Investigating Preparatory Alpha and Theta Oscillations in Motor Sequence Learning: An ERD/ERS Study

Nathan Sakirov

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University of Twente - Department of Cognition, Data and Education (CODE)

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First supervisor - Dr. Russell W. Chan

Second supervisor - Prof. Dr. Rob Van der Lubbe

Abstract

While several theoretical frameworks support the cognitive processes entailed in motor sequence learning (MSL), its underlying neurocognitive mechanisms are far from delineated. We aimed to further elucidate the neurocognitive mechanisms of MSL through the investigation of oscillatory activity in the preparation of motor sequences. Previous research has indicated theta oscillations to facilitate executive and working memory processes, and alpha oscillations to promote required motor inhibition within motor preparation. Thus, a new analysis was performed on a previously unpublished EEG dataset with respect to alpha and theta event-related desynchronization (ERD) and synchronization (ERS) patterns in motor preparation. Based on the Go/No-Go Discrete Sequence Production (DSP) paradigm, eighteen participants practised four sequences in six practice blocks and executed familiar and unfamiliar sequences in a test block the following day. Alpha and theta ERD/ERS values were extracted for the test block to contrast between motor preparation for familiar and unfamiliar dominant-hand sequences. For the theta band, analyses revealed predominant ERS in the preparatory period, despite a temporary shift from ERD (starting at -1400ms) to ERS for familiar sequences that was most prevalent (starting at -300ms) in right pre-frontal regions. General ERD was found for the alpha band within motor preparation. While no overall significant change between the two sequence types was identified, interaction analyses revealed a significant increase in ERD for familiar sequences in early preparation (starting at -1300ms), which subsequently decreased (starting at -400ms) in mid-frontal regions. Overall, our results support the relevance of theta oscillations for the storage and retrieval of temporal sequence information within working memory, and the subsiding nature of variable inhibitory properties entailed in preparatory alpha oscillations.

Keywords: Motor Sequence Learning, Motor Preparation, ERD/ERS, ERDS, EEG, DSP, Alpha, Theta

Investigating Preparatory Alpha and Theta Oscillations in Motor Sequence Learning: An ERD/ERS Study

The investigation of motor sequence learning (MSL) is a scientific endeavour that is intricately woven into daily human functioning. A wide variety of our daily activities, ranging from basic tasks such as tying one's shoelaces to more complex tasks such as playing the piano, are products of the goal-directed acquisition of motor sequences that become increasingly simple and automated over time (Chan et al., 2018; Moisello et al., 2011). MSL is thus understood as the process through which a "sequence of motor actions is performed with increasing spatial and temporal accuracy" (Dahms et al., 2019, p. 271).

Therein, repeated practice facilitates the integration of individual movements into synchronized series of actions that require diminishing amounts of effort and attentional monitoring (Abrahamse et al., 2013; Doyon et al., 2018). While the ability to perform movement sequences quickly and accurately is imperative for a wide variety of motor skills, its absence also poses a significant hindrance to basic human functioning (Ariani & Diedrichsen, 2019). In total, investigating the facilitating mechanisms of MSL is imperative to be able to pinpoint the potential avenues through which MSL performance may be improved.

However, to achieve this, we must first understand and provide theoretical support for its underlying cognitive processes. A considerable amount of research throughout the last decades provided invaluable insight into the cognitive mechanisms of MSL (Cohen et al., 1990; Rosenbaum et al., 1995; Verwey, 2001). One of the more recent and notable developments pertains to the Cognitive Framework for Sequential Motor Behaviour (C-SMB, Verwey et al., 2015). Thereby, the C-SMB has guided the development of contemporary literature in the field by elucidating the role of perceptual, central, and motor execution processing levels in MSL. However, such theoretical models are predominantly, albeit not exclusively, contingent upon the availability of decades of behavioural research, thus mainly utilizing insights generated from behavioural measures (Verwey et al., 2015).

Despite the established relevance of these frameworks, support for the underlying neural mechanisms of MSL is comparatively underrepresented (Ariani & Diedrichsen, 2019; Diedrichsen & Kornysheva, 2015; Doyon et al., 2018). This holds specifically true when leveraging the utility of neurophysiological evidence to support and supplement behavioural results (Abrahamse et al., 2016). To contribute to a consolidated picture of the facilitating factors of MSL, this study aims to further elucidate the neurocognitive mechanisms of MSL through the investigation of their associated preparatory oscillatory activity.

The DSP Task and Motor Preparation

However, the extent to which our investigations can positively contribute to the current understanding of MSL is contingent upon the selected experimental paradigm. Amongst other task types, one of the most prevalent experimental paradigms to investigate MSL was developed by Verwey (1999) by the name of the Discrete Sequence Production (DSP) task. In experiments that utilize the DSP paradigm, numerous discrete sequences (in the form of key presses) are performed as a response to spatially corresponding visual stimuli displayed on a computer monitor. Experiments utilizing the DSP paradigm have provided central insight into the theoretical foundations of MSL. This is due to its ability to tease out the development of sequence representations and subsequent inferences that can be made about various types of sequential motor behaviour (Verwey, 1999; Verwey et al., 2015).

The sequences entailed in the DSP paradigm are practised approximately 500 to 1000 times, which leads to the eventual automatization of sequence execution. This allows for the investigation of effects related to the acquisition of new sequences through the presentation of unfamiliar and familiar sequences in a testing phase. Commonly, familiar sequences are executed faster and more accurately than unfamiliar sequences, suggesting that different processes are responsible for their respective execution (De Kleine & Van der Lubbe, 2011; Verwey, 2001; 2021). Contrasting between familiar and unfamiliar sequence performance may thus shed light on the facilitating mechanisms of successful MSL. This is the main experimental manipulation that this thesis is centred upon.

Go/No-Go DSP Task. One fundamental issue entailed within the original DSP task is that preparation and anticipation of evincing motor responses may commence simultaneously while executing a preceding response. In a revision of the original DSP task, entitled the Go/No-Go DSP Task (De Kleine & Van der Lubbe, 2011), two additional signals (go and no-go) are presented to participants prior to sequence reproduction. Participants are only prompted to reproduce a sequence when followed by a go signal. Unlike the original DSP task, this new iteration thus allows the separation of the motor preparation phase from motor execution and post-movement (De Kleine & Van der Lubbe, 2011). For the scope of this thesis, we argue that this distinction is imperative to provide further insight into the neurocognitive mechanisms of MSL.

Motor Preparation. Facilitatory processes that enable sequence execution occur before movement execution. On a basic task level, a well-replicated phenomenon is heightened performance (such as higher response speed) when relevant task information about the anticipated movement is provided prior to the signal for movement execution (Leuthold et al., 1996). Moreover, Nazari et al. (2016) indicate that motor preparation of a planned action facilitates a more accurate completion of a time reproduction task. Furthermore, de Kleine & Van der Lubbe (2011) have shown that the demand for general motor preparation and visual working memory significantly decreases when executing familiar as compared to unfamiliar sequences within the more complex DSP paradigm. The execution of motor sequences can thus strongly benefit from motor preparation. Considering the available evidence, we will focus on the mechanisms that are entailed in the preparation of motor sequences in this thesis.

The Neurocognitive Mechanisms of Motor Sequence Learning

In consideration of the role of the DSP paradigm and the motor preparation phase, we will now turn our attention to the underlying neurocognitive mechanisms of MSL and the tools that can be utilized to investigate them. The goal-directed activity of MSL leverages basic properties of cognitive and motor control, requiring the intentional coordination and regulation of behaviour selection. Simultaneously, unwanted and inappropriate habitual actions must be suppressed, which jointly correspond to the imposed task demands (Dixon, 2015; Latash, 2012).

To illustrate these properties within a DSP paradigm, presented stimuli must initially be visually attended to for a predetermined period of time. This refers to sustained visual attention (Klimesch, 2012). As attended stimuli (in the form of sequences) also need to be successfully remembered and ultimately retrieved, MSL is contingent upon the episodic encoding of stimulus information into working memory (De Kleine & Van der Lubbe, 2011; Rozengurt et al., 2016). The online maintenance of the temporal order information within working memory, as dictated by the order of the visual stimuli, is pivotal to facilitate the correct execution of sequential behaviour (Crivelli-Decker et al., 2018). To simultaneously prevent unwanted action, processes of proactive inhibition occur during motor preparation (Pfurtscheller & Neuper, 2003). Pro-active (as opposed to reactive) inhibition refers to the required inhibition throughout the anticipation and preparation of a motor sequence that may or may not be executed after an execution signal (Van der Lubbe et al., 2021). In total, the fundamental functionality entailed in basic executive processes, sustained visual attention, the encoding of stimulus information into working memory and simultaneous motor inhibition are thus crucial mechanisms that enable and facilitate MSL.

Electroencephalography. To investigate the neural dynamics of such mechanisms, researchers have started utilizing neuroimaging techniques to unravel the spatiotemporal characteristics of their associated brain activity (Berlot & Diedrichsen, 2020; De Lucia et al., 2011). A particularly useful tool to enable such spatiotemporal investigation pertains to the utilization of electroencephalography (EEG) (Van der Lubbe et al., 2021). Herein, the predominant methodology throughout the past decades has been the analysis of Event-Related Potentials (ERP) (Chan et al., 2020; De Kleine & Van der Lubbe, 2011; Swarnkar & Miyapuram, 2020). While ERP analyses serve an important function in the investigation of MSL's neurocognitive mechanisms, ERPs reflect only one method of approximating their underlying neural dynamics. ERPs are event-related transients that reflect the synchrony of neuronal populations at specific temporal timings, while only partially capturing the temporal dynamics of frequency-specific oscillatory activity (Burgess, 2012). An alternative methodology that allows for the full consideration of frequency-specific oscillatory activity was popularized by Pfurtscheller & Lopes da Silva (1999) by the name of Event-related desynchronization and synchronization (ERD/ERS).

Event-Related Synchronization and Desynchronization

Event-related desynchronization and synchronization (ERD/ERS) serves as a methodological tool to investigate non-phase locked decreases (ERD) and increases (ERS) in oscillatory power relative to a specified baseline in predetermined frequency ranges. This means that a singular region of interest (i.e. location on the scalp) can display ERD and ERS at the same time (Pfurtscheller & Lopes da Silva, 1999). Pfurtscheller and & Lopes da Silva (1999) outline three essential factors that determine oscillatory properties. Firstly, the neural dynamics that characterise the occurrences of ERD and ERS are contingent upon intrinsic membrane properties and their dynamics in relation to synaptic processes. Furthermore, oscillatory strength is mirrored by the strength of interconnected networks, such as cortico-cortical or thalamo-cortical feedback loops. Lastly, oscillations are at a dynamic interplay with the modulating nature of local and general neurotransmitter systems. ERD/ERS thus reflects various states of synchrony that can manifest at different frequency bands (Pfurtscheller & Lopes da Silva, 1999).

Despite the potency of ERD/ERS to elucidate the neurocognitive mechanisms of sequential behaviour, its scientific application in MSL has been scarce. Nonetheless, a few key studies have recently provided further insight into the oscillatory activity that underlies MSL (Crivelli-Decker et al., 2018; Meissner et al., 2018; Van der Lubbe et al., 2021). In reconsideration of the previously outlined working memory and motor inhibition processes entailed in MSL, we suggest the particular involvement of the theta (4-8Hz) and alpha (8-13Hz) frequency bands in motor preparation (Crivelli-Decker et al., 2018; Meissner et al., 2018;

Pfurtscheller, 2003). The functional relevance of theta and alpha oscillations will thus be evaluated within the following sections.

Theta Oscillations

Theta oscillations have been continuously associated, and are suggested to play an integral role, in working memory functions and executive processes (Burke et. al, 2014; Klimesch et al., 2001). Furthermore, motor learning may be facilitated by theta oscillations through the coordination of sensory and motor brain activity, indicating that sensorimotor integration is particularly sensitive to changes in theta power (Bland & Oddie, 2001). Moreover, theta power is also indicated to promote episodic encoding and retrieval, while simultaneously contributing to the maintenance of temporal order information within working memory (Crivelli-Decker et al., 2018). We consider this functionality essential to the facilitation of MSL in a DSP paradigm, as a five-sequence stimulus temporal order must be maintained throughout motor preparation to enable the correct execution of sequences. Furthermore, Crivelli-Decker et al. (2018) identified a preferential relation of theta oscillations for the promotion of faster reaction times on subsequent trials in a semantic sequence-learning task.

Additionally, the effects of increases in theta power for sequence learning have been demonstrated in a neurofeedback study by Rozengurt et al. (2016). Via real-time positive EEG feedback and the employment of a visual target for goal theta power, participants were instructed to dynamically regulate target theta power through the exertion of directed mental effort. Ultimately, the employed theta neurofeedback paradigm promoted early consolidation of sequences. These results are in line with previous findings, demonstrating that directed theta power increases are potent to increase memory performance and promote learning decay protection (Reiner et al., 2014). Additionally, in a magnetoencephalography (MEG) study that contrasted oscillatory activity between Parkinson's disease (PD) patients and healthy controls, Meissner et al. (2018) found that increases in theta power in motor preparation (approximately 400ms before sequence reproduction) were associated with successful sequence learning.

Mid-Frontal Theta. Novel evidence for the topography of theta oscillatory activity points to the relevance of mid-frontal theta oscillations in MSL. Therein, Van der Cruijsen et al. (2021) indicate the facilitation of motor learning through theta power, which was particularly evident across Fz and FCz electrodes. The mid-frontal channels Fz and FCz approximately reside over the (dorsal anterior) cingulate cortex (CC) area, which is commonly associated with the allocation of mental resources to accomplish goal-directed tasks (Cohen et al., 2011; Van der Cruijsen et al., 2021). We thus argue that the functional properties of theta activity over CC may be potentially central to enable successful MSL. In total, Van der Cruijsen et al. (2021) indicate that theta power is an accurate indicator of successful motor learning and does not merely reflect perceived difficulty during training. In addition, Van der Lubbe et al. (2021) observed a small increase in theta power within motor preparation by contrasting motor imagery with motor preparation and execution. The change in theta power was most prevalent within mid-frontal channels, similar to the observed effects by Van der Cruijsen et al. (2021). Considering the emerging evidence on the role of mid-frontal theta oscillations in MSL, we thus seek to further investigate and validate these novel findings in this thesis.

Alpha Oscillations

Oscillations in the alpha band reflect key functions that are central to the cognitive processes that facilitate MSL. In general, alpha oscillations are consistently linked to processes of sustained attention and general motor inhibition (Pollok et al., 2014; Sauseng et al., 2010). Alpha oscillations that are observed over motor areas are also commonly referred to as mu oscillations. Crucially, Pfurtscheller & Neuper (2003) have shed light on the inhibitory properties of mu oscillations. Therein, mu ERD across the contra-lateral and ipsilateral hemispheres (closer to movement onset) can commonly be observed approximately 2 seconds prior to the onset of a self-paced finger movement. In total, the utility of a desynchronized mu rythm lies in the facilitation of information processing in motor preparation and in the dynamic regulation of required inhibition before movement onset (Pfurtscheller & Neuper, 2003).

Furthermore, Van Dijk et al. (2008) provided evidence in line with this alpha inhibition hypothesis. In their study, they investigated the role of alpha oscillatory activity in the modulation of visual perception through the presentation of visual stimuli. Therein, they identified that increases in pre-stimulus posterior alpha power negatively interfere with the discrimination ability for visual stimuli. Alpha oscillations thus serve the purpose of functional inhibition of unnecessary movements, ultimately modulating the gain of the dorsal visual stream (Jokisch & Jensen, 2007). Van Dijk et al. (2018) strengthened this assessment by indicating that changes in alpha oscillatory activity are not explained by changes in vigilance. Additionally, Zhuang et al. (1997) demonstrated that alpha power declined during initial learning of a serial reaction time task (SRTT; see Robertson et al. (2007)), followed by a peak in ERD over the C3 electrode when explicit knowledge has fully been accrued. After fully attaining explicit knowledge, the ERD subsided shortly after. This was attributed to the inhibitory functions entailed in alpha power. However, Zhuang et al. (1997) did not discriminate between different motor phases but rather averaged absolute alpha power for every block.

Pre-Frontal Alpha. Most available evidence points towards the relevance of alpha power over the primary motor cortex (M1: C3 and C4 electrodes) (Zhuang et al. 1997) and posterior brain regions (De Kleine & Van der Lubbe, 2011; Helfrich et al., 2017). Nonetheless, we suggest that investigating frontal persistent alpha activity in motor preparation may be imperative to fully understand the role of alpha oscillations in MSL. As motor preparation is a state without occurring movement, the predominantly investigated areas over M1 may be less relevant than pre-frontal areas that relate stronger to top-down control for the preparation of motor sequences (Pollok et al., 2014; Wang et al., 2016). Moreover, changes in alpha power have been associated with the facilitation of motor learning over (pre-)frontal areas during learning in an implicit sequence learning task (Moisello et al., 2013). Jointly motivated by the top-down control properties of frontal alpha oscillations (Wang et al., 2016), the absence of movement within motor preparation, and the findings on the relevance of (pre-)frontal alpha power in sequence learning (Moisello et al., 2013), we will thus explore the role of pre-frontal alpha oscillations in this thesis. We hope to thereby expand upon the available literature on M1 and posterior alpha oscillatory activity.

The Current Study

Through this study, we aimed to investigate the role of theta and alpha ERD/ERS in the preparation of familiar, as opposed to unfamiliar, motor sequences that were performed with the dominant hand in a Go/No-Go DSP paradigm. By contrasting the preparation of familiar and unfamiliar sequences in an EEG dataset, we sought to further elucidate the neurocognitive mechanisms of MSL in terms of their underlying oscillatory activity.

For theta oscillations, we firstly (1) expected a relative increase of theta power in motor preparation when compared to a specified baseline (preparatory ERS) for both unfamiliar and familiar sequences (Meissner et al., 2018). Secondly, based on the findings of Rozengurt et al. (2016) on the facilitating properties of theta power, we predicted (2) that this theta ERS would further increase for familiar as opposed to unfamiliar sequences. Thirdly, considering the findings of Van der Cruijsen et al. (2021), we believed (3) that this increase of theta ERS in the preparation of familiar sequences would be most pronounced within mid-frontal regions. Regarding alpha oscillations, we first hypothesized that (4) a relative decrease of alpha power in comparison to a specified baseline in motor preparation (preparatory ERD) would unfold for both unfamiliar and familiar sequences (Pfurtscheller & Neuper, 2003). Secondly, in consideration of the findings of Zhuang et al. (1997), we expected (5) alpha ERD to decrease when preparing familiar as opposed to unfamiliar sequences. Lastly, we believed that (6) this decrease of alpha ERD for familiar sequences would be most pronounced within pre-frontal regions (Moisello et al., 2013; Wang et al., 2016)

Methods

Dataset

The analysis of this thesis was performed on a previously recorded and unpublished EEG dataset, which was based on the implementation of the Go/No-Go Discrete Sequence Production (DSP) paradigm as part of a doctoral dissertation by de Kleine (2008). In the following sections, only the experimental details that are relevant to the analysis of this thesis were reiterated. For full experiment documentation, please refer to the doctoral dissertation by de Kleine (2008).

Participants

In the original study, eighteen students (14 females, $M_{age} = 22$) from the University of Twente served as participants. All participants declared normal (or corrected-to-normal) vision. Additionally, participants' average handedness score was collected, as per Annet Handedness Inventory (Annett, 1970), indicating that every participant could be categorized as right-handed. Participants provided informed consent before the experiment and received credits within the university credit system SONA upon completion. The original study was originally approved by the ethics committee of the faculty of Behavioural, Management and Social Sciences (BMS), and the current new analysis of the dataset was approved by the same committee under request number 230697.

Stimuli and Task

The DSP paradigm requires participants to complete a multitude of trials, each following a predetermined structure. Thereby, participants positioned their little finger on the ";" key, their ring finger on the "l", their middle finger on the "k" and their index finger on the "j" key. For every trial, five stimuli were presented, followed by a go or no-go signal that indicated whether a sequence needed to be replicated or not. When a go signal was presented, the trial was to be subsequently executed through the sequence of five spatially corresponding key presses. Participants were informed to reproduce the sequence as quickly as possible.

Each trial started with a 1000 millisecond display of a fixation cross in the middle of the screen and eight horizontally aligned squares, four on each side of the cross. Subsequently, one of the squares turned yellow for 750 milliseconds, repeating sequentially five times in total. The default screen was then displayed for 1500 milliseconds, representing the motor preparation interval. Afterwards, the fixation cross was coloured either red (for 6% of trials) or blue (for 94% of trials). A red fixation cross (displayed for 3000ms) indicated a no-go signal, meaning that no sequence needed to be executed. When a blue fixation cross was displayed, the sequence was to be executed by pressing the keys that spatially correspond to the previously shown yellow squares. For the preparation phase, participants were instructed to fixate their eyes on the cross in the centre of the screen. Please refer to Figure 1 for an overview of the displayed stimuli.

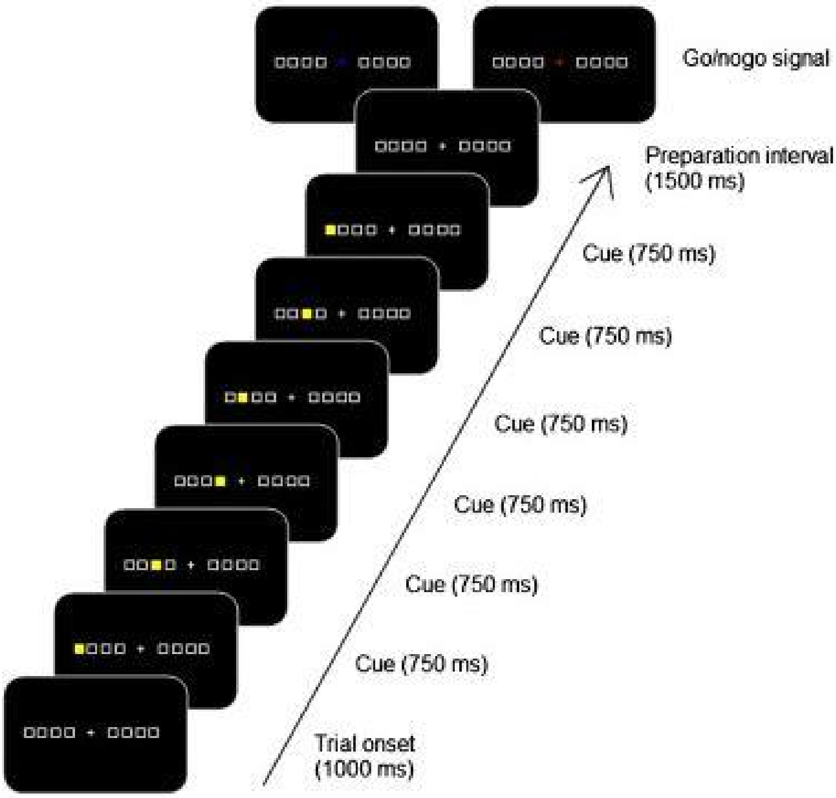


Figure 1. *Stimuli of the Go/No-Go DSP Paradigm.* Here, the sequence of stimulus display is indicated for a singular trial. The temporal properties of the indicated sequence are annotated on the time axis and are depicted in milliseconds. From: *Cognitive control of sequential motor behaviour*, by E. de Kleine, 2008, University of Twente (Doctoral dissertation).

Testing occurred on two separate days, while the first day was dedicated to the performance of five practice blocks. Eight sequences for each participant were practised twelve times within any given block. Within the practice phase, four of these eight sequences were practised with the dominant hand. A twenty-second pause was incorporated halfway through a given block, while each block was concluded with a two-minute pause. This pause was extended to ten minutes for every second block. On the next day, another practice block commenced, followed by three testing blocks. EEG was recorded for each of the testing blocks after a ninety-minute break for electrode attachment. Each testing block consisted of twelve unique sequences, consisting of four familiar, four unfamiliar and four mirrored (inverted) sequences. As each testing block was identical, only the first testing block contained novel sequences that were encountered for the first time. For the scope of the analysis in this thesis, only the first testing block was thus considered to contrast unfamiliar and familiar dominant-hand sequence preparation. Therein, two right-hand unfamiliar and two right-hand familiar sequences were performed as part of the testing block.

To prevent finger-specific effects on sequence performance within and across participants, the sequences entailed in the original study were counterbalanced across every participant for the practice and the test phase. To eliminate sequence-specific effects, the unfamiliar sequences of one sequence group participants were adopted to be the unfamiliar sequences for a second group. As this thesis is concerned with the performance of sequences with the dominant hand, all familiar and unfamiliar right-hand sequences, and their distribution across participants, can be found in Appendix A and B.

Apparatus

The experiment itself was displayed on a 17 inch monitor, situated 60cm in front of the participants and was run through a Pentium 4 computer. EEG recordings were made through 61 Ag/AgCI electrodes that were placed in compliance with the extended 10/20 system. EEG data was supplemented by electro-oculogram (EOG, bipolar) and electro-myography (EMG, both forearms) recordings with a Quick-Amp amplifier and were collected through Brain Vision Recorder (v1.05). During recording, the method of online average referencing was used. An impedance of <5 kilo-ohm was maintained and a sampling rate of 500Hz was employed.

Data Analysis

EEG Processing

Prior to any EEG (pre-)processing, an event-marker glossary of the stored EEG data was reconstructed on the basis of the associated behavioural data and the stored experimental scripts. Furthermore, each stored raw EEG file was preliminarily visually assessed for potential corruption and major artefacts (such as dead channels and prolonged noisy sections) within the Brainstorm toolbox (v3.221102) (Tadel et al., 2011) in MATLAB (R2023a) (MathWorks Inc., 2023). Due to corruption of the BrainVision *vmrk* (event-marker) files in participants three and four, they were excluded from further analysis. In total, sixteen participants were thus processed.

Eventually, further EEG (pre-)processing was performed within the MNE-Python environment (v1.4.2) (Gramfort et al., 2013). For the full MNE-Python script, please refer to Appendix C. Firstly, a low bandpass filter of 0.1HZ and an upper bandpass filter of 40Hz were applied to the data. After thorough visual inspection, an Independent Component Analysis (ICA) was performed to clean the data of physiological artefacts. Visual inspection for the detection of ocular, muscular and cardiac artefacts was supplemented by the function *find-bads-eog* entailed in MNE python, which provided recommendations for the removal of ICA components that matched the ocular signals captured by EOG channels. On average, 3.07 ICA components were removed from each EEG data file per participant.

Subsequently, the continuous data was epoched and indexed to discriminate between right-hand familiar and unfamiliar sequences. Motor preparation epochs were created for the timeframe of 1500ms up until 0ms before the execution signal, while the baseline was defined as -6500 to -5500ms before the execution signal. To obtain time-frequency data, Morlet wavelets were created for the alpha and theta band (run with three cycles) for three regions of interest: left-prefrontal (LPF; electrodes F1, F3 and F7), right-prefrontal (RPF; electrodes F2, F4 and F8) and mid-frontal (CC; electrodes Fz and FCz, overlaying the cingulate cortex region) (Van der Cruijsen et al., 2021). Please refer to Figure 2 for a visual representation.

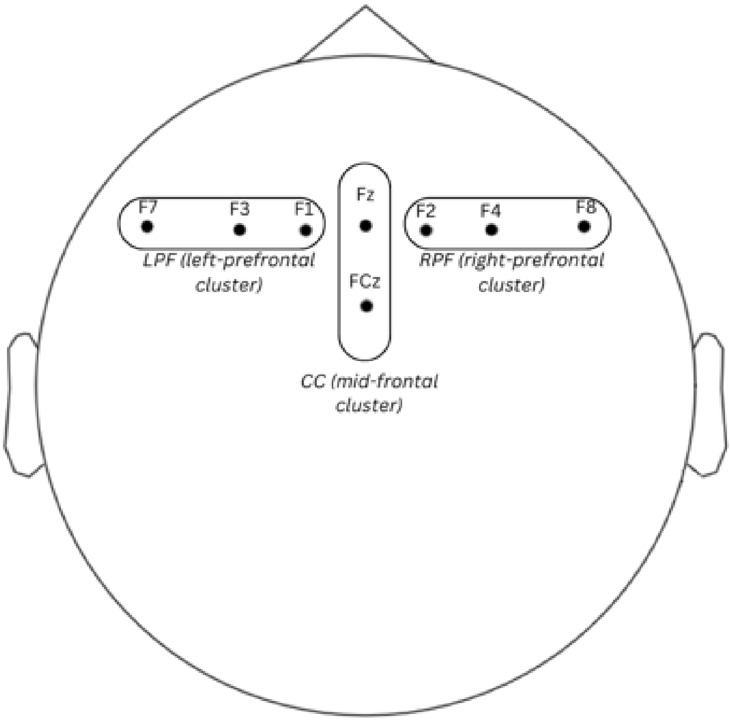


Figure 2. Left-prefrontal, right-prefrontal and mid-frontal electrode groupings. The LPF cluster indexes left-prefrontal regions through electrodes F7, F3 and F1, while the RPF cluster indexes right-prefrontal regions through electrodes F8, F4 and F2. The CC cluster indexes mid-frontal regions through electrodes Fz and FCz.

ERD/ERS and Linear Mixed Regression

The power outputs of the Morlet wavelets were further processed to obtain ERD/ERS values in the form of percentages. The Morlet outputs were subsequently limited to the relevant timeframes of -1500ms to 0ms (preparation), and -6500ms to -5500ms (baseline) before the execution signal. All other power outputs relating to the timeframe in-between were disregarded, while power outputs of the channels for each respective cluster were merged. Then, the data was segmented into 100ms intervals, calculating the means of every 50 consecutive values as dictated by the sampling rate of 500Hz. Subsequently, ERD and ERS were calculated as the percentage change of power relative to the baseline for each ROI, as suggested by Pfurtscheller (1999). ERD and ERS were then segmented for the theta (4-8Hz) and alpha (8-13Hz) frequency, while including the overlapping 8Hz frequency for both output variables.

The obtained ERD and ERS values were statistically analysed through linear mixed regression (LMER) via the lme4 package (v1.1-33) within RStudio (using R v4.2.1) (RStudio Team, 2023). LMER was specifically employed to control for the variance of random factors associated with the subject variable (Chan et al., 2018). Henceforth, two separate models were created with alpha ERD/ERS (Alpha) and theta ERD/ERS (Theta) as the respective outcome variables. As the main experimental manipulation entailed the preparation of familiar versus unfamiliar sequences, Condition (familiar or unfamiliar) was included as a predictor variable. Furthermore, the three pre-determined regions of interest (ROI: RPF, LPF, CC) and the sixteen time points in 100ms intervals (Time: 1500ms to 0ms) entailed in the motor preparation phase served as two additional predictors. Finally, analyses of variance (ANOVAs), including type II Wald chi-square tests ($\alpha = 0.05$), were performed on both LMER models. As the main experimental manipulation refers to the comparison of familiar and unfamiliar sequences, only significant interactions that include Condition were reported in the results. Additionally, whenever such significant interactions were found, additional post-hoc tests were performed and reported.

Results

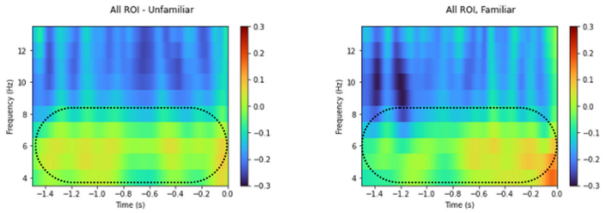
Theta ERD/ERS

An analysis of LMER models with theta ERD/ERS (Theta) as the outcome variable, and with Condition (familiar, unfamiliar), ROI (LPF, RPF, CC) and Time (-1500 - 0ms) as predictor variables was performed. Thereby, we found a significant main effect of Condition on Theta $\chi^2(1, n = 16) = 20.61$, $p < .001$, signifying that there is a significant difference in theta synchronization between the preparation of familiar and unfamiliar sequences. Additionally, a significant interaction of Condition x Time, $\chi^2(15, n = 16) = 204.58$, $p < .001$, was found, illustrating that the effect of familiar versus unfamiliar sequence preparation on theta synchronization varies as a function of the sixteen timepoints entailed in motor preparation. Moreover, a significant three-way interaction of Condition x Time x ROI was identified $\chi^2(30, n = 16) = 77.94$, $p < .001$, indicating that the effect of Condition on Theta based on the sixteen timepoints developed differently for the three regions of interest.

Post-hoc tests indicated that for CC, in the range from -1400ms to -1100ms (3 timepoints; $p < .01$) and at the timepoint -800ms ($p < .01$), lower theta synchronization for familiar as opposed to unfamiliar sequences was yielded. Conversely, at the timepoint -200ms ($p < .01$) significantly higher theta synchronization was identified for the familiar condition. Pertaining to LPF and RPF, a similar pattern was observed. For LPF, theta synchronization in the familiar condition was significantly lower in the range from -1300 to -1100ms (3 timepoints, $p < .01$) and at timepoint 0 ($p < .05$), while it was significantly higher at timepoints -600ms to -500ms ($p < .05$). Lastly, the differences were most pronounced within RPF, as theta synchronization was significantly lower for familiar sequences in the range from -1400ms to -800ms (7 timepoints; $p < .01$) and significantly higher from -300ms to 0ms (4 timepoints; $p < .01$). This three-way interaction is visualized within Figure 3, supplemented by their associated time-frequency representations based on Morlet wavelets.

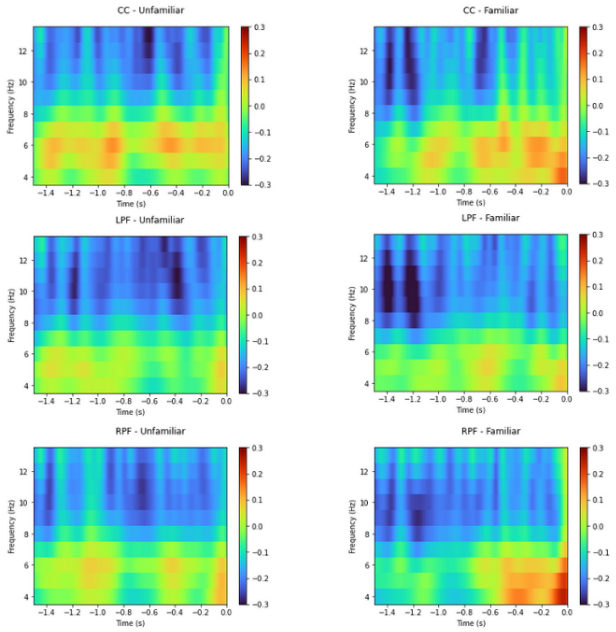
Panel 1

Time Frequency Representations, All ROI



Panel 2

Time Frequency Representations based on ROI



Panel 3

Theta ERD/ERS: Interaction Plot (Condition*ROI*Time)

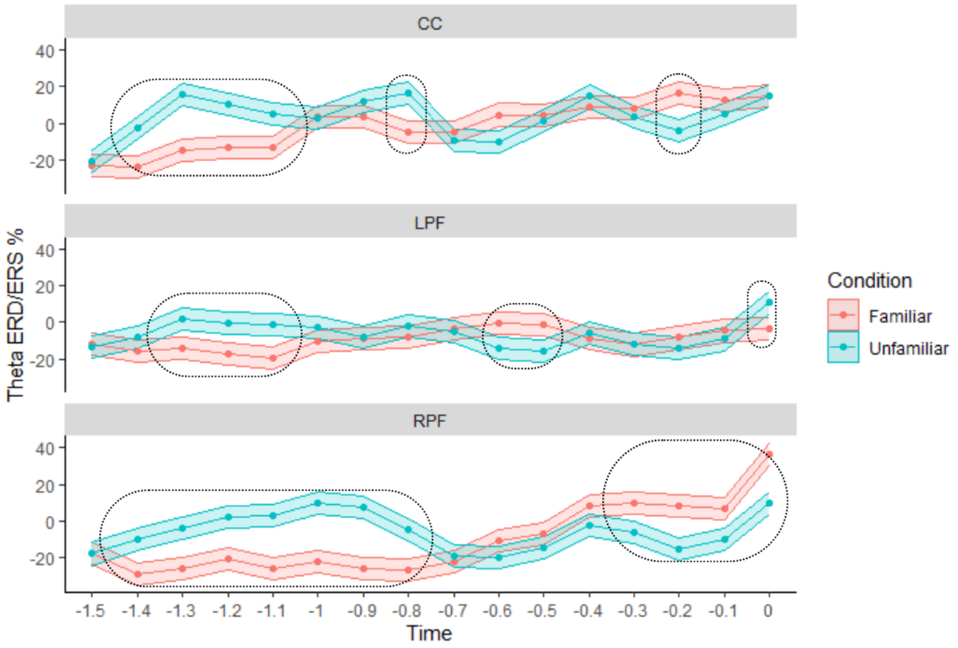


Figure 3. **1)** *Time-Frequency-Representations (TFR) for all ROI*. Within theta frequencies (4-8Hz - marked by a dotted line) predominant ERS (green to red gradient) can be seen for the motor preparation period and the significant main effect of Condition on Theta (Unfamiliar: Left, Familiar: Right) is illustrated. **2)** *TFR based on ROI* and **3)** *Three-Way Interaction Plot for Theta ERD/ERS* illustrate the significant Condition*ROI*Time interaction. Significant timepoints are marked by dotted lines in panel three and supplemented with their respective time-frequency properties in Panel two (ROI matched by height). Most noticeably, a shift from ERD (starting -1400ms) to sharp ERS (-300ms) for familiar sequences can be identified within RPF.

Alpha ERD/ERS

Furthermore, the LMER analysis with alpha ERD/ERS (Alpha) as the dependent variable and with Condition, ROI and Time as predictors revealed the following results. We identified no significant main effect of Condition on Alpha, $\chi^2(1, n = 16) = .07$, $p = .78$, indicating no significant difference in alpha synchronization between the familiar and unfamiliar condition. However, two significant two-way interactions were found. Thereby, significant interactions of Condition x Time, $\chi^2(15, n = 16) = 162.33$, $p < .001$, and Condition x ROI, $\chi^2(2, n = 16) = 14.04$, $p < .001$, were identified, illustrating that the effect of familiar versus unfamiliar sequence preparation on alpha synchronization varies as a function of the sixteen timepoints entailed in motor preparation, and the three regions of interests, respectively. Moreover, a significant three-way interaction of Condition x Time x ROI was identified $\chi^2(30, n = 16) = 80.61$, $p < .001$, highlighting that the difference between the familiar and unfamiliar condition, based on the sixteen different timepoints, differed as a function of the three regions of interest.

Post-hoc tests revealed significantly lower alpha synchronization for familiar sequences in CC within the range of -1300ms to -1100ms (3 timepoints, $p < .05$) and the timepoint 0 ($p < .05$), and significantly higher alpha synchronization in the timepoint -700ms ($p < .01$) and the range of -400ms to -100ms (3 timepoints, $p < .01$). Additionally, for LPF, alpha synchronization was significantly lower for familiar sequences in the range of -1300ms to -1200ms ($p < .01$) and the timepoint 0ms ($p < .01$), and significantly higher at the timepoint -700ms ($p < .05$), the range of -400ms to -300ms (2 timepoints, $p < 0.05$) and the timepoint -100ms ($p < .05$). Lastly, within RPF, familiar sequences elicited significantly lower alpha synchronization in the range from -1100ms to -900ms (3 timepoints, $p < .05$) and significantly higher alpha synchronization at the timepoint -600ms ($p < .05$). The significant Condition x ROI x Time interaction is depicted in Figure 4, alongside the corresponding time-frequency representations.

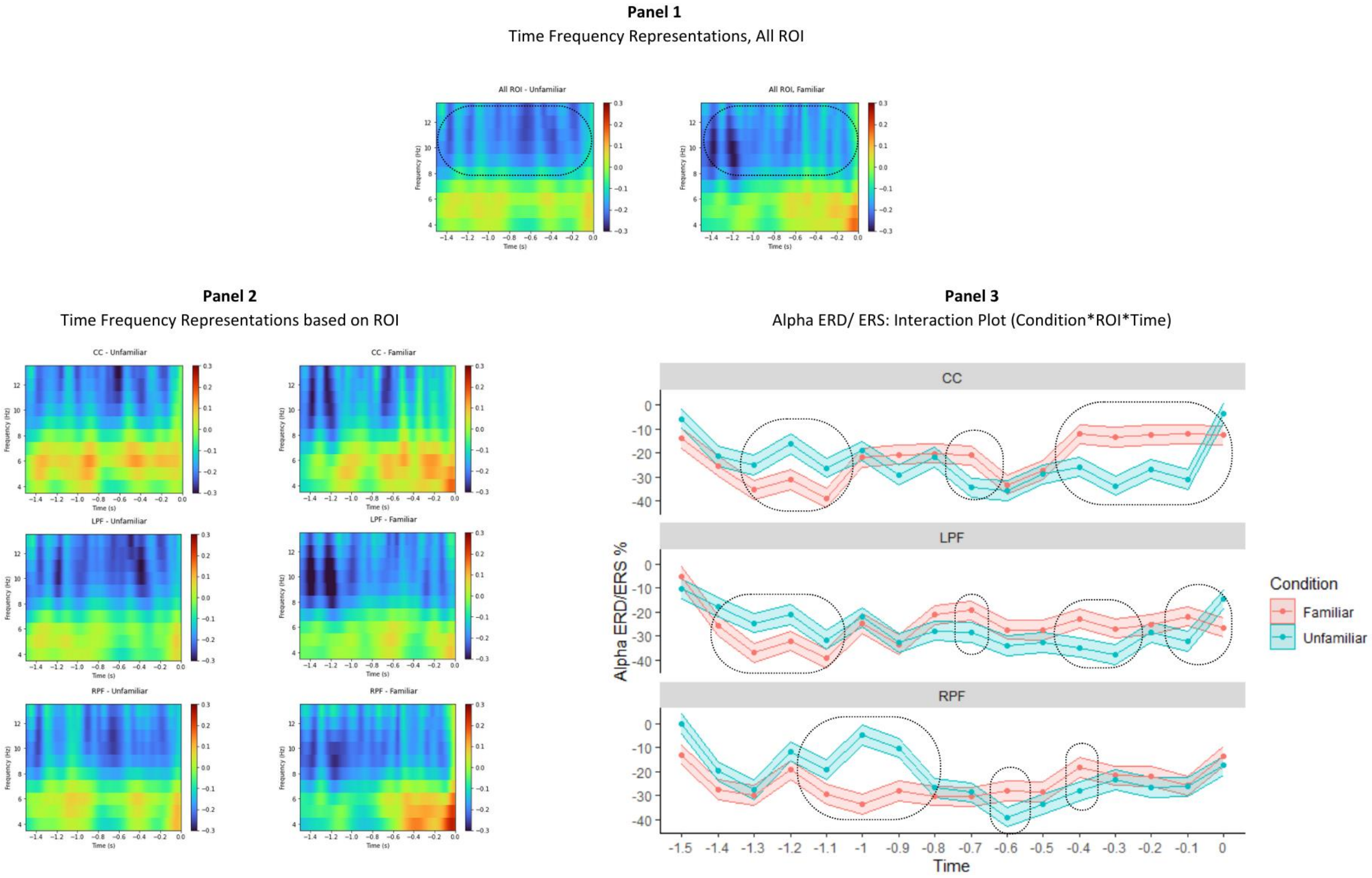


Figure 4. 1) *Time-Frequency-Representations (TFR) for all ROI*. Within the alpha band (8-13Hz - marked by a dotted line) predominant ERD (green to blue gradient) is discernible for the motor preparation period and the insignificant main effect of Condition on Alpha (Unfamiliar: Left, Familiar: Right) is demonstrated. **2)** *TFR based on ROI* and **3)** *Three-Way Interaction Plot for Alpha ERD/ERS* illustrate the significant Condition*ROI*Time interaction. Significant timepoints are marked by dotted lines in panel three and supplemented with respective TFRs in panel two (ROI matched by height). Most prominently, an increase of ERD (starting at -1300ms) for the familiar condition and the subsequent decrease of ERD (starting at -400ms) can be seen within CC.

Discussion

The goal of our study was to investigate the role of theta and alpha oscillations in the preparation of familiar as opposed to unfamiliar dominant-hand sequences. Regarding our hypotheses for theta oscillations, we first (1) identified predominant theta ERS throughout the preparatory period. This was in line with our expectations (Meissner et al., 2018). While unfamiliar and familiar sequence preparation significantly differed in associated theta synchronization, we did (2) not observe the expected general increase of theta ERS (Rozengurt et al., 2016) for familiar as opposed to unfamiliar sequences in the entire motor preparation period. Conversely, we identified predominant ERD for familiar sequences at the beginning of motor preparation, which shifted to ERS closer to the execution signal. Furthermore, these differences in theta synchronization were, contrary to our expectations, (3) not most pronounced within mid-frontal regions (Van der Cruijsen et al., 2021), but rather within right-prefrontal regions. For alpha oscillatory activity, our results indicate (4) general ERD throughout motor preparation. This was also in line with our expectations (Pfurtscheller & Neuper, 2003). However, familiar as opposed to familiar sequence preparation did (5) not significantly differ in alpha synchronization, thus alpha ERD did not generally weaken for familiar sequences. This is in opposition to our expectations (Zhuang et al., 1997). Nonetheless, when considering the three regions of interest and the timepoints in motor preparation, we did find stronger alpha ERD at the beginning of motor preparation, and weaker alpha ERD closer to the execution signal for familiar sequences. This difference, contrary to our expectations, was (6) not most pronounced in pre-frontal clusters (Wang et al., 2016) but rather in the mid-frontal cluster.

Theta ERD/ERS

We identified predominant theta ERS within motor preparation, which points towards the facilitating properties of theta power for executive functioning and working memory processes (Burke et. al, 2014; Crivelli-Decker et al., 2018; Klimesch et al., 2001; Rozengurt et al., 2016). However, we did not observe theta ERS throughout the entire preparatory period. Most pronounced in right-prefrontal regions, we rather found significant timepoints where ERD occurred for familiar sequences (as opposed to ERS for unfamiliar sequences) at the beginning of the motor preparation period (-1400ms to -800ms). This subsequently shifted to ERS for familiar sequences (as opposed to ERD for unfamiliar sequences) towards the end of the preparation period (starting at -300ms). We believe that this shift in temporal dynamics, and the shift from relative power decrease to increase, is associated with the differential loading of information that is selectively relevant to imposed task demands (Crivelli-Decker et al., 2018). Here, differences in task demands refer to the anticipation of either unfamiliar or familiar sequence execution.

Thus, for unfamiliar sequences, encoding of novel stimulus information into working memory occurs mainly post-stimulus provision and therefore closer to the onset of the preparation period. Conversely, the opposite mechanism occurs within preparation for familiar sequences. Novel stimulus information is not encoded after attending to intra-trial sequence stimuli, precisely because the sequence is already known and well-practiced. Consequently, information for eventual sequence execution is retrieved closer to the end of the preparation period and is therefore loaded into working memory in closer temporal proximity to the prompted execution of a familiar sequence.

This interpretation is in line with the findings of Crivelli-Decker et al. (2018), which indicate the relevance of theta oscillations for the maintenance of temporal order information within working memory. Moreover, a recent study by Champion et al. (2023) provides potential context to the mechanisms by which such temporal order information is maintained in working memory. Thereby, persistent activity amplitudes may be stored through a phase-locking mechanism, which allows a given neural circuit to produce sequential activity that ultimately encodes spatially corresponding stimulus patterns. Given that the exact processes underlying information maintenance in working memory are still being delineated by cognitive neuroscience, Champion et al. (2023) provide us with a reasonable foundation for the neural underpinnings of our results.

When contrasting our results with the findings by Meissner et al. (2018), our identified significant theta increase before the execution signal for familiar sequences is in line with their observed effects of sequence learning enhancement through theta power increases. Here, the timeline of theta increase is strikingly similar, as our results indicate the most pertinent increase starting at -300ms prior to the execution signal, just as Meissner et al. (2018) reported in their study. However, their approach was centred around the elucidation of differences in oscillatory activity as a result of altered cortico-basal-ganglia circuits in Parkinson's disease (PD) patients (Beudel et al., 2016). When connecting these outcomes, our results tentatively indicate that increases in theta synchronization (occurring closer to sequence execution) promote working memory processes, which may be imperative for functional MSL in both PD and healthy subgroups.

As our tertiary hypothesis was rejected, namely that differences between the two conditions would be most prevalent in the mid-frontal cluster (CC), our results do not fully conform with the findings of Van der Cruijsen et al. (2021). However, the facilitative properties of theta oscillations identified by Van der Cruijsen et al. (2021) were bound to the motor execution phase, which was not considered in this study. Hence, it is thus likely that processes of facilitation occur at different focal points throughout the entire temporal range of a motor sequence trial (Spampinato & Celnik, 2017). In addition to this, there is some degree of disaccord for the role of theta oscillations within MSL in further relevant literature.

While Van der Lubbe et al. (2021) observed a slight increase of theta power in the motor preparation phase of a DSP task, increases in theta power were not mainly attributed to the encoding and loading of sequence information into working memory. Alternatively, they were rather seen to mainly reflect global inhibitory interactions (Buzsaki, 2006, as cited in Van der Lubbe, 2021). This attribution serves as an alternative interpretation of the working-memory centred examination of theta oscillations within this thesis. Coupling this insight with the role of prefrontal cortices, not only for working memory processes (D'Ardenne et al., 2012), but also for inhibitory mechanisms during motor preparation (Duque et al., 2012), this alternative interpretation could thus also be consistent with our finding that conditional differences were most prevalent in the right pre-frontal region (RPF).

Additionally, some MSL studies point in the opposite direction, namely that decreases in theta power facilitate MSL. This was, for instance, illustrated by a recent study of Lump et al. (2023), in which sequence learning effects were associated with decreases in theta power. Our results are thus inconsistent with the data presented by Lum et al. (2023). Lum et al. (2023) outline that the facilitating theta increases observed by Meissner et al. (2018) occurred largely due to maladaptive responses to processing patterns entailed in visual sequence stimuli. They deemed this maladaptive response to likely occur in PD patients. As our results indicate the facilitating effects of theta power increases also for a healthy study population, we provide support for the obtained results by Meissner et al. (2018). Further research should clarify and provide further evidence to solve this disaccord entailed in contemporary literature.

Alpha ERD/ERS

Firstly, as we found general alpha ERD for the motor preparation phase, the previously indicated preparatory and inhibitory properties of a desynchronized rhythm within the alpha band for sequential motor behaviour were affirmed (Pfurtscheller, 1999; Pfurtscheller & Neuper, 2003; Van Dijk et al., 2008). In contrast to the temporal unfolding of theta ERD/ERS, we identified no shift from ERD to ERS in alpha oscillatory activity. When considering all regions of interest and timepoints, alpha ERD was consistently identified throughout the full preparation period. Thus, it is highly likely that alpha ERD occurs in to prevent unwanted movements and to prime a correct execution of sequences (Pfurtscheller, 1999; Pfurtscheller & Neuper, 2003), regardless of the to-be-executed sequence type. However, more nuanced statements can be made when considering an additional shift in temporal dynamics for the relative strength of ERD within the CC region (mid-frontal cluster). Here, familiar sequences elicit stronger ERD closer to the beginning of the preparation period (as opposed to weaker ERD for unfamiliar sequences, starting at -1300ms), which then shifts towards weaker ERD for familiar sequences (as opposed to stronger ERD for unfamiliar sequences, starting at -400ms) towards the end of motor preparation.

We consider the fundamental facilitating mechanism of this temporal disparity to be an increased demand for inhibition that occurs immediately post-stimulus provision. As familiar sequences are known and well-practised, stronger motor inhibition may be more relevant immediately after sequence recognition. Thus, inhibition may pertain to the prevention of movement that has become increasingly habitual due to repeated exposure to familiar sequences in the training phase. This does not occur for unfamiliar sequences, precisely because of their novelty and consequential lack of repeated exposure. As we move closer to the end of the preparation phase and towards movement execution, the demand for inhibition decreases for well-practised sequences and increases for entirely novel sequences. In total, we argue that this shift in the strength of ERD in this study mirrors a variable demand for motor inhibition that is contingent upon repeated exposure to sequence stimuli.

Similar to this pattern of variable inhibition demand, Zhuang et al. (1997) reported a pattern of peaking alpha ERD, up until explicit knowledge within the SRTT task was acquired and subsided shortly after. This, in essence, reflects the identified pattern that was found in this study, though some notable differences must be enunciated. Firstly, Zhuang et al. (1997) did not only utilize a different MSL task paradigm (SRTT), but they also set the alpha frequency boundaries to 9-11Hz. As upper alpha bandwidth (10-13Hz) was found to be most sensitive to finger movements (Pfurtscheller & Neuper, 2003), it is reasonable to argue that any similarities between this study and the one conducted by Zhuang et al. (1997) must always be viewed tentatively due to potential differences that may have been elicited through the consideration of varying alpha bandwidths.

Nonetheless, the results by Zhuang et al. (1997) also provide us with potential context for the mid-frontal cluster to predominantly reflect this pattern, as they identified a peak in ERD that was maximal for the central C3 electrode over M1. This is largely in line with the postulations of alpha (mu) ERD across motor regions by Pfurtscheller (1999). This does not preclude the possibility that pre-frontal regions are also indicative of variable demands on motor inhibition (Wang et al., 2016), as RPF did reflect a significantly stronger alpha ERD after the presentation of a familiar sequence stimulus. Rather, more central regions may nonetheless be more potent to display such shifts in variable inhibition demand, despite the absence of movement within the preparation phase. To assess this claim more holistically, future investigations of pre-frontal alpha oscillations should thus be complemented by including activity over M1 (through the central C3/C4 electrodes) within their study design. In total, our identified pattern of an alpha ERD increase, followed by a subsequent decline, may be a facilitating factor of successful MSL and ought to be investigated more comprehensively in future research.

Limitations and Future Directions

One of the key limitations of this study pertains to the fact that electroencephalographic recordings can only uncover the role of cortical structures in MSL. However, contemporary literature has indicated the importance of subcortical brain structures (such as the basal ganglia) for MSL facilitation (Ruiz et al., 2014; Turner & Desmurget, 2010). Any derived conclusions and implications of this study are thus inherently tied to cortical activity, potentially providing an incomplete overview of the neural dynamics of MSL. Additionally, the study employed a limited overview of the three motor phases, as only the motor preparation phase was considered within the analysis. As, for instance, illustrated by the results of Van der Cruijsen et al. (2021) or Van der Lubbe et al. (2021), insights from the motor execution or post-movement phase (and potentially, motor imagery) can be vital to fully grasp the role of oscillatory activity within MSL. Any obtained results thus only apply to the preparation of motor sequences and should ideally be supplemented with data on their subsequent execution. Lastly, the employed counterbalancing within our dataset was potentially ineffective in fully eliminating sequence-specific effects, as only two sequence clusters (groups that received the same sequences) were entailed in the practice phase. These sequences were eventually distributed across participants in the test phase, thereby influencing the obtained data of our analysis. Furthermore, as two participants that received the same sequence cluster were excluded from subsequent analysis (Participants 3 and 4; see Appendix A for sequence overview), sequence-specificity of the obtained results cannot fully be excluded.

Direct recommendations for further research pertain to the supplementation of the acquired results on alpha and theta ERD/ERS with behavioural data, such as reaction times (Abrahamse et al., 2016). Consequently, facilitatory mechanisms of successful motor sequence execution would not only be supported through oscillatory patterns, but also through their direct association with behavioural outcomes. As this study employed a block-level analysis, future research should also investigate the oscillatory dynamics on single sequence trial level. Particularly when matching behavioural outcomes with ERD/ERS data, single trial reaction time prediction may be possible through the identification of respective facilitating and inhibiting oscillatory patterns. This, for instance, would be highly interesting to investigate in light of the previously identified facilitating properties of theta oscillations for current and future trial performance (Crivelli-Decker et al., 2018; Rozengurt et al., 2016). Additionally, behavioural outcomes may not only pertain to the subsequent execution of sequences but could also be systematically investigated in view of learning decay (Reiner et al., 2014), as retention of sequential motor behaviour is an important part of MSL (Moisello et al., 2011).

Conclusion

The broader scope of this study was to investigate the role of frequency-specific oscillatory activity in MSL. Therein, we investigated preparatory theta and alpha ERD/ERS in a recorded EEG dataset and accrued initial evidence for facilitatory neurocognitive mechanisms of MSL. Most strikingly, a significant increase in theta ERS in close temporal proximity to evincing sequence execution was found for the preparation of familiar sequences. In line with the corresponding results of previous studies, we suggest an imperative role of theta oscillations for the successful encoding and retrieval of temporal sequence information within working memory. As a result, increases in theta power may benefit motor performance and thus lead to faster and more accurate sequence execution. Moreover, the identified pattern of an increase of alpha ERD for familiar sequences, followed by a subsequent decline in ERD, shed light on the variable and subsiding nature of inhibitory processes of alpha oscillatory activity. In total, our study further elucidated the oscillatory differences entailed in the temporal dimensions of sequence preparation through the contrast of well-practised sequences and entirely novel sequences. Nonetheless, our study only focused on the neural underpinnings of such sequence preparation and is yet to be re-evaluated in the light of corresponding behavioural outcomes.

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Appendix A

Practice Sequences

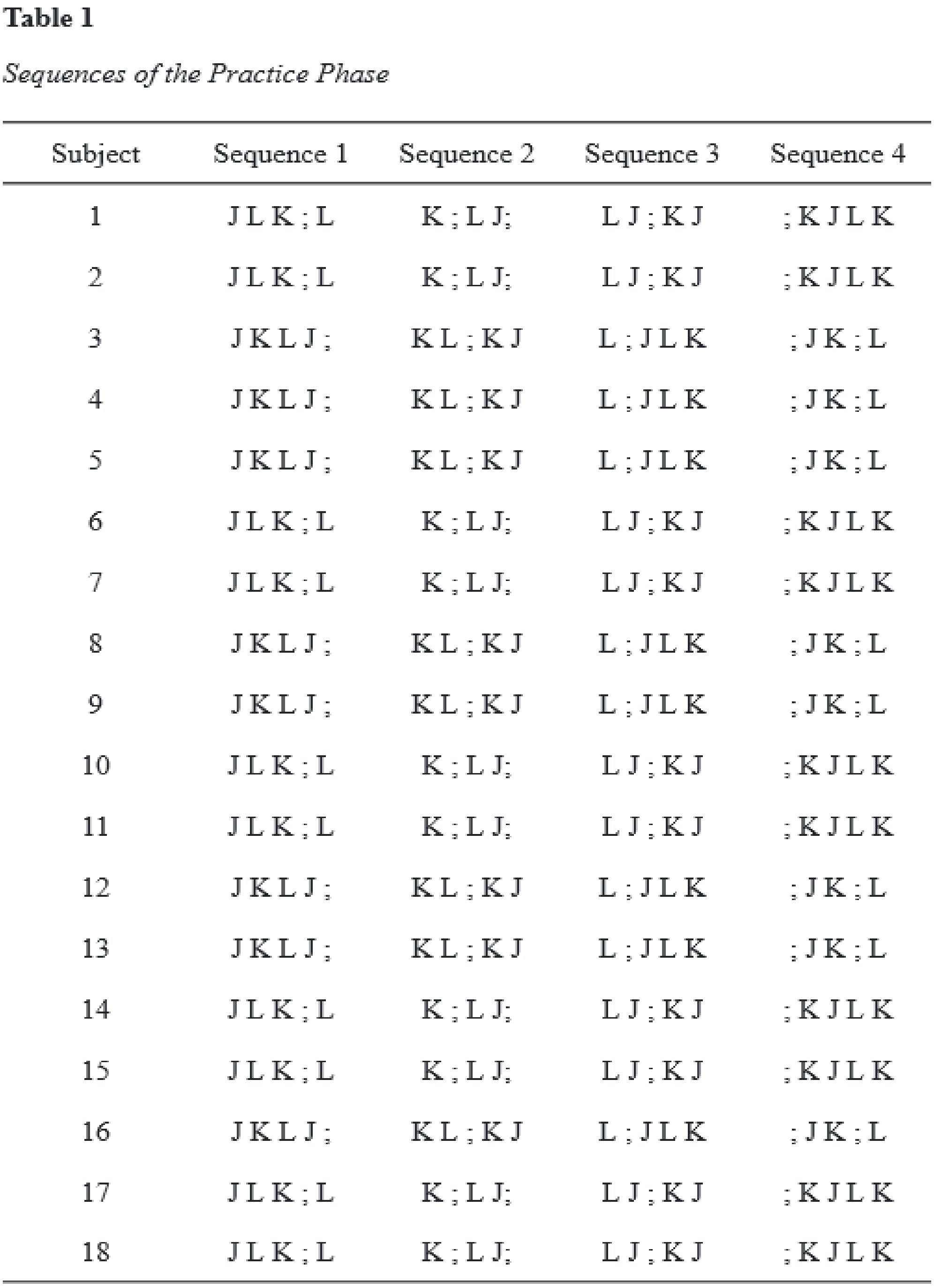


Table 1

Sequences of the Practice Phase

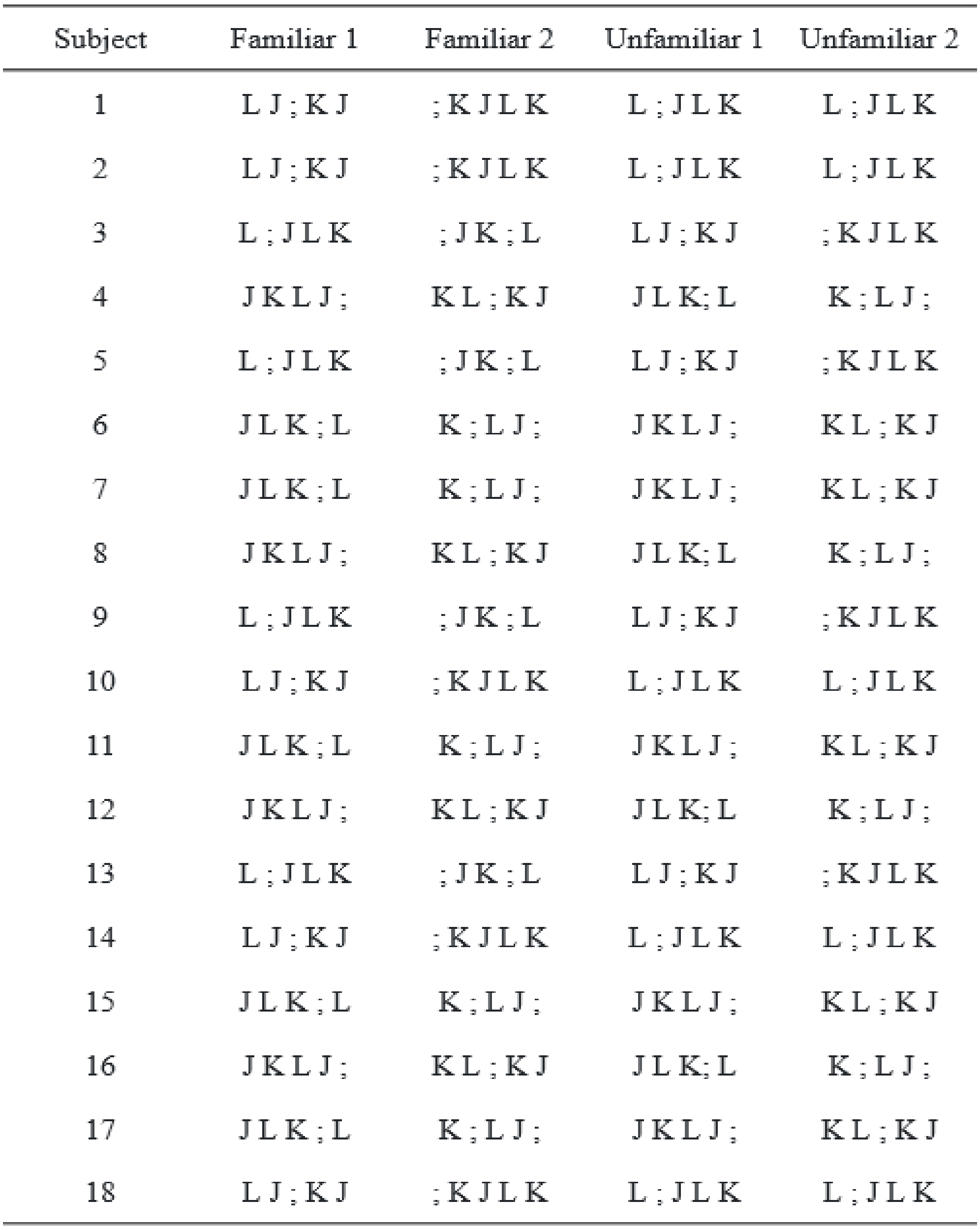
Subject	Sequence 1	Sequence 2	Sequence 3	Sequence 4
1	J L K ; L	K ; L J;	L J ; K J	; K J L K
2	J L K ; L	K ; L J;	L J ; K J	; K J L K
3	J K L J ;	K L ; K J	L ; J L K	; J K ; L
4	J K L J ;	K L ; K J	L ; J L K	; J K ; L
5	J K L J ;	K L ; K J	L ; J L K	; J K ; L
6	J L K ; L	K ; L J;	L J ; K J	; K J L K
7	J L K ; L	K ; L J;	L J ; K J	; K J L K
8	J K L J ;	K L ; K J	L ; J L K	; J K ; L
9	J K L J ;	K L ; K J	L ; J L K	; J K ; L
10	J L K ; L	K ; L J;	L J ; K J	; K J L K
11	J L K ; L	K ; L J;	L J ; K J	; K J L K
12	J K L J ;	K L ; K J	L ; J L K	; J K ; L
13	J K L J ;	K L ; K J	L ; J L K	; J K ; L
14	J L K ; L	K ; L J;	L J ; K J	; K J L K
15	J L K ; L	K ; L J;	L J ; K J	; K J L K
16	J K L J ;	K L ; K J	L ; J L K	; J K ; L
17	J L K ; L	K ; L J;	L J ; K J	; K J L K
18	J L K ; L	K ; L J;	L J ; K J	; K J L K

Appendix B

Test Sequences

Table 2

Sequences of the Test Phase



Subject	Familiar 1	Familiar 2	Unfamiliar 1	Unfamiliar 2
1	L J ; K J	; K J L K	L ; J L K	L ; J L K
2	L J ; K J	; K J L K	L ; J L K	L ; J L K
3	L ; J L K	; J K ; L	L J ; K J	; K J L K
4	J K L J ;	K L ; K J	J L K; L	K ; L J ;
5	L ; J L K	; J K ; L	L J ; K J	; K J L K
6	J L K ; L	K ; L J ;	J K L J ;	K L ; K J
7	J L K ; L	K ; L J ;	J K L J ;	K L ; K J
8	J K L J ;	K L ; K J	J L K; L	K ; L J ;
9	L ; J L K	; J K ; L	L J ; K J	; K J L K
10	L J ; K J	; K J L K	L ; J L K	L ; J L K
11	J L K ; L	K ; L J ;	J K L J ;	K L ; K J
12	J K L J ;	K L ; K J	J L K; L	K ; L J ;
13	L ; J L K	; J K ; L	L J ; K J	; K J L K
14	L J ; K J	; K J L K	L ; J L K	L ; J L K
15	J L K ; L	K ; L J ;	J K L J ;	K L ; K J
16	J K L J ;	K L ; K J	J L K; L	K ; L J ;
17	J L K ; L	K ; L J ;	J K L J ;	K L ; K J
18	L J ; K J	; K J L K	L ; J L K	L ; J L K

Appendix C

MNE Python Script

Github repository for this thesis