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„Disturbances in Early Event-Related Potentials of Epilepsy Patients in Working and Semantic Memory“

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Vorwort

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Eidesstattliche Erklärung

Hiermit versichere ich, Felicitas Huber, dass ich die vorliegende Diplomarbeit selbstständig verfasst, andere als die angegebenen Quellen und Hilfsmittel nicht benutzt und mich auch sonst keiner unerlaubter Hilfe bedient habe. Dieses Diplomarbeitsthema habe ich bisher weder im In- noch im Ausland in irgendeiner Form als Prüfungsarbeit vorgelegt. Diese Arbeit stimmt vollständig mit der vom Begutachter beurteilten Arbeit überein.

Wien, im Mai 2015

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Unterschrift

Abstract

Epilepsy patients' working and semantic memory were investigated. Event-related potentials were recorded from a sample of drug-resistant epilepsy patients (*n*=34) and controls (*n*=38) in response to a working memory task (Sternberg Task) requiring participants to distinguish new from memorized words and a semantic memory task (Lexical Decision Task) where participants were required to discriminate between words and pseudowords. In addition, behavioral data on working and semantic memory were gathered via a Verbal Working Memory test from the Inventory for Memory Assessment and via a Identical Word Meaning test from the Wilde Intelligence Test 2. Continuous EEG was recorded from 64 channels and a common average reference was applied offline. EEG was filtered between 0.1 and 10 Hz (12dB/octave) and a notch filter of 50 Hz was applied. Epilepsy patients performed significantly worse than controls on neuropsychological memory tests and EEG tasks and demonstrated slower reaction times. Results show decreased amplitudes of the N1 (100-230 ms) across paradigms as well as decreased P1 amplitude (70-130 ms) for memorized words in epilepsy patients. N1 component latency for epilepsy patients was prolonged for memorized words/words in the Sternberg and Lexical Decision task, respectively. These results provide support for disturbances in early processing during working and semantic memory retrieval in epilepsy patients, indicating attentional deficits as well as slowed overall processing.

Abstract (deutsch)

Arbeits- und semantische Gedächtnisleistungen einer Stichprobe von therapierefraktären EpilepsiepatientInnen wurden untersucht. Die Arbeitsgedächtnisleistungen von Personen ohne (*n*=38) und mit Epilepsie (*n*=34) wurden mittels des Subtest “Verbales Arbeitsgedächtnis” des IGD (Inventar für Gedächtnisdiagnostik) und auf physiologischer Ebene mittels eines Sternberg Tasks bei simultaner Aufzeichnung ereigniskorrlierter Potentiale erfasst. Leistungen im semantischen Gedächtnis wurden anhand des Subtest “Gleiche Wortbedeutungen” des WIT-2 und anhand erreigniskorrlierter Potentiale während eines Lexical Decision Tasks erhoben. Elektroenzaphlographische Aktivität wurde an 64 Kanäle aufgezeichent, eine common average – Referenz (offline berechnet) wurde verwendet. Personen mit Epilepsie zeigten niedrigere Leistungen und verlangsamte Reaktionszeiten sowohl im Arbeitsgedächtnistest als auch im semantischen Gedächtnistest. Auf physiologischer Ebene konnten eine reduzierte N1 Amplitude (100-230 ms) in beiden Tasks sowie eine reduzierte P1 Amplitude (70-130 ms) bei Wörtern die zuvor gemerkt werden sollten festgestellt werden. Die Latenzzeit der N1 Komponente war außerdem bei EpilepsiepatientInnen bei gemerkten Wörtern im Sternberg Task und bei Wörtern im Lexical Decision Task länger. Diese Ergebnisse deuten auf Störungen in frühen Prozessen der Informationsverarbeitung bei semantischen und Arbeitsgedächtnisprozessen hin und könnten Aufmerksamkeitsdefizite sowie verlangsamte Informationsverarbeitung indizieren.

Abstract-Extended

Aims. Memory problems in drug-resistant epilepsy patients were investigated on a (a) behavioral level including memory tests' scores, on a (b) physiological level including event-related potentials (ERPs) during memory retrieval and on a (c) subjective level, gathering self-report data on subjective memory. Since sleep has been shown to play an important role for memory functioning, a subjective measure of sleep quality was included also.

Methods. A sample of drug-resistant epilepsy patients (N = 34) and controls matched for gender and age (N = 38) were assessed with neuropsychological working memory (Verbal Working Memory test, subtest of the Inventory for Memory Assessment) and semantic memory (Identical Word Meaning test, subtest of the Wilde Intelligence Test 2) tests. Additionally, ERPs were recorded from healthy subjects in response to a word recognition Sternberg Task and a Lexical Decision Task requiring participants to discriminate between words and pseudowords. The Sternberg Task and the Lexical Decision Task were chosen as EEG paradigms to monitor and measure visual working and semantic memory retrieval, respectively. EEG was recorded from 64 channels and a common average reference was applied offline. The Pittsburgh Quality of Sleep Index score (PSQI) as well as various subjective memory scores were compared across groups.

Results. Generally, epilepsy patients performed significantly worse than controls on neuropsychological memory tests and EEG tasks and demonstrated slower reaction times. A significant difference in early processing, specifically in the P1 and N1 visual ERP components between epilepsy and control group was found. Specifically, results show decreased amplitudes of the N1 across paradigms as well as decreased P1 amplitude for memorized words in epilepsy patients. Additionally, N1 component latency for epilepsy patients was prolonged for memorized words/words in Sternberg and Lexical Decision task, respectively. There was no significant group difference between sleep quality scores. Healthy controls showed more significant and higher correlations between subjective memory and objective memory performance.

Conclusion. These results provide support for disturbances in early processing during working and semantic memory retrieval in epilepsy patients, indicating attentional deficits as well as slowed overall processing. These neurophysiological results were mirrored in worse memory performance on memory tests and slower reaction times.

Für meine Familie

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A. Introduction

Epilepsy is the most frequent serious neurological condition worldwide affecting all ages, races, and social classes (Neligan, Hauser, & Sander, 2012). The most common complaint in epilepsy patients is memory difficulty (MacAllister & Schaffer, 2007) and epilepsy patients have worse performance on standardized neuropsychological memory tests (e.g., Hermann, Seidenberg, Schoenfeld, & Davies, 1997; Moore & Baker, 2002; Oyegbile et al., 2004).

Since this is a significant issue for epilepsy patients, it is surprising that relatively few studies have investigated neural underpinnings of memory problems in epilepsy with event-related potentials (ERPs), even though they provide important temporal information on cognitive processing. Hence, this study aimed to not only replicate findings of reduced memory performance on psychological tests in the epilepsy group, but also to determine neurological processes underlying disturbed memory processing via ERPs. Specifically, early sensory processes were of interest, that is, P1 and N1 components, since monitoring early components is helpful in assessing attention, vigilance, and gating of sensory inputs (Pratt, 2011). Most importantly, investigating early components is necessary to determine whether epilepsy disturbs early sensory processes, which precede all cognitive activity.

Since sleep has been shown to repeatedly play an important role in memory functioning (Bear, Connors, & Paradiso, 2007; Diekelmann & Born, 2010; Maurer, Weeß, & Schredl, 2013), a quality of sleep measure was included as well. Additionally, even though the existence of memory problems is well-documented in the literature, relationships between subjective memory and performance on standardized memory tests remain elusive and non-significant (Elixhauser, Leidy, Meador, Means, & Willian, 1999; Marino et al., 2009; Piazzini, Canevini, Maggiori, & Canger, 2001; Thompson & Corcoran, 1991). To elucidate these relations, several different subjective memory measures were applied in this study to comprehend how accurately epilepsy patients estimate their memory ability compared to controls.

In the following paragraphs, the current state of research on epilepsy and memory as well as neuroanatomical locations and electrophysiological indicators of memory and early information processes will be reviewed. As they are of special interest, P1 and N1 components will be discussed thoroughly. This will be succeeded by a discussion on past ERP research of memory and epilepsy. Finally, literature on sleep quality and subjective memory in epilepsy patients will be discussed.

1. The Current State of Research

1.1. Epilepsy

Epilepsy is the most common serious neurological condition in the world, with an annual incidence of around 50 cases per 100 000 in developed countries and a worldwide prevalence of a little more than 50 million altogether (Neligan et al., 2012; Ngugi, Bottomley, Kleinschmidt, Sander, & Newton, 2010). It affects all ages, social classes and crosses all geographic boundaries. The prevalence rate is even higher in resource-poor countries due to limited or no access to medical services and treatment (Neligan et al., 2012). According to the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE), epilepsy is defined as a "disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure" (Fisher et al., 2005, p. 470). In epilepsy, the cause or predisposition for seizures stays the same over time. Also, seizures do not have specific precipitants such as metabolic disturbances or drug withdrawal but are unprovoked (Berlit, 2013; Smithson & Walker, 2012). Another characteristic of epilepsy is that it is not one entity but encompasses a rather heterogeneous group of conditions with wide variability in etiology, manifestations, and therapy (Baumgartner, 2001; Chang & Lowenstein, 2003; Smithson & Walker, 2012).

Epileptic seizures are due to continuous, abnormally synchronized electrical discharges of large groups of neurons (Zeman, Kapur, & Jones-Gotman, 2012) and can be broadly classified into two types, that is, generalized and focal (partial) seizures (Hall, Isaac, & Harris, 2009). Generalized seizures, in contrast to focal ones, are characterized by initial synchronous discharges over both hemispheres and may be a result of global brain cellular abnormalities (Hall et al., 2009). Generalized seizures encompass absence, myoclonic, atonic, and grand mal (also known as tonic-clonic) seizures (Berlit, 2013). Focal seizures, in comparison, originate from a localized cortical area and are frequently associated with a structural abnormality (Hall et al., 2009). Most focal seizures originate within one hemisphere. Focal or partial seizures can be further subdivided in simple focal and complex focal seizures. Whereas simple focal seizures do not impair consciousness, complex focal seizures do and can even initiate secondary generalized tonic-clonic seizures (grand mal; Berlit, 2013). Patients experiencing complex focal seizures usually do not remember the seizure itself.

The most common type of focal epilepsy is temporal lobe epilepsy (TLE), which is also the most common form of all epilepsies (Elger, Helmstaedter, & Kurthen, 2004; Engel, 1996). Sixty percent of focal seizures originate in the temporal lobes, and frontal lobes are the second most common point of origin (Ferrie & Walker, 2012). TLE is associated with cell loss in the hippocampus and its surrounding areas and has a potential for drug-resistance (Howard, Andres, & Mazzoni, 2013). An important distinction in classification is made between mesial, structural, and non-lesional epilepsy. Mesial TLE is characterized by the presence of hippocampal sclerosis or hippocampal atrophy (Engel, 1996), whereas structural epilepsy is described by the occurrence of any other lesion (e.g., tumors, vascular abnormalities, or cortical dysplasia). Non-lesional epilepsy can be defined as epilepsy without a tumor, vascular malformation, neuronal migrational disorder, encephalomalacia or other potentially epileptogenic neocortical lesion (Baumgartner, 2001; Elger et al., 2004; Oliva, Meckes-Ferber, Roten, Desmond, Hicks, & O'Brien, 2010).

1.2. Memory

Memory refers to a complex and dynamic system, which is used to retain and draw on information that is no longer present (Tulving & Craik, 2000). While memory is the means by which we store and access information, memory processes are the mechanisms associated with processing information, i.e., encoding, storage, and retrieval processes (Crowder, 1976 as cited in Tulving, 1995). Since a comprehensive discussion of memory goes beyond the scope of this thesis, only the two memory systems investigated, i.e., working memory and semantic memory, shall be described here.

1.2.1. Working Memory

Miller, Galanter, and Pribram presumably first introduced the term working memory in 1960 while referring to an immediate type of memory:

> we should like to speak of the memory we use for the execution of our Plans as a kind of quick-access, "working memory." There may be several Plans, or several parts of a single Plan, all stored in working memory at the same time. (Miller et al., 1960/2013, p. 65)

The term was then famously adopted by Baddeley and Hitch in 1974 to introduce the first version of their working memory model, thereby emphasizing the differences to the prevailing modal model at the time (for a review see Baddeley, 2003). Presently, the

working memory model conceptualizes working memory as a limited capacity system, which allows the temporary storage and manipulation of information (Baddeley, 2003; Cowan, 2001). In the most recent version of the model, working memory provides a crucial interface between perception, long-term memory, and action; information is received from both sensory input and long-term memory presentations (Baddeley, 2003).

At its core, working memory reflects the idea that information often has to be readily available to perform complex mental operations. Thus, it is critically important in cognition and is necessary for many cognitive abilities, such as reasoning, language comprehension, learning, planning, and spatial processing (Baddeley & Hitch, 1974; D'Esposito, 2007).

It is apparent by the numerous empirical studies on working memory that are published each year that the working memory model is one of the most widely known memory models in use today, though it has undergone modifications since its introduction by Baddeley and Hitch in 1974. The model proposes that working memory is the combination of a controlling attentional mechanism called the central-executive and a number of subsidiary slave-systems: the phonological loop, the visuospatial sketchpad, and the most recent addition to the model, the episodic buffer (Baddeley, 2000).

The central executive has overall attentional control and coordinates activities within the slave systems (Baddeley & Hitch, 2010). It is modality-free, has limited processing capacity and deals with any cognitively demanding task (Baddeley, 2000). The core role of the central executive is the control and allocation of attention within the working memory system while not actually being able to store any information (Baddeley, 2000, 2007). Overall, the central executive seems to consist of various separate but related executive control processes: the capacity to focus attention, to divide attention between two or more tasks and to control access to long-term memory (Baddeley & Hitch, 2010; Baddeley, 2007).

The most widely researched and prominent subsystem is the phonological loop. The phonological loop holds information in a phonological (speech-based) form (Baddeley & Hitch, 1974). It consists of two subcomponents itself, (a) a passive phonological store directly concerned with speech perception and (b) an articulatory rehearsal process linked to speech production that gives access to the phonological store (Baddeley & Hitch, 2010). This implies that words presented auditorily are processed differently than words presented visually. When presenting words in the auditory modality, words have a direct access to the phonological store. In contrast, words presented visually only gain access through

subvocal articulation, i.e., they have only indirect access to the phonological store by being articulated out loud. Thus, memory traces in the phonological store might stem directly from auditory input or from subvocal articulation of a visually presented item (Baddeley, 2000).

The visuo-spatial sketchpad stores and manipulates spatial and visual information (Baddeley & Hitch, 1974). In everyday life, for instance, it is used for the representation of mental maps when navigating a complex building. The visuospatial sketchpad can be divided into visual, spatial, and possibly kinaesthetic components (Baddeley & Hitch, 2010).

The episodic buffer is the most recent addition to the working memory model. It holds and integrates information from the phonological loop and the visuo-spatial sketchpad, i.e., it combines visual, verbal, and spatial information (Baddeley, 2000). This multidimensional common store is supposedly controlled by the central executive, though the relationship between episodic buffer and central executive is still under scrutiny (e.g., Baddeley, Allen, & Hitch, 2011). All incoming information is converted into coherent chunks, scenes, or episodes (no matter their code) as multi-dimensional representations (Baddeley, 2000). It is also assumed that the episodic buffer connects verbal and visuo-spatial subsystems to long-term memory (Baddeley et al., 2011). Thus, the episodic buffer is thought of as a temporary multidimensional store that functions as interface between the subsystems of working memory, long-term memory, and the central executive (Baddeley et al., 2011).

1.2.2. Semantic Memory

The idea that memory is not one single unitary faculty but comprises multiple memory systems was first proposed as early as 1890 (James, as cited in Squire, 2004). Since then, a clearer and more concrete classification of long-term memory has evolved by adding a biological framework (see Figure 1; Squire, 2004). This classification distinguishes between declarative and nondeclarative memory. Whereas the former refers to the capacity for conscious recollection about facts and events and is usually what is meant by memory in everyday language, the latter comprises procedural knowledge and is expressed by performance (Squire, 2004). Declarative memory enables comparisons between already learned material and supports encoding of memories via relationships between contents (Squire, 2004). Nondeclarative memory, on the other hand, encompasses several specialized performance systems, which are, when needed, reactivated by

structures where learning initially occurred (Squire, 2004). These two memory systems are differentiated by their operating principles: Declarative memory is able to detect and encode what is unique about a particular event, whereas nondeclarative memory is able to gradually extract common elements from a series of separate events (Squire, 2004).

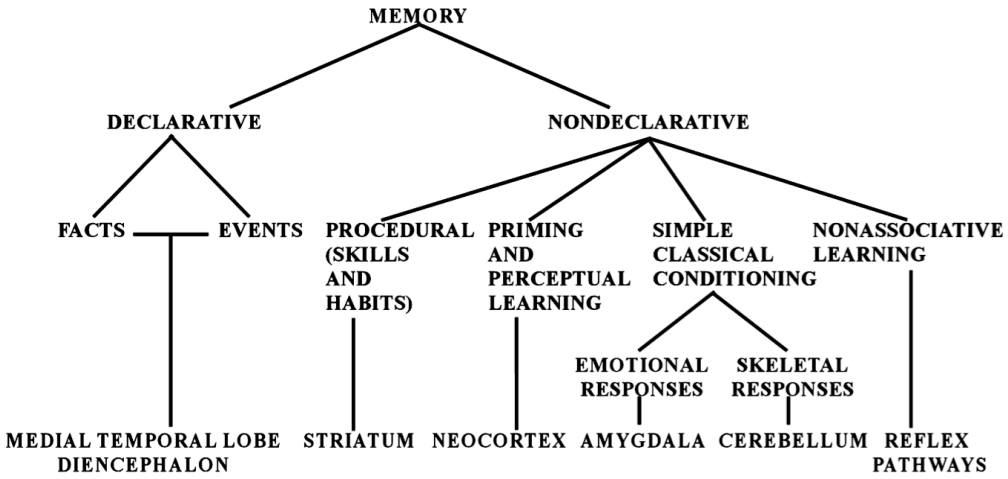

Figure 1. A taxonomy of long-term memory systems (Squire, 2004, p. 173).

According to Tulving (1983), declarative memory can be further subdivided into semantic memory (facts and general world knowledge) and episodic memory (past personal events experienced in a particular place and time). The former encompasses facts about the world, for instance, the meaning of a word, knowing what pepper is or the name of the current chancellor of Austria, whereas the latter includes re-experiencing a particular event in its original context such as a birthday party or graduation. Since semantic memory is concerned with word meaning it was particularly relevant to investigate.

Declarative memory is reliant on structures in the medial temporal lobe and the diencephalon (Squire, 2004). Skills/habits, priming, emotional responses, skeletal musculature, and nonassociative learning are dependent on structures of the striatum, neocortex, amygdala, cerebellum, and reflex pathways, respectively (see Figure 1).

1.3. Epilepsy and memory

People with epilepsy show weaker performance on objective neuropsychological tests (for a complete review see Zeman et al., 2012). Specifically, it has been demonstrated repeatedly that people with epilepsy have reduced memory and learning abilities, more attention and concentration problems, slower information processing, language deficits, and executive dysfunction when compared to people without epilepsy (e.g., Hermann et al., 1997; Moore & Baker, 2002; Oyegbile et al., 2004). Among all neuropsychological

complaints, memory deficits are the most prominent for people with epilepsy (MacAllister & Schaffer, 2007). This is why it is crucial to investigate them.

Another reason why investigating memory in epilepsy patients is important is that it is a prerequisite for many higher, complex cognitive functions (Baddeley & Hitch, 1974; D'Esposito, 2007). Memory capacity appears to reflect important and stable cognitive capability in individuals and is strongly predictive of performance on a variety of high-level aptitude measures (Perez & Vogel, 2011). For instance, good performance on memory tests is a predictor of fluid intelligence, abstract reasoning, and reading comprehension measures (Cowan, Fristoe, Elliott, Brunner, & Saults, 2006; Engle, Tuholski, Laughlin, & Conway, 1999; Kane, Kathryn, Conway, & Engle, 2001; Kyllonen & Christal, 1990). Also, disruptions in working memory are often linked to pathological cognitive states, for example, attention disorders, dementia, or, depression (Gold, Wilk, McMahon, Buchanan, & Luck, 2003; Morris & Baddeley, 1988; Rinck & Becker, 2005; Sonuga-Barke, Dalen, Daley, & Remington, 2002).

As temporal lobe epilepsy was the most common epilepsy type in the sample analyzed it is important to mention that TLE has commonly disabling effects on memory functioning (Elger et al., 2004). Cell loss in the hippocampus and surrounding areas (which is rather common in TLE) results in memory difficulties such as episodic memory impairments, as well as impairments in long-term consolidation and remote memory (Bell & Giovagnoli, 2007). Left-sided TLE, specifically, is characterized by verbal memory deficits, particularly in long-term consolidation and retrieval (Elger et al., 2004; Hermann et al., 1997) and is also associated with learning and working memory (Helmstaedter, Grunwald, Lehnertz, Gleißner, & Elger, 1997). Patients with right-sided TLE show deficits in spatial memory, identification of famous faces, delayed face recognition, and recognition of emotional facial expression (Breier et al., 1996; Glosser, Salvucci, & Chiaravalloti, 2003; Meletti et al., 2003; Milner, 2003). Other factors that can contribute to memory problems in epilepsy patients include the epileptic seizures as such or anti-epileptic drugs (AEDs; Grippo, Pelosi, Mehta, & Blumhardt, 1996).

Event-related potential studies have shown that epilepsy patients perform worse in both working memory (Grippo, Pelosi, Holly, Hayward, Barrett, & Blumhardt, 1994; Grippo et al., 1996) and semantic memory measures (Giovagnoli, 1999; Giovagnoli, Erbetta, Villani, & Avanzini, 2005; Messas, Mansur, & Castro, 2008), showing impaired performance and slower reaction times compared to controls. Before discussing these ERP findings and neurophysiological underpinnings of memory problems in epilepsy patients,

however, neuroanatomical structures and the location of memory shall be briefly reviewed first.

1.4. Neuroanatomical Structures and Localization of Memory

All functions relevant to information processing and memory are organized within the cerebral hemispheres (Crossman & Neary, 2010). Primary visual processes are located in the occipital lobes and language functions (speech, reading, writing, and calculation) are organized in the regions of the frontal, parietal, and temporal lobes adjacent to the left lateral sulcus (Crossman & Neary, 2010). It is a widespread assumption that frontal lobes play an important part in executive control, although there are differing opinions on the extent of separate localizability of different executive functions (Duncan & Owen, 2000; Shallice, Marzocchi, Coser, Savio, Meuter, & Rumiati, 2002).

Most important for this study are probably the structures in the medial aspects of the temporal lobes as they form part of the limbic system and are responsible for learning new information as well as recollecting from experience (Crossman & Neary, 2010). Bilateral disorders of the medial temporal lobes and limbic system, for instance, lead to loss of memory function (Crossman & Neary, 2010). Additionally, event-related functional magnetic resonance imaging (fMRI) studies have identified patterns of neural activation in the medial temporal lobe and prefrontal cortex for items recognized in the retrieval phase during encoding (Kircher et al., 2008; Qin, van Marle, Hermans, & Fernandez, 2011).

When it comes to localizing individual working memory systems, findings have been supporting the view that working memory is a result of interaction between the prefrontal cortex (PFC) and several other structures in the brain, rather than localized to a specific area (D'Esposito, 2007). It is assumed that subcomponents of working memory are to be thought of as constructs rather than distinct cerebral entities. The phonological loop, for instance, appears to work by integrating neural processes of perception and speech production (Buchsbaum & D'Esposito, 2008).

Posteromedial regions and parieto-hippocampal areas appear to play a significant role in the successful retrieval of episodic and maybe also semantic information (McCormick, Moscovitch, Protzner, Huber, & McAndrews, 2010; Vannini, O'Brien, O'Keefe, Pihlajamäki, LaViolette, & Sperling, 2011). Additionally the hippocampus has repeatedly been implicated in long-term memory processing, though its specific role is still unclear and under scrutiny (Schneider & Fink, 2013). In sum, it seems that primary visual processes are located in the occipital areas; temporal lobe, prefrontal cortex, and hippocampal interactions seem to be important for memory.

1.5. Electrophysiological Indicators of Cognitive Processes

This study analyses electrophysiological processes from electroencephalograms (EEGs) to investigate cognitive operations that are active while performing working and semantic memory tasks. Neurophysiological techniques have become a useful source of information when answering questions about working memory (Luck, 1998). One major advantage of an EEG is its high temporal resolution, meaning that unlike behavioral measures, electrophysiological responses are not exposed to temporal delay - they happen momentarily (Mecklinger, 1992). Because electrical potential travels close to the speed of light, transmission through the brain, meninges, skull, and scalp is essentially instantaneous and it is often possible to identify when a given process occurred to within a few milliseconds (Kappenman & Luck, 2011). Questions of time delay in semantic match-mismatch conditions, for instance, were answered with this technique (for a review see Kutas & Federmeier, 2011 or Van Petten & Luka, 2012).

Thus, analysis of EEGs enables close observation of the various stages of information processing from input to output/reaction, and much more precise analysis is possible than when working solely with behavioral measures. A basic assumption when using this method is that there are systematic relationships between processes of information processing and electrophysiological processes (Mecklinger, 1992). Specifically, information processing and event-related potential voltage changes are assumed to happen simultaneously (Donald, 1979 as cited in Trimmel, 1990). The information processing approach as such proposes that mental activities can be conceived as information processing systems (Mecklinger, 1992). It rests on the notion that information is being processed and transformed/manipulated in various stages. The mind computes a variety of different descriptions or representations of even a single stimulus, which implies that there are separable mental representations or codes (Cherry, 1953 as cited in Pashler, 1998; Posner, 1978). Hence, information is stored in specific places while being processed (Galotti, 2008). Reactions or output are considered results of a sequence of processing steps. The information-processing approach dominated cognitive psychology in the 1960s and 1970s and remains influential today.

The EEG is a useful tool to assist in detecting and understanding memory dysfunction in epilepsy patients (Grippo et al., 1996). It provides objective quantitative data on the timing and adequacy of cognitive processing in working and semantic memory as well as the associated behavioral processes and response preparation (e.g., Ruchkin, Canoune, Johnson, & Ritter, 1995). Thus, to observe information processing directly,

specifically in working and semantic memory tasks, it was deemed necessary to record electrophysiological activity. The following paragraphs shall give the reader unfamiliar with electroencephalography a very short introduction in how an EEG works and how it is used in current research.

1.5.1. EEG, The ERP technique, Components

The EEG constitutes the "sum of many different sources of electrical activity within the brain" (Luck, 1998, p. 263). It depicts momentary changes in brain activity, i.e., voltage changes, and consists of a summation of electrical activities by populations of largely neurons (Lopes da Silva, 2009). Specifically, electrical and magnetic fields that are generated in association with synchronous nerve cell activity are recorded (Hillyard & Anllo-Vento, 1998).

Event-Related Potentials (ERPs) are voltage fluctuations in the ongoing EEG that are time-locked to an event, for instance the onset of a stimulus or the execution of a manual response (Kappenman & Luck, 2011). The ERP waveform as such reflects the summation of postsynaptic potentials (PSPs) that occur simultaneously in large numbers of cortical pyramidal cells (a type of neuron) that are orientated in a similar manner (Luck, 2014). These PSPs are "a result of changes in electrical potential that occur when ion channels open or close in response to neurotransmitters binding with receptors on the postsynaptic cell membrane, which leads to flow of ions into or out of the cell" (Kappenman & Luck, 2011, p. 5). To clear up a common misconception it is worth mentioning that ERPs represent the inputs to a group of neurons rather than the outputs of those neurons, that is, ERPs do not reflect action potentials (Kappenman & Luck, 2011).

However, most ERPs are rather small in comparison with the ongoing EEG activity (Kappenman & Luck, 2011). Only in recent years it has become possible to extract neural responses associated with specific events or processes from the EEG with a signal averaging technique called event-related potential technique (ERP technique; Luck, 2014). To apply this averaging procedure, a stimulus must first be repeated several times. Then, the segment of EEG following each stimulus is extracted. After extracting all segments for all individuals, EEG segments are averaged together into a single waveform (Luck, 1998; Trimmel, 1990). It is assumed that any activity consistently time-locked to the stimulus onset will remain in this average, whereas any activity that is unrelated to the stimulus will average out, provided a sufficient number of trials are available (Luck, 1998; Trimmel, 1990). With this technique, specific electrical responses (voltage changes) are linked in

time to a definite sensory, cognitive, or motor event, for instance a word or an image (Luck, 2014; Trimmel, 1990). To sum up, ERPs are stimulus-evoked brain responses recorded form the human scalp, time-locked to an event (sensory, motor, or cognitive) and calculated by additive averaging.

The result of the averaging process is an average ERP waveform, which consists of a number of positive and negative voltage deflections called "components" (Luck, 1998). Conceptually, Luck (2014, p. 66) defines an ERP component as "a scalp-recorded neural signal that is generated in a specific neuroanatomical module when a specific computational operation is performed". Each component reflects different activity from a different set of brain areas and a large number of different components can be observed under different conditions (Hillyard & Kutas, 1983; Luck, 1998). The N400 component, for instance, is seen as part of the normal brain response to words and other meaningful (or potentially meaningful) stimuli (first discovered by Kutas & Hillyard, 1980; for review see Lau, Phillips, & Poeppel, 2008). Each component is named for its polarity (P for positive or N for negative polarity) and its position within the waveform, e.g., "P1" and "N1" stand for the first positive-going and negative-going component after stimulus onset, respectively (Luck, 1998). Some components are named slightly differently, e.g., "P170" or "N400", and here the numbers indicate the exact time of peak (Luck, 1998). As similar naming conventions are used for both auditory and visual ERP components, it is necessary to note that solely visually evoked potentials were investigated here.

Traditionally, ERP components can be broadly classified into three categories, namely (a) *exogenous sensory* components, (b) *endogenous* components, and (c) *motor* components (for a more thorough discussion on classifications see Trimmel, 1990). Exogenous sensory components are mainly determined by external stimulus characteristics (e.g., physical properties of a stimuli), which is why they are also called stimulus driven components (Luck, 2014; Näätänen, 1992). Endogenous components, which mostly depend on the subject's intentions and actions, are voluntary and show great variability and flexibility in accordance with the subject's varying internal state and behavior. These components vary, for instance, as a function of attention or task relevance. These are often elicited in the absence of external stimulation, and it is possible that disparate stimuli elicit the same component if their task-roles are equivalent (Donchin, Ritter, & McCallum, 1978; Näätänen, 1992). Motor components accompany the preparation and execution of a given motor response (Luck, 2014). Since the time course of a component indicates the period during which the corresponding brain area is active, early components generally reflect

sensory processing and later components usually reflect higher cognitive processes and motor-related activity (Luck, 1998).

Before describing early ERP components, two essential terms, amplitude and latency, need to be explained first. Amplitude constitutes the difference between the mean prestimulus baseline voltage and the largest positive- or negative-going peak within a time window (Luck, 2014; Polich & Kok, 1995). It is assumed that the amplitude of an ERP component denotes the intensity of activation of neural structures, that is, the intensity of information processing (Kok, 1990). It is closely related to the timing of information processing, which has been termed latency. Latency is the time from stimulus onset to the point of maximum positive amplitude within the same time window (Luck, 2014; Polich & Kok, 1995) and appears to reflect timing of stages of information processing (Kok, 1990). In contrast to reaction time measures, especially early components give more specific information with respect to the timing and duration of processing stages, whereas reaction time merely reflects total processing output (Ritter, Simson, Vaughan, & Macht, 1982 as cited in Kok, 1990). The next section shall outline amplitude and latency variations in early components and their associated cognitive processes.

1.5.2. Attentional modulation of early processing stages

At any given moment, all internal and external events in our surroundings are constantly in competition for control of our perception, memory, and behavior. However, most received inputs are irrelevant. Therefore, Luck (1998) describes the primary role of selective attention as the focusing of cognitive processing resources on a subset of available information while ignoring the rest. This allows cognitive resources and behavioral outputs to be concentrated on limited information (Luck, 1998). Consequently, perception and awareness of the whole world around us is influenced or at least dependent upon early selection processes, in which attention selects relevant inputs to be perceived and recognized (for a review of support for early selection and the locus of selection debate see Driver, 2001). It shall be noted that today, it is assumed that selective attention influences both early sensory and later, postperceptual information processing stages (Luck, Woodman, & Vogel, 2000).

There is a plethora of studies supporting the notion that attention acts at very early, perceptual levels of information processing (e.g., Downing, 1988; Hawkins, Hillyard, Luck, Mouloua, Downing, & Woodward, 1990). In 1964, Haider, Spong, and Lindsley first applied electrophysiological methods to study visual-spatial attention in humans. ERPs elicited by a vigilance task were examined. Specifically, participants had to respond to

interspersing dim flashes with a button press and were instructed to not respond to continuously presented brighter flashes. Findings showed systematic variation of early amplitudes corresponding with fluctuations in vigilance during the course of the task. Decreasing detection efficiency over time corresponded to a decrease of amplitude and increase of latency of what is now known as N1. This suggests that amplitude of the N1 is tied to levels of attention.

A different study by Posner, Snyder, and Davidson (1980) employing cues indicating test stimuli location found that test stimuli at the precued, i.e., attended, location are usually detected faster and/or more accurate compared to test stimuli at unattended locations. These results provide support for altering of stimulus processing by spatial attention. Other studies employing similar cuing techniques corroborate these results as they found larger P1 amplitudes over visual cortex for validly cued targets and shorter reaction times (f.e., Hillyard, Luck, & Mangun, 1994).

Since Haider et al.'s study in 1964, a plethora of papers have shown that P1 and N1 components are modulated by spatial attention (for review see Luck et al., 2000). In sum, these ERP results have been interpreted as a gain control mechanism (f.e., Eason, 1981), implying that attending to a location increases the gain/amount of sensory input received from that location (Luck et al., 2000; Mangun, 1995). This is then reflected in an increase in amplitude in the latency range of the P1 and N1.

P1, the first positive-going component in the waveform, is estimated to typically onset 60-90 ms postimulus with a peak between 100-130 ms (Luck, 2014). Following the P1 wave is the N1 wave (Luck, 2014). Several N1 subcomponents form the N1 peak, even though they are not necessarily functionally related (Luck, 2014). The earliest N1 subcomponent peak occurs 100-150 ms poststimulus at anterior electrode sites. At least two posterior N1 components peak 150-200 ms postimulus, arising from parietal cortex and lateral occipital cortex, respectively (Luck, 2014). Both P1 and N1 components are related to the processing of visual stimuli and are modulated by attention but also by the subject's state of arousal (Luck, 2014). To control for arousal level, ERP paradigms typically use identical physical stimuli to compare attended versus not attended locations.

The P1 and N1 components have been localized to visual areas in lateral extrastriate cortex and inferior occipital-temporal cortex (e.g. Gomez Gonzalez, Clark, Fan, Luck, & Hillyard, 1994; Hopf, Vogel, Woodman, Heinze, & Luck, 2002; Natale, Marzi, Girelli, Pavone, & Pollmann, 2006). Since P1 and N1 are the earliest components influenced by spatial attention, it has been argued that spatial attention cannot affect

sensory processing before extrastriate visual cortex. Still, this does imply that attention influences sensory coding to some extent.

1.6. Event-Related Potentials Research on Memory

1.6.1 Working Memory

As the Sternberg task was applied in this study to measure working memory, the subsequent paragraph shall shortly describe results of previous studies investigating ERPs via Sternberg tasks. First, however, it is important to have a closer look at the procedure of a Sternberg memory task itself. In 1966, Saul Sternberg presented participants with a short list of one to six digits and asked them to hold the list in short-term memory (Sternberg, 1966). Shortly thereafter, participants were presented with test digits and had to decide whether they had appeared in the list of digits they had been asked to memorize earlier (Sternberg, 1966). This task effectively measures how well people compare sensory information with representations that are active in memory (Gazzaniga, Ivry, & Mangun, 2002). The time between stimulus and response is occupied by a so-called memory scanning process (Sternberg, 1966). It has been used to show that items are retrieved sequentially, not at once and that every one of the stored items are compared to the target, regardless of whether a match for the target is found sooner (serial and exhausting processing hypothesis; Gazzaniga et al., 2002).

One of the major advantages of the Sternberg paradigm is that it allows a separate analysis of encoding, retention/maintenance and recognition/retrieval processes. This may be why the Sternberg paradigm has been used widely in cognitive neuroscientific studies of memory in the last decade (e.g., Jensen, Gelfand, Kounios, & Lisman, 2002; Rypma, Berger, Genova, Rebbechi, & D'Esposito, 2005). Thus, this paradigm is ideal for investigating temporal development during different stages of working memory processing (e.g., Jensen et al., 2002).

Electrophysiological correlates of short-term memory using versions of the Sternberg task have been widely studied. Potentials recorded during memorization as well as during correct identification of the probes include a late positivity most prominent parietally (P300, 300-800 ms; Luck, 2014; first described by Sutton, Braren, Zubin, & John, 1965) and most previous studies have been concerned with this component. The P300 has been shown to be affected by size of memorized set, stimulus type, position of probe in set, and age of the subject (Adam & Collins, 1978; Marsh, 1975; Patterson, Pratt, & Starr, 1991; Pfefferbaum, Ford, Roth, & Kopell, 1980; for a review see Polich & Kok,

1995 or Polich, 2007). For instance, non-lexical stimuli elicit a larger late positivity amplitude compared to lexical stimuli, and visual stimuli evoke a larger late positivity than auditory stimuli (Patterson et al., 1991; Pratt, Erez, & Geva, 1997). This suggests additional processing of non-lexical, non-auditory stimuli. Another study using a modified Sternberg paradigm with digit identification and matching of three memory sets with different loads (one, three, and five digits) found the P300 and to a lesser extent the P145 had significantly longer latencies to new items compared to memorized items (Pelosi, Hayward, & Blumhardt, 1998). The N270 latency to single digits was longer for new items and the latency of the P300 increased markedly with increasing set size (Pelosi et al., 1998). These longer latencies have been linked to efficiency of stimulus detection and speed of information processing (Kok, 1990; Pontifex, Hillman, & Polich, 2009), indicating that increasing set size has a slowing effect on speed of information processing and that memorized items are processed quicker compared to new items. The meaning of the P300 itself is still under much scrutiny, although the context updating hypothesis (for review see Donchin & Coles, 1988) has received much attention.

ERP working memory research focusing on early components have demonstrated that N1 and P2 amplitude are influenced by positioning, i.e., N1 and P2 amplitude showed larger amplitudes in response to first and second memorized item compared to all other stimuli (Wolach & Pratt, 2001). This indicates that first and second items received higher levels of attention than any of the other items. Conley, Michalewski, & Starr (1999) find similar results and showed decreased N1 amplitude with increasing set size. When investigating differences in early components between memorized items and new items (or distractors), lower N1 amplitudes were found for distractors compared to memorized digits (Wolach & Pratt, 2001). These results suggest that distractors had not been paid as much attention to as relevant memorized digits. Lower attention allocation to distractors compared with memorized items also point towards an early point of discrimination between memorized items and distractors (Picton & Hillyard, 1974 as cited in Wolach & Pratt, 2001).

Other research found that P1 and N1 amplitudes were not significantly affected by experimental condition, that is, no significant effect of memorized set size or probe type on P1 and N1 latencies and amplitudes were found during memory scanning (Pratt, Michaelweski, Barrett, & Starr, 1989; Pelosi, Holly, Slade, Hayward, Barrett, & Blumhardt, 1992; Wolach & Pratt, 2001). This has been interpreted as there being no early attentional differences for memorized words compared to new words or for memory load.

1.6.2. Semantic Memory

In a lexical decision task as was used for semantic memory analysis here, subjects usually have to complete a recognition judgment and are asked to respond as quickly as they can to indicate whether a target item is a valid word or a nonword/pseudoword. In other words, subjects are asked to verify if a string of letters is a word during a response time task. This task has been used in exploring semantic memory processes in the past (e.g., Holcomb & Neville, 1990; Meyer & Schvaneveldt, 1971).

Most ERP studies focusing on language, long-term memory representations and semantic, syntactic and discourse structures investigate the N400 response. The N400 is a broad negative deflection that starts 200-300 ms after word presentation and peaks after approx. 500 ms (first discovered by Kutas & Hillyard, 1980; for review see Lau et al., 2008). It is most often associated with semantic anomaly but can also be evoked by most meaningful stimuli (e.g., isolated words, faces, and pictures; Lau et al., 2008). The N400 is now regarded as part of a normal response to words and speech-based information (Kutas & Federmeier, 2000; Lau et al., 2008). Pseudowords, like the ones used in the Lexical Decision Task, can also evoke the N400 and produce more negative potentials compared to words at central or centro-parietal electrode sites (Hauk, Davis, Forder, Pulvermüller, & Marslen-Wilson, 2006; Kutas & Federmeier, 2000). This increase in the amplitude of pseudowords has been associated with heightened difficulties in lexically accessing pseudowords compared to words (Lau et al., 2008).

Differences between pseudowords and words have been found in early components as well. Word recognition studies investigated with ERP components found a difference between words and pseudowords reflected in the ERP as early as 112 ms, followed by a word frequency effect (Sereno, Rayner, & Posner, 1998). In most studies, however, early differences between words and pseudowords have been seen around 200 ms (Dehaene, 1995 as cited in Hauk et al., 2006; Hinojosa, Gomez-Jarabo, & Rubia, 1999; for review see Hinojosa, Martin-Loeches, & Rubia, 2001). Other researchers have found early neurophysiological differences between word categories (lexical vs. semantic), which suggests differential activation for lexical and semantic information (for example, Martin-Loeches, Hinojosa, Fernandez-Frias, & Rubia, 2001; Pulvermüller, Assadollahi, & Elbert, 2001). Taken together, these findings seems to suggest that brain activity is modulated by the meaning of a stimulus even at early processing stages.

1.7. Event-related Potentials Research on Memory and Epilepsy

When conducting research with children with benign well-controlled epilepsy, a different cortical activation pattern during a visual working memory task was found compared to controls (Myatchin, Mennes, Wouters, Stiers, & Lagae, 2009). Specifically, ERPs following target stimuli elicited higher amplitudes between 250 and 425 ms poststimulus in the epilepsy group, which coincided with time window of target-non-target stimulus discrimination in that task (Myatchin et al., 2009). This has been interpreted as increased processing effort for epilepsy patients compared to controls.

Studies with adult epileptic patients paint a different picture. In a study utilizing an auditory memory scanning paradigm with a sample of 17 temporal lobe epilepsy patients with complex partial seizures, a reduced amplitude of the N170 and prolonged latencies of the N290 waves were identified (Grippo et al., 1994). N170 wave in patients decreased further as memory load increased (Grippo et al., 1994). Simultaneously, longer reaction times and an increased slope of reaction time/set size relationship was found (Grippo et al., 1994). It was hypothesized that prolonged latencies reflect slowed processing time. Significant waveform alterations that occur this early support the hypothesis that abnormalities of early stages of processing may contribute to the memory difficulties experienced by TLE patients.

A follow-up study by Grippo et al. (1996) was conducted because intellectual differences between patient and control group existed in the previous one (cf. Grippo et al., 1994). Slower reaction times and reduced N170 amplitudes were identified again as well as a broad late negative shift between 577 and 735 ms in TLE patients. A subgroup of epilepsy patients with abnormal memory function showed a delayed P250 component, a delayed and attenuated N290 wave and abnormal positive shift between 262 and 315 ms after probe presentation. Additionally, there was a further positive shift between 315 and 420 ms as memory load increased (Grippo et al., 1996). This points toward substantial differences between epilepsy patients and controls early and later in the ERP waveform during a Sternberg Task.

Semantic memory processing of temporal epilepsy patients has similarly shown to be different, in that a reduced N400 amplitude under match and mismatch conditions was found (Miyamoto, Katayama, Kohsaka, & Koyama, 2000). Interestingly, there were no differences found in the late positive and contingent negative variation components (Miyamoto et al., 2000). Patients with left TLE did not have statistically significant effects of either word repetition or congruity on their ERPs (Miyamoto et al., 2000). The reduction

in N400 amplitude may indicate weaker strength of processing or even disturbed speech-based processing in epilepsy patients.

1.8. Sleep Quality

A significant factor that is crucial for physiological memory function and may also contribute to memory complaints is quality of sleep (Hancock & Larner, 2009). Many researchers have argued that sleep, specifically REM sleep, has an important role in memory, especially procedural and emotional memory (Bear et al., 2007; Maurer et al., 2013). Sleep is important for memory consolidation (and maybe integration) and stabilizes as well as enhances memory contents (for review see Diekelmann & Born, 2010; Bear et al., 2007; Maurer et al., 2013). For instance, depriving humans or rats of REM sleep can impair their ability to learn a variety of tasks, and some studies were able to show an increase in the duration of rapid eye movement (REM) sleep after an intense learning experience (Bear et al., 2007). In a different study by Karni, Tanne, Rubenstein, Askenasy, and Sagi (1994), participants were instructed to perform a task (identifying the orientation of a small line in peripheral vision) and showed performance improvement not only with practice, but also between evening and morning. This indicates a strengthening of memory during sleep for this type of learning. Additionally, there have also been suggestions that sleep deprivation influences encoding (Van Der Werf et al., 2009) which would subsequently negatively impact memory performance. More recent studies also point toward a connection between Non-REM sleep and declarative memory performance (Maurer et al., 2013). This is especially interesting as semantic memory was investigated.

A number of studies have reported on worse sleep quality of epilepsy patients (e.g., De Weerd et al., 2004; Ottman et al., 2011). Sleep disturbance, obstructive sleep apnea, insomnia and excessive daytime sleepiness (EDS) have all been shown to be quite common among epilepsy patients (Alanis-Guevara, Pena, Corona, Lopez-Ayala, Lopez-Meza, & Lopez-Gomez, 2005; Khatami, Zutter, Siegel, Mathis, Donati, & Bassetti, 2006; Maganti, Hausman, Koehn, Sandok, Glurich, & Mukesh, 2006; Piperidou et al., 2007) and it has been argued that sleep disturbance is more than twice as prevalent in patients with partial epilepsy than in controls (Kwan, Yu, Leung, Leon, & Mychaskiw, 2009). Epileptic patients have disrupted sleep with increased latency to sleep onset, increased number and duration of awakening, and increased duration of sleep stages 1 and 2 (Mendez & Radtke, 2001).

1.9. Subjective Memory

Over the last 300 years there has been little doubt that people with epilepsy suffer from memory impairment and it has been argued that epilepsy affects memory more than any other cognitive function (for review see Hall et al., 2009; Helmstaedter, Hauff, & Elger, 1998; Piazzini et al., 2001). Approximately 20-50% of patients with refractory epilepsy have poor memory (Hendriks, Aldenkamp, van der Vlugt, Alpherts, & Vermeulen, 2002) and epilepsy patients report that memory difficulties have one of the greatest adverse effects on their quality of life (Fisher et al., 2000). Despite the overwhelming body of literature on the existence of memory problems in people with epilepsy, a plethora of studies were not able to find a significant relationship between subjective memory complaints and performance on neuropsychological/objective memory tests and measures (Sunderland, Harris, & Baddeley, 1983*;* Vermeulen, Aldenkamp, & Alpherts, 1993) and several studies found a surprising lack of correlation between the two (Elixhauser et al., 1999; Marino et al., 2009; Piazzini et al., 2001; Thompson & Corcoran, 1991). For example, some studies have shown that TLE patients present with memory complaints, but perform adequately when assessed objectively with standardized memory tasks (Gallassi, Morreale, Lorusso, Pazzaglia, & Lugaresi, 1988; O'Shea, Saling, Bladin, & Berkovic, 1996). Conversely, patients with deficient test performance sometimes do not complain (Gleißner, Helmstaedter, Quiske, & Elger, 1998). Overall, there is no strong imperative to assume that objective performance on psychometric tests correlates highly or consistently with subjective memory (Hall et al., 2009).

The reason for this “no-correlation-effect” has been the topic of much debate and it has been suggested that self-reports may reflect objective impairment of specific memory components such as verbal and visual short-term memory but not of abstract reasoning, fluency or shifting attitudes which are the focus of many neuropsychological measures (Giovagnoli, Mascheroni, & Avanzini, 1997). Another possible explanation is that self-reports correlate with memory test scores, but not with those usually used to explore frontal functions (Thompson & Corcoran, 1991). An alternative possibility is the confounding influence of mood on self-reported memory performance and it has been argued that affective status explains more variance in subjective memory complaint than objective memory performance (O’Shea et al., 1996). Due to the high complexity of this issue, it was decided to include and analyze several memory self-report measures and monitor relationships with objective memory performance.

2. Hypotheses and Aims

Current ERP research on memory and epilepsy patients has focused primarily on the P3 component, postsurgical and AED-dependent impacts (e.g., Grippo et al., 1994; Grippo et al., 1996). However, the contribution of deficits in early visual processing has rarely been explored. The present work contributes to this gap in knowledge by monitoring early processing during a Sternberg Task and a Lexical Decision Task in epilepsy patients with poor treatment outcome. To effectively distinguish among different stages of information processing and how this has an impact on memory, the event-related potential technique was employed. The high temporal resolution of ERPs was considered especially advantageous to investigate early perceptual stages and memory-related operations. The aim of this study is therefore to identify ERP components sensitive to group differences and to clarify if and how early processing stages are disrupted. We were specifically interested in the possible contribution of early visual-processing deficits as they may cause a delay for all subsequent information processing including memory retrieval and output. Neuropsychological Tests were used beforehand to estimate the presence of memory differences between the groups on a behavioral level. Sleep quality was investigated as well to estimate the influence of sleep as a potential moderator variable. Additionally, self-report of memory problems was investigated with questionnaires, since research has shown that performance on objective tests may not correspond to self-report of memory functioning in epilepsy patients.

The following hypotheses are proposed:

Hypothesis 1: Moore and Baker (2002) have shown that epilepsy patients demonstrate difficulties when performing memory and language tasks. These findings have been corroborated by Oyegbile et al. (2004) who found worse memory function and worse performance across measures of intelligence, language and executive function in a sample of epilepsy patients with intractable temporal lobe epilepsy. Therefore it was hypothesized that epilepsy patients have lower scores on working memory and semantic memory tests compared to controls, in paper pencil and EEG format.

Hypothesis 2: Grippo et al. (1994) as well as Miyamoto et al. (2000) have investigated epilepsy patients' memory problems with event-related potentials and have shown prolonged reaction times for patients in working and semantic memory tasks, respectively. Based on these findings, the second hypothesis proposes that epilepsy patients have slower reaction times on working and semantic memory EEG tasks compared to controls.

Hypothesis 3: In their investigation of epilepsy patients' ERPs during memory tasks, studies by Grippo et al. (1994, 1996) and Miyamoto et al. (2000) have shown decreased amplitudes and longer prolonged latencies for patients. Hence, it was hypothesized that N1 and P1 components have longer latencies and decreased amplitudes in epilepsy patients compared to controls.

Hypothesis 4: As De Weerd et al. (2004) and Ottman et al. (2011) have found worse quality of sleep reports in epilepsy patients and sleep problems seem to be quite common among this patient group (Alanis-Guevara et al., 2005; Kwan et al., 2009), it was hypothesized that epilepsy patients report worse sleep quality than controls.

Since past research has shown that epilepsy patients will not evaluate their memory performance accurately, different subjective memory measures have been employed to investigate the relationship between different subjective memory measures and actual objective performance on working memory and semantic memory tests.

B. Methodology

In line with the "3-Ebenen-Ansatz", three different levels of analysis have been included in this investigation, (a) the physiological level, (b) the behavioral level, and (c) the subjective level (Birbaumer, 1975 as cited in Trimmel, 1990).

1. Design

The study followed a cross-sectional, quasi-experimental two-group design, consisting of a patient group (epilepsy patients) and a control group (healthy individuals). Control group was matched for gender and age (+/- 4 years) to control for both of these variables. For the neuropsychological tests, dependent variable consisted of the mean accuracy score (correct answers), and independent variable was group. Paired t-tests were used to analyze group differences. Behavioral data of the EEG-Paradigms were analyzed in the same way, with dependent variables being reaction time and accuracy score (correct answers) and the independent variable being group. With regard to the physiological data, dependent variables were amplitudes and latencies of the components under investigation and independent variables were group (between-subjects-factor), stimuli (within-subjects-factor), paradigm (within-subjects-factor), and location (within-subjects-factor). These factors were investigated via a Mixed ANOVA for each component with group as between-subjects factor. Amplitudes and latencies were analyzed separately. Concerning analysis of questionnaire data, the dependent variable constituted PSQI score (where higher scores represent more severe sleep problems), and independent variable was group. Group differences were analyzed via paired t-test. For the self-report memory measures, self-report scores were analyzed, with higher scores indicating more subjective memory problems. Each of these self-report measures' relationship with objective memory performance was assessed by the Spearman correlation coefficient for each group.

2. Materials and Procedure

2.1. Basic Information

2.2.1. Socio-demographic Information

Demographic data and social variables including date of birth, gender, marital status, education, employment, nationality, and mother tongue were collected with a questionnaire created for the study designed by Weberberger (2014) and Ifkovits (2014).

2.2.2. Handedness

Handedness was established via a handedness quotient on the Edinburgh Handedness Inventory (Oldfield, 1971). A quotient of ≥40 indicates right-handedness, ≤40 indicates left-handedness, and subjects with a quotient between the two are considered ambidextrous.

2.2.3. Language Ability Test

To make sure poor performance on memory measures were not due to low language ability levels, a language ability test was given to participants. Spelling, vocabulary and grammar were investigated (Derungs, n.d.). Exclusion criteria was a score of less than 90 percent (less than 18 out of 20).

2.2. Neuropsychological Tests

Subjects were given questionnaires and tests individually with the whole process lasting 30 minutes maximum. Tests and questionnaires were given to each participant in the same order, to avoid any other interference on performance.

2.2.1. Subtest Verbal Working Memory

The Verbal Working Memory measure used is a subtest of the "Inventar zur Gedächtnisdiagnostik" (IGD; Baller, Brand, Kalbe, & Kessler, 2006). The instructor read a list of words out loud, and participants were instructed to memorize only words containing the letter *r*. Half of these words were targets (words with *r*: Schnur, Sturm, Becher, Traube, Reifen, Karton, Mauer), half were distractors (words without *r*: Fahne, Küste, Zweig, Weste, Blüte, Biene, Tasche). After the instructor was finished reading, participants were instructed to write down all of the memorized words containing *r* on a piece of paper with a time limit of 45 seconds. The whole procedure was repeated three times, i.e., there were three "trials", with word list and instructions remaining the same.

2.2.2. Subtest Identical Word Meaning

The subtest Identical Word Meaning is part of the Wilde Intelligence Testing-2 battery (Kersting, Althoff, & Jäger, 2008) and was used to measure semantic (long term) memory. For each of 20 words in total, participants were asked to identify, out of five alternatives, the word with the most similar/identical meaning. A time limit of 90 seconds was set for each participant. This task was chosen due to its similarity to other semantic memory measures used in previous studies (cf. Messas et al., 2008; Smith & Lah, 2011).

2.3. EEG Paradigms/Experimental Procedure

2.3.1. Sternberg Task

To measure Verbal Working Memory during EEG recording, a modified Sternberg Task (Chao & Knight, 1996; Ergen, Yildirim, Uslu, Gürvit, & Demiralp, 2012; Sternberg, 1966) with words was created similar to the continuous memory recognition task in Papanicolaou et al. (2004; task designed by Dr. Karin Trimmel and already used previously by Weberberger (2014)). In line with classic recognition paradigms, participants were asked to memorize and later recognize a set of five words, a paradigm which has been used to illicit old-new ERP effects in the past (Ergen et al., 2012; Guo, Duan, Li, & Paller, 2006). The task consisted of a study/encoding phase and a recognition/retrieval phase. In the former, participants were asked to memorize a list of five consecutively presented words (Freiheit, Meinung, Beweis, Vorteil, Gedanke), in the latter, participants had to indicate whether the word was one of the memorized set or not. Words were German nouns rated three or less on the abstract-concreteness mean scale by Paivio, Yuille, and Madigan (1968) and had a word frequency of 9 to 21 per million of words.

The study/encoding phase started with a notice to click once to start and to memorize the following five words ("Zum Starten bitte klicken! Bitte merken Sie sich die folgenden 5 Wörter!"). Words were presented for 1000 ms each with a randomized 1500-2200 ms Interstimulus Interval (ISI) between stimuli. The study/encoding phase lasted no more than 20 seconds in total. When neither stimuli nor instructions were present, a white colored central fixation cross was displayed in the middle of the screen to minimize eye movement and indicate stimulus location.

The retrieval/recognition phase started with a notice to click once to start the first trial („1. Durchgang. Zum Starten bitte klicken!"). Participants were then presented with a list of 10 words presented one at a time. For each word, a recognition judgment had to be made, i.e., participants had to click a green colored left mouse button with a "J" for "Ja" response (yes, item belongs to previously memorized set) and a red colored right mouse button with "N" for "Nein" response (no, item does not belong to memorized set/is a new word). In each trial, 5 memorized items (targets) were randomly interspersed with 5 new items (distractors). Distractors, i.e., new words not on the previously presented study list, were chosen according to the same criteria as targets (see above). Sequence of stimuli was balanced and pseudorandomized.

After the first trial, a notice appeared on the screen to click once to start the second trial ("2. Durchgang. Zum Starten bitte klicken!"). This notice appeared before each new trial. In total, the retrieval/recognition phase was divided into 9 trials with 10 probes per trial. Overall, forty-five words served as target (memorized words) and 45 words served as distractor stimuli (new words). Words were presented for 1000 ms each with a randomized 1500-2200 ms Interstimulus Interval (ISI) between stimuli (See Figure 2). The recognition phase took no more than 5 minutes. When neither stimuli nor instructions were present, a central fixation cross was displayed in the middle of the screen to minimize eye movement and indicate stimulus location.

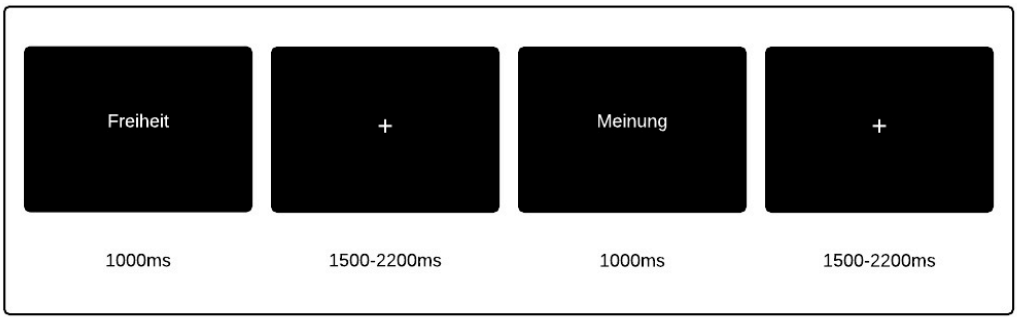

Figure 2. Experimental Paradigm, Sternberg Task. ISI and word presentation time are displayed as well as an example of a target and a distractor item.

2.3.2. Lexical Decision Task

Participants were instructed to decide whether a given word was a word that actually existed in the German language or was a pseudoword/nonword. Lexical Decision Tasks are a good way to measure semantic memory (f.e., Frishkoff, Perfetti, & Westbury, 2009). The task was created based on previous research, designed by Dr. Karin Trimmel and already used previously by Ifkovits (2014). Forty-eight rare words with low word frequency were chosen via the search engine „COSMAS II" (Institut für Deutsche Sprache, n.d.). Words taken into analysis were exclusively words occurring one to five times per million words in the German language and consisting of four to six letters (16 words with four, five, and six letters each; Wagenmakers, Steyvers, Raaijmakers, Shiffrin, van Rijn, & Zeelenberg, 2004). Forty-eight pseudowords were created from rare words as well, also consisting of 16 words with four, five, and six letters each (Barca & Pezzulo, 2012; Wagenmakers et al., 2004). The procedure for creating pseudowords was as follows: in words with one syllable a vowel or a consonant was replaced with a different vowel or a different consonant, respectively. For words with two or more syllables, two or more letters were replaced (Albrecht & Vorberg, 2010; Jones, Marsh, & Hughes, 2012;

Wagenmakers et al., 2004). All pseudowords were pronouncable and orthographically similar to „real“ words (Barca & Pezzulo, 2012; Curran, 1999; Wagenmakers et al., 2004). The decision regarding the number of words/pseudowords were based on previous research (e.g., Albrecht & Vorberg, 2010; Barca & Pezzulo, 2012).

The lexical decision task was presented on a computer screen. Words were presented for 1000 ms each with a randomized 1500-2200 ms ISI between stimuli (see Figure 3). When neither stimuli nor instructions were present, a white-colored central fixation cross was displayed in the middle of the screen to minimize eye movement and indicate stimulus location. If participants believed the word was an actual word, they were instructed to click on a green colored left mouse button with a “J” for “Ja” response (yes, item is a real word). If participants believed the presented stimulus was not a real word, they clicked a red colored right mouse button with “N” for “Nein” response (no, word is not a real word).

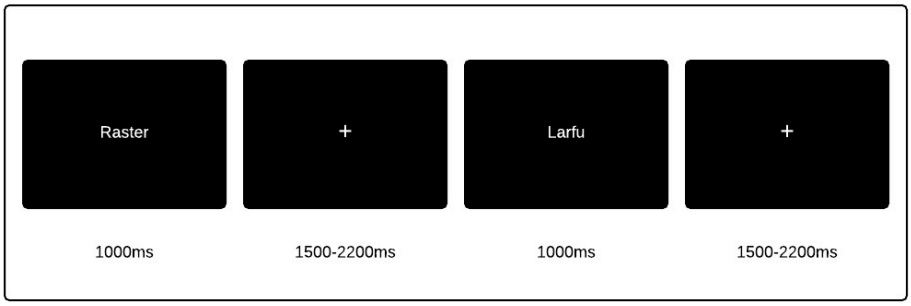

Figure 3. Experimental Paradigm, Lexical Decision Task. ISI and word presentation time are displayed as well as word and nonword examples.

A practice trial preceded the actual lexical decision task, in which four stimuli (two words and two pseudowords) were presented. This was done to ensure that participants understood instructions. If this was the case, the lexical decision task was initiated. Overall, the lexical decision task lasted five minutes and 20 seconds.

2.4. Questionnaires

2.4.1. The Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) is one of the most frequently used standardized measures to assess subjective sleep quality (Doi et al., 2000). It was included to measure sleep quality during the previous month. This instrument has been previously adapted to German (Riemann & Backhaus, 1996) and has been validated showing good sensitivity and specificity (Doi et al., 2000; Fichtenberg, Putnam, Mann, Zafonte, &

Millard, 2001; Wittchen et al., 2001). The PSQI total score has also shown good reliability (Cronbach's alpha = .77; Doi et al., 2000). A total of 18 items were used to evaluate seven components of sleep quality: sleep efficiency, frequency of sleep disturbance, sleep latency and duration, day dysfunction due to sleepiness, overall sleep quality and medication use. Each component is rated on a 0–3 severity scale referring to the frequency of each disturbance (0 = not in the past month, 1 = less than once a week, 2 = once or twice a week, 3 = three or more times a week). The PSQI provides a global score with a range of 0–21, with higher scores indicating more sleep complaints.

2.4.2. Subjective Memory Questionnaire

Four subjective memory measures from four different past studies were integrated into one subjective memory questionnaire put together by the author: A Visual Analogue Scale (100 mm in length; 10-point-Likert scale) was the first item on the memory questionnaire. This scale was consistent with the one used by Andelman, Zuckerman-Feldhay, Hoffien, Fried, and Neufeld (2004). Each subject was asked to provide an overall rating of his/her memory on a scale of 0 to 100 with 0 referring to the worst possible memory ("sehr schlechtes Gedächtnis") and 100 referring to the best possible memory ("sehr gutes Gedächtnis"). The next item on the questionnaire was a four-category rating item where subjects rated the degree to which their memory was a nuisance in everyday life, ranging from not a nuisance, mild, moderate, to severe nuisance ("Wie sehr beeinträchtigt Sie ihr Gedächtnis im Alltag?" "gar nicht", "etwas", "mäßig", "sehr"; also used by Blake, Wroe, Breen, & McCarthy, 2000). This item was coded on a 1-4 severity scale, with 1 indicating that memory was a severe nuisance in everyday life and 4 indicating that memory was not a nuisance. The last items were taken from the Quality of Life in Epilepsy Inventory (QOLIE-89, Version 1.0; Devinsky et al., 1995). The first item asked participants to circle a number from 1 to 4 indicating if they had any trouble with their memory in the past four weeks (1 = yes, a great deal to 4 = no, not at all; "Hatten Sie in den letzten 4 Wochen Probleme mit Ihrem Gedächtnis?" "1= ja, sehr große Problem", "4 = nein, überhaupt nicht"). For the subsequent four items, participants had to circle a number from 1 to 6 for how often in the past weeks they had trouble remembering (a) names of people, (b) where they put things, (c) things people tell them, and (d) things they read hours or days before (1 = All of the time, " = most of the time, 3 = a good bit of the time, 4 = some of the time, 5 = a little of the time, 6 = none of the time).

3. Sample description/Participants

Patients participating in the study were diagnosed with focal epilepsy (mostly temporal lobe epilepsy, TLE) and were in the process of being evaluated for epilepsy surgery at the General Hospital Vienna ("Allgemeines Krankenhaus Wien"). All patients suffered from medically refractory seizures despite treatment with Antiepileptic Drugs (AEDs) and as such remained drug resistant. All participants, except two in patient and one in control group were right-handed as defined by a handedness quotient $\geq$40 on the Edinburgh Handedness Inventory (Oldfield, 1971). For the EEG-Analysis, only right-handed individuals were included. None of the participants had a language ability score lower than 90 percent. Patients had no other neurological diseases involving the central nervous system (CNS). Healthy individuals were matched for gender and age (+/- 4 years) as the control group. The study was approved by the Ethics Committee of the Medical University of Vienna.

4. EEG Data Recording and Analysis

EEG signals were recorded with a DC-amplifier system and the software "BrainVision Recorder Version 1.20" (Brain Products, Germany) from 64 electrodes in standard locations covering the whole scalp (Jasper, 1958) and referenced to electrode FCz. Three additional electrodes were attached, two below both eyes to measure horizontal eye movements (HEOGs) and one beside the right eye to monitor vertical eye movements and eye blinks (VEOG). Continuous EEG was recorded at 1000 Hz sampling rate (measurement every .001 seconds).

The EEG data were analyzed for ERPs with the "BrainVision Analyzer software 2.0.4.368" (Brain Products, Germany). Offline, a common average reference was applied and EEG was filtered between 0.1 and 10 Hz (12 dB/octave, Butterworth Zero Phase Filters) and a notch filter of 50 Hz was applied. Eye movement and blink artifacts were corrected semiautomatically, with eye artifacts being selected automatically and then visually inspected for accuracy afterwards. The continuous EEG signal was divided into epochs from 100 ms before to 1000 ms after stimulus onset. Epochs were corrected relative to a 100 ms pre-stimulus baseline. Only correct response trials were included in the ERP averages. Trials with eye artifacts, response errors, body movements/EMG activity during epoch and prestimulus baseline were excluded from analysis. Epochs were averaged separately for each condition in both tasks. All subjects with less than 30 trials per stimulus type (because of artifacts or incorrect responses for each stimuli/probe type), and all left-

handed individuals were excluded from analysis. Overall, 23/25 patients and 28/27 controls were included for analysis in the Sternberg and Lexical Decision task.

C. Results

1. Descriptive Analysis

Thirty-eight healthy controls (20 males and 18 females, average age 37.24, 37 right handed and 1 left handed, mean number of education years 13.85) were recruited and matched for age and gender to epilepsy patients. Thirty-four patients with a diagnosis of epilepsy participated (18 males, 16 females, average age 38.8, 32 right handed and 2 left handed, mean number of education years 11.08). In over half (23 patients) epileptogenic focus was found within the temporal lobe, three had frontal lobe foci, one parietal and seven unspecified (see Table 1).

Table 1.
Clinical Data of Epilepsy Patients

Patient	Age	Epilepsy	Side	Focus	Classific.	Duration(yr)	Seizure Frq.*	Seizure Frq. **	Onset
VP07	25	TLE	left	temporal	n. lesional	7.00	up to 10/m	0/y	18th ly
VP14	45	TLE	-	temporal	n. lesional	40.67	.3-.5/m	0/y	5th ly
VP15	26	-	right	unspec.	n. lesional	15.42	15-25/m	0/y	11th ly
VP19	56	TLE	left	temporal	mesial	55.58	2-3/3 m	2-3/y	1st ly
VP20	38	TLE	right	temporal	n. lesional	12.67	unclear	216/y	26th ly
VP21	60	TLE	right	temporal	structural	42.42	5/m	unclear	18th ly
VP22	38	FLE	left	frontal	sturctural	26.67	30/m	0/y	12th ly
VP23	29	TLE	right	temporal	n. lesional	2.58	8-12/m	0/y	27th ly
VP24	52	TLE	right	temporal	mesial	48.33	6-9/m	1/y	4th ly
VP25	32	PLE	right	parietal	n. lesional	18.67	5/m	0/y	14th ly
VP26	46	TLE	right	temporal	mesial	43.00	2/m	0/y	3rd ly
VP27	37	TLE	right	temporal	n. lesional	19.25	4/m	0/y	18th ly
VP28	34	TLE	left	temporal	mesial	9.08	3-5/m	0/y	25th ly
VP29	26	FLE	right	frontal	DVA	13.17	unclear	12/y	13th ly
VP30	20	-	right	unspec.	n. lesional	16.33	unclear	4-6/y	4th ly
VP31	38	FLE	left	frontal	structural	.58	.7/m	0/y	38th ly
VP32	38	TLE	right	temporal	structural	1.75	12/m	0/y	37th ly
VP33	30	-	left	unspec.	n. lesional	9.08	4/m	4/y	21st ly
VP34	34	TLE	left	temporal	n. lesional	20.67	.12-.24/m	0/y	14th ly
VP35	50	-	-	unspec.	structural	31.67	3/m	0/y	19th ly
VP43	26	TLE	right	temporal	structural	1.00	2-5/m	0/y	25th ly
VP45	23	-	right	unspec.	n. lesional	3.00	12-16/m	1/y	20th ly
VP46	54	TLE	left	temporal	mesial	35.00	3-4/m	6/y	19th ly
VP48	48	-	right	unspec.	n. lesional	1.00	4-8/m	0/y	47th ly
VP49	52	TLE	right	temporal	n. lesional	6.00	1/m	6/y	46th ly
VP50	32	TLE	right	temporal	mesial	5.00	12-16/m	0/y	27th ly
VP52	23	TLE	left	temporal	mesial	6.00	28-84/m	0/y	17th ly
VP54	54	TLE	left	temporal	n. lesional	18.00	unclear	6/y	36th ly
VP55	32	-	L+R	unspec.	structural	10.00	5-45/m	0/y	22nd ly
VP56	30	TLE	left	temporal	structural	-	28/m	0/y	30th ly
VP63	65	TLE	left	temporal	structural	3.00	1-3/m	0/y	62nd ly
VP64	20	TLE	left	temporal	structural	0.4	0.16/m	2/y	20th ly
VP65	57	TLE	left	temporal	mesial	51.00	4-8/m	0/y	6th ly
VP67	50	TLE	left	temporal	structural	28.00	2-6/m	3/y	22nd ly
M±SD	38.8±12.7					18.24±16.6	9.3±12.05	8±37.4	21.4±13.6

Note. Side = hemisphere of epileptogenic zone; focus = lobe of epileptogenic zone; ly = life years; duration = years between epilepsy onset and test date

Fourteen patients showed no epileptogenic lesion, in eleven a structural abnormality such as a tumor or other lesion was found. Hippocampal sclerosis and/or

atrophy could be identified in eight patients (mesial TLE). The average duration of the seizure disorder was 18.24 years (*SD* = 16.6, range 0.4 to 55.58 years). The estimated mean number of complex partial seizures per month was 9.3 (*SD* = 12.05, range 1-2 per year to 1-3 per day). Six patients were on antiepileptic drug (AED) monotherapy, the remainder were on polytherapy.

2. Behavioral Analysis

2.1. Neuropsychological Tests

As hypothesis was directional based on previous research, a paired one-tailed t-test each was carried out for the "Verbal Working Memory" and the "Identical Word Meaning" test. Assumptions of normality distribution for differences were met.

2.1.1. Subtest "Verbal Working Memory" (IGD, Inventory for Memory Assessment)

There was a significant effect for group, $t(33) = -4.13$, $p = .000$, with control group receiving higher scores than patient group (see Table 2).

Table 2.
Means and S.D.s of psychological test scores and EEG paradigms for patients and controls

	Controls				Patients	
	n	Mean	S.D.	*p*	Mean	S.D.
Psychological Tests						
Verbal Working Memory test	34	17.4	2.5	**	14.26	3.5
Identical Word Meaning test	34	15.3	3.8	**	9.8	4.36
EEG Paradigms						
Sternberg T. Score	32	86.09	6.8	*	82.3	9.7
Lexical Dec. T. Score	31	94.26	3.1	*	92.8	2.94
Sternberg T. RT	32	.735	.096	*	.786	.12
Lexical Dec. T. RT	31	.82	.19	*	.95	.24

Note. * $p < .05$, ** $p < .001$.

2.1.2. Subtest "Identical Word Meaning" (WIT-2, Wilde intelligence testing-2)

There was a significant effect for group, $t(33) = 4.69$, $p = .000$, with control group receiving higher scores than patient group (see Table 2).

2.2. EEG Paradigms

Paired one-tailed t-tests (directional hypothesis) were carried out on reaction times and accuracy of response (sum of correct responses) in both Sternberg and Lexical decision tasks. Reaction times (RTs) and responses were recorded online for all the

participants. Subjects who did not respond or misunderstood the task had to be excluded from analysis. Assumptions of normality of differences were met.

2.2.1. Sternberg Task

Two one-tailed paired *t* tests revealed that reaction times were significantly faster in the control group compared to the patient group ($t(31) = -1.95$, $p = .03$) and that controls reached a significantly higher mean accuracy score than patients ($t(31) = 1.85$, $p = .037$). In other words, controls reacted more quickly and accurately than patients (see Table 2).

2.2.2. Lexical Decision Task

Two paired *t* tests (one-tailed) were performed. There was a significant effect for group, $t(30) = 1.75$, $p = .046$, with control group having more correct responses than patient group. As with the Sternberg task, control group also showed significantly faster reaction times than patient group $t(30) = -2.27$, $p = .015$ (see Table 2).

Table 2 demonstrates that the overall accuracy was significantly lower in patients than controls in all memory measures. Analyses of reaction times show that controls also had faster reaction times in both EEG paradigms. Figure 4 was created to visualize these results, showing how control group has more correct responses across all memory measures. It also shows that Paper-Pencil tests evoked greater differences between groups, while also being more difficult overall. This was by design, since a sufficient number of correct trials were need for ERP analysis.

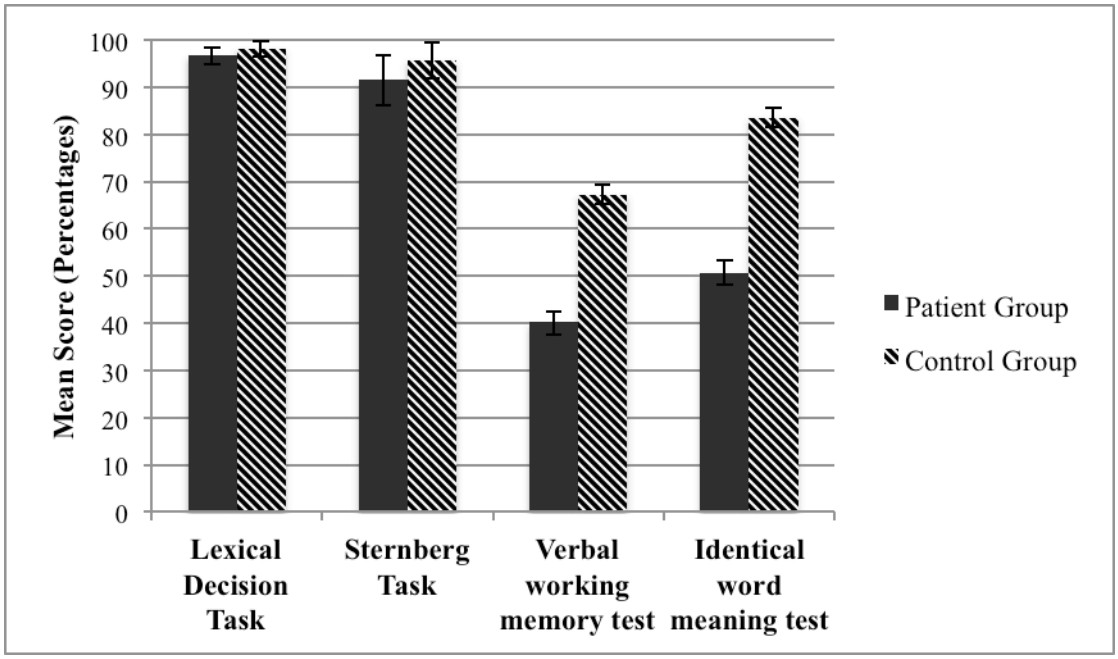

Figure 4. Average percentage of correct responses per group in each task and corresponding standard errors.

3. ERP Analysis

Upon visual inspection of ERP grand averages, time windows for P1 and N1 components were defined as 70–130 ms and 100–230 ms, respectively. As P1 and N1 peaks were rather well-defined, peak amplitudes and peak latencies for these were measured and considered as dependent variables in statistical analyses (cf. Handy, 2005). Independent variables were group (between-subjects-factor: control group vs. epilepsy group), stimuli (within-subjects-factor: memorized word/word vs. new word/pseudoword), paradigm (within-subjects-factor: Sternberg Task vs. Lexical Decision Task), and location (within-subjects-factor: POz/Oz for N1, O1/O2 for P1). Twox2x2 Mixed ANOVAs were applied to the two aforementioned components in the ERP data analysis. To measure effect size, partial etas squared were reported. Significance levels were set at the conventional level (.05). As P1 and N1 are reported largely over parieto-occipital areas and the generators of N1 and P1 are assumed to be in this region (Hopf et al., 2002; Warbrick, Arrubla, Boers, Neuner, & Shah, 2013), electrodes of interest were located in this area and subsequently included in the analysis. Specifically, electrodes POz and Oz were included for N1 analysis and electrodes O1 and O2 for P1 analysis. After exclusion of left-handed individuals and participants with fewer than 30 trials, 23 epilepsy patients and 28 controls were included in N1 component analysis. Twenty-five epilepsy patients and 27 controls were included in P1 component analysis. Difference in sample sizes between P1 and N1 component is due to different electrode selection.

3.1. ERP Tasks

Figure 5 and Figure 6 show the grand average ERP waveforms for the Sternberg Working Memory Task and the Lexical Decision Task at the occipital and parietal-occipital sites included in analysis in response to the two stimulus types. They represent a summary of the between and within-group effects for the P1 and N1 components described below. Curves are displayed from 100 ms before stimulus to 1000 ms after stimulus. The first prominent peak occurs around 100 ms, followed by a negative deflection around 160 ms. Negative is poled upwards. Figure 7 and Figure 8 provide an overview of all grand average ERPs across the scalp for the Sternberg Working Memory Task and the Lexical Decision Task, respectively. Figures were exported from the Brain Vision Analyzer software 2.0.4.368. Lines blue/black indicate target and distractor conditions for the control group, lines green/red indicate target and distractor conditions for the epilepsy group.

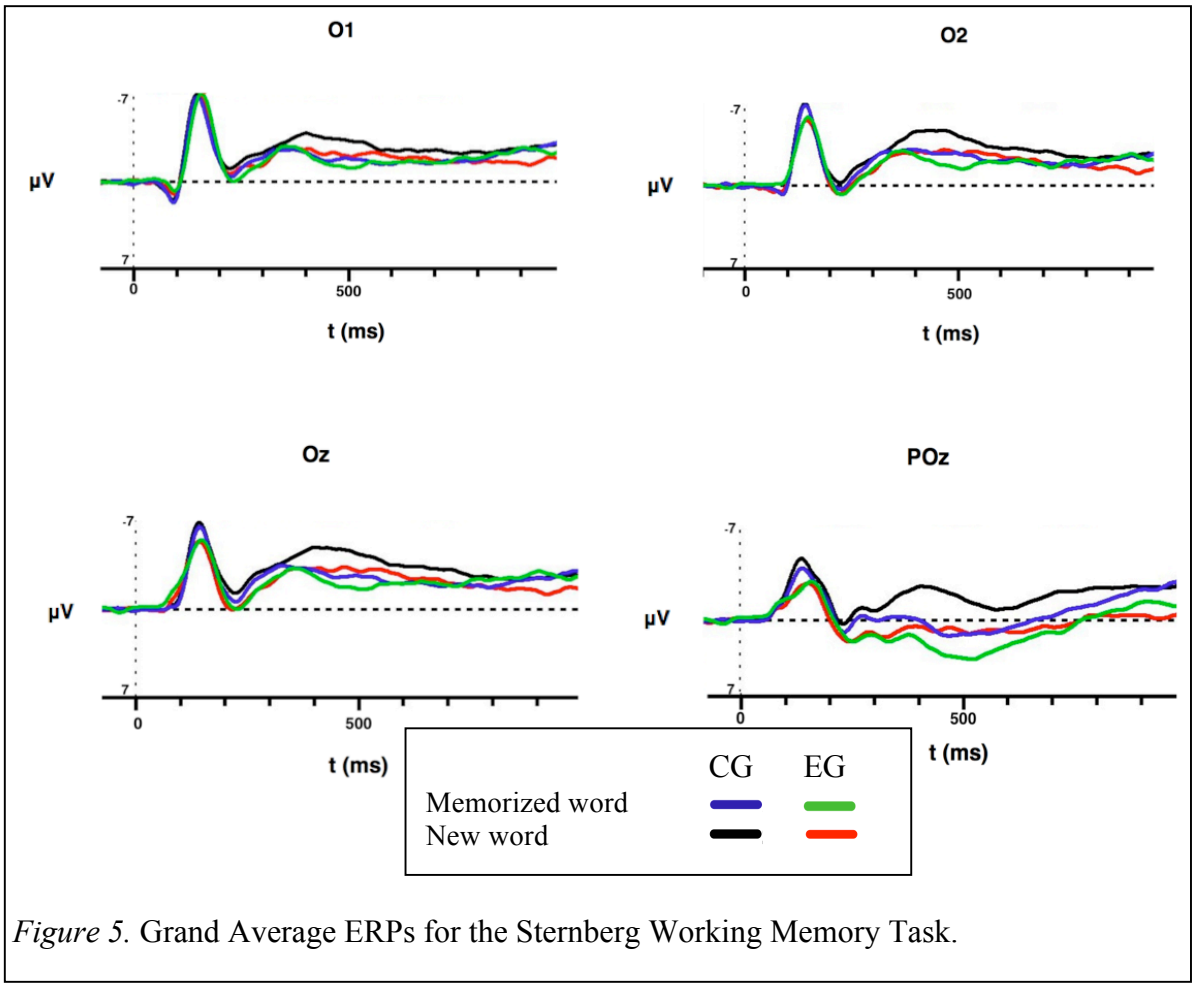

Figure 5. Grand Average ERPs for the Sternberg Working Memory Task.

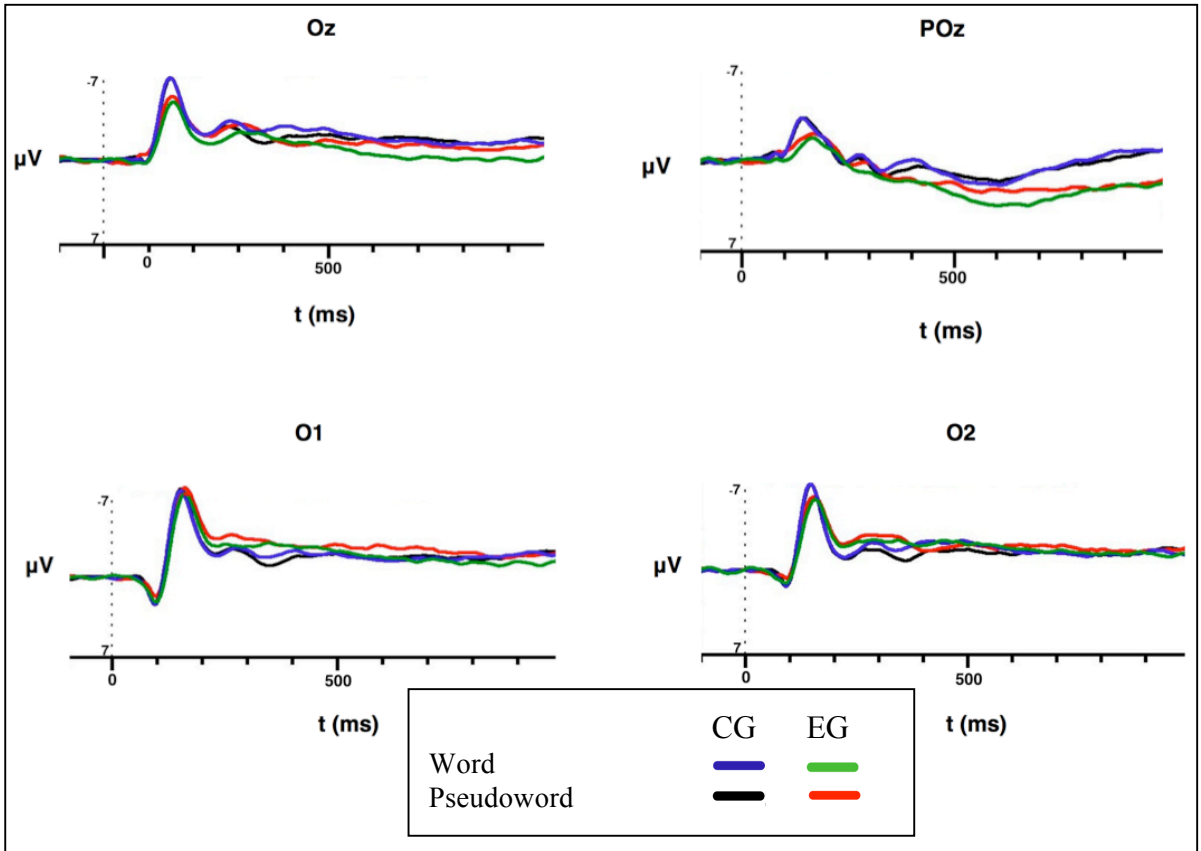

Figure 6. Grand Average ERPs of the Lexical Decision Task.

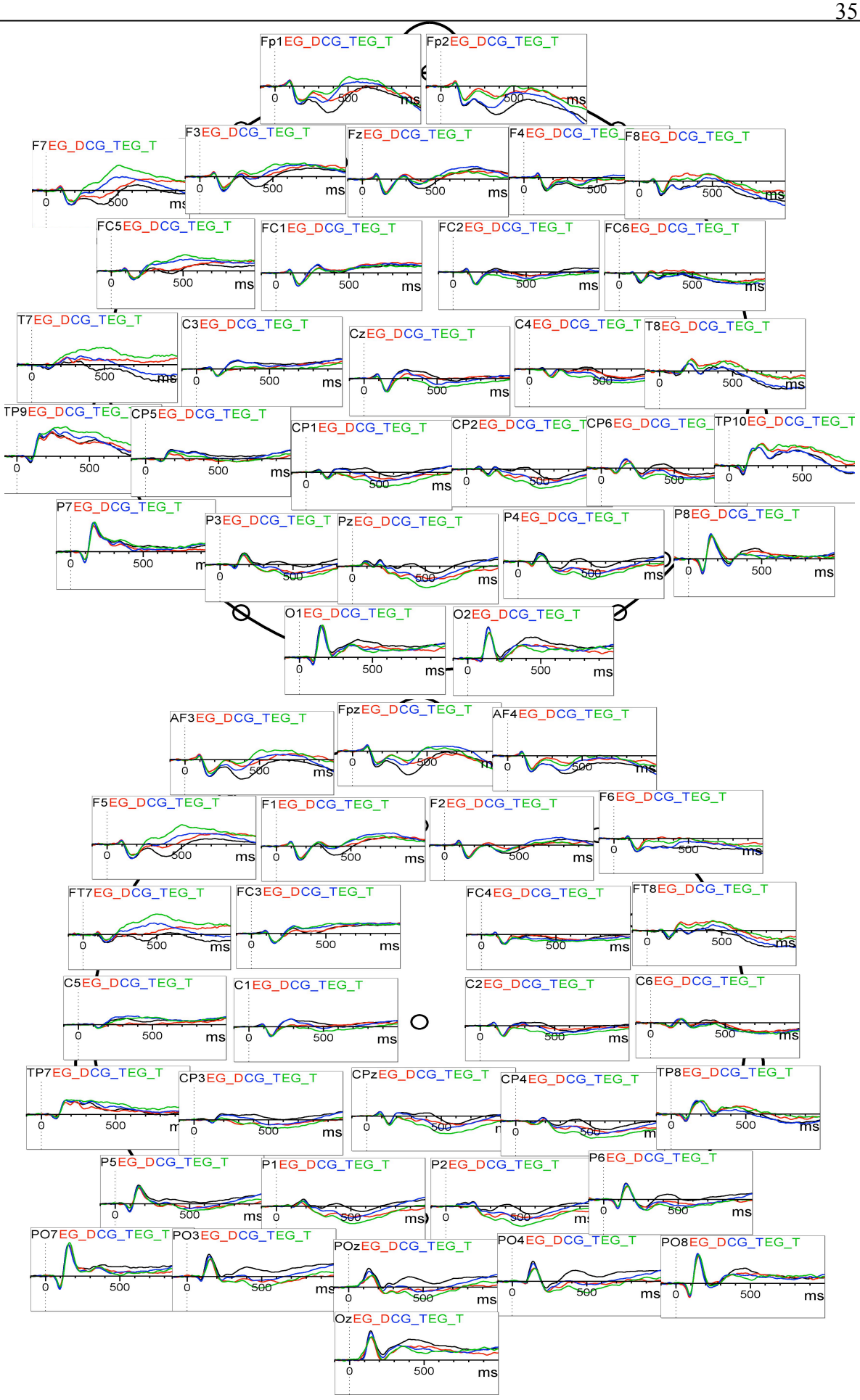

Figure 7. Grand Average ERPs for the Sternberg Working Memory Task across the scalp.

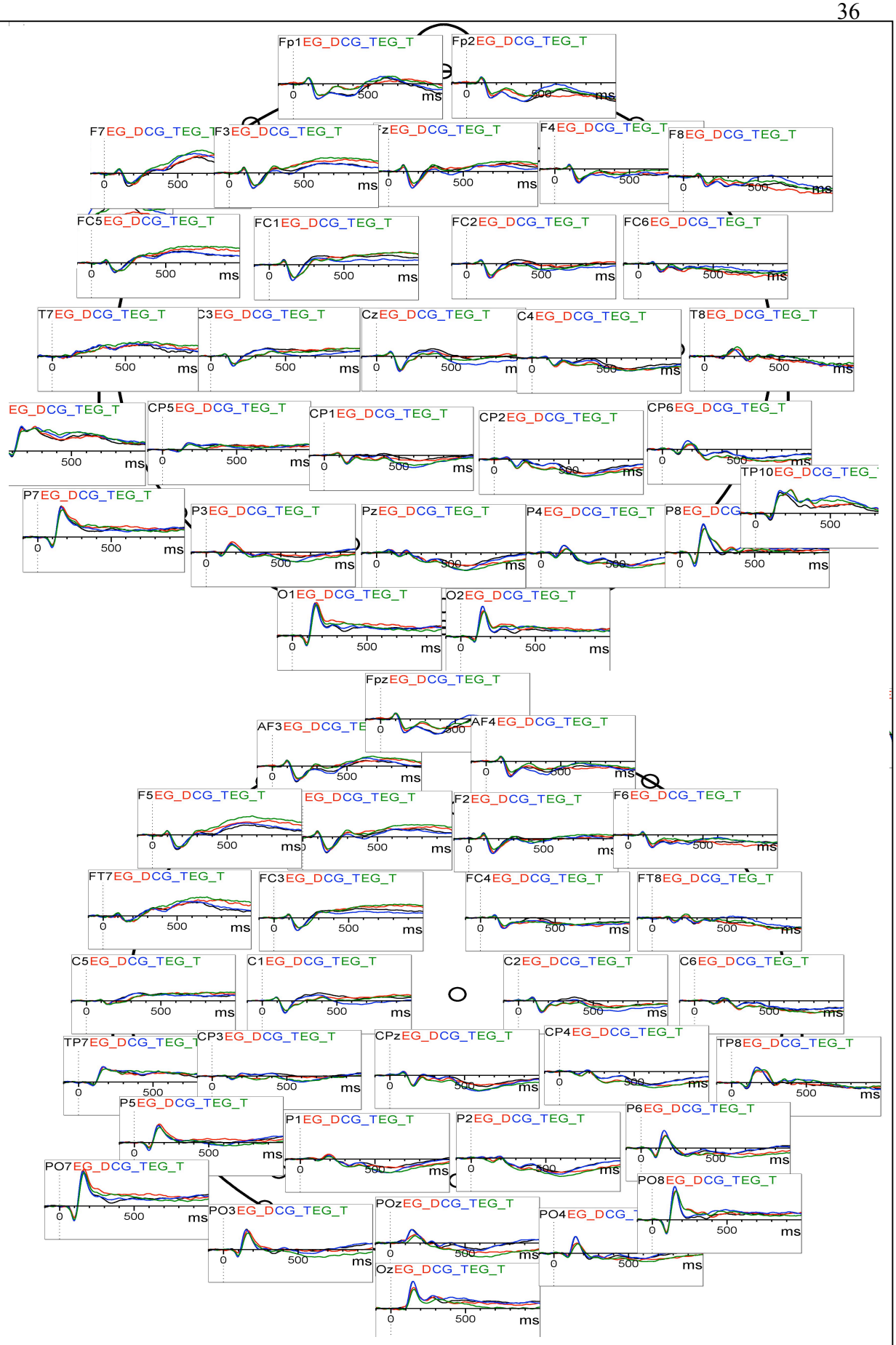

Figure 8. Grand Average ERPs for the Lexical Decision Task across the scalp.

The P1 (70-130 ms)

A 2 (group: control vs. patient) x 2 (stimuli: target vs. distractor) x 2 (paradigm: Sternberg Task, Lexical Decision Task) Mixed ANOVA was performed on peak amplitude and peak latency each. Regarding P1 amplitude analysis, assumptions of homogeneity of variances were met (Levene's Test: for Sternberg Task-Target, Lexical Decision Task-Target, Sternberg Task-Distractor, and Lexical Decision Task-Distractor $p = .42$, $p = .71$, $p = .07$, $p = .08$, respectively). A significant stimuli x paradigm x group interaction was found ($F(1, 50) = 4.18$, $p = .046$, partial $\eta^2 = .077$), with control group showing larger amplitudes than patient group (see Figure 9). Interestingly, while control group showed larger amplitudes for memorized words in the Sternberg Task, epilepsy group showed larger amplitudes for new words in this paradigm (see Figure 9).

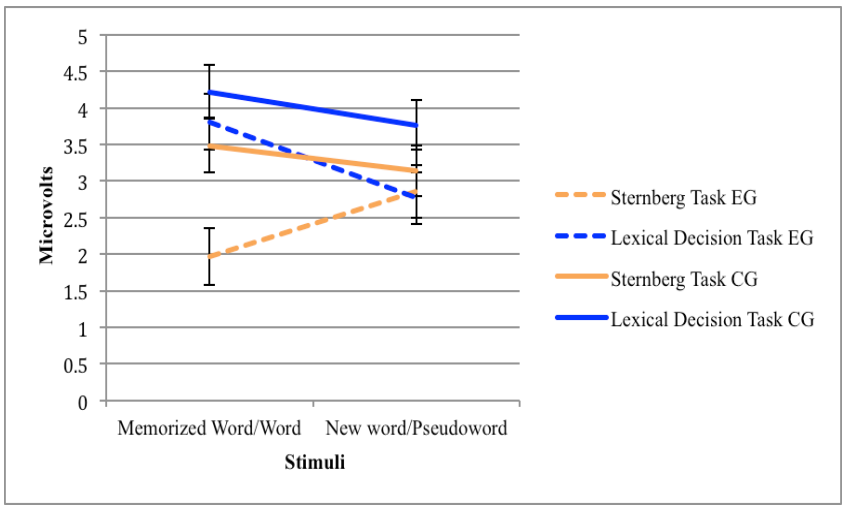

Figure 9. Significant stimuli x paradigm x group interaction for P1 Amplitude.

There was a significant stimuli x paradigm interaction as well ($F(1, 50) = 5.23$, $p = .026$, partial $\eta^2 = .095$), with memorized words having smaller amplitudes than new words in the Sternberg Task, but actual words having larger amplitudes than pseudowords in the Lexical Decision Task. A significant main effect for paradigm was identified ($F(1, 50) = 4.95$, $p = .03$, partial $\eta^2 = .09$) which showed larger amplitudes for the Lexical Decision Task compared to the Sternberg Task overall. None of the other main effects or interactions were significant (see Table 3).

Table 3.

Amplitude and Latency Analysis of P1 Component

df = 50	P1 Component					
	Amplitude			*Latency*		
	F	*p*	P. η^2	F	*p*	P. η^2
Group	.78	.38	.015	.77	.39	.015
Stimuli	.73	.39	.014	.0	.99	.0
Paradigm	4.95	**.031***	.09	9.73	**.003***	.16
Stimuli x group	.34	.56	.007	.12	.73	.0
Paradigm x group	.08	.7	.002	.2	.65	.00
Stimuli x group x paradigm	4.18	**.046***	.07	.00	.95	.00

Concerning P1 latency analysis, assumptions of homogeneity of variances were met (Levene's Test: For Sternberg Task-Target, Lexical Decision Task-Target, Sternberg Task-Distractor and Lexical Decision Task-Distractor $p = .14$, $p = .12$, $p = .095$, $p = .93$, respectively). There was a significant main effect of paradigm ($F(1, 50) = 9.73$, $p = .003$, partial $\eta^2 = .16$), with peak latencies of Sternberg Task being significantly shorter than peak latencies of the Lexical Decision Task. None of the other main effects or interactions reached significance (see Table 3).

The N1 (100-230 ms)

A 2 (group: control vs. patient) x 2 (stimuli: target vs. distractor) x 2 (paradigm: Sternberg Task, Lexical Decision Task) Mixed ANOVA was performed on peak amplitude and peak latency each. Regarding N1 amplitude analysis, assumptions of homogeneity of variances were met (Levene's Test: for Sternberg Task-Target, Lexical Decision Task-Target, Sternberg Task-Distractor, and Lexical Decision Task-Distractor $p = .89$, $p = 96$, $p = .93$, and $p = .55$, respectively). A significant main effect for group was identified ($F(1, 49) = 6.35$, $p = .015$, partial $\eta^2 = .115$), with control group having significantly larger, i.e., more negative, amplitudes compared to epilepsy group across paradigm and stimuli (see Figure 10).

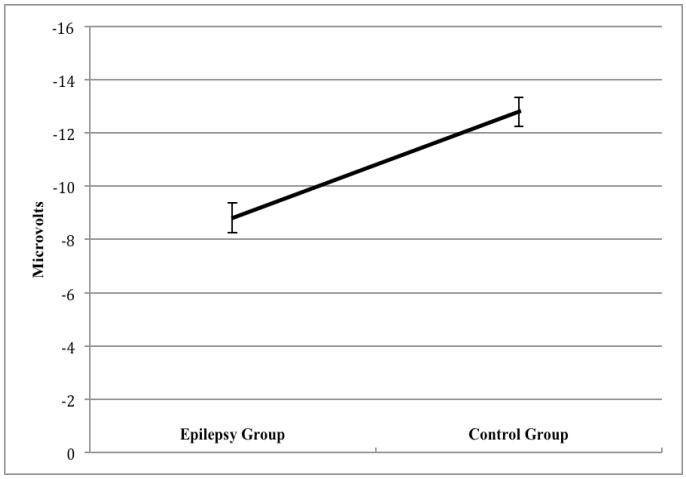

Figure 10. N1 Amplitudes across paradigms and stimuli.

Additionally, a significant main effect for stimuli was found ($F(1, 49) = 8.8$, $p = .005$, partial $\eta^2 = .15$) indicating higher amplitudes for new words/pseudowords than memorized words/words. None of the other main effects or interactions were significant (see Table 4).

Table 4.

Amplitude and Latency Analysis of N1 Component

	N1 Component					
df = 49	*Amplitude*			*Latency*		
	F	*p*	P. η^2	F	*p*	P. η^2
Group	6.35	**.015***	.115	2.6	.113	.05
Stimuli	8.8	**.005***	.15	.811	.37	.016
Paradigm	.35	.55	.007	8.5	**.005***	.148
Stimuli x group	1.76	1.9	.035	5.6	**.02***	.104
Paradigm x group	1.4	.24	.03	.08	.78	.002
Stimuli x group x paradigm	3.35	.07	.064	.001	.97	.0

Concerning N1 latency analysis, assumptions of homogeneity of variances were not met in one condition, the Sternberg-Task target condition (Levene's Test: for Sternberg Task-Target, Lexical Decision Task-Target, Sternberg Task-Distractor, and Lexical Decision Task-Distractor $p = .016$, $p = .33$, $p = .54$, and $p = .86$, respectively). However, since Box-Test revealed homogeneity of variance-covariance matrices ($F= 2.7$, $p > .001$), it was decided to continue with the analysis. A significant stimuli x group interaction was identified ($F(1, 49) = 5.6$, $p = .02$, partial $\eta^2 = .10$). Besides epilepsy group showing longer peak latencies overall, epilepsy group showed significantly shorter peak latencies for the new word/pseudoword condition than for the memorized word/word condition. This

pattern was reversed in controls. This means that in the control group, there were longer latency periods for new words/pseudowords than for memorized words/words (see Figure 11). Additionally, there was a significant main effect for paradigm ($F(1, 49) = 8.5$, $p = .005$, partial $\eta^2 = .15$) which showed longer N1 peak latency periods for the Lexical Decision Task compared to the Sternberg Task. None of the other interactions or main effects reached significance (see Table 4).

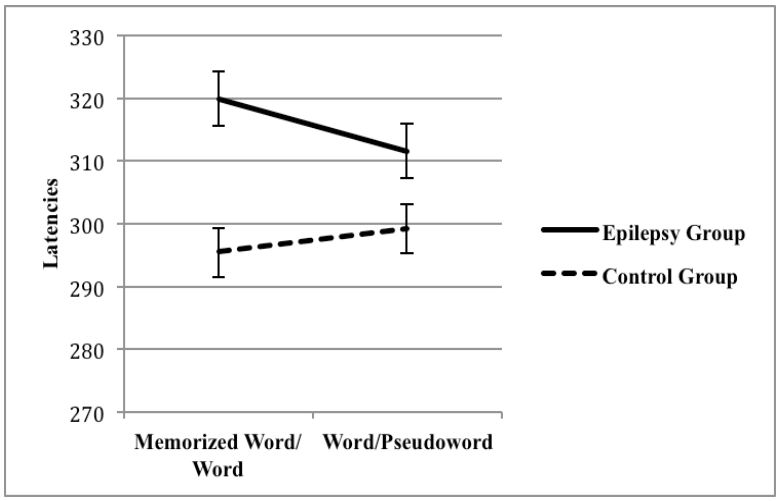

Figure 11. Significant stimuli x group interaction for N1 latency.

4. Questionnaire Data Analysis

The questionnaires discussed below were implemented after the first 20 patients were tested. Hence, sample size was reduced to 14 patients and 14 controls and began with VP43 (see Table 1). In this reduced sample, average age was 40.18. Eighteen males and 10 females participated overall (patients and controls were again matched for age and gender). The mean number of education years was 12.27. Eleven patients had epileptogenic focus within the temporal lobe.

4.1. Pittsburgh Quality of Sleep Index

The PSQI scores of patients and healthy controls were compared using a Wilcoxon Signed-ranks-test (nonparametric test was chosen due to self-report nature of the questionnaire, cf. Field, 2013). The PSQI total score includes sleep efficiency, frequency of sleep disturbance, sleep latency and duration, day dysfunction due to sleepiness, overall sleep quality, and medication use and was not significantly different between the two groups ($Z = -1.12$, $p = .26$). However, medians as well as means for each group indicate a trend for worse sleep quality in epilepsy patients (EG: $Mdn = 5.2$, CG: $Mdn = 3.33$).

Participants in the control group had a mean total sleep quality score of 4.64. In contrast, participants in the epilepsy group had a mean total sleep quality score of 6.69. Whereas the total mean and median PSQI score in control group was below the cut off level of five, the total mean and median PSQI score in epilepsy group was above the cut off level of five.

4.2. Subjective Memory Questionnaire

Correlations between the subjective memory measures and psychological tests were calculated separately for epilepsy patients and controls to examine relationships between actual memory abilities and perceived memory skills. Spearman correlation coefficients are displayed in Table 5. For the four-category rating item coding had to be reversed since it asked participants to rate how much of a problem memory was (1 = not a nuisance, 4 = severe), whereas for the other memory measures higher scores indicated better memory.

Table 5.
Correlations self report memory questionnaire and tests

	Epilepsy Group			Control Group		
Questionnaires	VAS	Q	QoL	VAS	Q	QoL
Verbal Working Memory	.49	**.618***	-.05	**.61***	.46	**.59***
Identical Word Meaning	.18	-.25	-.225	.15	.39	-.106
Sternberg Task	.22	.26	.03	.37	**.60***	**.65***
Lexical Decision Task	**.55***	**.61***	-.29	**.75***	**.596***	**.65***

Note. *p<.05

On the whole, control group showed more significant, higher, and more positive correlations between subjective and objective memory measures. Specifically, control group had seven significant objective-subjective memory correlations compared to three significant correlations in epilepsy group (see Table 5). For the epilepsy patients correlations between the subjective memory measures and the psychological tests was on the whole very weak or non-existent (see Table 5), with only three of twelve significant correlations overall. Two of these included the subjective four-category rating item. For the control group all psychological memory tests showed two to three significant correlations with subjective memory measures, with the exception of the Identical Word Meaning Task, which did not show any significant correlations in either group across all subjective measures.

D. Discussion

Epilepsy patients' working and semantic memory was examined on a behavioral, physiological, and subjective level compared to healthy controls. In the past, it has been shown repeatedly that people with epilepsy show a number of cognitive problems, including reduced memory performance, learning problems as well as attention and concentration deficits (Hermann et al., 1997; Moore & Baker, 2002; Oyegbile et al., 2004). As memory deficits are one of the most pervasive and apparent problems for epilepsy patients (MacAllister & Schaffer, 2007), one aim of this study was not only to replicate reduced memory performance on psychological tests in the epilepsy group, but also to determine neurological processes underlying disturbed memory processing. It has been previously suggested that EEG is a useful tool to assist in detecting and understanding memory dysfunction in epilepsy patients (Grippo et al., 1996) as it provides objective quantitative data on the timing and adequacy of cognitive processing. Hence, electrophysiological correlates during memory retrieval were recorded and analyzed by extracting even-related potentials. Processes specifically in the early stages of information processing, that is, P1 and N1 components, were of interest since monitoring such early components can be used to assess attention, vigilance, and gating of sensory inputs, i.e., to investigate whether epilepsy patients' sensory processing is disturbed (Pratt, 2011). Thus, measuring these components can elucidate whether epilepsy patients' sensory processing is disturbed before all cognitive activity happens (Pratt, 2011). Relatively little has been done so far in the area of ERP research on memory functioning in epilepsy patients. Most findings have reported reduced amplitudes and prolonged latencies in epilepsy patients (Grippo et al., 1994; Grippo et al., 1996; Miyamoto et al., 2000), which is why it was hypothesized that this would be similar in the sample analyzed.

Besides behavioral and physiological memory functioning, the role of sleep quality was investigated also. The role of sleep in memory has been increasingly under investigation in the past decade. The beneficial effects of sleep on memory consolidation, enhancement (Diekelmann & Born, 2010; Maurer et al., 2013), and the detrimental effects of sleep deprivation on learning (Bear et al., 2007) and memory performance (Karni et al., 1994) indicate the importance of sleep on memory, especially because recent literature has suggested a connection between Non-REM sleep and declarative memory performance (Maurer et al., 2013). Importantly, a number of studies provide support for worse sleep quality and increased sleep disturbance in epilepsy patients compared to healthy controls (De Weerd et al., 2004; Kwan et al., 2009; Ottman et al., 2011; Piperidou et al., 2007). To

shed light on this, subjective quality of sleep ratings were compared between epilepsy and control group.

Additionally, the relationship between objective memory performance and subjective memory was of interest. Several studies have not found a significant relationship (Elixhauser et al., 1999; Piazzini et al., 2001; Sunderland et al., 1983; Vermeulen et al., 1993), indicating that epilepsy patients cannot adequately judge their memory performance. While some studies have shown that epilepsy patients complain but do not show memory deficits (Gallassi et al., 1988; O'Shea et al., 1996), others have found that patients with deficient memory do not complain (Gleißner et al., 1998), which might be due to not remembering memory problems.

In the subsequent sections, firstly findings regarding behavioral measures of working and semantic memory tasks in Paper Pencil and EEG format for both groups will be discussed. Secondly, event-related potential results will be lined out, focusing on P1 and N1 peak amplitude and latency exclusively. Lastly, results of sleep quality ratings and subjective memory measures are examined. Main conclusions are based on statistical analyses performed on memory scores, ERP peak amplitudes and latencies as well as subjective memory and sleep quality ratings.

1. Behavioral Measures

Performances on psychological tests and EEG tasks as well as reaction times were significantly affected by group. The epilepsy group had significantly lower scores across all psychological tests, i.e., working and semantic memory tests, in paper pencil and EEG format, and longer reaction times to probes in the EEG tasks. This supported the hypothesis that (1) epilepsy patients have lower scores on working and semantic memory tests in both formats and (2) epilepsy patients show slower reaction times on EEG working and semantic memory tasks. These findings mirror the results from Moore and Baker (2002) and Oyegbile et al. (2004), which demonstrate that temporal lobe epilepsy patients show poorer performance for remembering verbal material and have worse overall memory performance. Slowed speed of processing in epilepsy patients also seems to be one of the main difficulties associated with epilepsy; this is reflected not only in the significantly longer reaction times of patients during EEG memory tasks but also supported by findings of Grippo et al. (1994) who found longer reaction times for epilepsy patients in working memory tasks, and Miyamoto et al. (2000) who found longer reaction times for epilepsy patients during semantic processing, though the difference was not significant which might have been due to small sample size (10 patients). Prolonged reaction times in

epilepsy patients have also been associated with abnormal perceptuo-motor skills and reduced speed of processing in epilepsy (Trimble & Thompson, 1986), which could also stem from antiepileptic drug treatment (Reynolds, 1983). Generally, longer reaction times have been associated with difficulties in sensory/perceptual processing (Jensen, 2006). Overall, these results suggest slowed speed of processing, decreased processing efficiency and presumably might lead to prolonged memory scanning time for epilepsy patients.

2. ERPs

Results of ERP analyses provide support for information processing differences between epilepsy patients and healthy controls at very early processing stages. Neural responses during memory retrieval differed between patients and controls already in P1 (70-130 ms) and N1 (100-230 ms) ERP components. The N1 complex was characterized by decreased amplitudes, i.e., less negative amplitudes, for patients across stimuli conditions and paradigms in total. A similar trend was found for the P1 component, although here a different activation pattern for stimuli conditions in the Sternberg working memory task (stimuli x paradigm x group interaction) was identified: while control group showed significantly larger, i.e., more positive, amplitudes for memorized words, epilepsy group showed significantly more positive amplitudes for new words.

In general, it is believed that the amplitude of an ERP component reflects intensity of information processing (Kok, 1990). Specifically, P1 and N1 amplitudes have been shown to be affected by attentional allocation and arousal (Haider et al., 1964; Luck, 2014); since all probe items had the same physical characteristics, it could be argued that these findings (decreased amplitudes) indicate reduction in epilepsy patients' levels of attention and/or an increase in their distractibility (Grippo et al., 1994). Hence, these results imply more attention allocation to stimuli in healthy controls, an attentional deficit, increased distractibility and subsequently decreased sensory input for epilepsy patients overall and for memorized words in the Sternberg task especially. The decrease in P1 amplitude for memorized words in patient group suggests attentional disturbance in the retrieval and maybe encoding of memorized words especially. It has been shown in the past that attention and distractibility can cause faulty encoding and have an important effect on performance testing in epilepsy (Bornstein, Pakalnis, Drake, & Suga, 1988; Delaney, Prevey, & Mattson, 1986). These interpretations are also supported by behavioral results, which show significantly lower accuracy in memory tasks for epilepsy patients compared to controls. It seems that early sensory disturbances might influence later, more endogenous memory processes.

Findings also show longer latencies for epilepsy patients in the N1 component as well as a difference in latencies for stimuli between groups. Whereas the ERP waveform for the control group was characterized by longer peak latencies for new words/pseudowords than memorized words/words, this pattern was reversed in the epilepsy group. Since latencies are believed to indicate timing of certain brain activation (Kok, 1990), these results suggest a slowed processing speed for memorized words/words for epilepsy patietns starting already 100-230 ms poststimulus. This might translate into slower information processing overall and also a slowing of later memory processes, causing, for instance, prolonged memory scanning times. These findings tie in nicely with results from behavioral measures, which show prolonged reaction times for the epilepsy group. No such latency differences were found for the P1 component, maybe because slowed speed of processing does not start until 100-230 ms poststimulus, the N1 component range. Overall, these findings support the hypothesis that epilepsy patients show decreased amplitudes in P1 and N1 ERP components (3), similar to findings by Grippo et al. (1994, 1996) and Miyamoto et al. (2000). Additionally, these findings contributed to elucidating semantic and working memory processing disturbances in epilepsy patients.

Regarding stimulus conditions, it was found that N1 amplitude was characterized by higher amplitudes for new words/pseudowords compared to memorized words/words. For the Sternberg working memory task the same pattern was found for the P1 component (i.e., memorized words showed smaller amplitudes than new words). Both of these findings are contrary to previous results by Wolach and Pratt (2001), who showed lower N1 amplitudes for new words. However, the effect found in the present study might be driven by the performance of the patient group, who demonstrated lower amplitudes overall. For the Lexical Decision task these results are in line with previous studies by Dehaene (1995 as cited in Hauk et al., 2006), and Sereno et al. (1998) who all found higher amplitudes for pseudowords. This has been interpreted as an increased processing effort due to difficulty in lexically accessing these items in memory (Lau et al., 2008). Findings also show larger amplitudes for the Lexical Decision Task compared to the Sternberg Task in the P1 component, and longer latencies for the former in both P1 and N1 components. This illustrates the differences between the paradigms and memory types with shorter latencies indicating that working memory is, unsurprisingly, more readily and quickly available than semantic memory.

Visual inspection of all grand average ERPs across the scalp (see Figure 7 and 8) shows also interesting activity in the frontocentral electrodes. Follow-up analysis (see Appendix) showed that the N1 activation at frontocentral electrodes (positive voltage at frontal sites) follows a similar pattern than at parieto-occipital locations. In fact, a stimulixgroupxhemisphere interaction for N1 amplitude and a stimulixgroup interaction for N1 latency was found, very similar to results from parieto-occipital regions (see Figure A1 and Figure A2). Thus, it could be speculated that these activities represent two sides of the same coin. Of course, source modeling on high density EEG recordings would need to be performed to further investigate whether a single dipole is at work at both parietal-occipital and frontocentral locations here. What might also be important for future studies analyzing this question is if and how epileptogenic zones influence this dipole.

The present study is one of few studies focusing on disturbances of early information and memory processing in epilepsy patients. Early attentional deficits might explain or contribute to reduced performances of epilepsy patients on memory tests. Similar results have been found in elderly individuals (for a review see Gazzaley, 2011) indicating the importance of monitoring early sensory processes in individuals with pathologies or memory problems. As for the underlying cause of these early disturbances, it has been speculated in the past that these deficits might be due to pathological abnormalities of epilepsy syndrome itself or it may be that the pathology involves connections to memory structures (Grippo et al., 1996). Secondary generalized seizures or anti-epileptic drugs (AEDs) could also result in defective memory by distant effects independent of origin of seizures (Grippo et al., 1996).

3. Questionnaire Data

Although epilepsy patients perceived themselves to have worse sleep quality compared to controls, results did not reach a significant level. However, since mean and median PSQI scores of patient group were above the PSQI cut off score of five, which has been used repeatedly to distinguish between good (PSQI < 5) and bad sleepers (PSQI > 5; Doi et al., 2000; Wittchen et al., 2001), these results do suggest that epilepsy patients are bad sleepers overall. Hence, the hypothesis that (4) epilepsy patients report worse sleep quality than controls could be partially supported. Evidence for worse sleep quality for epilepsy patients has been found in the past, for instance by De Weerd et al. (2004) and Ottman et al. (2011). Since the data also point in this direction, the fact that there were no group differences could be attributed to small sample size (n = 13) and requires replication with a larger sample of epilepsy patients in the future.

Comparisons between subjective memory measures and psychological tests indicate that healthy controls estimated their memory performance better than epilepsy patients. In the control group participants had higher, i.e., more positive, and a larger number of significant subjective-objective memory correlations. In other words, healthy individuals rated their memory performance higher and performed higher on memory tests as well. Specifically, control group performances on all memory tests correlated significantly with two to three subjective memory measures, with the exception of the Identical Word Meaning Task, which did not show any significant correlations in either group across all subjective measures. This might be due to task difficulty, since this task was the hardest of all memory tests, with both control and epilepsy group achieving lowest of all memory tests' scores. The Lexical Decision Task achieved significant correlations across all subjective memory measures, which might be due to low task difficulty as it was the easiest of all tasks, with both control and epilepsy group achieving highest scores across all memory tests.

When analyzing subjective memory measures, no systematic pattern could be identified. The quality of life in epilepsy memory items correlated significantly with three memory tests. The visual analogue scale and the four-category rating item correlated with two. Overall, it seems that healthy individuals can rather accurately judge their memory performances with the self-report measures applied.

For the epilepsy patients, correlations between the subjective memory measures and the psychological tests were weak; only three correlations of twelve in total were significant. These results are supported by studies from Elixhauser et al. (1999), Marino et al. (2009), Piazzini et al. (2001), and Sunderland et al. (1983) who found no significant relationships between subjective memory complaints and performance on objective memory tests as well. Interestingly, correlations between two measures of memory performance (Verbal Working Memory and lexical decision task) of epilepsy patients and the subjective memory four-category rating item reached significance, probably because of the way the question was posed: it was the only item asking participants how much of a problem memory was for everyday life compared to overall ratings of memory and questions asking quantification of trouble remembering in the past four weeks. This indicates that the higher performance on the Verbal Working Memory and lexical decision tasks, the less memory was seen as nuisance in everyday life. Since Verbal Working Memory is vital for everyday life, this correlation seems rather plausible. However, it needs to be taken into account that the Lexical Decision Task was the easiest of all tasks,

with both control and epilepsy group achieving highest of all memory tests' scores. Thus, it might be that overestimation of memory skills contributes to the significant correlation with the subjective rating item in this task.

In sum, epilepsy patients seem to experience difficulties in their awareness of memory problems. Since confounding influences of mood and affective status were not controlled for but have been named as possible explanations for epilepsy patients' problems when evaluating their memory (O'Shea et al., 1996), interpretations of results remain tentative until future studies replicate findings controlling for confounders.

4. Final Conclusion and Remarks

The main finding of this combined behavioral, ERP, and self report study is that drug-resistant epilepsy patients not only perform significantly worse on objective memory tests and show slower reaction times compared to their matched controls, but also that differences in brain activity emerge very early during working and semantic memory tasks. To elaborate, worse memory performance of the patient group was reflected in decreased N1 and P1 amplitudes and prolonged N1 latencies during memory retrieval. This suggests decreased attentional levels and/or increased distractibility in epilepsy patients already during the 70-230 ms range. These findings (lower attention levels, increased distractibility in patients) have been demonstrated in the past (cf. Bornstein et al., 1988). Additionally, patients cognitive processing seems to be slower from approx. 100-230 ms onwards, translating into slower information processing overall and also a slowing of later memory processes, maybe even causing prolonged memory scanning times.

Especially interesting was also the reversed pattern for amplitude increase for memorized words compared to new words between groups in the Sternberg task. It seems that memorized words were not paid the same level of attention to by patients compared to controls, even though they were instructed to memorize them in the encoding phase. If this is a results of reduced attention during studying or retrieving items is difficult to say. Since participants were asked to memorize only five words, ERPs in the encoding phase could not be analyzed and thus conclusions about whether attentional deficits are present in the encoding phase as well cannot be drawn.

At the behavioral level, epilepsy patients' scored significantly lower than their matched controls in a paper pencil Verbal Working Memory task, a paper pencil Identical Word Meaning task measuring semantic memory, as well as in a Sternberg word recognition task (visual working memory) and a lexical decision task (semantic memory). These memory deficits across all measures show the pervasiveness and dissemination of

memory problems in epilepsy. Additionally, as previously mentioned, reaction times were significantly slower for epilepsy patients in the EEG tasks, which corresponds to findings of prolonged N1 latencies.

Self-report data on sleep quality indicate a trend of worse sleep quality for patients, which might be due to the syndrome itself. It could also be related to affective status, such as depressive moods or anxiety. If sleep quality were indeed worse in epilepsy patients, questions of causality would be important to address as well. Hence, the role of sleep quality on memory in epilepsy needs to be further investigated in the future. Patients are also impaired in their awareness of their memory ability. However, as with sleep quality, the influence of mood is unclear and needs to be controlled for in future research.

Future research might also consider including more sources of information. For instance, not only memory tasks employed during EEG recording, but also during fMRI scanning could be investigated. Although EEG is has very high temporal resolution, functional magnet resonance imaging (fMRI) might be better suited to answer questions regarding the influence of epilepsy on functional neuroanatomy of memory function. Hence, while this study has now provided insight on attentional deficits, fMRI studies might be helpful in investigating how these deficits are related to epileptogenic focus and compensation strategies.

Concerning the clinical importance of these results, Berry et al. (2010) have shown benefits from perceptual discrimination training for working memory in older adults aiming to ameliorate age-related memory deficits. Since memory complaints are significant for epilepsy patients, it is worth investigating whether perceptual and attentional training would improve working memory for epilepsy patients. This would most probably improve quality of life for many patients.

Conclusively, this study provides evidence for disturbance in early processing during memory retrieval for epilepsy patients, indicating attentional deficits as well as slowed overall processing, which is assumed to be reflected in memory impairment in epilepsy. The causal role of the epilepsy syndrome itself (for instance, hippocampal cell loss), seizures or AEDs remain to be answered.

Appendix

In the following, results from a follow-up analysis conducted on the N1 component at frontocentral locations will be described. Identical sample and analysis procedure was used as explained in section C-1 and B-4. Time window for N1 component was again defined as 100-230 ms, analyzed were peak amplitudes and latencies. Independent variables were group (between-subject factor: control group vs. epilepsy group), stimuli (within-subject-factor: memorized word/word vs. new word/pseudoword), paradigm (Sternberg Task vs. Lexical Decision Task), and hemisphere (right vs. left) for location FC1/FC2 and FC3/FC4. A 2x2x2x2 Mixed ANOVA at selected frontocentral locations was performed. A 2 (stimuli: target vs. distractor) x 2 (paradigm: Sternberg Task, Lexical Decision Task) x 2 (lateralization: left vs. right) Mixed ANOVA of selected frontocentral locations (location: FC1/FC2, FC3/FC4) with group as a between factor was performed on peak amplitude and peak latency. To measure effect sizes, partial etas squared were reported, significance levels was set at the convention .05 level. After exclusion of left-handed individuals and participants with fewer than 30 trials, 26 epilepsy patients and 28 controls were included in the analysis.

N1 Amplitude

A **significant group x stimuli x lateralization** interaction was found ($F(1, 50) = 6.74$, $p = .012$, partial eta squared = .12). As Figure A1 shows, control group showed higher amplitudes in the left hemisphere for both conditions, memorized words/words were more positive than new words/words in right and left hemisphere, whereas epilepsy group showed higher amplitude in the right hemisphere for distractor condition and higher amplitudes in the left hemisphere for target condition; while control group showed higher amplitudes for the target condition compared to distractor condition in both hemispheres, epilepsy patient group only showed higher amplitudes for the target condition in left hemisphere.

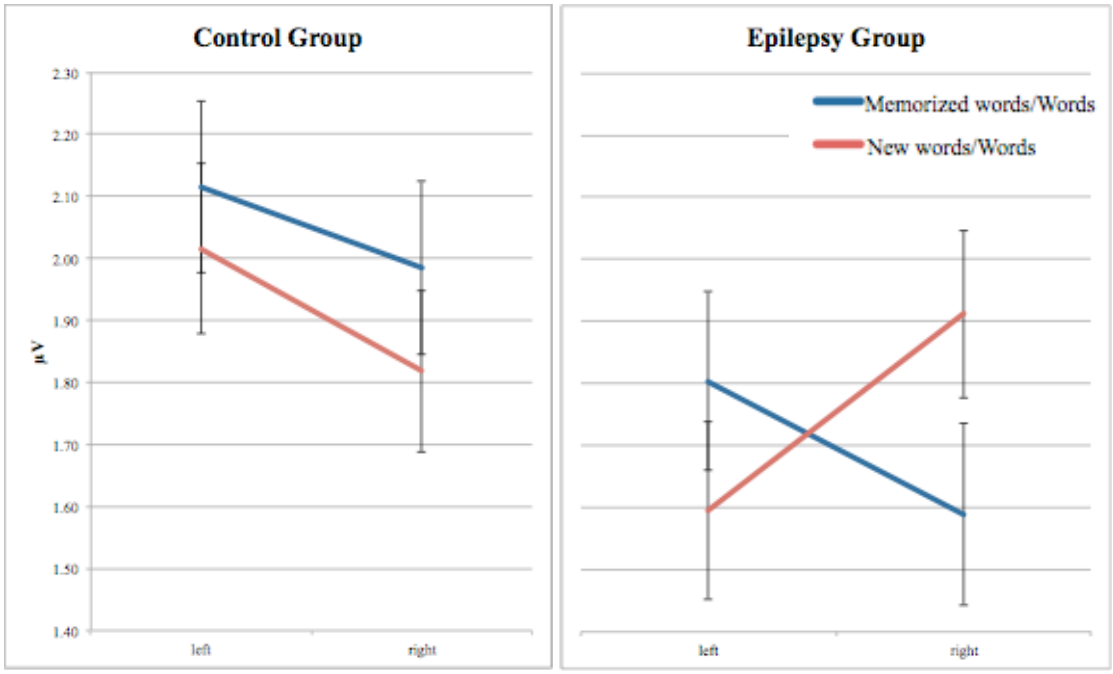

Figure A1. Significant group x stimuli x lateralization interaction.for N1 Amplitude.

N1 Latency

A significant **group x stimuli interaction** was found (F(1, 52) = 4.41, *p*=.041, partial eta squared = .08). Whereas epilepsy group showed longer latencies for memorized words/words, control group showed slightly longer latencies for new words/pseudowords than for targets (see Figure A2). The control group was faster in both conditions.

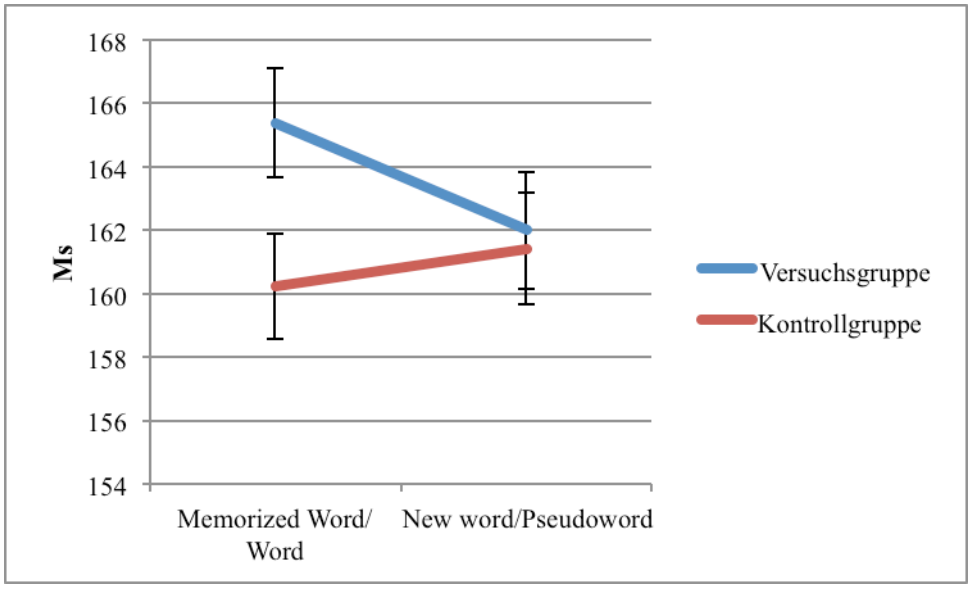

Figure A2. Significant group x stimuli interaction for N1 Latency.

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Schwerpunkt: Klinische Psychologie, Psychologische Diagnostik

Summer School Trauma & Resilience Juli 2014
Hebrew Universität Jerusalem, Israel
Schwerpunkt: Trauma, PTBS, Resilienz und "community preparedness"

Exchange Student, Joint Study Program Februar-August 2013
University of Western Australia, Perth
Schwerpunkt: Neuroanatomie und Neuropsychologie

Bachelor of Arts, English & American Studies 2008-2012
Universität Wien (abgeschlossen)

STIPENDIEN

Auslandsstipendium verliehen durch die „Hebrew University of Jerusalem" (2014)
Gerald Frank Brown Memorial Scholarship verliehen durch das "Government of Western Australia" (2013)
Leistungsstipendium aus den Mitteln des öst. Bundesministeriums für Wissenschaft, Forschung und Wirtschaft (2013)
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BERUFSERFAHRUNG

FORSCHUNGSARBEIT

Demonstratorin, Institut für Medizinische Psychologie, Med.Universität Wien Januar-Juni 2015

- Unterstützung bei Forschung in der Arzt-Patienten Kommunikation und Psychoonkologie (Dr. Birgit Hladschik-Kermer)
- Analyse von Längsschnittdaten über die Effektivität des Gesprächsführungscurriculums für MedizinstudentInnen
- Literaturrecherche über Psychoonkologie, Depression und Angst

Editor, Journal of European Psychology Students May 2014-present

- Betreuung des Review-Prozess von Manuskripten von Anfang bis zum Schluss
- Unterstützung der StudentInnen bei APA-Richtlinien-Konformität
- Kommunikation zwischen Autoren, Copyeditors, Lektoren und Layouteditors

Wissenschaftliche Praktikantin, Universität Wien September-Dezember 2013

- Social, Cognitive & Affective Neuroscience Unit
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- Hilfestellung bei Ethikantrag sowie Testpersonenrekrutierung

ANDERE

Schreibassistenz, Parlamentskorrespondenz Österreich September 2012-Januar 2015

- Korrekturlesen, Tippen und Hilfestellung vor allem an Plenartagen

Praktikum zum Diagnostizieren, Österreichisches Bundesheer Oktober 2012-Januar 2013

- Führen von Assessment- und Explorationsgesprächen zur Eignungsbeurteilung für Auslandseinsätze (unter Supervision)

Praktikantin, Kolpinghaus, Neuropsychologie Juli-September 2012

- Neuropsychologische Diagnostik (v.a. MMSEs)
- Beratungsgespräche
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Praktikantin, Krankenhaus Maria Ebene Juli-August 2010

- klinische-psychologische Diagnostik von alkohol- und medikamentenabhängigen Patienten
- Durchführung des kognitiven und autogenen Trainings

QUALIFIKATIONEN

TOEFL: 116 of 120

Lehrerfahrung: Leitung von Workshops zum wissenschaftlichen Schreiben für Psychologiestudierene (2014, Juni 2015)

IT: SPSS (inkl. SPSS-Syntax), Brain Vision Recorder & Analyzer, Content Management Systems (Wordpress), Macros, Anfänger in R and LaTex

Mitgliedschaften:

Executive Board of the European Federation of Psychology Students' Association (seit 2014)

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