004). Furthermore, considering that neocortical regions are responsible for the extended consolidation of newly acquired linguistic information, the middle STG's preservation could be crucial. Additionally, it's crucial for preserving language skills when other regions are damaged, as suggested by recent work by Gore et al. (2022), which found that middle STG activation in older individuals is linked to word learning, accuracy, and retention.

4.2. Materials and methods

Participants: Eight patients with aphasia (Four women; mean±SD age: 53.3±7.8 years, range: 44–65; years of education 13±2.3 years, range: 9–16) were recruited in the study. All were native Italian speakers. The eligibility criteria for individuals in the aphasia group encompassed an age range spanning from 18 to 85 years, confirmation of their first and single stroke via CT or MRI scan, enduring aphasia arising from the stroke, persisting for a minimum of 6 months from the onset of the stroke, as established through a comprehensive speech and language assessment and the capability to comprehend and execute instructions necessary for the completion of the experimental task. The diagnosis of aphasia and aphasia severity was determined using Aachen Aphasia Test (AAT)(IT-AAT: De Bleser et al., 1986; Luzzatti et al., 1994, 2006; Willmes et al., 1988). Two participants with aphasia only participated in the first session and then dropped out due to health reasons.

Written informed consent was obtained from all participants prior to participation.

Stimuli

The structure and the characteristics of the stimuli were the same as in experiment 2 of chapter 3. Novel objects have been chosen from Novel Object and Unusual Name (NOUN) and trisillabic pseudowords from Sulpizio et al. (2013) (See Appendix D and E).

ID	Age	SEX	Yeat of Education	Severity	Type	Etiology	Lesion Location
1	62	M	11	Mild	Broca	Haemorrhage	Left Frontal regions-insula
2	54	F	8	Severe	Broca	Ischemia	Left MCA (Frontal, insula)
3	44	M	16	Moderate	Fluent	Ischemia	Left MCA (parietal)
4	65	F	13	Severe	Global	Ischemia	Left parietal-temporal regions
5	45	F	13	Severe	Anomic	Ischemia	Left MCA stroke (caudate nucleus, putamen and internal capsule)
6	52	M	13	Mild	Conductive	Haemorrhage	Left temporal lobe
7	58	M	13	Mild	Fluent	Haemorrhage	Left parieto.temporal
8	47	F	8	Severe	Fluent	Haemorrhage	Left Frontal-Temporal

Table 3. Demographic and clinical data of participants with chronic aphasia.
Notes: M = male; F = female; MCA = middle cerebral artery.

Procedure

We implemented a single-blind sham-controlled crossover design. Participants underwent three stimulation conditions (anodal and cathodal tDCS and sham) in a counterbalanced order. Sessions were separated by seven days to avoid carryover effects and were administered at the same time of the day. During stimulation, participants were given a language learning paradigm (Implicit learning paradigm explained in Experiment 2 of Chapter 3.)

Transcranial Direct Current Stimulation Procedure:

The tDCS procedure was administered using a battery-operated Eldith Programmable Direct Current Stimulator from neuroConn GmbH. The stimulation was delivered through a pair of sponge electrodes, each measuring 5 x 5 cm, that were soaked prior to application. The stimulating electrode was strategically centered over the left superior temporal area, corresponding to the t3 position of the international 10–20 EEG system. The second electrode, serving as a reference, was positioned on the skin over the contralateral supraorbital region. Both anodal and cathodal tDCS were delivered at a current of 1 mA for a duration of 20 minutes in their respective sessions. Additionally, an ultra-short stimulation, lasting less than 30 seconds, was initiated at the start of the sham session. At the onset of all three sessions (anodal tDCS, cathodal tDCS, sham), the current was increased in a ramp-like fashion, as described by Nitsche, Liebetanz, et al. (2003). This elicited a brief tingling sensation on the scalp, which subsided within seconds, aligning with previous findings (Nitsche, Schauenburg, et al., 2003). In all sessions, the currents were gradually turned off over a span of a few seconds, a method that does not produce any perceptible sensations (Ambrus et al., 2012). This procedure was conducted out of the subject's field of view to ensure unbiased results. Language learning commenced at the beginning of the stimulation in each session and persisted for an additional 5 minutes after the conclusion of the tDCS or sham stimulation, totaling 25 minutes (similarly to Flöel et al., 2008).

4.3. Statistical analysis.

All analyses described in the subsequent sections were conducted using the R statistical software. However, the specific analytical approach varied depending on the dependent variable under consideration.

4.3.1. Recognition Task

Preliminary descriptive statistics were computed including mean accuracies and standard error across the different age groups, conditions of learning, and time points. Additionally, the Exact Binomial Test was employed to determine if performance significantly exceeded chance levels. These analyses facilitated an overview of task performance trends and variations across the specified conditions.

Inferential statistical analyses were conducted using lme4 package for generalized mixed modeling. Generalized Mixed Models (GMM) were calculated for performance at the recognition task with subjects as random intercepts. Fixed factors included conditions of tDCS stimulation (anodal, cathodal, and sham), time (immediate learning and after one week), aphasia severity and lesion location. Severity classification was given by the results at the AAT battery test and gross lesion location was either anterior (frontal) or posterior (non-frontal- based on previous studies. See Peñaloza et al., 2016 and Vadinova et al.,2020). The random intercept for subjects was incorporated to account for the variability and repeated measurements within these units.

4.3.2. Learning Curve

For the learning curve variable, a multilevel regression approach was adopted, specifically employing growth curve analysis (GCA) based on a second-order orthogonal polynomial model to probe temporal changes in learning curves (Mirman, 2014). The analysis incorporated fixed effects for time (block), stimulation condition, severity and lesion location alongside random effects for participants corresponding to various time points. As the outcome variable was binary (correct or incorrect response), logistic GCA was the chosen method for data analysis. Model comparisons were undertaken to evaluate condition disparities concerning specific time-related elements. In orthogonal polynomial models, the intercept denotes the overall average outcome, the linear term signifies the linear trajectory, and the quadratic term represents the curvature.

4.4. Results

4.4.1. Recognition test - Descriptive statistics

In the recognition tests, all conditions consistently demonstrated mean accuracy rates significantly above the chance level at time one, as determined by the Exact Binomial Test. Specifically, the mean accuracy was 0.653 for the anodal condition, 0.597 for the cathodal condition, and 0.542 for the sham. However, under the anodal condition and the sham condition, accuracy results under chance after one week (Time 2): Participants achieved a mean accuracy of 0.403 under the cathodal condition at Time 2 (p-value = 0.210), and a mean of 0.306 under the sham one (0.708).

4.4.2. Recognition test- Inferential statistics

A generalized linear mixed model (GLMM) was employed to investigate the effect of LESION location, CONDITION, TIME, SEVERITY, and tDCS condition on the accuracy of the recognition task of individuals with aphasia. The results revealed significant effects for SEVERITY, CONDITION, TIME, and tDCS CONDITION. We found a significant effect of TIME, indicating that as time progressed, there was a decrease in accuracy by about 0.7741 units regardless of the condition ($p < 0.001$). Among the tDCS CONDITIONs, the sham condition was associated with a lower performance by approximately 0.7530 units compared to anodal stimulation ($p = 0.0024$). While the cathodal condition also showed a trend towards lower accuracy, it wasn't statistically significant ($p = 0.0867$). When evaluating the effect of SEVERITY, individuals with severe aphasia showed a lower accuracy by approximately 0.7675 units compared to the reference group, those with mild aphasia ($p < 0.001$). Conversely, individuals with moderate aphasia did not demonstrate a significant difference in accuracy compared to those with mild aphasia (Estimate = 0.01312, SE = 0.338, $p = 0.96$). Finally, our analysis of the LESION site indicated that neither frontal nor posterior lesions had statistically significant differences on the response ($p > 0.05$). The estimates for frontal lesion and posterior lesion were -0.13469 and -0.12157, respectively. However, the interactions between LESION location, SEVERITY, TIME, and tDCS CONDITION did not significantly influence accuracy (all p-values > 0.05).

When setting the cathodal stimulation as referent, the anodal stimulation was associated with an increased performance by approximately 0.4225 units compared to the cathodal stimulation, though this was marginally significant ($p = 0.0867$). The sham condition showed a decrease in accuracy by about 0.3305 units compared to the cathodal condition, but this effect was not statistically significant ($p = 0.1787$).

When examining the effect of SEVERITY, individuals with severe aphasia demonstrated a lower accuracy by approximately 0.7675 units than those with mild aphasia ($p < 0.001$). Lastly, when considering the LESION location, there was no statistically significant difference in performance associated with either frontal or posterior lesions when compared to the reference lesion site.

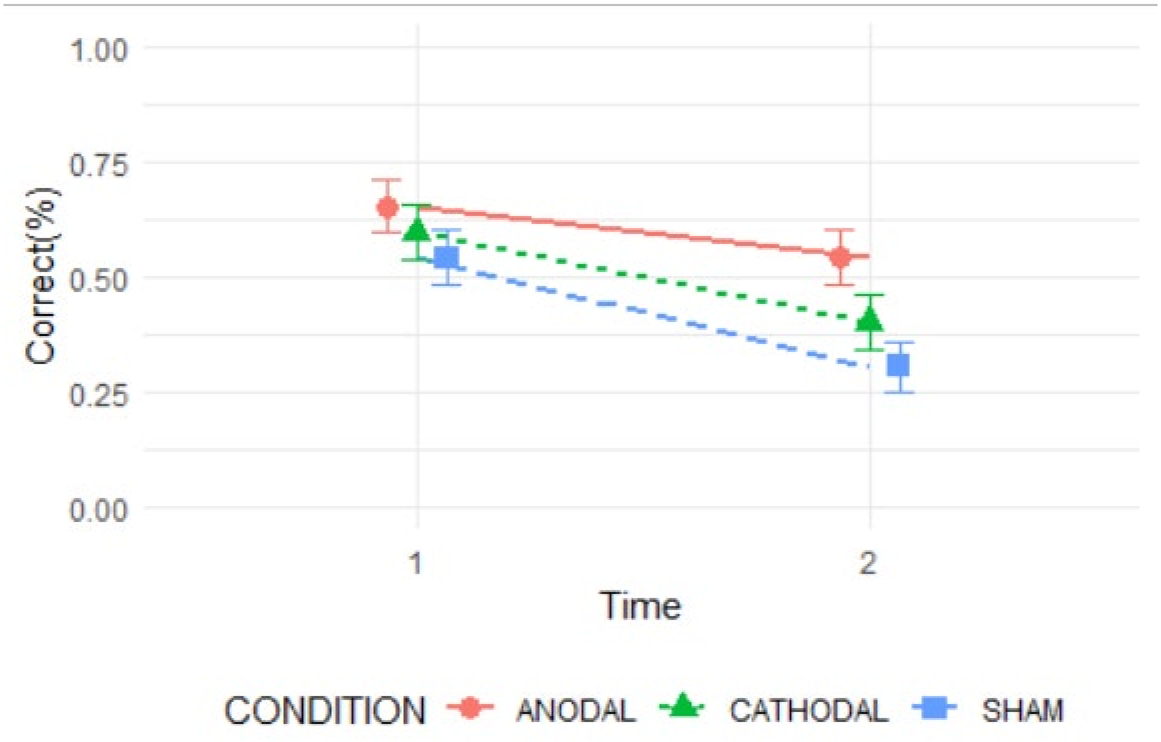


Fig.9 Comparison of recognition task for participants with aphasia and matched controls immediately and after one week.

4.4.3. Learning curve

With the Growth Curve Analysis, we examined the trajectory of ACCURACY across the five different blocks. The model incorporated both linear and polynomial terms for BLOCK to capture the learning curve's shape. Furthermore, we investigated the effects of three key predictors: CONDITION, LESION, and SEVERITY. Random effects were introduced to account for individual variability among the participants (ID). Our analysis of the BLOCK variable revealed a significant linear trend (estimate:

41.755, $p < 2e-16$), indicating a notable increase in ACCURACY as block numbers advanced. However, the quadratic term (poly(BLOCK, 2)2) did not reach statistical significance, suggesting a consistent linear trajectory without substantial curvature across block numbers. Shifting focus to the impact of tDCS CONDITION, we found compelling evidence of its influence on the learning curve. When considering the linear component of the learning curve, we observed evidence that both cathodal and sham conditions had a notable negative impact compared to the anodal one (cathodal estimate: -0.85804, $p < 2e-16$; sham estimate: -0.87908, $p < 2e-16$). This aligns with the significant coefficients seen in the interaction terms "cathodal condition:poly(BLOCK, 2)1" (approximately -36.87022) and "sham condition:poly(BLOCK, 2)1" (approximately -35.36097). Both coefficients were negative and significantly different from zero, indicating that in both the cathodal and sham conditions, the linear increase in accuracy with each block was significantly slower compared to the anodal condition. Turning to the quadratic component of the learning curve, the interaction terms "cathodal condition: poly(BLOCK, 2)2" (approximately -2.62287) and "Sham condition :poly(BLOCK, 2)2" (approximately 4.23898) had coefficients that were close to zero. This suggests that the CONDITION (cathodal and SHAM) had little impact on the quadratic aspect of the learning curve. In other words, regardless of whether participants received cathodal or sham tDCS, their quadratic learning pattern did not significantly deviate from the anodal condition.

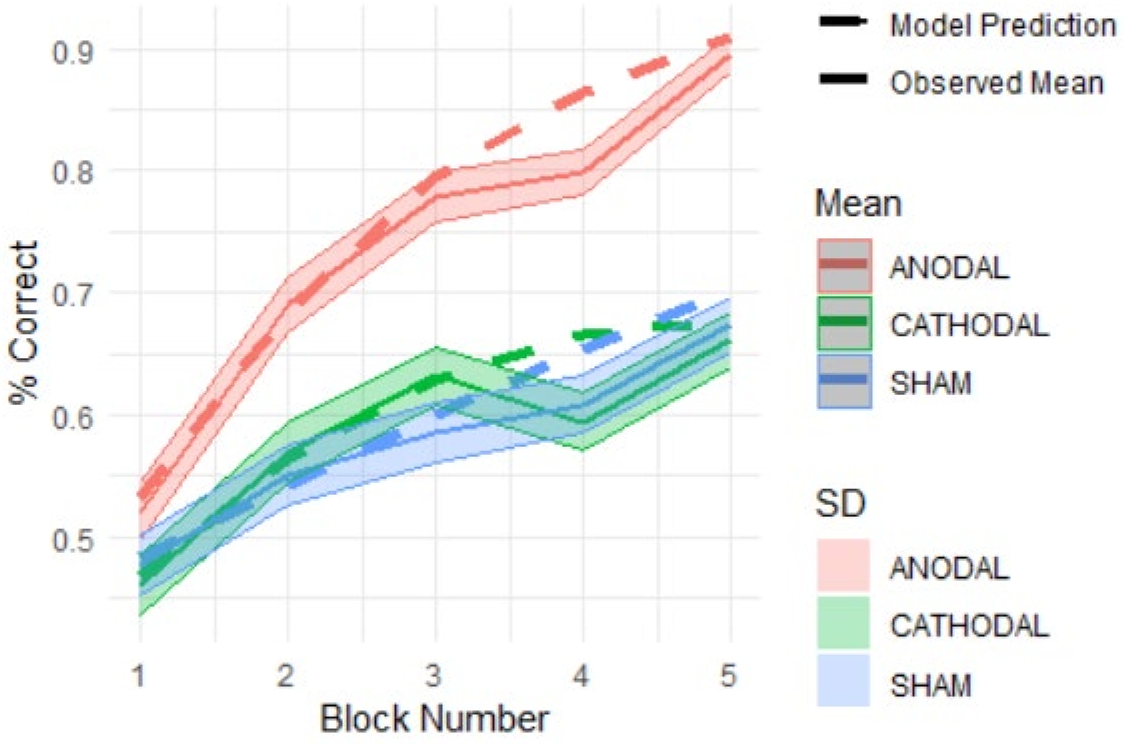


Fig.10. Comparison of learning curves for different tDCS stimulations. The observed (dash) and logistic GCA model fit (lines) learning curves are depicted for the three groups.

Regarding the impact of LESION location on ACCURACY, our analysis revealed consistent findings for both the linear and quadratic components of the learning curve. Specifically, we found that lesion location, whether frontal or posterior, did not have a statistically discernible impact on ACCURACY. In both cases, the coefficients associated with these lesion locations were non-significant, indicating that ACCURACY did not significantly differ based on whether the lesion was located in the frontal or posterior region ($p > 0.05$). This could be given by the fact that the sample size is small, and the groups are imbalanced, with 3 pwa with anterior lesions against 5 with posterior ones.

Lastly, we explored the role of SEVERITY in shaping the learning curve. Moderate aphasia does not show a statistically significant relationship with the linear term of BLOCK ($p = 0.9001$), Severe aphasia, on the other hand, exhibits a strong negative relationship with the linear term of BLOCK ($p < 0.001$), indicating significant differences in learning. No levels of severity shows a statistically significant relationship with the quadratic term of BLOCK ($p = 0.8813$ and $p = 0.4740$, respectively).

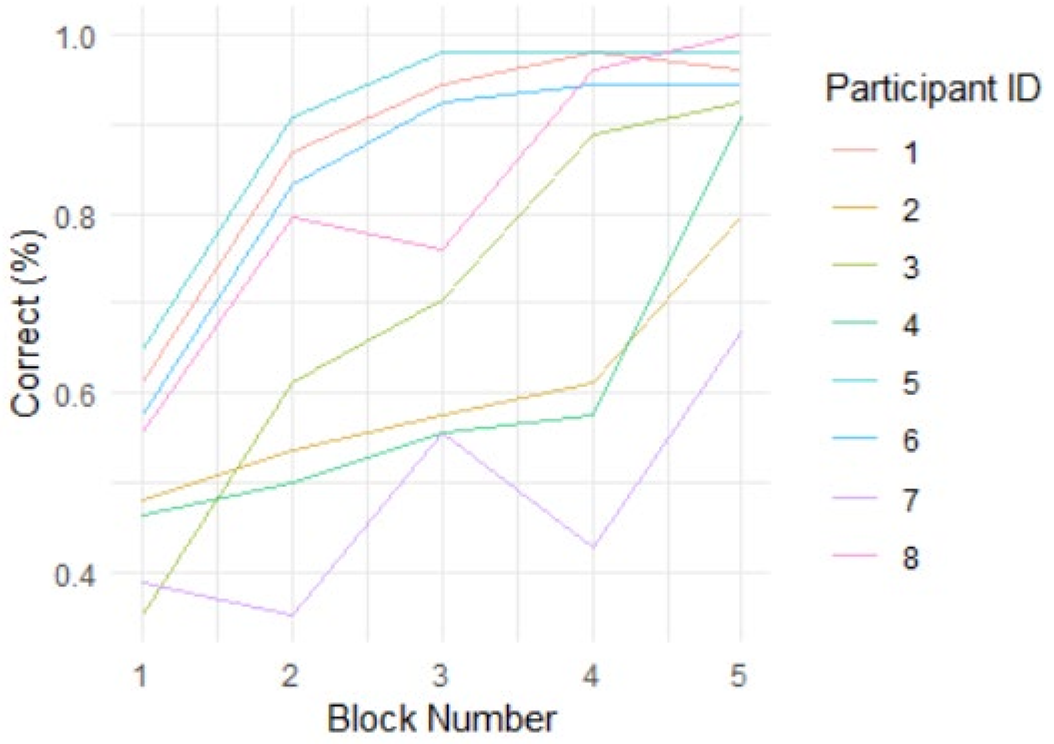
4.4.5. Individual variability

Our analysis of recognition accuracy among participants with aphasia reveals intriguing patterns of individual variability. Among our participants, we identified cases where word-referent recognition accuracy was deemed significant (probability < 0.33) and those where it did not reach the significance threshold (probability ≥ 0.33).

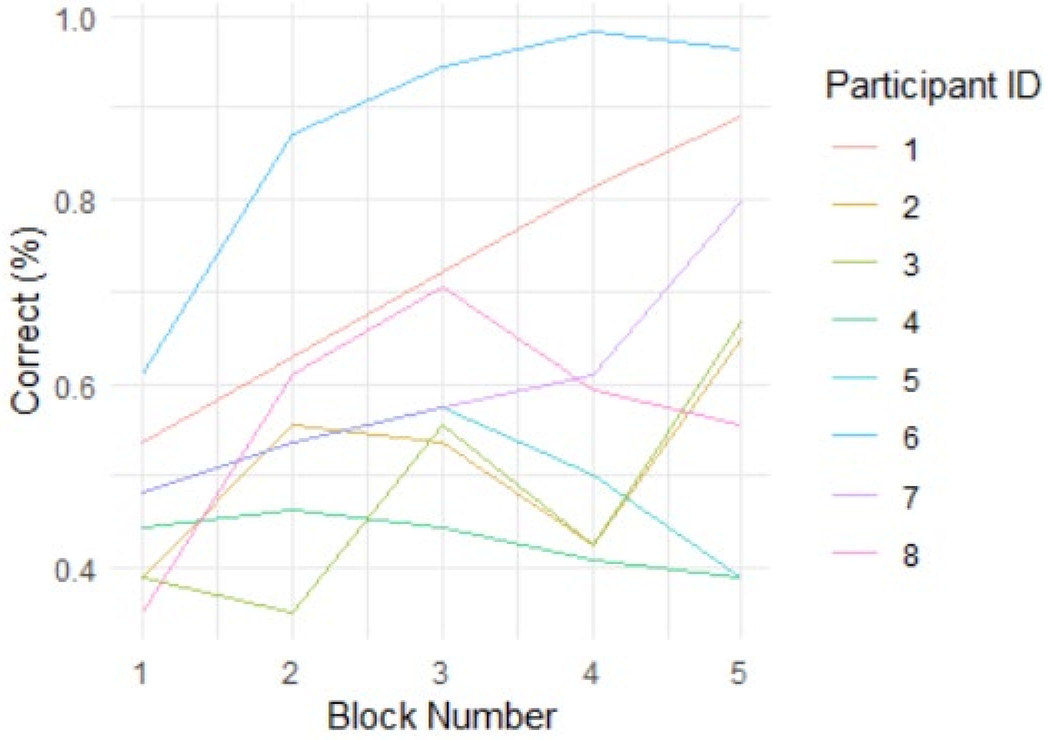
Among the participants in our study, three consistently demonstrated above-chance performance across all stimulation conditions at the initial time point (TIME 1). However, upon revaluation at TIME 2, these patterns shifted. At TIME 2, Participant 1's performance dipped below chance levels in both the cathodal and sham stimulation conditions, indicating a decline in word-referent recognition accuracy. Similarly, Participants 3 and 7 experienced a decrease in recognition accuracy, falling below the chance threshold, specifically in the sham condition at TIME 2.

In contrast, six out of seven participants exhibited above-chance word-referent recognition accuracy in the anodal stimulation condition at both TIME 1 and TIME 2, highlighting the consistency of this stimulation's positive effect on their recognition abilities. However, Participant 4 stood out as an exception, as they failed to demonstrate significant recognition accuracy across all time points and conditions, and this could be influenced by her severe global condition. Notably, five participants maintained significant above-chance performance in the immediate testing, even after exposure to the sham condition, indicating a level of resilience in their word-referent recognition skills. Under cathodal stimulation, six participants displayed significant above-chance results, showcasing the potential benefits of this stimulation method. Interestingly, Participant 8 achieved notable accuracy levels specifically under cathodal and sham stimulation at TIME 2, despite having a severe fluent condition and a lesion in the left Frontal-Temporal regions

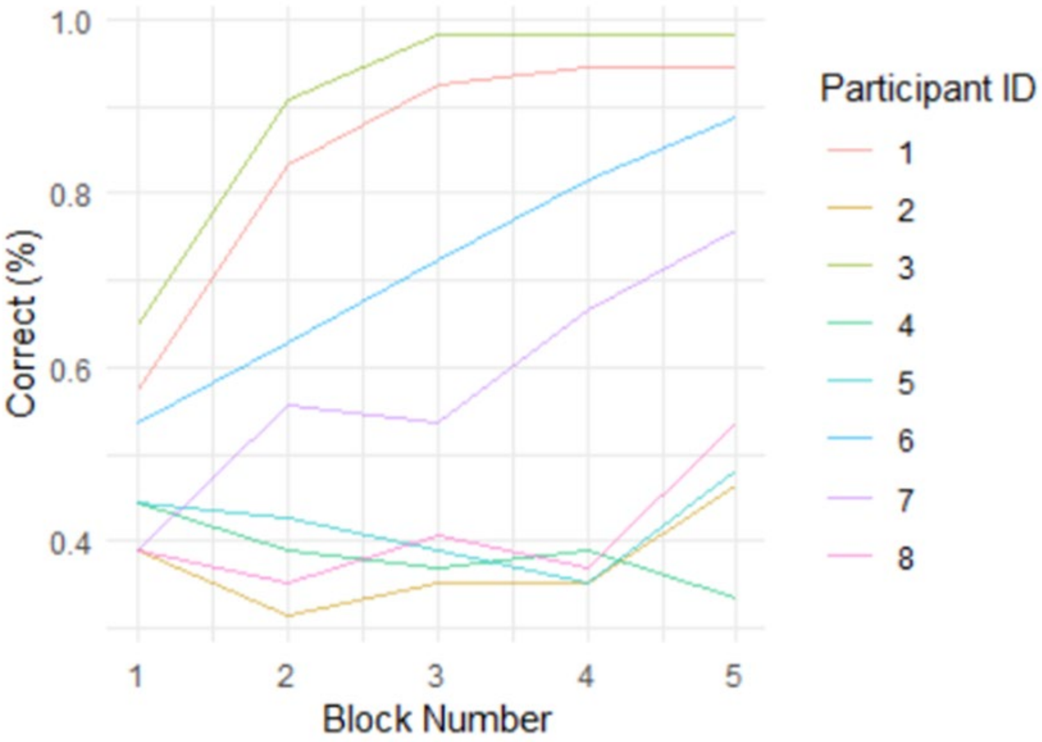
In the analysis of learning slopes, we observed varying levels of individual performance among our participants. The majority of participants demonstrated positive slopes, indicating that they exhibited a noticeable improvement in their learning over time. This suggests that these individuals were able to grasp the learned material more effectively and adapt to the changing experimental conditions. Notable examples include participants with participants 1, 2, 3, 6, 7, and 8, who displayed positive learning slopes across different conditions. Conversely, a smaller subset of participants displayed non-positive slopes, indicating either minimal improvement or even a decline in their learning performance over time. Participants with ID 4 and 5in the cathodal and SHAM conditions demonstrated non-positive slopes, suggesting that they may have encountered challenges in learning the material or adapting to the experimental conditions. The severe global condition of Participant 4 and her extended lesion in the left parietal-temporal regions might be a contributing factor. Similarly, Participant 5's severe anomic condition and lesion in the left MCA, specifically in subcortical regions like the caudate nucleus and putamen, could hinder her performance in an implicit learning task.



A. ANODAL CONDITION



B. CATHODAL CONDITION



SHAM CONDITION

Fig. 11. Individual variability in performance across learning blocks. Panel A depicts the individual performances of participants under anodal stimulation, Panel B depicts the individual performances of participants under cathodal stimulation, Panel C depicts the individual performances of participants under SHAM stimulation,

4.5. Discussion

The primary objective of our study was to delve into the potential of transcranial direct current stimulation in augmenting implicit learning among post-stroke aphasia patients. Our findings, concerning implicit novel vocabulary learning and its correlation with tDCS condition, lesion location and aphasia severity, enrich the expanding literature on the role of tDCS in aphasia rehabilitation. Remarkably, in the context of post-stroke aphasia, the impact of tDCS on novel vocabulary learning remains uncharted and to our knowledge, this is the first study investigating it. In fact, although there is a growing body of literature on the effect of tDCS on aphasia therapy outcome, it's pivotal to differentiate between learning new linguistic material and re-learning during typical anomic therapy, as they likely engage different mechanisms.

In our study we found a significant effect of anodal tDCS on both the immediate recognition tests and the learning curve. Concerning the immediate performance, we discerned a distinct influence of the stimulation condition on accuracy. anodal conditions outperformed both cathodal and sham conditions, resonating with findings from studies on healthy populations. For instance, Antonenko et al., 2016, highlighted the potential of transcranial alternating current stimulation (tACS) over the superior temporal lobe in enhancing cognitive processes, while Flöel et al., 2008, targeting the same area, posited the potential of anodal tDCS in language learning enhancement with our same implicit learning paradigm.

Based on the findings from the logistic GCA, it appears that the type of tDCS condition (anodal, cathodal, and sham) had a significant impact on the rate of learning, as reflected by the steepness of the learning curve over blocks. Specifically, participants who received anodal tDCS demonstrated a significantly steeper learning curve compared to those who received cathodal and sham tDCS. This suggests that anodal tDCS may enhance the rate at which participants acquired new skills or knowledge over time, leading to faster learning.

Consistent with our prior studies, this study reveals that time exerts a pronounced effect on accuracy regardless of the tDCS condition. Such findings echo the findings of Balboa-Bandeira et al. (2020), who noted moderate enhancing effects of transcranial electrical stimulation (tES) on language learning, but these effects waned in follow-up data. In contrast, Bucur and Papagno's (2019) meta-analysis further revealed a significant effect of tDCS on naming scores both immediately post-treatment and during follow-up. Nevertheless, compared to rTMS that showed a medium to large effect, the effect of tDCS was small to medium. Moreover, the authors qualified the studies using the Physiotherapy Evidence

Database (PEDro) and the modified Sackett Scale and found out that, while studies with rTMS were qualified with moderate to high GRADE, studies with tDCS had a low level of evidence.

Moreover, we had an effect of severity both in the recognition task and during the learning task. Specifically, we found that individuals with severe aphasia had significantly lower accuracy compared to those with mild aphasia, while those with moderate aphasia showed no significant difference with the latter group. Furthermore, when analyzing the learning curves, individuals with severe aphasia exhibited slower initial learning, leading to a significant negative relationship with the linear term of learning blocks.

The intricate relationship between learning ability and aphasia severity has been the focal point of numerous studies. Our study contributes to this dialogue, suggesting that the benefits of tDCS might be modulated by individual factors such as aphasia severity. Without the use of tDCS, as already mentioned in Chapter 3, studies examining the association between learning ability and aphasia severity yielded equally mixed findings with some studies showing no significant associations between aphasia severity and SL and AGL(Peñaloza et al., 2015; Cope et al., 2017; Schuchard and Thompson, 2017), while other reporting a significant association for SL in CSL tasks and in AGL involving linear rules of pseudoword sequences (Cope et al., 2017; Peñaloza et al., 2022). Similarly, to our experiment, in a study conducted by Peñaloza et al. (2016) on cross-situational learning in individuals with aphasia, it was observed that participants with milder aphasia exhibited rapid learning, which plateaued after a few blocks. In contrast, individuals with more severe aphasia demonstrated slower learning, ultimately reaching a similar level of proficiency by the end of the seven learning blocks. When looking at tDCS, in the 2017 study by Norise et al., the effects of tDCS on chronic non-fluent aphasic patients were explored, with a focus on identifying predictors for language fluency recovery. The researchers hypothesized that baseline severity might influence post-stimulation improvement. Their results confirmed that those with more severe initial language deficits experienced the most significant improvement, especially in discourse productivity. This improvement was most evident in word-level production tasks. While some measures, like the Western Aphasia Battery, didn't correlate with fluency outcomes, the severity in specific tasks might predict improvement in those areas. The findings highlight the potential of tDCS interventions for chronic and severely affected individuals, suggesting that the effects of tDCS might be more pronounced in certain patient subgroups. However, the study had limitations, including a small sample size.

Finally, we also probed the impact of lesion location, a crucial determinant in therapeutic outcomes. However, our data did not indicate a significant influence of lesion location on tDCS-induced accuracy improvements. This could be given by the small sample size but also by the fact that we chose to stimulate an area that is usually not affected in PWA.

Our study, while providing insights into the application of tDCS for patients with aphasia, had several limitations that warrant consideration. Firstly, the small sample size of just eight participants, half of whom were very severe patients, limits the generalizability of our findings to the broader aphasia population. This is further complicated by the variability in lesion sites among our participants, which could introduce inconsistencies in the effects of tDCS. Variability can provide valuable insights. For instance, in the study conducted by Vadinova et al. (2020), they chose to incorporate both individuals with post-stroke aphasia having frontal lesions and those with posterior lesions. Their aim was to explore the substantial involvement of the left inferior frontal gyrus in implicit statistical learning. This decision made it particularly intriguing to assess individuals both with and without an intact LIFG region. However, it's important to note that our sample size was insufficient to draw conclusions on the involvement of specific areas.

Moreover, our reliance on the 10-20 EEG system, while standardized, might not have been the most precise method for our study. Lefaucheur et al. (2017) have emphasized the importance of accurate targeting of specific brain regions for optimal therapeutic outcomes with tDCS. The 10-20 EEG system doesn't account for individual anatomical variations, size and morphology (Kim et al., 2016), potentially leading to variability in targeting and outcomes. MRI-guided neuronavigation, which takes into account individual brain anatomy, could offer a more precise approach (De Witte et al., 2018). Moreover, we decided to use 1 mA based on the majority of the studies used in learning studies in healthy individuals and in linguistic experiments in PWA, nevertheless changing in calibrating stimulation intensity can be decisive in achieving optimal outcomes. In a study by Fiori et al. (2019), the effects of high-definition transcranial direct current stimulation (HD-tDCS)—a more targeted version of tDCS—on language recovery in aphasia patients were examined. This research specifically sought to determine the differential impacts of two current intensities1 mA (with a current density of approximately 0.0259 A/cm^2) versus 2 mA (with a current density of approximately 0.0519 A/cm^2), on verb naming. Conducted as a double-blinded crossover study, two sets of ten aphasic individuals underwent either active cathodal HD-tDCS or a sham treatment, targeting the right counterpart of Broca's area, while engaging in a verb naming task. Each stimulation condition was administered over five consecutive days, with a week-long break between conditions. Notably, only the group receiving the 2 mA intensity displayed significant improvements in verb naming, which persisted a week post-intervention, whereas the 1 mA group showed no such gains.

Adding to the complexity, we found an important inter-variability among participants. Shah-Basak et al. (2015) highlighted the significant individual variability in response to different tDCS montages. Their findings underscore the necessity of a tailored approach, as not all subjects benefited most from the same tDCS montage. This individual variability is a crucial reminder of the importance of personalizing tDCS treatment approaches, especially for patients with chronic post-stroke aphasia. Nevertheless, despite these challenges, our study took place in a clinical setting where personalizing tDCS is not always easy, for this reason, we had the clear aim to stimulate an area of responsible learning, which might remain unaffected in aphasia.

In our study, we utilized single session tDCS and observed no significant learning outcomes after one week. However, many researchers suggest that to realize the full potential of tDCS, it should be administered over multiple days or even weeks, a method termed multisession tDCS. Different authors, like Meinzer et al., (2014), Perceval et al., (2020) and Reis et al., 2009 posited that multisession tDCS could influence memory consolidation in healthy individuals and may be more beneficial than a single session. Similarly, in aphasia research, findings suggest that conducting over five sessions can yield improved long-term outcomes, as underscored in a (2021) review by Zettin and colleagues. When combined with behavioral exercises, this approach seems to promote favorable neural adaptations, akin to the processes of long-term potentiation, as described by Cirillo et al. (2017). Consequently, it's plausible that aphasia patients might benefit from more extended tDCS sessions for optimal learning results. Had we conducted more than a single session, our findings might have been different.

Finally, our sessions featuring distinct vocabularies were spaced only a week apart, which might have caused some overlap or confusion. One participant did report this feeling of confusion, yet his learning outcomes consistently remained above average.

4.6. Conclusion

Our exploration into the potential of tDCS for aphasia rehabilitation has shed light on its multifaceted implications, underscoring the importance of individualized approaches in therapeutic interventions. While our findings offer promising avenues for enhancing language recovery, they also emphasize the need for a deeper understanding of the intricate interplay between individual factors, lesion locations, and stimulation conditions. The limitations of our study, particularly concerning sample size and lesion considerations, highlight the necessity for further comprehensive research. As the field of aphasia rehabilitation continues to evolve, it is imperative that we harness the potential of tools like tDCS, ensuring that their application is both evidence-based and tailored to the unique needs of each patient. This endeavor not only holds promise for refining therapeutic strategies but also paves the way for a future where individuals with aphasia can access more effective and personalized treatment options.

CHAPTER 5: General discussion and conclusion

5.1. Summary and relevance of the thesis

The primary objective of this thesis was to investigate novel word acquisition, particularly in the context of healthy aging and aphasia. This exploration was two-fold: firstly, we aimed to juxtapose explicit (conscious and intentional) learning against its counterpart, implicit (unconscious or automatic) learning—a realm that, albeit pivotal, remains relatively uncharted. Secondly, we embarked on an investigation of the potential augmentation of this learning process through the utilization of transcranial direct current stimulation (tDCS), targeting the middle superior temporal gyrus (STG)—a region predominantly unaffected in aphasia, especially in non-fluent pwa, and known to be associated with implicit learning.

The significance of this endeavours stems from the imperative to understand the nuances of language acquisition post-stroke, which has profound implications both theoretically and clinically (Brady et al., 2016; Dignam et al., 2016).

From a theoretical viewpoint, discerning the aptitude of these individuals to learn new words can refine our understanding of the interplay between language processing and learning systems in an injured brain (Ferguson, 1999). This probe also illuminates how such interactions influence therapeutic outcomes in aphasia, particularly concerning anomia treatments. Acquiring new words necessitates understanding new word forms, the meanings they encapsulate, and their inter-associations (Gupta and Tisdale, 2009). Thus, evaluating this cognitive prowess in post-stroke Aphasia patients can shed light on the foundational mechanics underlying anomia therapy, whose primary objective revolves around reinforcing the linkage between word forms and their meanings. This is pivotal in reinstating access to pre-existing yet elusive lexical knowledge (Basso et al., 2001). Notably, memory and learning architectures might be instrumental in bolstering these weakened form-meaning associations, in re-establishing lexical pathways, and in forging connections amongst pre-existing or new linguistic representations

(Coran et al., 2020). A proposition has been put forth suggesting word learning could augment therapy-induced recuperation, potentially through brain plasticity processes such as the formation of new neural connections (Kelly and Armstrong, 2009). Moreover, an in-depth examination of word learning dynamics in aphasia can offer profound insights into the pivotal cerebral regions facilitating word learning in healthy adult brains, thereby enriching theoretical expositions of language therapeutic effects post-neural damage. While the efficacy of language therapy in post-stroke Aphasia patients is well-documented (Brady et al., 2016), the foundational mechanics propelling linguistic enhancement remain elusive (Dignam et al., 2016). If learning mechanisms are indeed central to therapy-driven recuperation, then integrating learning theories becomes paramount in sculpting a comprehensive theory of linguistic rehabilitation (Ferguson, 1999). Such a theory should be poised to unveil the neural substrates of the recovery trajectory, decipher the cognitive bases of behavioral enhancements, and pinpoint procedures optimized for desired therapeutic outcomes (Hinckey, 2002). The synthesis of cognitive and learning paradigms with neurological findings can lay the groundwork for a holistic theory of aphasia therapy, possibly illuminating the essence of transformation beyond mere impairment (Hinckey, 2002).

Clinically, assessing the word-learning competence of post-stroke Aphasia patients has ramifications for therapeutic strategization and prognostications concerning linguistic recuperation (Helm-Estabrooks, 2002). Anomia therapy, for instance, stands to gain from paradigms of word learning capacities in neurologically intact adults (Basso et al., 2001). To this end, Chapter 2 shifts its focus to examine language learning in older individuals, challenging the prevailing belief that age serves as a barrier to language acquisition. Despite cognitive declines often associated with aging, such as decreased working memory and slower processing speeds, the chapter highlights the enduring plasticity of the elderly brain, which remains receptive to new linguistic experiences. However, it's important to note that older adults exhibit a more gradual and consistent learning pattern than their younger counterparts. The dominance of explicit learning observed initially might, over time, align with implicit learning, thanks to the long-term retention attributes of implicit memory. An interesting find was that the duration of education played a more significant role under explicit learning scenarios than under implicit ones.

If learning is indeed central to language therapy, understanding the neural, linguistic, and cognitive factors that either support or hinder word learning becomes essential for tailoring effective aphasia treatments. Such interventions would be designed to holistically address deficits, integrating individual patterns of language processing, broader cognitive functions, and distinct learning preferences and capabilities. Additionally, a thorough evaluation of learning abilities in those with post-stroke Aphasia can provide predictive insights into recovery trajectories and how patients might respond to language interventions. While direct assessments of learning abilities don't necessarily provide a clear indication of recovery potential or treatment responsiveness, they do offer a measure to assess the effectiveness of learning mechanisms. These assessments can then be used to predict treatment outcomes and the longevity of the treatment's effects. With this backdrop, Chapter 3 delves into aphasia therapy, drawing connections between linguistic learning abilities in aphasic individuals and language rehabilitation strategies. The chapter underscores the importance of a deeper understanding of language learning in aphasia and particularly emphasizes the promising role of implicit language learning in aphasia treatment, given its durable nature. Two experiments further explore the proficiency of learning under both implicit and explicit conditions, revealing a comparatively stable trend of implicit learning among aphasic individuals. This chapter also investigates the impact of factors such as aphasia severity and lesion location on language learning abilities, emphasizing the challenges posed by severe aphasia and analysing the role of frontal lesions in word learning, particularly their influence during implicit learning stages.

Lastly, in alignment with various academic perspectives, if learning truly plays a foundational role in the therapeutic process, then exploring techniques to enhance such learning capabilities is crucial. Such techniques could form the cornerstone for targeted language-based rehabilitation strategies (as discussed in Basso et al., 2001; Breitenstein et al., 2004; Kelly & Armstrong, 2009; Flöel et al, 2008), with tDCS being a prime example. Chapter 4 embarks on this journey, assessing the potential of tDCS over the middle STG in boosting implicit learning in individuals with post-stroke aphasia. The findings indicate that both anodal and cathodal tDCS conditions fare better than the sham condition. The chapter suggests that individual factors, such as the severity of aphasia, might modulate tDCS effect.

5.2. Speech Language Therapy and Learning principle

Learning and language are intricately intertwined in the process of aphasic recovery. Research has consistently shown that the ability to acquire new words and the response to language therapy are closely related. For instance, Tuomiranta et al. (2014) emphasized the connection between effective word learning skills and the successful reacquisition of vocabulary, both being anchored in preserved cognitive functions. Similarly, Dignam et al. (2016) identified a significant link between immediate therapy gains and receptive word learning. Schuchard et al. (2017) delved into the relationship between implicit learning and response to implicit language treatment, while Silagi et al. (2020) compared the effects of implicit and explicit training methods, underscoring the potential of both approaches in treating individuals with aphasia. Collectively, these studies underscore the pivotal role of learning in enhancing language capabilities and the potential of tailored therapeutic interventions in fostering recovery in aphasic individuals.

5.3. Considering Implicit Learning and tDCS in Clinical Practice

In recent years, there has been a renewed interest in understanding the best interventions for aphasia, particularly concerning word retrieval challenges. Various treatments, rooted in explicit learning methods, have been at the forefront of this research (Nickels, 2002). Response Elaboration Training (RET) is one such method where individuals with aphasia provide verbal responses to stimuli. The clinician then models these responses, reinforcing and elaborating upon them, guiding the individual to generate a more refined response (Wambaugh et al., 2013). Another prominent method, Semantic Feature Analysis (SFA), focuses on helping individuals with aphasia identify the primary semantic properties of challenging words. For instance, if the word "fridge" poses a difficulty, cues about its location or usage may be given to activate its semantic connections (Boyle, 2004; Maddy et al., 2014; Maher & Raymer, 2004). The Verb Network Strengthening Treatment (VNeST) enhances lexical retrieval within sentential contexts, spotlighting verbs and their related roles (Edmonds et al., 2009; Edmonds & Babb, 2011).

Additionally, Word Retrieval cueing strategies provide phonological or semantic cues to aid word recall (Wambaugh et al., 2002; Webster & Whitworth, 2012).

While explicit methods remain dominant, there is growing interest in the potential of implicit learning therapies for aphasia. Some researchers, (see for instance C. Davis et al., 2009; C. H. Davis & Oliver, 2012), underscore this, although their primary focus remains on syntactic abilities, such as Oral Reading for Language in Aphasia (ORLA), which employs reading training without an overt instructional component on syntax, leveraging repeated exposure to the same stimulus during reading (Cherney, 2010). Other implicit learning methods include structural priming, which aims to enhance speech production through repeated exposure to certain sentence structures (J. Lee et al., 2019). Similarly, masked repetition priming involves presenting target image names briefly alongside distracting stimuli, aiming to implicitly boost naming abilities (Silkes, 2018). Moreover, Errorless therapy, often referred to as “Errorless learning,” emphasizes the importance of preventing mistakes during the learning process. By structuring tasks in a way that minimizes the chance of errors, and by providing immediate feedback before an error occurs, the therapist ensures that the individual is consistently reinforced with correct responses. The underlying belief is that by preventing errors, the process of memory consolidation is enhanced, leading to more effective learning. Some studies suggest that errorless therapy is as effective as traditional hierarchical cueing therapy, while others indicate that error-prone therapy might be more effective in certain scenarios (S. Abel et al., 2005).

The findings from the thesis under discussion propose that a blend of both explicit and implicit learning in anomia therapy could be advantageous. While explicit learning may provide an initial advantage, implicit learning exhibits greater durability and appears to support the retention of learning material over time. Moreover, this type of learning could be preserved and compensate when explicit learning is not impaired. Finally involving partially different neural mechanisms potentially not interested by the lesion usually present in aphasic patients, exploiting such mechanisms may be more proficient. Such insights echo broader sentiments on implicit incidental learning conditions that maintain consistent cognitive strategies and low attentional demands. There is evidence suggesting that individuals with agrammatic aphasia may face challenges benefiting from explicit instructions when tasks involve high working memory demands and they may rely on implicit learning easily (Breitenstein et al., 2004; Schuchard & Thompson, 2015).

Several researchers highlight the potential of leveraging principles from implicit statistical learning and memory research to enhance treatment outcomes for children and adults with developmental language disorders (Aguilar et al., 2018; Finestack & Fey, 2009; Grunow et al., 2006; Plante et al., 2014; Plante & Gómez, 2018; von Koss Torkildsen et al., 2013). By seamlessly blending these principles with established treatment techniques, the learning process can be accelerated and broadened (Fey & Finestack, 2009). Plante and Gomez (2018) proposed five principles from statistical learning studies, which, while designed for developmental disorders, have potential relevance in aphasia treatment.

For instance, the Regularity Principle underscores our natural inclination to identify patterns in the information we encounter. Applied clinically, two factors—frequency of occurrence and consistency—are pivotal. Traditional learning paradigms favor high-frequency, dense input, promoting rapid assimilation. However, children with developmental language disorders and PWA may require double the exposure to discern vocabulary. Our study supports this, revealing improved retention in PWA after they were exposed to fewer associations at double the frequency. This mirrors the therapeutic efficacy of "massed practice" as highlighted by Breitenstein et al. (2004). Over the last two decades, Constraint-Induced Language Therapy (CILT), a therapeutic approach that restricts the use of compensatory communication strategies, encouraging verbal communication in aphasia patients, has gained traction (Zhang et al., 2017). However, Fridriksson & Hillis (2021) suggest that the CILT's effectiveness might owe more to increased therapy intensity than restricting non-verbal communication. A 2022 meta-analysis by RELEASE pinpointed the benefits of intensive, tailored speech-language therapy (SLT) for optimal PWA recovery (RELEASE, 2022).

Building on the Regularity Principle is the Variability Principle, emphasizing the strategic alteration of non-target language input. This principle, introduced by Gómez (2002), postulates that increased variability in non-target elements enhances learning. Subsequent studies confirmed this approach's potency in vocabulary acquisition (Aguilar et al., 2018; Alt et al., 2014). However, its direct application in PWA remains uncharted territory, suggesting a potential avenue for exploration.

An associated concern is the potential downside of excessive variability, leading us to the Input Principle. It emphasizes viewing all linguistic input as viable for implicit learning. With the inevitable inconsistencies in language, learners must discern regular patterns. Evidence suggests that even in normal development, it can be challenging to differentiate correct from incorrect input. PWA shows particular difficulty with irregular verbs, although results vary (Faroqi-Shah & Friedman, 2015; López-Barroso & de Diego-Balaguer, 2017)). Inconsistent input in therapy could hamper recovery, making structured, consistent input imperative. In aphasia therapy, the need for consistent and structured input is paramount to navigate these inconsistencies, solidify language patterns, and promote relearning. Errorless Learning dovetails with the Input Principle, emphasizing the prevention of errors during the learning phase. This approach is particularly fitting for aphasia therapy, where consistent correct input is vital. By focusing on accurate and immediate feedback, Errorless Learning ensures PWA are not exposed to erroneous patterns, fostering robust language structure comprehension and bolstering learner confidence (Middleton et al., 2022).

Lastly, the Memory Principle accentuates the importance of adequately encoding learned information for subsequent retrieval. While individuals with aphasia may show aptitudes in both implicit and explicit learning, as this thesis and the current Literature show, retention often lags behind their healthy counterparts. Techniques like repeated retrieval and memory reconsolidation can aid in this endeavor. The act of retrieval has been shown to solidify new memories (McGregor et al., 2022;Leonard et al., 2019). The concept of memory reconsolidation, wherein a reactivated memory can be reinforced or updated, can be useful in treatment.

Besides implementing memory and learning principles into clinical practice, a way of augmenting traditional therapeutic methods is the use of tDCS which has shown significant promise. In their last review, Breining and Sebastian (2020) and Elsner et al. (2020) highlighted tDCS's potential to amplify conventional therapy outcomes, in a parallel review, Balboa-Bandeira (2020) found tDCS to enhance implicit and explicit language learning mechanisms in healthy participants.

Our study aligns and unifies these findings, suggesting enhanced learning in aphasia patients through tDCS.

It's vital to emphasize that while we have foundational therapeutic methods grounded in evidence-based medicine, each patient brings their unique nuances. Hence, while these standardized therapies are indispensable for consistency and replicability, there is a burgeoning need for individualized therapies. This tailored approach should take into consideration the intricacies of memory, learning, and neuroplasticity principles. The importance of personalization holds true not only for behavioral interventions but also for neuromodulation techniques, indicating a trajectory where research is headed.

In conclusion, the fusion of both explicit and implicit learning strategies in anomia therapy emerges as a captivating avenue. The insights from implicit learning, when synergized with avant-garde modalities like tDCS, suggest a significant shift in therapeutic strategies.

While this thesis, along with current literature, provides a foundational understanding of these combined methodologies, there is a pressing need for more extensive studies, especially with larger participant samples, to further elucidate and refine their efficacy.

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Embarking on this doctoral journey has been one of the most challenging yet rewarding experiences of my life, and there are many incredible individuals who have provided unwavering support, invaluable advice, and moments of joy along the way. In this space, I take a moment to express my deepest gratitude to each of them.

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Appendix A

Pseudo-words employed in Experiment 1, 2 and 3 taken by Basso et al., 2001.

Lasba
Grole
Zaclo
Nuspo
Norli
Velba
Mible
Bippo
Vorpa
Pilca
Nunco
Lansi
Cirli
Bepri
Pirga
Lorba
Bleti
Lutre
Fimpo
Dresi
Svife
Dongi
Lerpo
Milvo
Svuna
Gilne
Tucce
Revra
Filco
Tiblo
Rundo
Galpo
Silpo
Lecri
Glove
Lorfe
Pasbi
Clesi
Tabri
Drelo
Fitre
Trulo
Nirgo
Senci
Relga
Sdeta
Sbulo
Lovri
Dippa
Zirve
Zilci
Zunde
Nipra
Pruso
Nulge
Rembe
Docle
Tepro
Furra
Dunl

Appendix B

Images employed in Experiment 1 and Experiment 2. from the Novel Object and Unusual Name (NOUN) Database (see http://www.sussex.ac.uk/wordlab/noun), a free tool for researchers offering images of novel objects and unusual names (Horst & Hout, 2016)

Appendix C

Images employed in Experiment 3 from the Novel Object and Unusual Name (NOUN) Database (see http://www.sussex.ac.uk/wordlab/noun), a free tool for researchers offering images of novel objects and unusual names (Horst & Hout, 2016)


















Appendix D

Pseudo-words employed in Experiment 4 taken by Sulpizio et al., 2013.

Bivata
Nediro
Gumica
Tadiro
Fobita
Botile
Vorita
Gediro
Revoro
Zabata
Potora
Tufita
Tamile
Dulica
Segoro
Vupita
Gerile
Losile
Zicata
Vobero
Vurola
Sepica
Nipata
Zimero
Lemero
Cibima
Lufero
Dapola
Bisile
Nebola

Appendix E

Images employed in Experiment 4 from the Novel Object and Unusual Name (NOUN) Database (see http://www.sussex.ac.uk/wordlab/noun), a free tool for researchers offering images of novel objects and unusual names (Horst & Hout, 2016)