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Time Perception in Mesial Temporal Lobe Epilepsy Patients

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Introduction

Time Perception

The internal perception of how quickly time is progressing or how much time has passed since an event occurred is known as subjective or psychological time (Meck, 2005). The human's capacity to time events in the seconds to minutes range controls the subjective perception of time-passing and enables the human to identify what is occurring in our surroundings and when to react to it (Piras et al., 2014). It has been demonstrated that the capacity to gauge objective time is largely stable, only changing in the presence of severe mental problems, brain disease, or pharmacological disturbances (Meck, 1996; Paule et al., 1999). Given that timing ability is a sensitive measure of information processing, and that temporal perception can impact various cognitive processes, it is postulated that interval timing is a reliable construct to examine cognitive dysfunctions after brain damage (Piras et al., 2014). The ability to estimate time is a sensitive indicator of whether a brain injury has affected the underlying neuronal substrate. Whether temporal distortions are a sign of or a cause for the cognitive and behavioural symptoms of neuropsychiatric illnesses will become more clear with further study on neurological and psychiatric patients (Piras et al., 2014).

This research paper aims to explore the relationship between mesial temporal lobe epilepsy and time perception. To achieve this, the paper will delve into various theories of time perception and timing classification. It will conduct a thorough analysis of time perception from both behavioural and neuroanatomical perspectives and also examine the hemispheric lateralisation of timing. Furthermore, the paper will investigate the correlation between time perception and the mesial temporal lobe.

Scalar Expectancy Theory

The Scalar Expectancy Theory (SET), also known as the internal clock model (Treisman, 1963), is widely regarded as the most influential model in the psychological timing literature.

It postulates that as soon as an event to be timed begins, an attention-controlled switch closes, permitting pulses from an internal pacemaker to be gathered into an accumulator (Piras et al., 2014). The present pulse count held in working memory is then contrasted with a value recorded in reference memory, and when the two values match sufficiently, a decision rule produces time estimation (Treisman, 1963). This explanation claims that arousal, vigilance, attention, working memory, episodic memory, and decision-making are substantially correlated with interval timing (Buhusi & Meck, 2009; Meck, 2005; Penton-Voak et al., 1996; Wearden et al., 1999). While internal timing and temporal memory are separate systems, they are linked by the frontal-striatal loops to enable the execution of timing sequences required for duration discrimination (Meck, 1996). As dopaminergic functions in the basal ganglia impact internal timing in the seconds-to-minute-range and cholinergic functions in the frontal cortex impact memory and attentional mechanisms (Coull et al., 2011; Meck, 1996), tailored manipulations can be planned to selectively modify the respective functions of the information processing phases defined by the SET (Coull et al., 2012).

As internal duration judgments depend on the number of pulses gathered into the accumulator, behavioural and pharmaceutical manipulations of the internal clock's effective pace can impact these estimations (Piras et al., 2014). The more pulses gathered, the longer the time period is perceived to be and vice–versa (Piras et al., 2014). One can alter the pace of perceived time by inducing small increases in arousal, for instance, by presenting sequences of click-tones (Penton-Voak et al., 1996). Injections of drugs that are considered to enhance dopaminergic function, such as methamphetamine, cocaine, and nicotine, cause the transient underestimation of interval duration since interval timing has been theorised to depend on an ideal level of dopaminergic activity in corticostriatal circuits (Coull et al., 2011; Meck, 1996). This behaviour modification is known as "clock pattern" and states that the criterion number of clicks is collected in a shorter amount of time because a putatively faster

clock creates the comparison representations while the normal duration representations (e.g., 400 ms) are produced by a regular clock speed (e.g., 350 ms; Coull et al., 2011). In contrast, medications that are considered to decrease dopaminergic function (such as antipsychotics) cause an overestimation of interval length since they slow down the clock during testing, resulting in a lower accumulation of the criterion amount of clock ticks (Buhusi & Meck, 2002; Coull et al., 2011).

Beat-Frequency Model

Another widely postulated model for internal timing is the beat-frequency model, which states that certain subpopulations of neurons encode durations. Those subpopulations of neurons oscillate at various synchronised frequencies and reset at the start of the stimulus that will be timed (Miall, 1989). The term "beat frequency" refers to the oscillatory rate at which a population of in-phase neurons reacts, and the term "beat period" describes the interval between two time points at which the population of neurons reacts in phase (Hartcher-O'Brien et al., 2016). Various durations can be encoded and distinguished due to the numerous possible sub-ensembles formed from a group of neurons. Striatal medium spiny neurons may be able to perform these calculations (Matell et al., 2003). The idea that the brain areas containing striatal medium spiny neurons are involved in time perception was supported by lesion and neuroimaging studies (Coull et al., 2008; Meck et al., 2008).

Functional Taxonomy of Timing: Explicit and Implicit Timing

Regarding the functional taxonomy of timing, a critical distinction is made between mechanisms involved in tasks during which the aim is to consciously provide an approximate of time passed (*explicit timing*) and tasks for which the aim is non-temporal but can be aided by a presumably incidental temporal context (*implicit timing*; Coull & Nobre, 2008). *Motor timing* (i.e., adjusting motor responses to externally or internally set time periods in the range of milliseconds and seconds) and *perceptual timing* (i.e., time approximation and

distinction of time periods of milliseconds and seconds) are other subcategories of timing functions (Coull & Nobre, 2008).

In explicit timing tasks, motor timing is the representation of a time period or inter-stimulus interval (ISI) with a motor act (Coull & Nobre, 2008). An example of motor timing is the *temporal reproduction task*, where subjects either continuously press a button to indicate a pre-defined time period or press the button after a certain amount of time has passed (Coull & Nobre, 2008). Another example is the *paced finger-tapping task*, where a motor response, such as pressing a button, is initially performed synchronously to a sensory stimulus with a regular ISI (synchronisation phase). Then, the sensory stimulus terminates, and the subjects must continue pressing the button at the previously learned pace (continuation phase). Thereby, ISIs can be characterised as isochronous or rhythmic (Coull & Nobre, 2008).

Furthermore, perceptual timing in explicit timing tasks typically requires the subject to decide whether one time period or ISI was shorter or longer than another one (Coull & Nobre, 2008). For instance, in *temporal discrimination tasks,* participants contrast the durations of two sensory stimuli—a probe and a target—stored in working memory. With a delayed discriminatory response, if the probe was shorter, longer or the same as the target, temporal estimations are measured (Coull & Nobre, 2008).

Implicit timing, also known as temporal expectation (Coull & Nobre, 2008), future-oriented attending (Barnes & Jones, 2000) or anticipation of event timing (Ghose & Maunsell, 2002)) utilises temporal information to increase motor or perceptual performance (Coull & Nobre, 2008). For example, stimuli appearing at an expected time trigger faster and more accurate responses than those appearing unexpectantly (Niemi & Näätänen, 1981). In implicit timing tasks, the primary goal for the subject is non-temporal, but the underlying subconscious temporal abilities are tested. For instance, in the *temporal pre-cue task,* an association is

taught between a cue and a short or long ISI, and the subject has to react as fast as possible when the target appears (Coull & Nobre, 2008). This can be deliberately predicted with the previously learned target-specific cue that either indicates a short or long period before the target stimulus. In the *serial prediction task*, subjects have to press a button whenever a probe sequence of ISIs is equal to a previously learned temporal pattern of ISIs (e.g., between tones, there is first a 2 s interval, then 5 s and lastly 1 s before the last tone; Coull & Nobre, 2008). Temporal expectations can be built unintentionally ("exogenously") as a by-product of a regular stimulus appearance or intentionally ("endogenously") when the regular stimulus interval is noticed and used to inform deliberate action (Coull & Nobre, 2008).

Time Bisection Paradigm. One example of an explicit temporal discrimination task is the *time bisection task*, in which a long standard interval and a short standard interval are shown to the subjects, who then are instructed to judge whether a presented interval was more similar to the long or the short standard interval (Mioni et al., 2018). To estimate the accuracy of the subject's judgement, the point of subjective equality (PSE) is calculated, which indicates the specific duration at which the subject decided for "short" and "long" equally often (Mioni et al., 2018). In case the PSE is shifted from the midpoint, that is an indication of a deviant perception of time duration. For instance, a subject with a larger PSE perceived the durations longer than they were (Mioni et al., 2018).

Another indicator of time bisection performance is the Weber ratio (WR), where smaller values indicate a higher temporal sensitivity (Mioni et al., 2018). Killeen et al. (1997) suggested that the PSE reflects the pacemaker's velocity and that a reduced PSE indicates pacemaker acceleration (Meck, 1996). Therefore, as the PSE is increased, the pacemaker is thought to slow down, and consequently, the internal clock generates more variability (Gibbon et al., 1984).

Foreperiod Paradigm. The *foreperiod paradigm* illustrates an implicit timing task (Mioni et al., 2018). In such a task, participants must react to a stimulus presented after a warning signal. Depending on the duration of the foreperiod between the warning and the target signal, the participants' response times (RTs) may change. RTs are typically shorter for the short foreperiod blocks than blocks with long foreperiods only, known as the fixed foreperiod effect (Mattes & Ulrich, 1997; Vallesi et al., 2009). Shorter RTs in the short foreperiod blocks result from improved time estimates of short intervals compared to long intervals (Bausenhart et al., 2008).

Contrary to the fixed foreperiod paradigm, the outcomes often reverse when the short and long foreperiods are not presented in blocks but are randomly intermixed. In such paradigms, often, the RTs are lower for the long foreperiod trials, which is called the variable foreperiod effect (Niemi & Näätänen, 1981; Vallesi et al., 2009). Sequential effects are another phenomenon related to the variable foreperiod paradigm. That is the effect of shorter RT for short foreperiods if preceded by another short foreperiod instead of a longer foreperiod (Mioni et al., 2018). However, the RT at the present long foreperiod is fast regardless of the length of the prior foreperiod (Capizzi et al., 2015).

Behavioural Differentiation Between Explicit and Implicit Timing

Explicit and implicit timing can be differentiated not only theoretically but also behaviourally. This notion is supported by Mioni et al. (2018), who found impairment in explicit timing in patients with Parkinson's Disease (PD) while their implicit timing abilities were preserved. The PD patient group perceived time periods as shorter than they actually were, with a higher variability than the control group. At the same time, they showed normal foreperiod and sequential effects. The authors suggested that this specific deficit in the time bisection task in PD patients indicates that explicit timing is linked to the functioning of the basal ganglia (BG) and the dopaminergic connections, which are impaired in PD patients.

Furthermore, the selective impairment in temporal abilities of PD patients promotes the notion that timing can be differentiated into explicit and implicit timing.

Likewise, in a study with patients suffering from “beat deafness”, it was found that they had difficulties performing tasks that involved explicit rhythm but not implicit rhythm (Bégel et al., 2017). Those subjects had a perceptual deficit in beat tracking, but they could move a finger synchronously to the beat and perceive beat regularity while not paying attention to the rhythm. The authors suggested separate pathways for explicit and implicit beat rhythm perception (Bégel et al., 2017). Another study investigated the attention orientation of subjects with right frontal damage and found that orienting towards cued explicit information was impaired. At the same time, the performance was preserved when implicit rhythmic patterns were used (Triviño et al., 2011). Droit-Volet and Coull (2016) also demonstrated that explicit and implicit timing follow distinct developmental trajectories, with implicit timing being independent of age and temporal variability in explicit timing tasks decreasing as a function of age. An explanation for these trajectories may be that implicit timing abilities are derived from automatic processes which do not depend on age and the maturation of cognitive abilities (Reber, 1992). In contrast, explicit timing abilities improve with age because they partially depend on executive functions, which mature with the development of cognitive capacity (Droit-Volet, 2013).

To address the question of whether implicit and explicit timing rely on separate timing mechanisms, Herbst et al. (2022) conducted an auditory foreperiod task with constant and variable foreperiods, including pitch discrimination as an implicit measure of timing and duration discrimination as an explicit timing task. During those tasks, the participant's brain activity was recorded with magnetoencephalography (MEG). The results indicated no distinct neural dynamics when attention was directed to time, initiating the explicit timing task. According to the authors, this could show that explicit timing is encoded by the same

mechanism as implicit timing. Correspondingly, it was found that implicit temporal expectations can dynamically guide explicit temporal judgment by prioritising certain items held in working memory (Ede et al., 2017). Likewise, partial correlations between behavioural explicit and implicit measures were found (Coull et al., 2013). Other authors found that both tasks utilised the same internal representation of time, yet their external manifestation varied according to temporal task goals (Piras & Coull, 2011).

Accordingly, Herbst et al. (2022) hypothesised that, following a common encoding of temporal information, there are separate read-out mechanisms per task. This could explain why most studies found behavioural differences between the two tasks. In fact, their results showed that temporal predictability only improved performance in the implicit timing task and did not influence explicit timing performance. Thus, information on the temporal predictability of a stimulus may only be used implicitly and not deliberatively. However, there was an increase of pre-target-induced beta power in parietal and sensorimotor areas during implicit timing, which suggests that beta oscillations play a role in temporal prediction. Thus, implicit timing seems to be reflected in oscillatory neural dynamics and determines automatic sensory and behavioural responses, while no definite conclusions can be drawn about explicit timing in this respect (Herbst et al., 2022). Additionally, the authors pointed out no correlations between the performance in the explicit and implicit timing tasks. In summary, explicit and implicit timing mechanisms are at least partially dissociable and further investigation is needed to define the cognitive and neural processes that cause this differentiation in timing mechanisms.

Neuroanatomical Substrate of Explicit and Implicit Timing

The fact that explicit and implicit timing have been connected to separate neural regions adds more support to the idea that these two processes are distinct from one another. In particular, explicit timing has been frequently linked to the supplementary motor area (SMA),

cerebellum, BG, and right inferior frontal and parietal cortices (Coull & Nobre, 2008). Instead, the variable foreperiod effect in implicit timing has been connected to the lateral prefrontal cortex (Arbula et al., 2017; Triviño et al., 2010), while the sequential effect has been linked to the motor/premotor circuitry (Vallesi et al., 2007) and left subcortical structures (Triviño et al., 2016).

Explicit timing. In explicit timing, the functional magnetic resonance imaging (fMRI) research on perceptual (Livesey et al., 2007; Pouthas et al., 2005; Rao et al., 2001; Tregellas et al., 2006) or motor (Bengtsson et al., 2005; Bueti et al., 2008; Cunnington et al., 2002; Jahanshahi et al., 2006; Lewis et al., 2004) timing has consistently found activation in those important 'timing areas' (i.e., cerebellum, right inferior frontal and parietal cortices, BG, and SMA). Specifically in perceptual timing, when the requirements of a temporal discrimination task were elevated, either by prolonging the duration of the time period or by limiting the temporal range inside which two time periods are to be contrasted, activity in the anterior portion of SMA (pre-SMA), the right inferior frontal cortex, and BG increased (Pouthas et al., 2005; Tregellas et al., 2006). Livesey et al. (2007) demonstrated that even when the control task was substantially more challenging than the timing test, BG and inferior frontal cortex were still differentially activated during temporal discrimination. In particular, the BG are shown to be predominantly engaged when an initial representation of stimulus time is retained for subsequent recall during the encoding stage of perceptual timing tasks (Rao et al., 2001). This implies that the BG is engaged during the initial encoding of time, not during the later comparison phase of temporal estimation as the coincidence detection paradigm would predict (Matell & Meck, 2004).

Additionally, the BG are involved in motor timing tasks, such as motor reproduction tasks of time periods in which subjects have to perform motor responses that indicate the timed interval (Bueti et al., 2008). During the paced finger-tapping task, the BG are engaged while

continuing the motor response (Lewis et al., 2004). According to Coull and Nobre (2008), the co-activation of the BG with other areas, namely the cerebellum, SMA and inferior frontal cortex, may be determined by the task context. For instance, both the BG and the SMA were activated when subjects replicated timed intervals that sensory stimuli had earlier specified (Lewis et al., 2004). However, only the BG were engaged when subjects created a subjective internal model of a time interval and performed a self-initiated movement (Cunnington et al., 2002). This shows that the BG and SMA play different roles in the representation of time periods that are determined either internally or externally, respectively. The cerebellum tends to be more susceptible to subsecond rather than supra-second durations (Lewis & Miall, 2003) and is generally more frequently engaged in motor studies of explicit timing (e.g. Bueti et al., 2008) than perceptual timing studies.

To conclude, in explicit timing, regardless of the task requirements (manual/verbal replies (Bengtsson et al., 2005); sub/supra second intervals (Jahanshahi et al., 2006); perceptual/motor processing (Bueti et al., 2008), the BG are consistently engaged in time periods of at least a few hundred milliseconds. However, depending on the temporal context, additional areas, such as the SMA, inferior frontal cortex, and cerebellum, may be involved.

Implicit timing. The research on the neuroanatomical substrates of implicit timing can be divided into perceptual and motor timing research. In perceptual timing research, one can differentiate further between exogenous and endogenous temporal expectations. Exogenous temporal expectations and the incidental occurrence of predictable temporal dynamics have been investigated by utilising MEG and fMRI. A MEG study by Martin et al. (2008) illustrates increased activity in the cerebellum and parietal cortex during a choice RT task, which varied according to the hazard function. The *hazard function* is the "function of the conditional probability that a target will occur at a particular time, given that it has not

already occurred" (Coull & Nobre, 2008, p. 5). Furthermore, Pollok et al. (2008) found an increase in phase synchronisation between the cerebellum, subcortical structures and parietal cortex during tasks that foster motor synchronisation to predictable ISIs. In addition, fMRI studies have linked temporally predictable ISIs to activity in the left premotor and inferior parietal cortices (Dreher et al., 2002; Praamstra et al., 2006; Sakai et al., 2000). Also, increased activity was identified in the dorsal premotor cortex while synchronising responses to auditory rhythms in predictable ISIs (Chen et al., 2006).

Endogenous temporal expectations, the voluntary use of informative pre-cues to meliorate performance, were connected to the left inferior parietal cortex and cerebellum (Sakai et al., 2002). This was tested in a *sequence-learning paradigm*, where subjects improved their motor speed using temporally predictable ISIs (Sakai et al., 2002). When informative attentional pre-cues were used (*temporal pre-cue task*), the ventral premotor cortex and the left inferior parietal cortex were activated to predict stimulus onset and speed up the motor response (Coull et al., 2000). Even during a purely perceptional task, such as the *serial prediction task*, the ventral premotor cortex activated during temporally predictable ISIs (Schubotz & von Cramon, 2001). The observation that motor areas, such as premotor or inferior parietal cortices, are activated in both perceptual representations of actions and their execution suggests that the main goal of perceptual implicit timing is to enhance prospective motor function (Coull & Nobre, 2008).

In motor timing research, the cerebellum has been pointed out to be crucial, especially for event timing (Ivry et al., 2002). Patients with focal cerebellum lesions performed the finger tapping and intermittent circles task and showed more variability when performing the tasks with the impaired hand (ipsilesional) than with the unimpaired hand (contralesional) (Ivry et al., 2002). However, in the continuous cycles task, there was no difference in variability between the hands.

It appears that sequential effects are processed more automatically than the variable foreperiod effect (Mioni et al., 2018). While the variable foreperiod effect relies on the prefrontal structures connected to executive functions (Triviño et al., 2010), this is not true for sequential effects (Mioni et al., 2018). Sequential effects are preserved in the presence of prefrontal lesions (Triviño et al., 2010, 2011) and remain unaffected by working memory demands (Capizzi et al., 2013). Instead, neural structures linked to the sequential effects are the motor/premotor circuitry (Vallesi et al., 2007), left subcortical structures and inferior parietal cortex (Triviño et al., 2016). These structures are connected to a medial, subcortical network, which includes projecting fibres from the anterior cingulate to limbic structures, such as the thalamic nuclei and the ventral striatum (Jones et al., 2013). Due to this neural divergence, it has been suggested that sequential effects rely on brain regions that are more primitive and mature sooner than prefrontal structures (Vallesi & Shallice, 2007).

Conclusion. To summarise, the SMA, cerebellum, BG, and right inferior frontal and parietal cortices are implicated in explicit timing (Coull & Nobre, 2008), while the lateral prefrontal cortex (Triviño et al., 2010), motor/premotor circuitry (Vallesi et al., 2007) and left subcortical structures (Triviño et al., 2016) are linked to implicit timing.

Hemispheric Lateralisation for Explicit and Implicit Timing

The hemispheric lateralisation of explicit and implicit timing functions has been suggested by several authors (Geiser et al., 2008; Hosseini et al., 2020; Kagerer et al., 2002). When comparing implicit with explicit perceptual timing in a verbal rhythm task, the right temporoparietal areas were activated during the explicit timing task (i.e., judging whether a sentence was “isochronous” or “rhythmic”), and the left temporoparietal areas were linked to the implicit timing task (i.e. judging whether the sentence was a statement or a question, not noticing the rhythmic difference between the sentences; Geiser et al., 2008). Additionally, right hemisphere damage may lead to reduced accuracy in explicit timing tested by the

temporal reproduction task and left hemisphere damage may lead to difficulties in implicit timing tested by the temporal prediction task (Hosseini et al., 2020). Also, the right hemisphere was crucial for the explicit timing ability to reproduce durations longer than 2-3 s (Kagerer et al., 2002).

As motor control is left-lateralised (Rushworth et al., 2003), an overlap with the neural substrates of implicit timing was suggested (Coull & Nobre, 2008). The left hemisphere was found to be responsible for the feedforward specification of prospective motor dynamics, while the right hemisphere primarily compares the current limb position in space to the intended goal position using sensory feedback (Serrien et al., 2006). Coull and Nobre (2008) suggested that temporal processing functions in parallel in the two hemispheres. While implicit timing (left hemisphere) utilises previously learned temporal information to predict stimulus duration or onset, in explicit timing tasks (right hemisphere), the current stimulus duration is recorded in working memory and compared to the incoming sensory feedback. To sum up, the literature has found a general pattern of right-hemispheric activity in explicit timing and left-hemispheric activity in implicit perceptual timing (Coull & Nobre, 2008).

Time Perception and the Mesial Temporal Lobe

The mesial temporal lobe (MTL) is a crucial brain area for time perception. Specifically, the hippocampus plays a crucial role in the cortico-striatal circuitry involved in interval timing. For instance, a neuroimaging study found that the hippocampus and striatum work together when processing implicit temporal expectations from mnemonic associations, which highlights the role of the hippocampal-striatal network in the processing of temporal associations (van de Ven et al., 2020). Also, a competitive interaction was found between hippocampal and striatal areas, which led to the conclusion that if one system was damaged, the other system was facilitated (Poldrack & Packard, 2003). This effect may be due to the direct projections from the dorsal striatum to the MTL, which have been linked to interval timing, as illustrated in Figure 1 (Matell et al., 2003; Meck, 2005, p. 4). Also, animal studies have found increased dopaminergic transmission in the dorsal striatum due to hippocampal lesions, which may lead to time perception alterations (Lipska et al., 1992; Meck, 2005).

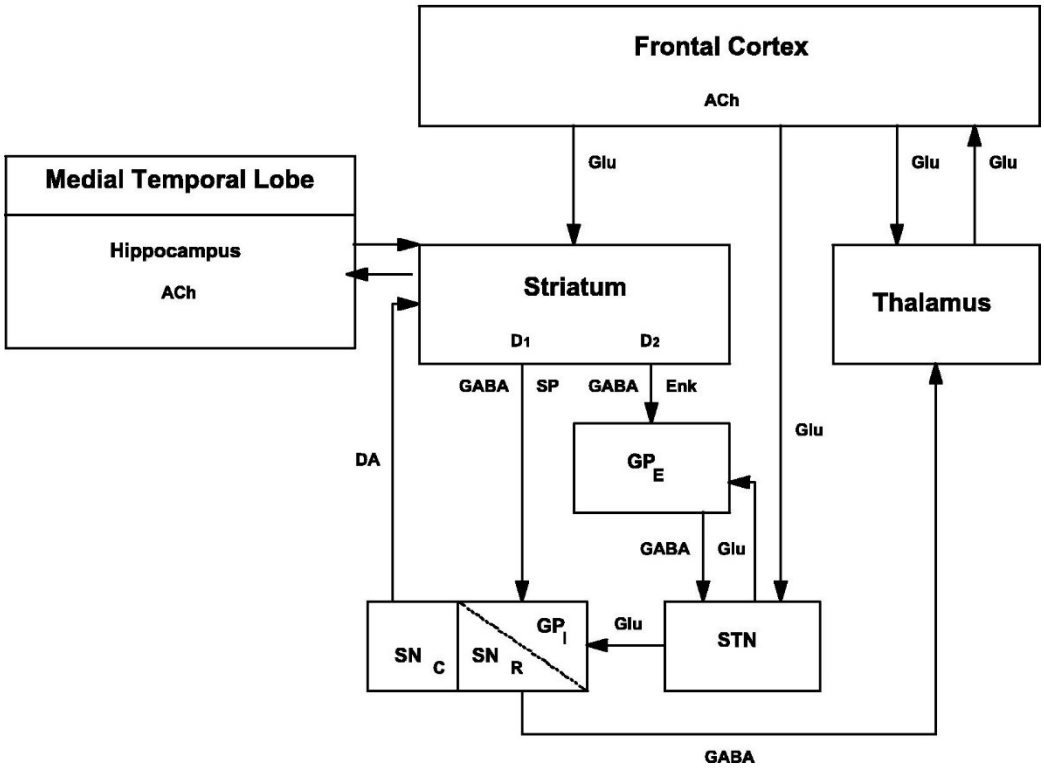

Figure 1. *A model of the neurotransmitter networks and corticostriatal/hippocampal circuitry that are thought to be involved in time perception in the seconds- to minutes range. Matell and Meck (2000, 2004) provide characterisations of these anatomical connections as well as how cortico-striatal coincidence detection and subsequent thalamocortical feedback affect the temporal control of behaviour. "Ach, acetylcholine; Glu, glutamate; SP, substance P; Enk, enkephalin; GABA, c-aminobutyric acid; DA, dopamine; D1, dopamine D1 receptor subtype; D2, dopamine D2 receptor subtype; GPE, globus pallidus external capsule; GPI, globus pallidus internal capsule; SNC, substantia nigra pars compacta; SNR, substantia nigra pars reticulata; and STN, subthalamic nucleus" From Meck, W. H. (2005). Neuropsychology of timing and time perception. Brain and Cognition, 58(1), p. 4. Copyright © 2004 Elsevier Inc. All rights reserved.*

Animal research provides additional evidence for the involvement of the MTL, including the hippocampus, in time perception. Using single-cell recordings, researchers found that specific

cells in the hippocampus, called “time cells”, have distinct firing patterns depending on the point in time an event occurred in a sequence (MacDonald et al., 2011). Time cells are thought to represent the flow of time in memory sequences and fire parallel to those hippocampal cells responsible for space, which integrates time and space in the hippocampus (Eichenbaum, 2014). This leads to the conclusion that the hippocampus provides a crucial mechanism for the organisation of various experience elements into a coherent representation in memory (Eichenbaum, 2014).

More evidence for the involvement of the MTL in timing stems from fMRI studies. Utilising multivoxel pattern similarity analysis of their fMRI data, Sherman et al. (2023) found that longer duration judgements were associated with greater temporal pattern change in the MTL, specifically the left hippocampus. The authors postulate that this pattern change is associated with subjective duration judgements. Pattern stability in the left hippocampus has been connected to an individual’s memory of temporal proximity. More specifically, greater pattern dissimilarity was thought to appear when remembered events were farther apart (Ezzyat & Davachi, 2014). These results add to mounting evidence that the hippocampus is involved in short-term temporal processing, but further research is required to determine whether and how the observations apply to other groups (e.g. different age groups, individuals with neurological disorders; Sherman et al., 2023).

Explicit Time Perception and the Mesial Temporal Lobe

Several authors have found explicit timing impairments in patients with MTL damage (Drane et al., 1999; Ehrlé et al., 2001; Melgire et al., 2005; Noulhiane et al., 2007; Palombo et al., 2016; Perbal et al., 2000, 2001; Richards, 1973; Vidalaki et al., 1999; see Table 1). One historical study is the case of the individual H.M., who underwent resection of both MTLs and experienced severe memory impairment thereafter (Richards, 1973). In a time reproduction task, H.M. systematically underestimated longer time intervals (20-300 s), while

his timing abilities were intact for shorter time intervals (1-20 s). Eisler and Eisler (2001) concluded that temporal lobe structures, such as the hippocampus, are implied in the task instruction maintenance in the short-term memory while accumulated clock readings are kept even without regular temporal lobe function.

However, there are mixed results on the duration range affected by MTL impairments. A recent study found that amnestic patients with MTL damage showed impairments in the temporal judgments of long durations (>4 min) but not short durations (<90 s) (Palombo et al., 2016). This study suggests that the hippocampus is crucial for temporal duration estimations in the order of minutes but not the order of seconds. In contrast, a case study of an amnestic patient with MTL damage investigated the temporal production and reproduction of three temporal durations in the second range (5, 14 and 38 s; Perbal et al., 2000). Similarly to the H.M. case, the patient demonstrated a systemic underestimation in the reproduction of durations in the second range (14 and 38 s) compared to the control group. Perbal et al. (2001) repeated the task paradigm with 18 epilepsy patients who underwent a unilateral MTL resection and found that participants with right MTL lesions underestimated all three durations compared to patients with left MTL lesions and controls. However, they underestimated the durations only in the production task, not in the reproduction task, as documented before by Perbal et al. (2000). The authors assumed that those underestimations stem from distorted conventional units saved in long-term memory retained by the right MTL which renders it essential in translating a duration into an accurate time production.

The Right MTL in Explicit Timing. Several studies have examined the lateralisation of explicit time perception in the MTL and highlighted deficits in patients with right MTL damage (Drane et al., 1999; Melgire et al., 2005; Perbal et al., 2001; Vidalaki et al., 1999). One study compared the time judgements of 53 unilateral TLE patients with the ones of 24 healthy controls following a Wada assessment (Drane et al., 1999). Candidates with

medically intractable epilepsy underwent a unilateral amobarbital injection to evaluate their language and memory functioning before performing an anterior temporal lobectomy. After the resolution of the drug effects, the participants had to judge how long it had been since the administration of the drug. Both patients with left and right TLE underestimated that time period after receiving the injection in the right hemisphere. Similar to healthy controls, patients with left TLE estimated time more precisely when they knew that they would be asked for a time judgment after the second amobarbital dose. This is an example of a prospective timing task in which the participants are informed about the later time estimation task before the time period begins. However, this effect only occurred when the second amobarbital dose was injected into the left hemisphere. Patients with right TLE did not improve their time judgements under those conditions. This led the authors to conclude that the right MTL was critical to accurate time judgements (Drane et al., 1999).

Another study demonstrated that TLE patients with right-sided lesions showed greater variability and reduced sensitivity in time bisection and time reproduction tasks with periods from 500 ms to 8 s (Vidalaki et al., 1999). Additionally, Melgire et al. (2005) found that the duration judgements of patients with right MTL resections were more variable than the control group's judgements in all tested duration ranges (milliseconds and seconds) and conditions (auditory and visual stimuli). The authors suggested that the right temporal lobe was responsible for the decision-making in temporal estimation, specifically when the present signal duration is contrasted with previously learned short and long time periods, as in the time bisection task.

The Left MTL in Explicit Timing. Some studies have highlighted the role of the left temporal lobe in explicit timing (Ehrlé et al., 2001; Noulhiane et al., 2007; Samson et al., 2001). For instance, a significant impairment in auditory temporal abilities for brief time periods (i.e., between 10 and 100 ms) was found in TLE patients with left-sided lesions

compared to right TLE patients and controls (Ehrlé et al., 2001; Samson et al., 2001). However, no deficit was found for longer time periods. Another study tested the production of time intervals and verbal estimation of time in patients with either right or left MTL resection (Noulhiane et al., 2007). They found that patients with left MTL lesions were impaired in both tasks, while right MTL lesion patients only showed impairments in time production. Both patient groups overestimated 1 to 8-minute durations in the time production task. The authors reasoned that the shorter subjective time perception may be caused by insufficient attention allocation to the time intervals. The time production task is an example of a prospective timing paradigm as described above, while the verbal estimation task is an example of a retrospective timing paradigm in which the participants are not informed about a later time estimation task before the target time period begins (Noulhiane et al., 2007). Since the left MTL group exhibited impairments in retrospective timing, while the right MTL patients did not, it can be claimed that the left MTL is essential for estimating time in retrospect. Taken together, those studies suggest that the left and right MTL may play different roles in explicit time perception.

Implicit Time Perception and the Mesial Temporal Lobe

Since no studies directly tested implicit timing abilities in MTL patients utilising paradigms such as the foreperiod task, a study about temporal order (involving sequencing, recency and list discrimination) was taken into account. Palombo and Verfaellie (2017) proposed that the MTL may not only be involved in the explicit judgement of temporal order tasks but also in their implicit assessment. To support that claim, they cite a study by (Schapiro et al., 2014), which utilised a paradigm that yielded the incidental encoding of sequences of shapes, scenes, tones or syllables, which were displayed in temporal regularities with some items always co-occurring. The control group could discriminate the regularities from novel recombinations of the items, while the MTL patient was not. Moreover, the study ruled out

other explanations than impairment in incidental encodings, such as misunderstanding of the test instruction or inattention during the task, as the patient could point out which individual items were shown. The authors claim that the MTL is involved in extracting temporal regularities, which is important in implicit timing tasks (Schapiro et al., 2014). More evidence stems from functional neuroimaging research with healthy subjects. One fMRI study conducted an exogenous temporal expectation task aimed at engaging automatic, implicit timing abilities rather than deliberate, explicit ones (Li et al., 2012). They found an activation of the MTL, temporal parietal conjunction and thalamus related to their task paradigm. Taken together, there are indications that the MTL's role in implicit time perception should be further investigated.

Conclusion. Multiple studies have found explicit timing impairments in temporal lobe epilepsy (TLE) patients who underwent a unilateral MTL resection to relieve medically intractable epilepsy (Melgire et al., 2005; Noulhiane et al., 2007; Perbal et al., 2001), the Wada test to plan this resection (Drane et al., 1999) or suffered from unilateral hippocampal sclerosis (Ehrlé et al., 2001) or unilateral TLE in general (Vidalaki et al., 1999). Those studies specifically highlight the lateralisation of explicit timing abilities. Moreover, explicit timing tasks have been tested in amnesia patients with MTL damage (Palombo et al., 2016; Perbal et al., 2000; Richards, 1973). Those studies indicate that the MTL plays an important role in explicit time perception. However, the MTL's involvement in implicit time perception remains unclear in the current literature.

Table 1

Studies on Time Perception in MTL Patients

Author	Year	n° patients	Age patient/s	n° left MTL	Age left MTL	n° right MTL	Age right MTL	n° controls	Age controls	MTL SX or DX	Timing Task	Explicit/ Implicit	Modality	Time range
Richards	1973	1	47							Amnesia, MTL damage	TPro, TRepro	Explicit	-	1 - 300 s
Vidalaki et al.	1999	19		10	29.8±2.2	9	33.3±3.1	14	35.5±2.5	TLE	TRepro, TBT	Explicit	Visual	0.5 - 8 s
Drane et al.	1999	53		27	34.9±9.8	26	32±8.3	24	25.8±4.7	TLE, Wada	VET	Explicit	Visual	>15 min
Perbal et al.	2000	1	40					48	23.5	Amnesia, MTL damage	TPro, TRepro	Explicit	Visual	5 - 38 s
Perbal et al.	2001	18		9	35 (20-37)	9	33 (16-56)	11	32 (21-64)	TLE, MTL resection	TPro, TRepro	Explicit	Visual	5 - 38 s
Ehrlé et al.	2001	18		8	32 (25-44)	10	34 (17-52)	6	31 (22-55)	TLE, MTL damage	AD	Explicit	Auditory	80 - 1000 ms
Melgire et al.	2005	16		8	39 (24-47)	8	37 (26-61)	11	39 (25-51)	TLE, MTL resection	TBT	Explicit	Visual, Auditory	2 - 8 s; 50 - 200 ms
Noulhiane	2007	28		14	33.5±7.3	14	35.1±8.5	14	32.3±5.9	TLE, MTL resection	TPro, VET	Explicit	Visual	1 - 8 min
Palombo et al.	2016	8	57 (47-65)					14	62.6±10.1	Amnesia, MTL damage	VET	Explicit	Visual	40 s – 7 min 50 s

Note. Age, age in years; TLE, temporal lobe epilepsy; MTL, mesial temporal lobe; TRepro, temporal reproduction; TPro, temporal production; TBT, time bisection task; VET, verbal estimation task; AD, asynchrony discrimination.

Mesial Temporal Lobe Epilepsy

Epilepsy

One of the most prevalent and disabling chronic neurologic disorders is epilepsy (Devinsky et al., 2018). In a meta-analysis of 222 studies, Fiest et al. (2017) found that the lifetime prevalence of epilepsy was 7.60 per 1,000 people (95% CI 6.17-9.38), whereas the point prevalence of active epilepsy was 6.38 per 1,000 people (95% confidence interval [95% CI] 5.57-7.30). While seizures are the core symptom of epilepsy, not everyone who has seizures has epilepsy. An acute injury to the central nervous system (CNS) of a structural, systemic, toxic, or metabolic nature can cause epileptic seizures. Those seizures are acute manifestations of the injury and may remain a singular event when the underlying issue has been treated, or the acute phase has passed (Hesdorffer et al., 2009). In contrast, epilepsy patients suffer from *unprovoked* seizures, meaning they occur without precipitating factors (Beghi, 2020). The International League Against Epilepsy (ILAE) Epidemiology Commission suggests that two or more unprovoked seizures occurring more than 24 hours apart are required to classify an epilepsy case for population-based studies of epilepsy epidemiology (Thurman et al., 2011). The onset of those recurrent unprovoked seizures may be categorised as focal (arising in one hemisphere of the brain), generalised (arising in both hemispheres at the same time), or unknown (Fisher et al., 2018).

Epilepsy is a serious neurological condition which can greatly lower an individual's quality of life due to the recurring events of seizures and their aftermath. Moreover, the underlying aetiology of the seizures and adverse treatment effects can have impactful cognitive, neurological, psychological and social consequences (Beghi, 2020). In some cases, epilepsy can even lead to sudden, nontraumatic, unexpected death, termed Sudden unexpected death in epilepsy (SUDEP) (Nashef et al., 2012). SUDEP is thought to be caused by seizures and thereby induced cardiorespiratory alterations (Beghi, 2020). Although most epilepsy patients

can reach seizure freedom using antiepileptic drug (AED) therapy, around one third of the patients are resistant to the drugs. Drug resistance in epilepsy patients is the phenomenon wherein seizures cannot be completely controlled despite using multiple AEDs, either alone or in various combinations (Löscher et al., 2020).

Mesial Temporal Lobe Epilepsy

Patients suffering from the most prevalent form of partial epilepsies, mesial temporal lobe epilepsy (MTLE), are typically resistant to AED therapy (Uslu et al., 2019). MTLE is often caused by hippocampal sclerosis (HS), the most frequent underlying pathophysiology in TLE. However, the causal link between the emergence of MTLE and HS remains unclear (Uslu et al., 2019). While AED therapy typically has a poor long-term prognosis in MTLE-HS patients, surgical intervention is frequently reported as successful (Kumlien et al., 2002). In a study examining 83 patients with intractable MTLE, only 23% achieved seizure control on AEDs. However, following surgery, 72% of the individuals gained seizure freedom (Kumlien et al., 2002). It remains unclear why some MTLE patients experience intractable seizures while others benefit from AED treatment (Uslu et al., 2019).

The Effects of Surgery in MTLE Patients. To achieve permanent freedom from seizures, epilepsy surgery is a promising therapy option. For focal epilepsy, laser interstitial thermal therapy (LITT) can be used as a minimally invasive surgical intervention, which offers an alternative to resective surgery and delivers enduring results with moderate efficacy (Brotis et al., 2021). Also, LITT is thought to cause fewer cognitive deficits, especially when the dominant hemisphere is involved in MTLE (Donos et al., 2018). One study found that, in this case, even though a decline in verbal and narrative memory was noted, the naming function remained unimpaired (Donos et al., 2018). The authors postulated that the observed declines were small at the group level, and that further improvement in cognitive functions could be expected over the following months as the functional recovery post-surgery was not

concluded yet (Donos et al., 2018). This study sets a good example, highlighting the importance of evaluating cognitive deficits after a surgical intervention. Usually, the success of surgical interventions in epilepsy patients is measured mainly based on freedom from seizures or the continued use of anticonvulsants, which often does not adequately consider the impact on the complex reality of the patient's life.

During epilepsy surgery, cognitive functions may be impacted. For instance, after anteromedial temporal lobe resection in the language-dominant (typically left) hemisphere, a decreased naming ability was found, especially for unique objects, such as famous faces and landmarks (Drane et al., 2009). Additionally, right anteromedial temporal lobe resection impaired the ability to recognise those unique objects (Drane et al., 2009). Regrettably, those functions are not routinely assessed in the process of preoperative monitoring, even though they can seriously impact a person’s social, occupational and academic life (Drane et al., 2015). Besides the need for thorough cognitive assessment when planning a surgical intervention, understanding the scope of cognitive impairment in MTLE patients caused by the disease or its underlying aetiology is vital to plan other treatment possibilities that target well-being and social and occupational functioning.

Cognitive Impairment in MTLE Patients. Memory impairment is the most common cognitive deficit in MTLE-HS patients (Uslu et al., 2019). Verbal memory impairments were demonstrated in left MTLE patients, and nonverbal, visual memory impairments were found in right MTLE patients (Delaney et al., 1980). Memory deficits in right TLE patients can be seen as a disruption in a ventral visual processing system in charge of pattern recognition, object identification and facial memory (Barr, 1997). The view of strong lateralisation of verbal and spatial memory functions in the MTL was challenged by a study that found that right and left MTLE-HS patients did not differ in their spatial memory performance (Glikmann-Johnston et al., 2008). The integrity of both the right and the left

MTL proved important in navigating, learning and recalling objects and their locations (Glikmann-Johnston et al., 2008).

Moreover, working memory, executive functions and attention were associated with an abnormal connectivity between dorsal PFC and caudate in TLE patients (Riley et al., 2011). Interestingly, some authors examined cognitive abilities in drug-responsive and pharmacoresistant MTLE patients and found that the pharmacoresistant group performed worse on the attention tests (Uslu et al., 2019). The authors reasoned that the increased frequency of seizures in the pharmacoresistant group may cause verbal attention deficit. All MTLE-HS patients in this study demonstrated poor performance in frontal lobe function tests and memory, which points out the importance of the connection between the temporal lobe and prefrontal structures (Uslu et al., 2019). One study examining patients with childhood absence epilepsy (CAE) found that poor executive functioning was associated with decreased temporal sensitivity, reflected by the underestimation of time periods and high temporal variability in the time bisection task (Cainelli et al., 2019). The authors reason that there is an overlap of neural substrates (i.e. the frontostriatal system) involved in both time perception and CAE (Cainelli et al., 2019; Droit-Volet, 2013).

Time Perception in Mesial Temporal Lobe Epilepsy Patients

As discussed previously, there is evidence that time perception is compromised in MTLE patients (Melgire et al., 2005; Noulhiane et al., 2007; Perbal et al., 2001; Vidalaki et al., 1999). One study tested the performance of 19 patients with TLE in the temporal reproduction and time bisection task (Vidalaki et al., 1999). There were 10 TLE patients with left-hemisphere focus, nine with right-hemisphere focus and 14 healthy controls. When compared to the control group, timing ability was reduced in the right TLE group in both tasks. The left TLE group's differences from the controls were insignificant, even though their PSE was shifted leftward compared to the control group, which suggests a pacemaker

acceleration of the internal clock. The authors suggest that the right and the left temporal lobe were both involved in time perception in different ways. Both of the task paradigms used in this study tested explicit timing. Until this point, no studies have been conducted on TLE patients testing their implicit time perception.

The current study aims to examine the explicit as well as implicit timing abilities of patients with MTLE. To that end, 21 MTLE patients from the Center for Epilepsy in Erlangen and 20 neurologically healthy participants were examined using a foreperiod task as an implicit measure and a time bisection task as an explicit measure of timing abilities. Considering the findings of Vidalaki (1999), it is hypothesised that MTLE patients show decreased explicit timing abilities compared to healthy controls. Moreover, it is assumed that MTLE patients will perform worse on the implicit timing task than the healthy controls as the MTL may be involved in extracting temporal regularities, which are crucial for implicit timing abilities (Schapiro et al., 2014).

Hypotheses:

1. MTLE patients show decreased accuracy in the explicit timing task compared to healthy controls.
2. MTLE patients show decreased implicit timing abilities compared to healthy controls.

Materials

Participants

In this study, 21 epilepsy patients and 20 neurologically healthy subjects participated. The epilepsy patients were between 19 and 76 years old (M = 39.10, SD = 17.79) and the controls were between 23 and 79 years old (M = 45.90, SD = 15.85). There were 13 males and eight females in the patient group, and in the control group, there were six males and 14 females. All the epilepsy patients were recruited from the Center for Epilepsy in Erlangen, Germany. Based on the medical records (e.g. MRI data), patients with TLE and MTL alterations, such as hippocampal sclerosis, were selected. Six patients had MTL alterations on the right side, 11 on the left side and four had bilateral MTL alterations. Those MTL alterations were restricted to the hippocampus in seven cases (P01, P04, P06, P09, P10, P13, P14, P15), three patients had alterations that extended within the MTL cortices (P08, P16, P20) and 10 patients suffered from alterations extending beyond the MTL (P02, P03, P05, P07, P11, P12, P17, P18, P19, P21; see Appendix A). Nineteen patients received AEDs, such as Lamotrigin and Levetiracetam (see Appendix B). The control subjects were recruited from the researcher's peer group and had no history of psychiatric or neurological disorders. An overview of the demographic characteristics of both groups can be found in Table 2.

Table 2

Demographic Characteristics

	Patients		Controls	
	Mean	SD	Mean	SD
Age	39.1	17.79	45.9	15.85
Education	10.1	1.70	11.3	1.19
IQ	103.8	13.34	117.1	13.20

Note. Age: age in years; Education: education in years; IQ: verbal IQ tested with the MWT-B intelligence test.

Materials

Neuropsychological and Cognitive Examination

All tests were standardised, non-invasive and did not involve any health risks for the participants. The following tests assessed the participants' memory, naming abilities, verbal fluency, cognitive estimation and general intelligence.

Berlin Amnesia Test (BAT). The BAT is used for people aged 13 to 65 to assess learning ability and possible anterograde amnesia (Metzler et al., 2010). The test lasts 45 to 60 minutes and is divided into eight sub-tests designed to assess mild to severe mnestic deficits. Both figural-spatial and verbal memory performance are measured. The reliability of the BAT is considered high as the retest reliability is .93, .75, .90 and .95 for the four total scores. For this study, three verbal memory subtests were performed. The first subtest assessed the number of words recalled from a previously learned list of 20 words, further referred to as *Free Recall*. The second subtest required the subject to identify 15 previously learned words in a semantic context, further referred to as *Semantic Interference*. The third subtest used from the BAT assessed the participants' short-term memory and is called the

Digit-Span task. Specifically, the instructor read a three-digit span, and the participant had to repeat it correctly. If the current digit-span was recalled successfully, another digit would be added to the next digit-span. This task continued until the participant could not repeat the digit-span correctly.

Boston Naming Test (BNT). The BNT (Kaplan et al., 1983) tests the ability to name objects. In epilepsy patients, the BNT is commonly used to investigate seizure focus, as patients with left TLE show significantly worse performance than right TLE patients (Alessio et al., 2006). In a group of 51 epilepsy patients, the test-retest reliability after eight months was as high as .94 (Sawrie et al., 1996). The test consists of 60 line drawings of graded difficulty (from "bed" to "abacus") and takes 10 to 20 minutes to complete. Within a time span of 20 seconds, the participants were required to name the object in the drawing correctly (Spreen & Risser, 2003). More than 12 mistakes indicated impaired naming abilities.

Regensburg Verbal Fluency Test (RWT). The RWT is primarily used for neuropsychological patients aged 18 and over and is intended to record verbal fluency (Aschenbrenner et al., 2000). Subjects are given two minutes to generate words of a specific category, such as animals or words starting with the letter “s”. Two of the five subtests assess the ability to switch between two (formal lexical or semantic) categories. For example, one task is to name a sport and a fruit alternately. The various subtests have a retest reliability over three weeks between .72 and .89. In this study, the participants were required to state as many animals as possible within two minutes.

Cognitive Estimation Test (TKS). The TKS is suitable for the neuropsychological diagnosis of adolescents and adults with brain damage and takes about five minutes to complete (Berger & Rockenbauch, 2002). Noteworthy, the TKS has a reliability of .76 (Cronbach's alpha) and assesses cognitive estimation, which is supported by executive

functions and semantic knowledge. Specifically, the participants of this study were asked to rate the size, weight, and number of objects shown in photographs. Finally, they were asked to make time estimations based on questions such as “How long does a flight from Frankfurt to New York take?”.

Multiple-Choice Vocabulary Intelligence Test (MWT-B). The MWT-B tests verbal intelligence within five minutes and can be used with subjects aged 20 to 65 (Lehrl, 1999). For this purpose, the participants had to underline existing words, ignoring the pseudo-words (e.g. "Nale - Sahe - Nase - Nesa - Sehna"). There were 37 items, and the IQ was calculated based on the number of correctly identified words. For example, an average IQ of 100 was obtained when identifying 27 words correctly.

Timing Tasks

Subjects were seated in front of a computer screen (14”) with an approximate distance of 60 cm. The computer was used to run and record the experimental events via Psychopy Software (Peirce, 2009). The foreperiod task was first performed, and second, the time bisection task. After reading the instructions and going through a brief trial run, the experiment started, and three blocks of 42 trials each were performed for each task. As shown in Figure 2, both tasks used a grey circle with a cross inside on a white background to indicate time intervals. More specifically, the beginning of the time interval was marked by the line of the circle becoming noticeably thicker, and the appearance of the cross marked the end of the interval. The thin circle was shown for 500 ms, and the thicker circle was displayed for one of the following interval durations: 480, 720, 960, 1200, 1440, 1680, or 1920 ms. After this time interval, the cross appeared for 500 ms. Even though the task stimulus and general procedure were identical, the task instructions and the measured variables differed between the two tasks. The foreperiod task required subjects to respond as quickly as possible to the appearance of the cross by pressing the space bar; the target variable measured was response time. Instead, in

the time bisection task, participants had to memorise two standard durations, one short (480 ms) and one long (1920 ms), each shown 10 consecutive times. In the testing phase, the participants had to judge if the presented interval durations were more similar to the short or the long standard interval. As soon as the cross appeared in the middle of the circle, they were instructed to press the "s" key for "short" or the "l" key for "long". The PSE and the WR were considered the target variables for this task.

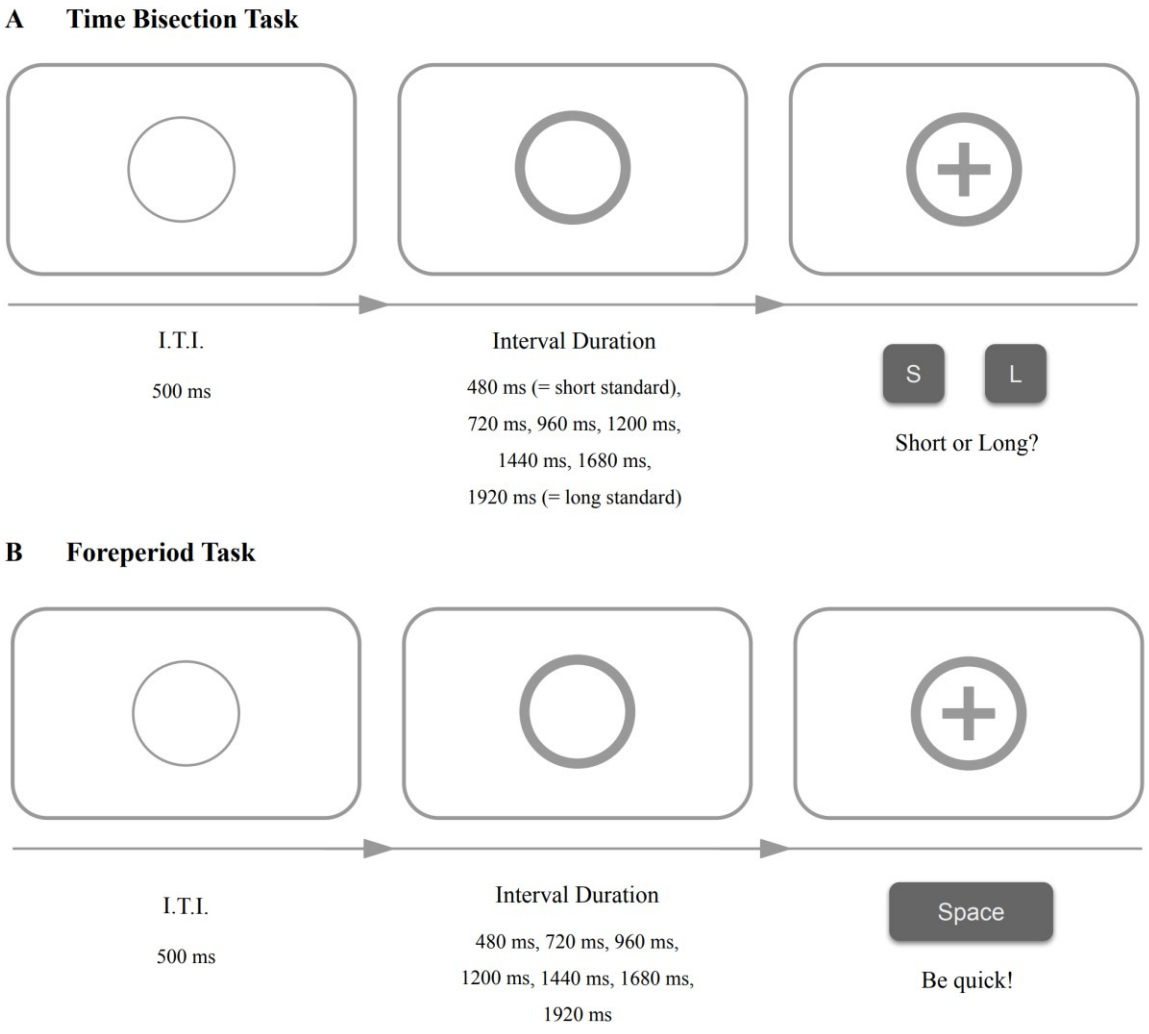

Figure 2. *A visual representation of the time bisection (A) and the foreperiod task (B).*

Procedure

Firstly, the participants were informed about the examination's nature, meaning and scope and signed informed consent (see Appendix C). Secondly, the aforementioned neuropsychological tests were administered. The patient group performed additional neuropsychological assessments, meaning supplemental subtests of the BAT and RWT, the Edinburgh Handedness Inventory (EHI; Oldfield, 1971) and the Incompatibility subtest of the Test of Attentional Performance (TAP; Fimm, n.d.). Thirdly, the participants performed the foreperiod task and the time bisection task. Taken together, the examination lasted about one hour, depending on the participants' performance.

Statistical Analysis

The statistical analysis was conducted using the R environment (http://R-project.org/). Firstly, missing values and reaction times below 150 ms were removed as they likely stemmed from anticipating the stimulus. Then, the z-scores of the interval duration (*Duration*), *Group*, *IQ* and *Age* variables were computed. For the time bisection task, a 7-point psychometric function was determined to plot the z-scores of *Duration* on the x-axis and the proportion of "long" responses on the y-axis. Furthermore, two indices were calculated, one for the perceived duration and one for temporal sensitivity. The index for the perceived duration, the PSE, indicated the stimulus duration at which subjects equally frequently replied "short" and "long". Whereas the WR, the index of temporal sensitivity, was calculated by dividing the standard deviation of the psychometric function by the midpoint duration (1200 ms). Next, the proportion of times the participant pressed "long" as a response was analysed using a generalised linear mixed model analysis with binomial assumptions including *Group* (patients vs controls), *Duration* (480 ms, 720 ms, 960 ms, 1200 ms, 1440 ms, 1680 ms, 1920 ms), *Age* and *IQ* and their interactions as fixed factors. Subjects were treated as random effects. A model including *Age* was found to be unreliable because of high collinearity. Thus,

Age was excluded from the model. Using the example of IQ, a significant main effect of *IQ* with a risk ratio lower than 1 would signify a curve shift to the right with an increasing IQ score. Similarly, a significant risk ratio below 1 would indicate a flatter curve for increasing IQ values, and a significant risk ratio greater than 1 for the main effect of *IQ* and *Duration* would indicate a steeper curve depending on the increase of the IQ.

For the foreperiod task, the RTs were inverted by dividing by -1000 (*iRT*) and plotted to confirm the normality assumption. A linear mixed model fit by REML t-tests using Satterthwaite's method, including *Group* (patients vs controls), *Duration* (480 ms, 720 ms, 960 ms, 1200 ms, 1440 ms, 1680 ms, 1920 ms) and *IQ* and their interactions as fixed factors was conducted to analyse the inverted reaction times. Thereby, subjects were treated as random effects. For example, a significant main effect for *IQ* and *Duration* would signify foreperiod effect changes depending on the subject's IQ. Meanwhile, to identify the foreperiod effect, a negative slope of the regression line has to be captured, indicating faster RTs with increasing interval durations. Thus, a positive main effect for *IQ* and *Duration* would imply a reduction of the foreperiod effect with increasing IQ.

Further, independent t-tests were conducted on the PSE, WR, foreperiod effect, neuropsychological test scores and demographic variables (i.e. age and education) to compare the performance of the patients and the controls. Additionally, the effect size was estimated with Cohen's *d*. Moreover, Pearson correlation coefficients were computed to assess the relationship between the abovementioned variables. Lastly, two subjects had to be excluded from the analysis. One control subject was aged above 76 years, and one patient did not complete one of the tasks.

Results

Neuropsychological Tests and Demographic Statistics

Firstly, the t-tests for Free Recall ($t_{(37)} = 5.05$, $p = <.001$), Semantic Interference ($t_{(37)} = 2.97$, $p = .005$), Naming Mistakes ($t_{(37)} = -3.21$, $p = .003$) and Language Fluency ($t_{(37)} = 4.33$, $p = <.001$) were significant, meaning that there was a difference in performance between patients and controls. Table 3 summarises the means, standard deviations and cut-off scores of the neuropsychological tests per group. Secondly, there was a positive correlation between age and IQ ($r = .57$, $p = <.001$), indicating that higher age was associated with higher IQ. Thirdly, the t-tests for education ($t_{(36)} = 2.43$, $p = .020$) and IQ ($t_{(37)} = 3.14$, $p = .003$) were significant, and both of the measures were higher in the control group (see Table 2).

Table 3

Neuropsychological Test Scores

		Patients		Controls	
	Cut-Off	Mean	SD	Mean	SD
Free Recall	<12	11.62	3.11	16.2	2.73
Semantic Interference	<26	26.57	2.34	28.6	1.85
Digit Span	<5	6.81	1.25	6.7	0.92
Naming Mistakes	>12	10.45	10.425	2.75	1.943
Language Fluency	<33	31.24	8.99	45.65	13.67
Cognitive Estimation	<11	10.55	2.72	11.74	1.85

Note. Cut-Off: Raw score which indicates a performance below average (z = -1); Free Recall: Free recall of a previously learned list of words (BAT Subtest 1); Semantic Interference: Finding the same words in a semantic context (BAT Subtest 2); Digit Span: Digit span forward, measures short-term memory (BAT Subtest 5); Naming Mistakes: Mistakes in the

Boston Naming Test; Language Fluency: Verbal Fluency Test (RWT), cut-off score depends on the age of the subject, <33 is the cut-off for the age group between 30 and 41 years; Cognitive Estimation Test: TKS in German.

Explicit Timing: Time Bisection Task

There was a significant effect for *Duration* (RR = 3.78, 95% CI [3.43, 4.17], p = <.001), indicating that the proportion of the response "long" increased when the interval duration increased. Thus, the experiment elicited the expected responses and was performed correctly overall. As illustrated in Figure 3, there was a significant interaction effect between *Group* and *Duration* (RR = 0.64, 95% CI [0.57, 0.72], p = <.001), indicating that the proportion of "long" responses decreases with increasing duration in the patient group. However, the interaction cannot be interpreted in isolation. Considering the strong positive main effect of duration, the small negative effect of the interaction between *Group* and *Duration* indicates an overall flatter curve and less precise temporal judgements in the patient group.

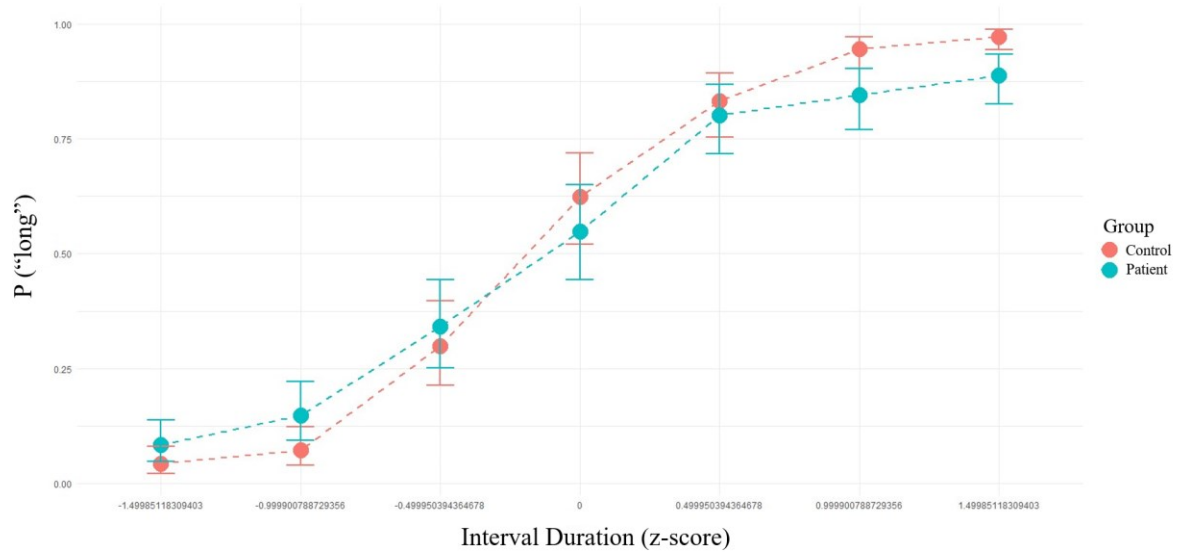

Figure 3. *This figure displays the psychometric curves of the time bisection task per group. The z-scores for each interval duration (i.e. 480 ms, 720 ms, 960 ms, 1200 ms, 1440 ms, 1680 ms, 1920 ms) are on the x-axis, and the proportions of "long" responses are on the y-axis.*

Additionally, there was a significant interaction effect between *Duration*, *IQ,* and *Group* (RR = 0.76, 95% CI [0.67, 0.86], p = <.001), demonstrating a flatter psychophysical curve in the patients with a higher IQ (see Figure 4).

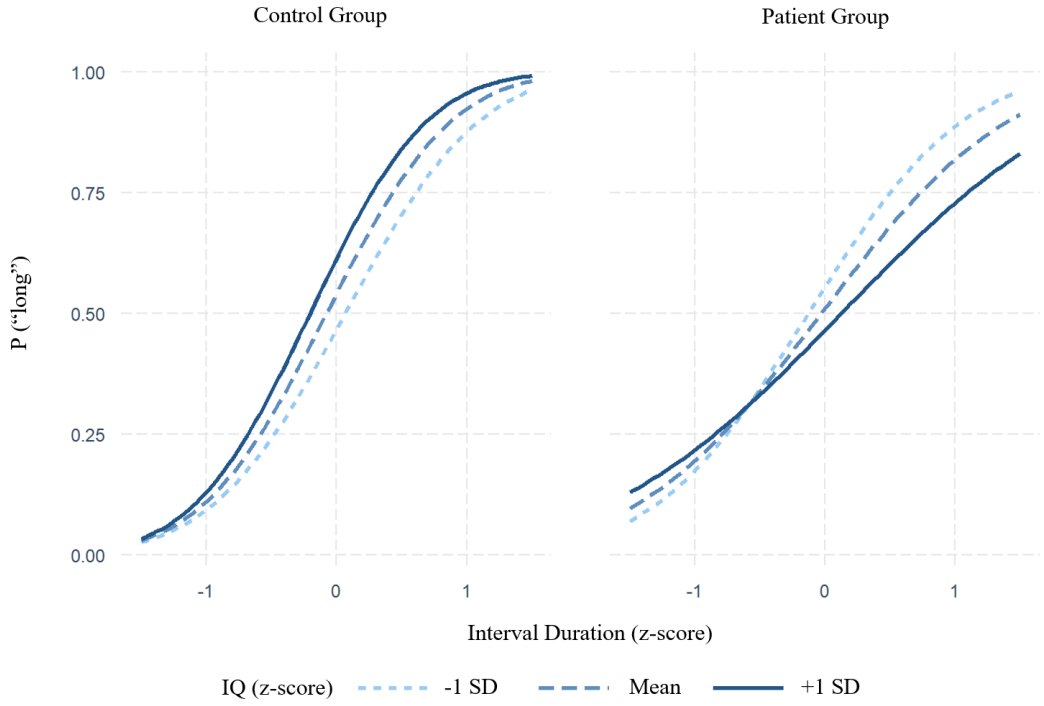

Figure 4. *The interaction effects of Duration, Group and IQ in the time bisection task. The z-scores of the Duration variable are on the x-axis, and the proportions of "long" responses are on the y-axis.*

Moreover, the WR of the patient group was higher than the control group's WR (patient's WR = 0.44, *SD* = 0.22; control's WR = 0.31, *SD* = 0.14), indicating a significantly lower temporal sensitivity in the patient group ($t_{(37)}$ = -2.24, p = .031). Also, the data conveys a negative correlation between the WR and education (r = -.39, p = .016) and two neuropsychological tests ($r_{(\text{Free Recall})}$ = -.44, p = .005; $r_{(\text{Fluency})}$ = -.34, p = .03). There was no significant difference between groups concerning the PSE ($t_{(37)}$ = -0.57, p = .572).

Implicit Timing: Foreperiod Task

There was a significant main effect for *Duration* ($F_{(10,4992)}$= -0.19, p = <0.001), meaning that all the subjects exhibited the foreperiod effect as their RTs became shorter with longer durations (see Figure 5).

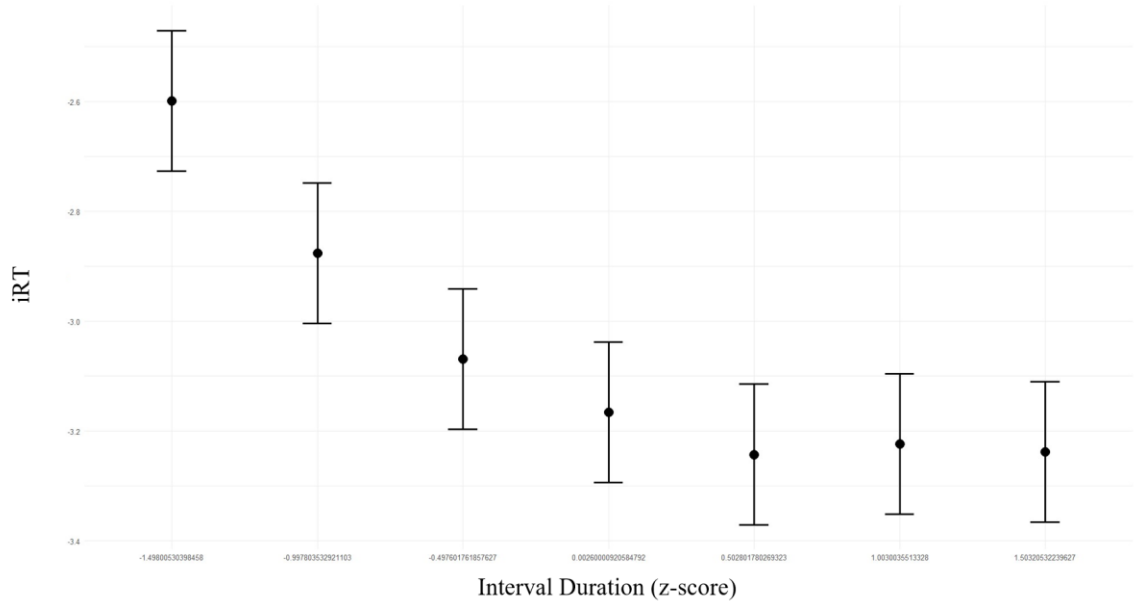

Figure 5. *This figure displays the foreperiod effect in the sample. The z-scores for each interval duration (i.e. 480 ms, 720 ms, 960 ms, 1200 ms, 1440 ms, 1680 ms, 1920 ms) are on the x-axis, and the inverted reaction times are on the y-axis.*

However, there were no significant effects for *Group* or *Duration* and *Group*. This means there was no statistical difference between the slopes of the foreperiod effects of controls and patients, as shown in Figure 6. Also, the main effect for *IQ* was insignificant.

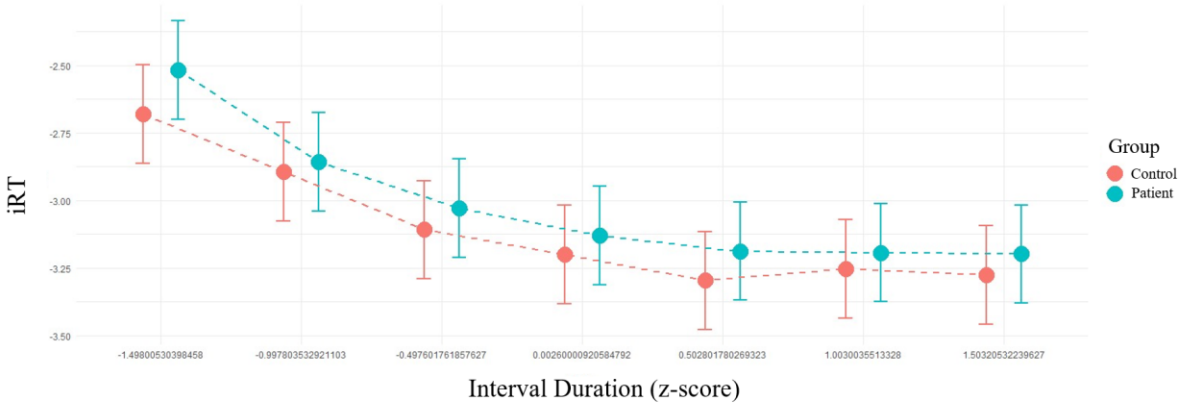

Figure 6. *This figure displays the foreperiod effect per group. The z-scores for each interval duration (i.e. 480 ms, 720 ms, 960 ms, 1200 ms, 1440 ms, 1680 ms, 1920 ms) are on the x-axis, and the inverted reaction times are on the y-axis.*

Discussion

Explicit and Implicit Timing

This study aimed to examine the explicit and implicit time perception of MTLE patients. First, it was found that MTLE patients were less precise in explicit temporal judgements than the control subjects. Moreover, the WR of the patient group was higher than that of the control group, reflecting lower temporal sensitivity in MTLE patients. As explicit timing abilities pose higher cognitive demands, it was expected that epilepsy patients with MTL alterations would demonstrate a worse performance than healthy controls. In line with those results, previous studies found that TLE patients with a right-hemisphere focus displayed lower temporal sensitivity in the time bisection task than the controls (Melgire et al., 2005; Vidalaki et al., 1999). Also, a study employing other explicit timing paradigms, such as time production or reproduction tasks, pointed out deficits in MTLE patients (Perbal et al., 2001). Indeed, the authors found that patients with right MTL lesions underestimated durations in the second range when they had to produce them but not when they had to reproduce them (Perbal et al., 2001). Even though the present study utilised another explicit timing task with durations in the millisecond range, the results confirm an explicit timing deficit in MTLE patients with right-hemisphere focus. According to Drane et al. (1999), the right temporal lobe is a critical structure for accurate, explicit temporal judgements.

Despite that, explicit timing deficits in MTLE patients with left-hemisphere focus were also reported (Ehrlé et al., 2001; Noulhiane et al., 2007; Samson et al., 2001). For instance, TLE patients with left-sided lesions showed a significant impairment in auditory temporal abilities durations in the millisecond range (Ehrlé et al., 2001; Samson et al., 2001). Another study found that patients with left MTL lesions were impaired in the production of time intervals and verbal time estimation (Noulhiane et al., 2007). To sum up, it is suggested in the literature that the left and the right MTL are implied in explicit time perception, which

confirms the results of the present study. Unlike the present study, previous studies on this topic differentiated between MTLE patients with right- and left-hemispheric focus. Nevertheless, the present study contributes to the literature by employing the time bisection task in MTLE patients.

One explanation for the poor accuracy of MTLE patients in explicit timing is an underlying timing deficit. Alternatively, the poor performance could reflect a temporal working memory deficit (Vidalaki et al., 1999). As the MTL was hypothesised to organise experiences into a coherent representation in memory (Eichenbaum, 2014; Uslu et al., 2019), it could be that the MTLE patients did not correctly memorise the standard interval durations or that they had difficulties retaining the interval durations shown during the experiment. Also, patients might have confused the current interval with a previously presented one, which made their scores more variable (Vidalaki et al., 1999). According to Perbal et al. (2001), deficits in explicit timing could be explained by distorted representation of durations in the long-term memory.

In the present study, three measures of memory were conducted. In two of them, the controls outperformed the patients (i.e. Free Recall, Semantic Interference). Nevertheless, the average performance of the patient group in the Semantic Interference task was within the norm and did not indicate a memory deficit in the patient group. Nevertheless, the mean score of the patients in the Free Recall task was slightly below average, as 45% of the patients did not produce a satisfactory number of recalled words. In addition, the lower the temporal sensitivity of a participant was, the fewer words they recalled from the previously learned list of words and the fewer animals they listed in the language fluency task. Therefore, a lower performance on explicit timing may be connected to memory and language functions. In line with that, Mioni, Grondin, et al. (2017) found lower temporal sensitivity and a greater underestimation in the time bisection task in PD patients with MCI. In another sample of PD patients, higher temporal variability in two explicit timing tasks was associated with lower

working memory and short-term memory (Perbal et al., 2005). Also, healthy controls with lower MMSE and semantic fluency scores performed worse on the time bisection task (Mioni et al., 2018). Similarly, less precise explicit temporal judgments were found in older subjects with higher MMSE scores, and the authors suggested that cognitive control functions may underly explicit time processing (Capizzi et al., 2022). All in all, those results suggest that cognitive functions influence the outcome of explicit timing tasks and that temporal abilities are not the only construct measured by the time bisection task.

Secondly, this study did not find a significant difference between MTLE patients' PSE and healthy controls' PSE. In particular, a reduced PSE in the patient group would indicate an acceleration of the pacemaker's velocity (Killeen et al., 1997; Meck, 1996). However, this study showed no evidence of pacemaker acceleration or deceleration in MTLE patients or healthy controls. Conversely, Vidalaki et al. (1999) showed that TLE patients with a left-hemisphere focus displayed a significant leftward shift of the PSE compared to the control group. Although, another study failed to reveal significant differences in the PSE of MTLE patients and controls as well (Melgire et al., 2005). Hence, the PSE alone may not be a reliable performance measure in the time bisection task.

Lastly, patients with higher IQs were less precise in their explicit timing judgements than patients with lower IQs. An explanation could be that the IQ test in this study assessed verbal IQ, which tends to improve over time and reach its peak around 50 years of age (Kaufman, 2001). Indeed, in the present sample, higher age was associated with a higher IQ score. Correspondingly, Capizzi et al. (2022) found that older and more compromised subjects delivered less precise explicit temporal judgements. Admittedly, the authors reasoned that this change displayed a deficit in overall cognitive function rather than in temporal processing. In any case, those results suggest that, instead of a high IQ, an increased age may have caused worse outcomes in the explicit timing task.

Overall, there was a larger difference between patients and controls in explicit timing abilities than in implicit timing abilities. MTLE patients, as much as healthy controls, benefitted from the elapse of time and reacted faster the longer they waited for the stimulus to appear. Even though the MTLE patients reacted generally slower than the healthy controls, they still displayed the foreperiod effect. Also, the foreperiod effect persisted in the subjects independently of their IQ. This result could be explained by the fewer cognitive demands implicit timing tasks pose compared to explicit timing tasks (Capizzi et al., 2022). In particular, the implicit timing task had a straightforward and non-temporal goal, as the participants simply had to respond to the appearance of a cross without memorising interval durations or judging time periods like in the explicit timing task. To our knowledge, no study has investigated the foreperiod effect in MTLE patients yet. Another paradigm designed to measure incidental encoding of temporal regularities has shown that controls could discriminate novel recombinations from the temporal regularities while the MTL patient was not (Schapiro et al., 2014). Instead, the present study could not confirm the involvement of the MTL in subconsciously extracting temporal regularities, as the foreperiod effect was preserved in the MTLE patients. In line with that, it has been reported that patients with another neurological disease, PD, showed spared implicit timing in the presence of impaired explicit timing (Mioni et al., 2018). Likewise, Bégel et al. (2017) found that subjects with "beat deafness" had difficulties with explicit rhythm but not implicit rhythm tasks. Also, patients with right frontal damage were impaired in deliberate attentional orientation to durations but performed normally when implicit rhythmic patterns were involved (Triviño et al., 2010, 2011). Taken together with the results of this paper, it is suggested that explicit and implicit timing abilities are distinct processes and that implicit timing is a more stable function not heavily influenced by brain damage or neurological diseases.

Limitations and Strengths

There are several limitations to this study which should be considered. Firstly, the IQ, education and neuropsychological test scores were significantly higher in the control group than in the patient group. As cognitive control processes were hypothesised to impact explicit temporal judgement (Capizzi et al., 2022), the patient group possibly displayed a lower temporal sensitivity because they had a lower IQ, education level and cognitive abilities. Future studies should match the control group to the patient group regarding IQ and education. Secondly, whether the time bisection task reflects explicit timing abilities or memory functions remains unclear. Future studies should work on differentiating those cognitive functions with a different paradigm for testing explicit timing.

Thirdly, the patient group was heterogeneous concerning the aetiology of the MTLE, the scope of brain damage, years of illness and age. Some patients had structural alterations of the hippocampus, while others had alterations outside the MTL as well. Also, the number of years suffering from the disease and the age differed greatly. Considering the small sample size, those differences between the patients created a highly heterogeneous sample. Future studies should create a more homogenous patient group restricted to hippocampal sclerosis cases and focused on a specific age group, as age can greatly influence the outcome of timing tasks (Capizzi et al., 2022). Fourthly, no distinction was made between MTLE patients with left-, right- or bilateral alterations in the statistical analysis. Previous studies have pointed out the lateralisation of time perception, and future studies should increase the sample size to analyse the patients according to the lateralisation of structural alterations and epileptic focus.

Nevertheless, this study adds to the literature because it was the first to examine implicit time perception utilising the foreperiod paradigm in MTLE patients. Few studies have examined explicit and implicit timing in the same experimental session. In doing so, this study contributes to the discussion about the differentiation of explicit and implicit time perception.

Future Directions

In the future, implicit time perception should be further investigated in different patient groups. The study of implicit timing may offer insights into the temporal processing of cognitively impaired patients as it poses fewer demands on cognitive control functions than explicit timing tasks (Capizzi et al., 2022). Specifically, an implicit measure of time perception is not influenced by other executive functions as much as explicit timing is. Consequently, it may be a more sensitive measure of cognitive impairment and uncover deficits in automatic subconscious processes. In general, more attention should be brought to temporal processing as it is crucial for organising and planning daily activities, such as executing an action at the right moment or judging the duration of an event to plan a future action (Cainelli et al., 2019). Also, future studies should investigate possible connections between implicit and explicit time perception and develop a model of time perception that integrates both timing aspects. After defining temporal functioning and impairment in various patient groups, it is also essential to think of an effective treatment for time perception dysfunctions. Patients could learn strategies to deal with their shortcomings and facilitate daily planning activities. For instance, patients could set reminders on their smartphones to facilitate performing actions at the right point in time. Moreover, patients could consult a psychologist or peer to write down daily tasks and their required time frames together. Memorising semantic knowledge about how long daily tasks usually take may assist the organisation of their day. Acquired semantic knowledge about temporal dimensions may compensate for diminished time sensitivity, and alarms may help the patients perform actions at the appropriate time. Overall, more research must be conducted on explicit and implicit time perception, and the impact of timing deficits in daily functioning must be determined to plan successful treatment interventions in the future.

Conclusion

Explicit and implicit timing abilities influence behaviour and underly daily decision-making and planning. Explicit timing is the deliberate estimation of a time period, while implicit timing describes the unconscious processing of temporal information. This study revealed explicit and implicit time perception alterations among MTLE patients. Overall, there was a larger difference between patients and controls in explicit timing abilities than in implicit timing abilities. MTLE patients showed lower temporal sensitivity in explicit timing, while their foreperiod effect in the implicit timing task was largely preserved. This study was the first to explore implicit timing in MTLE patients. Thus, further research is required to investigate the impact of timing deficits in different patient groups. Besides the neuropsychological assessments of memory, executive functions, language and attention, time perception should be routinely investigated in patients with MTL alterations.

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Appendix A

Demographic Characteristics of MTLE Patients

Patients	Aetiology	Age	Education	IQ	Illness
P01	HS	34	10	95	11
P02	TLE	76	8	124	8
P03	Cavernom	66	12	130	1
P04	HS	55	12	94	55
P05	Meningocele, EA	28	12	101	6
P06	HS	27	10	101	1
P07	Ischemia	20	12	100	9
P08	EA	30	8	100	1
P09	HS, MTL resection	54	8	100	17
P10	HS	27	10	100	2
P11	Lesion	24	12	100	7
P12	TBI	60	10	97	8
P13	HS	61	8	130	50
P14	HS	48	10	100	31
P15	HS	30	8	101	12
P16	Heterotopia	43	10	95	3
P17	HSV-Encephalitis	24		88	1
P18	Ischemia, right HC	19	12	100	9
P19	Cavernom	19	10	88	
P20	HS, MTL resection	31	8	101	31
P21	HS, aTL resection	54	12	130	52

Note. HS: hippocampal Sclerosis; TLE: temporal lobe epilepsy; EA: enlarged amygdala; MTL resection: mesial temporal lobe resection; Age: Age in years; Education: education in years; IQ: IQ tested by the MWT-B intelligence test: Illness: Length of Illness in Years.

Appendix B

Antiepileptic Drugs of MTLE Patients

AED therapy	N of patients	Patients
No AED therapy	2	P06, P09
Lamotrigin	9	P02, P03, P07, P08, P10, P11, P12, P14, P16
Levetiracetam	7	P04, P08, P15, P16, P17, P18, P19
Brivaracetam	4	P01, P12, P13, P21
Lacosamid	5	P01, P14, P17, P18, P20
Perampanel	2	P04, P10
Valproat	2	P05, P13
Oxcarbazepin	2	P07, P15
Pregabalin	1	P13
Clobazam	1	P13
Cenobamat	1	P21
Quetiapine	1	P21
Bisoprolol	1	P21

Note. AED: Antiepileptic drug.

Appendix C

Patientenaufklärung

Mesiale Temporallappenepilepsie - Auswirkungen auf das prospektive Gedächtnis und die Zeitwahrnehmung

Sehr geehrte Patientin, sehr geehrter Patient,

im Rahmen dieser wissenschaftlichen Studie wird überprüft, ob bestimmte Epilepsien mit Gedächtnis- und Zeitwahrnehmungsproblemen einhergehen. Dazu werden Epilepsiepatienten und gesunde Personen untersucht.

Die Studie besteht aus drei Teilen:

1. Neuropsychologische Untersuchung: Gedächtnis, Aufmerksamkeit, Intelligenz, Sprache
2. Computertest zur Zeitwahrnehmung „Explizite und Implizite Zeitwahrnehmung“: Auf einem Computerbildschirm werden Kreise gezeigt und Sie sollen mit einem Tastendruck reagieren, wenn ein Kreuz erscheint. Dieser Test hat zwei Teile:
    a. Sie drücken die Leertaste, wenn das Kreuz erscheint (unbewusste/implizite Zeitwahrnehmung).
    b. Sie prägen sich eine lange und eine kurze Zeitspanne ein und beurteilen dann, ob eine gezeigte Zeitspanne eher kurz (S-Taste) oder lang (L-Taste) war (bewusste/explizite Zeitwahrnehmung).
3. Virtuelles Gedächtnis Brettspiel „Virtual Week“: Dieses Spiel führt Sie durch Situationen aus dem Alltag und Sie werden gebeten sich Termine und Verpflichtungen einzuprägen und zum richtigen Zeitpunkt virtuell auszuführen.

Die gesamte Untersuchung wird hier im Epilepsiezentrum Erlangen stattfinden und ungefähr zwei Stunden in Anspruch nehmen. Im Anschluss an die Testung wird der verantwortliche Neuropsychologe die Ergebnisse der neuropsychologischen Untersuchung mit Ihnen besprechen. Dabei können Sie mehr über Ihre Gedächtnis- und Zeitwahrnehmungsfähigkeiten erfahren und einen Beitrag dazu leisten, epilepsiechirugische Eingriffe besser zu planen.

Diese Tests haben kein gesundheitliches Risiko, können jedoch durch die geforderte Konzentration belastend wirken. Bei zu hoher Belastung, ist ein Abbruch jederzeit möglich. Ihre Teilnahme an der Untersuchung ist selbstverständlich freiwillig und kann jederzeit ohne Angabe von Gründen beendigt werden. Die Nicht-Teilnahme oder Beendigung der Studie birgt selbstverständlich keinerlei Nachteile für die weitere medizinische Behandlung. Eine Aufwandsentschädigung wird bei dieser Studie nicht geboten.

Wenn Sie die Bereitschaft zeigen, an der beschriebenen Untersuchung teilzunehmen, tragen Sie dies bitte mit Ihrer Unterschrift ein. Mit Ihrer Unterschrift bestätigen Sie, dass Sie zum Zeitpunkt der Studie weder schwanger noch stillend sind.

Bei Rückfragen wenden Sie sich bitte an:

Dr. Michael Schwarz

Schwabachanlage 6

91054 Erlangen

Tel.: 09131 – 85 46148

Email: Michael.Schwarz@uk-erlangen.de

Einwilligungserklärung

Hiermit erkläre ich,

Vorname_____Nachname_____

Straße_____PLZ/Ort_____

geboren am_____ dass ich durch Herrn Dr. Schwarz, mündlich und schriftlich über das Wesen, die Bedeutung und Tragweite der wissenschaftlichen Studie „Mesiale Temporallappenepilepsie - Auswirkungen auf das prospektive Gedächtnis und die Zeitwahrnehmung“ informiert wurde und ausreichend Gelegenheit hatte, meine Fragen hierzu in einem Gespräch zu klären. Ich habe insbesondere die mir vorgelegte Patientenaufklärung vom _____ verstanden und eine Ausfertigung derselben und dieser Einwilligungserklärung erhalten. Ich bin bereit, an der wissenschaftlichen Untersuchung im Rahmen der o.g. Studie teilzunehmen. Mir ist bekannt, dass ich meine Einwilligung jederzeit ohne Angabe von Gründen und ohne nachteilige Folgen für mich zurückziehen und einer Weiterverarbeitung meiner Daten jederzeit widersprechen kann.

_____ _____

Datum, Unterschrift Patient

Hiermit erkläre ich, den/die o.g. Patient/in _____über Wesen, Bedeutung und Tragweite der o.g. Studie mündlich und schriftlich aufgeklärt und ihm/ihr eine Ausfertigung der Information (Patientenaufklärung) sowie dieser Einwilligungserklärung übergeben zu haben.

_____ _____

Datum, Unterschrift des Studienkoordinators

Datenschutzrechtliche Einwilligungserklärung *(Zutreffendes bitte ankreuzen)*

Studie: Mesiale Temporallappenepilepsie - Auswirkungen auf das prospektive Gedächtnis und die Zeitwahrnehmung

Studienleiter: Dr. Michael Schwarz (09131 – 85 46148; Michael.Schwarz@uk-erlangen.de)
Institution: Universitätsklinikum Erlangen, Epilepsiezentrum, Schwabachanlage 6 , 91054 Erlangen

Ich bin damit einverstanden, dass die einleitend genannte Person bzw. ein Mitarbeiter der einleitend genannten Institution Einblick in meine Original-Krankenunterlagen nimmt.

Ich stimme zu, dass Daten, die meine Person betreffen (hierzu gehören insbesondere auch Krankheitsdaten aus meinen Krankenunterlagen) unter der Verantwortung der oben genannten Institution in verschlüsselter Form

( ) für psychologische Studien mit der oben genannten Fragestellung gespeichert und verarbeitet werden.

Nach Art. 6 Abs. 2 Nr. 3c BayDSG können Ihre Daten ohne erneute Einwilligung zur Durchführung wissenschaftlicher oder historischer Forschung verwendet werden, wenn das wissenschaftliche oder historische Interesse an der Durchführung des Forschungsvorhabens Ihr Interesse an dem Ausschluss der Zweckänderung erheblich überwiegt und der Zweck der Forschung auf andere Weise nicht oder nur mit unverhältnismäßigem Aufwand erreicht werden kann,

( ) Ich bin mit dieser Regelung einverstanden.

Widerruf der Zustimmung zur Datenverwendung

Ich weiß, dass ich meine Zustimmung zur Verwendung meiner Daten jederzeit und ohne Angabe von Gründen gegenüber der einleitend genannten Institution bzw. Person widerrufen kann und dass dies keinen Einfluss auf meine etwaige weitere ärztliche Behandlung hat.

( ) Im Falle des Widerrufs bin ich damit einverstanden, dass meine Daten zu Kontrollzwecken weiterhin gespeichert bleiben. Ich habe jedoch das Recht, deren Löschung zu verlangen, sofern gesetzliche Bestimmungen der Löschung nicht entgegenstehen.

Bis zu einem Widerruf bleibt die Datenverarbeitung rechtmäßig.

Ich bin mir bewusst, dass im Falle einer anonymisierten Speicherung meiner Daten deren Löschung auf meinen Wunsch nicht möglich ist.

Hinweise zum Datenschutz

A. Allgemeine Angaben

a. Namen und die Kontaktdaten des Verantwortlichen sowie gegebenenfalls seines Vertreters:

Dr. Michael Schwarz

Schwabachanlage 6

91054 Erlangen

Tel.: 09131 – 85 46148

Email: Michael.Schwarz@uk-erlangen.de

b. Kontaktdaten des Datenschutzbeauftragten:

Krankenhausstraße 12

91054 Erlangen

Telefon: 09131 85-46810

Email: datenschutz(at)uk-erlangen.de

c. Rechtsgrundlage der Datenverarbeitung: Ihre Einwilligung

d. Dauer der Speicherung: 2 Jahre

e. Beschwerderecht: Sie können sich an Bayer, den Landesbeauftragten für den Datenschutz in München, als Aufsichtsbehörde wenden, wenn Sie der Ansicht sind, dass die Verarbeitung Ihrer personenbezogenen Daten rechtswidrig erfolgt.

B. Allgemeine Rechte

Das Recht auf Löschen und auf „Vergessenwerden“ ist eingeschränkt, soweit Ihre Daten für die wissenschaftliche Forschung erforderlich sind.

Näheres erfahren Sie hier:

1. Recht auf Löschung:

Sie haben das Recht, von dem Verantwortlichen zu verlangen, dass Sie betreffende personenbezogene Daten unverzüglich gelöscht werden, und der Verantwortliche ist verpflichtet, personenbezogene Daten unverzüglich zu löschen, sofern einer der folgenden Gründe zutrifft:

a) Die personenbezogenen Daten sind für die Zwecke, für die sie erhoben oder auf sonstige Weise verarbeitet wurden, nicht mehr notwendig.

b) Sie widerrufen Ihre Einwilligung, auf die sich die Verarbeitung stützte, und es fehlt an einer anderweitigen Rechtsgrundlage für die Verarbeitung.

c) Die personenbezogenen Daten wurden unrechtmäßig verarbeitet.

Sie haben keinen Anspruch auf Löschung, soweit Ihre Daten für wissenschaftliche Forschung erforderlich sind und die Löschung voraussichtlich die Verwirklichung der Ziele dieser Verarbeitung unmöglich macht oder ernsthaft beeinträchtigt,

oder

die Verarbeitung zur Geltendmachung, Ausübung oder Verteidigung von Rechtsansprüchen erforderlich ist.

2. **Mitteilungspflicht im Zusammenhang mit der Berichtigung oder Löschung personenbezogener Daten oder der Einschränkung der Verarbeitung:**

   Der Verantwortliche teilt allen Empfängern, denen personenbezogenen Daten offengelegt wurden, jede Berichtigung oder Löschung der personenbezogenen Daten oder eine Einschränkung der Verarbeitung mit, es sei denn, dies erweist sich als unmöglich oder ist mit einem unverhältnismäßigen Aufwand verbunden. Der Verantwortliche unterrichtet Sie über diese Empfänger, wenn Sie dies verlangen.

Das Recht auf Datenübertragbarkeit ist eingeschränkt oder ausgeschlossen, wenn die Forschung im öffentlichen Interesse liegt oder die Daten ein Geschäftsgeheimnis darstellen.

Näheres erfahren Sie hier:

1. **Recht auf Datenübertragbarkeit:**
   a) Sie haben das Recht, die Sie betreffenden personenbezogenen Daten, die Sie einem Verantwortlichen bereitgestellt haben, in einem strukturierten, gängigen und maschinenlesbaren Format zu erhalten, und Sie haben das Recht, diese Daten einem anderen Verantwortlichen ohne Behinderung durch den

Verantwortlichen, dem die personenbezogenen Daten bereitgestellt wurden, zu übermitteln, sofern die Verarbeitung mithilfe automatisierter Verfahren erfolgt.

b) Bei der Ausübung Ihres Rechts auf Datenübertragbarkeit gemäß Absatz a) haben Sie das Recht, zu erwirken, dass die personenbezogenen Daten direkt von einem Verantwortlichen einem anderen Verantwortlichen übermittelt werden, soweit dies technisch machbar ist.

c) Die Ausübung des Rechts auf Datenübertragbarkeit lässt das Recht auf Löschen der Daten unberührt. Dieses Recht gilt nicht für eine Verarbeitung, die für die Wahrnehmung einer Aufgabe erforderlich ist, die im öffentlichen Interesse liegt oder in Ausübung öffentlicher Gewalt erfolgt, die dem Verantwortlichen übertragen wurde.

d) Das Recht gemäß Absatz 2 darf die Rechte und Freiheiten anderer Personen nicht beeinträchtigen.

2. Werden personenbezogene Daten an ein Drittland oder an eine internationale Organisation übermittelt, so haben Sie das Recht, über die geeigneten Garantien gemäß Artikel 46 DSGVO im Zusammenhang mit der Übermittlung unterrichtet zu werden.

Hinweise:

Die in dieser Studie betriebene Forschung liegt im öffentlichen Interesse. Die Ausübung des Rechts auf Datenübertragbarkeit kann deshalb von Ihnen nicht ausgeübt werden.

C. Rechte, die durch den Forschungszweck beschränkt sind

Das Recht auf Berichtigung, Einschränkung der Verarbeitung und Auskunft ist ausgeschlossen, sofern diese Rechte voraussichtlich die Verwirklichung des

Forschungszwecks unmöglich machen oder ernsthaft beinträchtigen und die Beschränkung für die Erfüllung des Forschungszwecks notwendig ist.

Näheres erfahren Sie hier:

Sie haben als betroffene Person folgende Rechte,

sofern diese Rechte nicht voraussichtlich die Verwirklichung des Forschungszwecks unmöglich machen oder ernsthaft beinträchtigen und die Beschränkung für die Erfüllung des Forschungszwecks notwendig ist:

1. **Recht auf Berichtigung:**

   Sie haben das Recht, von dem Verantwortlichen unverzüglich die Berichtigung Sie betreffender unrichtiger personenbezogener Daten zu verlangen. Unter Berücksichtigung der Zwecke der Verarbeitung haben Sie das Recht, die Vervollständigung unvollständiger personenbezogener Daten – auch mittels einer ergänzenden Erklärung – zu verlangen.

2. **Recht auf Einschränkung der Verarbeitung:**

   Sie haben das Recht, von dem Verantwortlichen die Einschränkung der Verarbeitung zu verlangen, wenn eine der folgenden Voraussetzungen gegeben ist:

   a) die Richtigkeit der personenbezogenen Daten wird von Ihnen bestritten. Die Einschränkung der Verarbeitung kann in diesem Fall für eine Dauer verlangt werden, die es dem Verantwortlichen ermöglicht, die Richtigkeit der personenbezogenen Daten zu überprüfen;

   b) die Verarbeitung unrechtmäßig ist und Sie die Löschung der personenbezogenen Daten ablehnen und stattdessen die Einschränkung der Nutzung der personenbezogenen Daten verlangen;

c) der Verantwortliche die personenbezogenen Daten für die Zwecke der Verarbeitung nicht länger benötigt, Sie sie jedoch zur Geltendmachung, Ausübung oder Verteidigung von Rechtsansprüchen benötigen

Wurde die Verarbeitung eingeschränkt, so dürfen diese personenbezogenen Daten – von ihrer Speicherung abgesehen – nur mit Ihrer Einwilligung oder zur Geltendmachung, Ausübung oder Verteidigung von Rechtsansprüchen oder zum Schutz der Rechte einer anderen natürlichen oder juristischen Person oder aus Gründen eines wichtigen öffentlichen Interesses der Union oder eines Mitgliedstaats verarbeitet werden.

Haben Sie eine Einschränkung der Verarbeitung erwirkt, werden Sie von dem Verantwortlichen unterrichtet, bevor die Einschränkung aufgehoben wird.

3. Auskunftsrechte:

Sie haben das Recht, von dem Verantwortlichen eine Bestätigung darüber zu verlangen, ob Sie betreffende personenbezogene Daten verarbeitet werden; ist dies der Fall, so haben Sie ein Recht auf Auskunft über diese personenbezogenen Daten und auf folgende Informationen:

a) die Verarbeitungszwecke;

b) die Kategorien personenbezogener Daten, die verarbeitet werden;

c) die Empfänger oder Kategorien von Empfängern, gegenüber denen die personenbezogenen Daten offengelegt worden sind oder noch offengelegt werden, insbesondere bei Empfängern in Drittländern oder bei internationalen Organisationen;

d) falls möglich die geplante Dauer, für die die personenbezogenen Daten gespeichert werden, oder, falls dies nicht möglich ist, die Kriterien für die Festlegung dieser Dauer;

e) das Bestehen eines Beschwerderechts bei einer Aufsichtsbehörde;

f) Sie haben das Recht, vom Verantwortlichen eine Kopie der personenbezogenen Daten, die Gegenstand der Verarbeitung sind, zu erhalten. Für alle weiteren Kopien, die Sie beantragen, kann der Verantwortliche ein angemessenes Entgelt auf der Grundlage der Verwaltungskosten verlangen. Stellen Sie den Antrag elektronisch, so sind die Informationen in einem gängigen elektronischen Format zur Verfügung zu stellen, sofern Sie nichts Anderes angeben.

   Das Recht auf Erhalt einer Kopie darf die Rechte und Freiheiten anderer Personen nicht beeinträchtigen.

_____

Datum

_____

Name der Probandin / des Probanden

_____

Unterschrift