Frontal midline theta and cross-frequency coupling during short term memory and resting state

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A B S T R A C T

This paper aims to establish how frontal midline theta and theta-gamma coupling are altered by memory load as well as by recall performance during a verbal digit span task using an open EEG dataset. Traditional behavioral scores, as well as new measure were used, as the recall accuracy as a function of the order of the digits followed a sigmoid curve. The new behavioral score was strongly correlated with traditional measures. The EEG results show that neither the resting state theta nor the theta during the digit span task is predictive of the task performance. However, there was a strong positive correlation between cognitive load and theta power as well as a negative correlation between cognitive load and theta peak frequency during the task. These results are in line with earlier studies indicating that frontal midline theta is modulated by cognitive load rather than memory performance. Furthermore, there was an increased alpha-beta cross frequency coupling during resting state but that was not correlated with the performance of the upcoming memory task. During the task the cross-frequency coupling was minimal, and it did not correlate with memory performance nor with task load, that raises the possibility that EEG is not sensitive enough for cross-frequency coupling measures.

1. Introduction

Our ability to encode and remember the information that surround us relies upon our short-term memory (STM). This core mental faculty briefly retains a small amount of information to support a wide array of mental processes.

STM capacity has often been measured using a digit span task. A number of randomly selected digits are presented as stimulus items, and a participant has to reproduce the digit list after a short delay. The digit span task is easy to perform, and it is widely used as part of the Wechsler Adult Intelligence Scale (WAIS) in assessing and studying the memory span in different neuropsychiatric conditions(Jasinski et al., 2011; Kiewel et al., 2012; Olson, 2020).

There are number of studies that described the biological underpinnings of short-term memory using electrophysiological (Gosmann and Eliasmith, 2021; Masse et al., 2020) as well as neuroimaging studies (Emch et al., 2019; Yu et al., 2019).

EEG research over the past decades gathered evidence for the role of theta and gamma rhythms for STM (Klimesch, 1996; Klimesch and Doppelmayr, 1996). For example, an increase in the amplitude of frontal midline theta (FMT) activity was shown with higher cognitive load in memory tasks in both EEG (Gevins et al., 1997; Onton et al., 2005) and MEG studies (Jensen and Tesche, 2002; Osipova et al., 2006). Later on, it

was concluded that theta is not only restricted to memory formation and recall but more generally frontal midline theta is an index of increased need of cognitive control (Cavanagh and Frank, 2014).

It has also been shown that gamma-band power during successfully memorized trials are greater compared to those that are forgotten (Gruber et al., 2004; Herrmann et al., 2004; Jokisch and Jensen, 2007).

Moreover, brain oscillations in different frequency bands should not be considered as discrete and independent; rather, they represent coupled neuronal processes at different hierarchical levels (Buzsáki and Draguhn, 2004) across various spatial and temporal scales (Mento et al., 2018). It has therefore been proposed that such nested activity of different frequency bands may represent a reliable neurophysiological mechanism underpinning complex behaviors. One particular example of such nested oscillations that is important during STM could be observed in the hippocampus, where the high frequency oscillations power is modulated by the phase of theta frequency oscillations during memory tasks (Tort et al., 2009; Trimper et al., 2014). According to this theory (known as the theta-gamma code), one memory item is encoded in each gamma cycle while each theta-cycle encodes the sequence of all items held in storage (Lisman, 2010; Lisman and Buzsáki, 2008; Lisman and Jensen, 2013). The existence of such theta-gamma code in the human brain has been confirmed by several EEG studies, where increased theta-gamma cross-frequency coupling was observed during successful

memory formation, but not during incorrect encoding (Köster et al., 2014; Roux and Uhlhaas, 2014; Schack et al., 2002). Following the theory of theta-gamma coding, longer theta cycles could accommodate more gamma cycles, equivalent to sustaining memory for a greater number of items. Indeed, Kamiński (Kamiński et al., 2011) found that the theta cycle length during resting state correlated with short term memory capacity. However, recently Malenínská (Malenínská et al., 2021) failed to replicate this study and found no evidence on the relationship between resting state theta-short term memory.

Recently, there has been a renewed emphasis on the need for replication in cognitive neuroscience as number of studies could not be replicated (Collaboration, 2015). Following that "replication crisis", many researchers started to make their results openly available, and lately, there has been an initiative to replicate some EEG-findings independently by several different laboratories (Pavlov et al., 2021a).

Recently Pavlov et al. uploaded an open EEG-dataset recorded during a verbal digit span task (Pavlov et al., 2021b). The aim of this study is to use that open dataset to replicate some core findings regarding the role of frontal midline theta as well as the theta-gamma cross-frequency coupling during memory encoding. Furthermore, as the dataset also contains EEG-recordings during resting state, the relationship between resting state theta and the performance during digit span task could be clarified, and an additional argument could be made on the debate between (Kamiński et al., 2011) and (Malenínská et al., 2021).

The hypothesis of this study was that FMT power, as well as peak frequency is modulated by cognitive load, but not the accuracy of the memory recall, while based on earlier studies (Friese et al., 2013; Park et al., 2013; Heusser et al., 2016), the expectation was that theta-gamma phase-amplitude coupling is correlated with recall accuracy.

2. Materials and methods

2.1. Participants

This current study analyzed the dataset publicly available at openneuro.org. The following description of the participants, task, and EEG-setup is the same as reported by (Pavlov et al., 2021b). The original study included 86 healthy volunteers with normal or corrected vision and no history of neurological or mental disorder, and normal hearing. Due to technical failures, the final dataset consisted of 65 EEG recordings. Basic demographic data (age, gender, handedness, ocular dominance) was also collected for each participant. The experimental protocol was approved by the Ural Federal University ethics committee.

2.2. Digit span task

Each trial-sequence began with an exclamation mark for 0.5 s along with a recorded voice command "begin" – indicating the start of the trial. The exclamation mark was followed by an instruction to either memorize the subsequent digits in the correct order or to just listen to the digits without attempting to memorize them. The instruction was followed by a 3-s baseline period. Then either 5, 9, or 13 digits were presented auditorily with an inter-stimulus interval of 2 s. Each of the digits from 0 to 9 was used, and the mean duration of each digit was 664 ms (min: 462 ms, max: 813 ms). The last digit in the sequence was followed by a 3-sec retention interval. During the baseline, encoding, and retention intervals, participants were fixating a cross (1.2 cm in diameter) on the screen. In the memory condition, the participants were asked to recall each digit out loud in the correct order starting from the first one (i.e., serial recall). The retrieval was recorded by a computer microphone controlled by PsychoPy (Peirce, 2007). The participants had 7, 11, and 15 s for 5, 9, and 13 digit sequences, respectively, to recall the digits. The retrieval was followed by an inter-trial interval (ITI) of 5 s. In the control condition (passive listening), presentation of the digits and the delay period was followed immediately by an ITI of the same duration.

There were 9 blocks in total with 54 passive listening and 108 memory trials overall. Each block consisted of 3 control (one of each load) followed by 12 memory (4 trials on each level of load) followed again by 3 control trials. Before the main task, each participant completed 6 practice trials (3 passive listening and 3 memory trials). After each block, the participant had a self-paced break. After every 3 blocks, the participants took a longer break.

The behavioural responses were manually transcribed from the recorded speech by at least two scorers and the mismatching trials were then checked by one of the authors of the original dataset.

2.3. Recording setup

Before the WM task, resting state EEG for 34 min was recorded. The participants were seated in a comfortable chair and asked to close their eyes and to sit still. After the resting state recording, the participants were given instructions and proceeded with the WM task. A 64-channels EEG system with active electrodes (ActiCHamp, Brain Products, Germany) was used for the recording. The electrodes were placed according to the extended 10–20 system with FCz channel as the online reference and Fpz as the ground electrode. The level of impedance was maintained below 25 kOm. The sampling rate was 1000 Hz. The distance to the monitor was 80 cm. Two loudspeakers were placed on the sides of the monitor with 84 cm between them (62°). The measured loudness of the digit sounds was 70 dB SPL. The loudness was measured by placing a Mastech MS6701 sound level meter near where the participants' head was located. The luminance in the room was set to 380 lux. Further details of the recording setup can be found at the paper describing the dataset (Pavlov et al., 2021b).

2.4. Analysis

Matlab scripts that were used for the analysis are available at osf.io.

2.5. EEG-preprocessing

Pre-processing steps were performed within EEGlab (Delorme and Makeig, 2004). EEG data were first high-pass filtered (>0.5 Hz using FIR filter implemented in EEGlab). Then noisy channels were identified using automatic channel rejection toolbox implemented in EEGlab and then they were replaced by interpolation of the signal from adjacent channels. After that, the EEG data was resampled to 500 Hz. The continuous EEG-data were then epoched for each digit presentation trial (i.e. −0.5 to 1.5 s relative to digit presentation). After that independent components were computed. Components were labeled using IClabel toolbox within EEGlab, and those components that were labeled as <75% brain activity were rejected. The artifact-free EEG datasets pre-processed in EEGLab were then exported to MATLAB 2020b for further analysis.

Each epoch (−0.5 to 1.5 s relative to each digit presentation) was labeled by two factors (*Task* and *Load* where the *Task* indicated whether the subject needed to passively listen to the digits presented or to memorize them, and the *Load* was equal to the nth digit presented).

As the number of epochs with lower load naturally outnumbered those with higher load, each load-trials were resampled to match the number of the highest load condition using bootstrap resampling.

2.6. Resting-state EEG preprocessing

The pre-processing steps for the resting state recordings were similar to the task-EEG preprocessing steps, except that the data was not epoched, but the continuous data were subjected to the ICA and subsequent artifact-rejection.
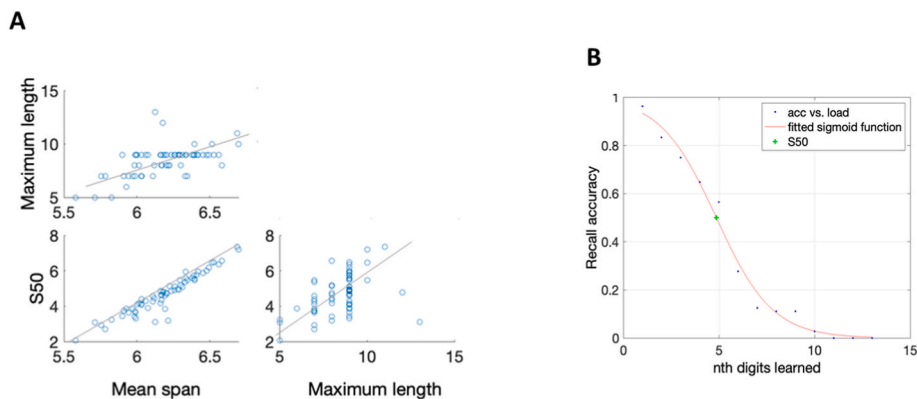
Fig. 1. Graphical overview of the relationships between behavioral scores of the digit span task (A), and the visual representation of the calculation of the S50, in one subject (B).

2.7. Behavioral analysis

Since the order of the length of the list was randomized and not increased as in common neuropsychological tests, the „Two Error Maximal Length" and „Two Error Medium Span" could not be calculated. However, the mean span (MS) and maximum length (ML) that relies on all the trial's data could be evaluated (Woods et al., 2011). The ML was calculated as the longest list correctly recalled during the task, and MS was evaluated based on (Woods et al., 2011): The hit rate for each list length (e.g., $5 = 1.0$, $9 = 0.35$, $13 = 0.1$, sum $= 1.45$) was added to the baseline value (that is 0.5 digits less than the shortest list length (i. e. 4.5).

If the performance was averaged across each nth digit presented, it has been observed that the performance as a function of the nth digit presented follows a sigmoid function. A sigmoid curve was fitted for each participants performance and then calculated the so-called S50 and the nth digits at with the recall accuracy is 50% (See Fig. 1 panel B).

As this new measure is relatively new in the literature (to our knowledge no one has reported this earlier) in order to relate to the other commonly used behavioral measure, the partial correlation coefficients were calculated between the behavioral measures across subjects.

2.8. Relationship between frontal-midline theta during task and task performance

The power-spectra of the frontal midline channels (Cz, Fz, Afz, F1, F3) was calculated using Fast Fourier Transform on the epoched EEG-data during the task. Then the relative theta power was averaged across the channels, as well as the peak frequency of the theta power, for each epoch. Then the linear regression was calculated for each subject between the nth digit presented and the theta power as well as between the nth digit presented and the theta peak frequency separately for the Listening condition and the Memory condition. The F-statistics of the individual linear regression were compared between the Listening and Memory conditions across subjects using Wilcoxon signed-rank test.

2.9. Resting state FMT - task performance

The power-spectra of the frontal midline channels (Cz, Fz, Afz, F1, F3) was calculated using Fast Fourier Transform on the resting state EEG-data. In order to have an equal sample from each participant, a random 2-min time-section of each recording was used. Then the relative theta power was calculated and averaged across the channels, as well as the peak frequency of the theta power. Then the correlation coefficient was calculated between the behavioral scores and the FMT-power as well as between the behavioral scores and the FMT-peak frequency.

2.10. Cross frequency coupling (CFC)

Consistent with previous publications (Cohen, 2014; Dimitriadis et al., 2018; Pahor and Jaušovec, 2014), the analysis of cross-frequency coupling (CFC) focused on channel Cz. While there are many form of CFC (Jensen and Colgin, 2007), this paper focuses on the phase-amplitude cross-frequency coupling.

The calculation followed the procedure described by Cohen, 2008, 2014. The following example will demonstrate the calculation of the PACz (the z-score of the phase-amplitude coupling) of one trial at a specific low and high frequency band. First the raw (cleaned) EEG-signal of the trial at the channel Cz was band-pass filtered to gamma band (30–70 Hz). Then, the power time-series of the previously filtered signal was calculated using Hilbert transform (a). The raw analytical signal of the channel Cz was then band-pass filtered to theta band (4–8 Hz) and the phase time series was calculated using again the Hilbert transform on the filtered signal (ϕ). The quantification of the phase-amplitude coupling was calculated using the equation suggested by earlier papers (Canolty and Knight, 2010; Cohen, 2014):

$$PAC = \left| n^{-1} \sum_{t=1}^{n} a_t e^{i(\varphi_t - \bar{\varphi})} \right|$$

where t is the time point, a the power of gamma at the time point t, i is the imaginary operator, ϕ is the phase angle of theta at the time point t and n is the total number of time points (that was corrected with a debiasing factor $\bar{\varphi}$ as suggested by(van Driel et al., 2015).

To avoid different confounds of the PAC, nonparametric permutation test was applied between the calculated PAC and the null-hypothesis distribution (Cohen, 2014). The null-hypothesis ditribution was calculated the same way as PAC but iteratively time-shifting the high-frequency filtered signal's power time-series. The PACz was calculated as the z-value between the generated null-hypothesis distribution and the PAC.

The PACz was calculated for each bin of the comodulogram (frequency for phase: 4–12 Hz, Frequency for amplitude (15–40 Hz). The filtering band-width was different for the lower (frequency for phase) and higher (frequency for amplitude) frequencies: for the lower frequencies, the bandwidth was 3 Hz, centered around the given low frequency, whereas for the higher frequencies, the bandwidth was set $\pm 0.4 \ast fx$ around the given high frequency fx.

2.11. Resting state CFC analysis

In case of resting state activity the PACz was calculated for the whole recording. In addition, the correlation between the three different behavioral measures and the PACz at each bin of the comodulogram was calculated. The correlation coefficients were then corrected for multiple

comparison using permutation testing.

2.12. CFC during task

In order to get longer time-segments for the CFC-analysis, the EEG-datasets during the task were reepoched in the following way: each epoch contained 5 digit presentation. There were six different conditions according to (1) the maximum number of digits presented so far and (2) the instructed task. Listen 5 for example corresponded to epochs that contained trials of the first 5 digit presentation, Listen 9 from the 5th to 9th digit Listen 13 from 9th to 13th digit (same in Memory condition). As the number of epochs with lower load naturally outnumbered those with higher load, each load-trials were resampled to match the number of the highest load condition using bootstrap resampling.

The PACz comodulogram for each condition was calculated and then RM-ANOVA on factors Task (Memory vs Listen) and Load (5 9 13) was applied and the results were corrected for multiple comparision using permutation testing.

At this point one could only proximate the effect of cognitive load and task on the cross-frequency coupling. To check how the CFC correlated with the performance, the average PACz during the Memory condition was calculated for each participant and then the correlation coefficient between the three different behavioral measures and the PACz at each bin of the comodulogram was calculated. The correlation coefficients were then corrected for multiple comparison using permutation testing.

As the results revealed non-significant CFC during either of task condition, the CFC analysis was repeated by excluding the time segment after 200 ms of the stimulus presentation to omit the spurious CFC that is driven by stimulus presentation (Cohen, 2014.). As there was no difference between the two calculation method the results contain the later calculation method.

3. Results

3.1. Behavioral data

As we observed that the accuracy as a function of the nth digit presented (load) follows a sigmoid curve, the load at which the fitted sigmoid curve was 50% was calculated (See Fig. 1 panel B) on top of the other commonly used measures such as the mean span and maximum length. The descriptive statistics of the behavioral scores are presented in Table 1.

As the S50 was a novel metric for quantifying performance on this task, we also calculated the correlation with more traditional behavioural measures. The strongest correlation was between MS and S50. See Table 2 for the correlation coefficients and Fig. 1 for graphical representation of these correlations for one particular subject. To provide evidence that the sigmoid relationship between accuracy and load was replicable across subjects and could be replicated if one only analyses the longest digit length, each subject's accuracy-load curve can be found in the supplementary material.

3.2. Relationship between resting state frontal midline theta and task performance

According to Kamiński (Kamiński et al., 2011), one could predict the short term memory capacity from the resting state theta activity. To

Table 1
Descriptive statistics of the digit span scores.

	Mean	STD	Min	Max
S50	4.71	1.11	2.00	7.34
ML	8.45	1.40	5.00	13.00
MS	6.19	0.23	5.60	6.70

Table 2
Correlation coefficients (and the corresponding p-values in parenthesis) between the behavioral scores of the digit span task.

	S50	ML	MS
S50	1	0.05 (0.7)	0.71(<0.001)
ML	0.05 (0.7)	1	0.44 (0.01)
MS	0.71 (<0.001)	0.44 (0.01)	1

Table 3
Correlation coefficients (and the corresponding p-values in parenthesis) between the behavioral scores and frontal midline theta during resting state.

	MS	ML	S50
FMT power	0.01 (0.78)	−0.03 (0.42)	0.03 (0.43)
FMT peak frequency	−0.06(0.21)	−0.05(0.32)	−0.05 (0.33)

check if the frontal midline theta during resting state was correlated with the behavioral performance the correlation between the various behavioral scores and the FMT power and peak frequency during resting state was calculated. There was no significant correlation between the frontal midline power and the behavioral measures, nor the FMT peak frequency and the behavioral performance (See Table 3 and Fig. 2 upper panel).

3.3. Relationship between frontal-midline theta during task and task performance

According to the theta-gamma coding model, one would expect a relationship between FMT and behavioural performance on this task. To that end, the relationship between FMT during task and behavioural performance was investigated by the correlation between the various behavioral scores and the FMT power and peak frequency during task. There was no significant correlation between the task performance and the FMT power during task nor with the FMT peak frequency (See Table 4 and Fig. 2 lower panel).

### 3.4. Frontal midline theta – load relationship

According to the theta-gamma code, and the hypothesised role of FMT in working memory function, we hypothesised that higher memory load would result in higher FMT power and slower theta (i.e. decreased theta peak frequency).

There was an increment of the FMT power that followed the memory load within the memory condition. Linear regression revealed strong relationship (mean regression coefficient across subjects = 0.12 ± 0.05 (−0.1-0.3)). (See Fig. 3). The regression between the frontal midline theta power and the presented digit order was significantly weaker (Wilcoxon $p < 0.001$) during listening condition (mean regression co-efficients across subjects = 0.01 ± 0.05(−0.1-0.13)). Simple t-test revealed that the coefficients during memory condition were significantly different from zero ($p < 0.01$), while the coefficients in listening condition was not ($p = 0.1$).

The relationship between FMT peak frequency and cognitive load revealed that the linear regression during memory condition (average regression coefficients in participants = −0.1 ± 0.05 (−0.15-0.1)) were significantly lower (Wilcoxon's $p < 0.01$) compared to listening condition (average regression coefficient = 0.02 ± 0.05 (−0.09-0.12)), indicating that the higher cognitive load resulted in a slower theta oscillation during memory condition. (See Fig. 4). Simple t-test revealed that the coefficients during memory condition were significantly different from zero ($p = 0.03$), while the coefficients in listening condition was not ($p = 0.09$).

Additionally, one could assume that the saturation curve that is observable during memory condition is due to the failed trials at the higher load condition. In other words, one would expect that the power
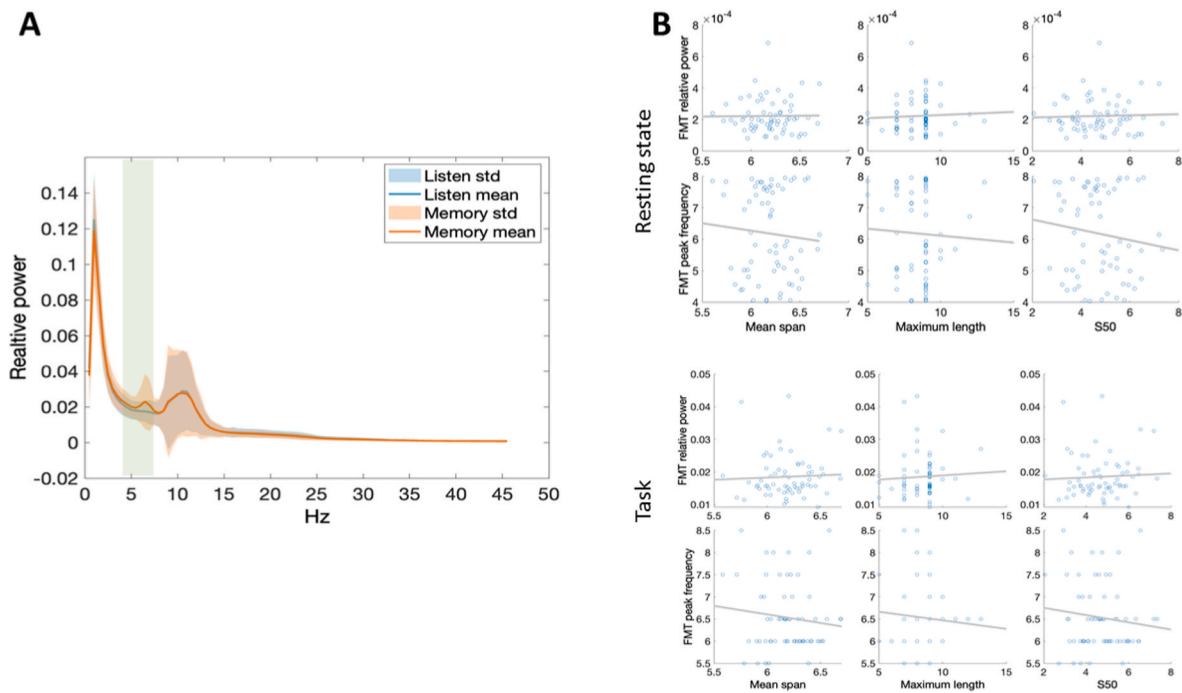
Fig. 2. Panel A shows the average power spectra of all the subjects over the frontal channels during Memory (red) and Listening (blue) condition. The green bar shows the theta frequency range used for the analyses. Panel B is the visual representation of the relationships between the behavioral scores and frontal midline theta during resting state (upper panel) and between the behavioral scores and frontal midline theta during digit span task (lower panel). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 4
Correlation coefficients (and the corresponding p-values in parenthesis) between the behavioral scores and frontal midline theta during task.

	MS	ML	S50
FMT power	0.04 (0.37)	0.05 (0.31)	0.05 (0.32)
FMT peak frequency	−0.11 (0.11)	−0.07 (0.14)	−0.1 (0.1)

of the FMT keeps increasing when one looks at the correctly recalled sequences, (and conversely, the theta peak frequency keeps decreasing) compared to the sequences that contains incorrect recalls. To that end, the difference on the theta power-load relationship and on the peak frequency-load relationship between the correct sequences and "all trials included" was investigated. As seen in the Fig. 5, the FMT power follows the assumption: i.e keeps increasing during correct sequences. However, in case of the FMT peak frequency, the peak frequency seems to decrease, but at higher load the peak frequency returns to higher frequency same as in case of the "all-trials included".

3.5. Cross-frequency coupling during task and resting state

Following the idea of theta gamma code one would assume that there is a relationship between theta-gamma CFC and memory performance. Furthermore, according the idea of Kaminscy et al., the behavioural performance is predictable from resting state activity. To that end the relationship between CFC (both during resting state and task) and behavioural performance was investigated.

For the sake of better overview this section does not contain p-values, but rather points to the relevant figures that represent the average PACz/correlation values at the comodulograms.

Increased (PACz>40) alpha-beta cross-frequency coupling was found during the resting state activity over the channel Cz (See Fig. 6 panel C). The correlation between the resting state PACz and the different behavioural measures however revealed non-significant correlation between the resting state cross-frequency coupling and the

memory performance (See Fig. 6 panel D).

The cross-frequency coupling during the task was much weak (maximum PACz<1) in both conditions, and there was no significant effect of task nor load on the coupling strength (See the average comodulograms of each condition in Fig. 6 panel A). Furthermore, there was no significant correlation between the coupling strength during memory condition and the behavioural measures (See Fig. 6 panel B).

4. Discussion

The current paper aimed to confirm the role of frontal midline theta in memory encoding during verbal digit span task. Overall, the EEG-results show that neither resting state theta nor the theta during the task is predictive to the memory recall accuracy. However, there was a strong positive correlation between cognitive load and theta power as well as a negative correlation between cognitive load and theta peak frequency during the task.

Regarding the behavioral data, the results show that the average STM capacity was in the normative range (Cowan, 2001; Miller, 1956). However, there are number of differences between the digit span task that is implemented in WAIS and the current task, that limited the number of measures that could be derived. Since the order of the length of list was randomized and not increased as in common neuropsychological tests, common digit span measures such as TE-ML and TE-TT could not be calculated. Interestingly, after plotting the average recall accuracy at each nth digit presented a sigmoid relationship was found. After a thorough search in the literature, no other paper was found that described such relationship between accuracy and the nth presented digit in digit span task, thus this paper is the first to describe such relationship. This observation should be considered when the commonly used digit span is utilized in clinical as well as during experimental studies. Furthermore, the validity and replicability of the measures derived from this function (the S50, i.e. the nth digit presented at which the accuracy is 50% calculated from the fitted accuracy-nth digit sigmoid curve) could not be investigated in the current study, and further
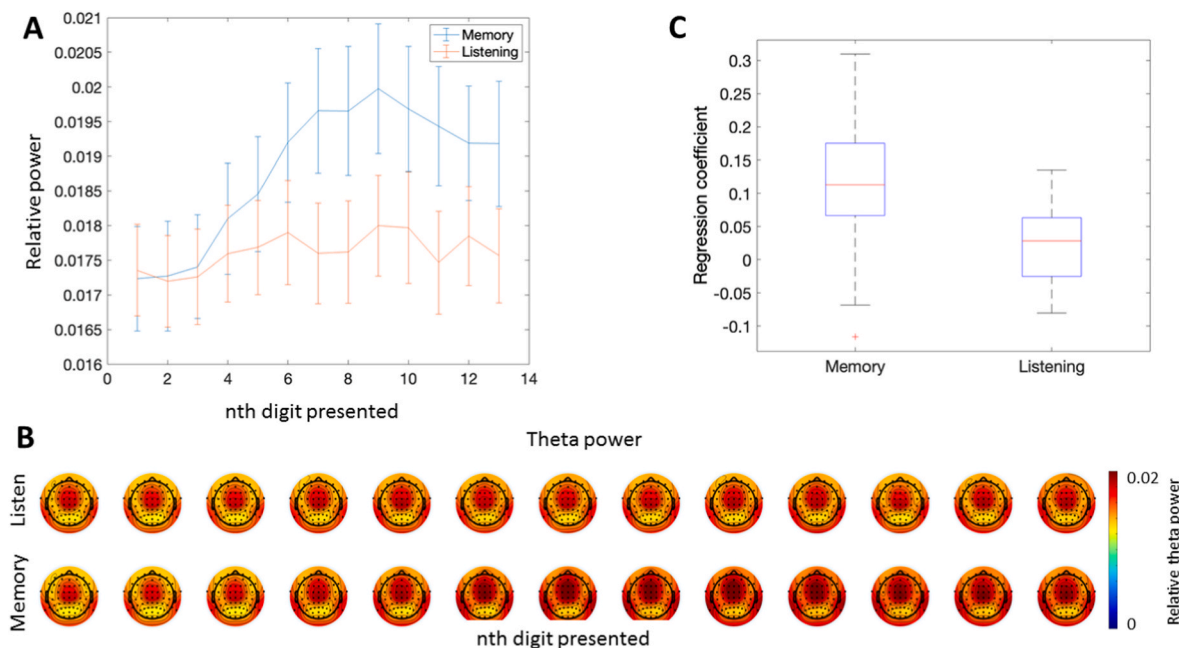
Fig. 3. *Frontal midline theta power – cognitive load relationship. Panel A shows the mean ± SD of the FMT power across subjects at each nth digit presented both during Memory and Listening condition. Panel B shows the average relative theta power at each nth digit presented both during Listening and Memory condition. The color represents the relative theta power. Panel C shows the distribution of the regression coefficients between FMT power and the nth digit presented in the two conditions. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)*
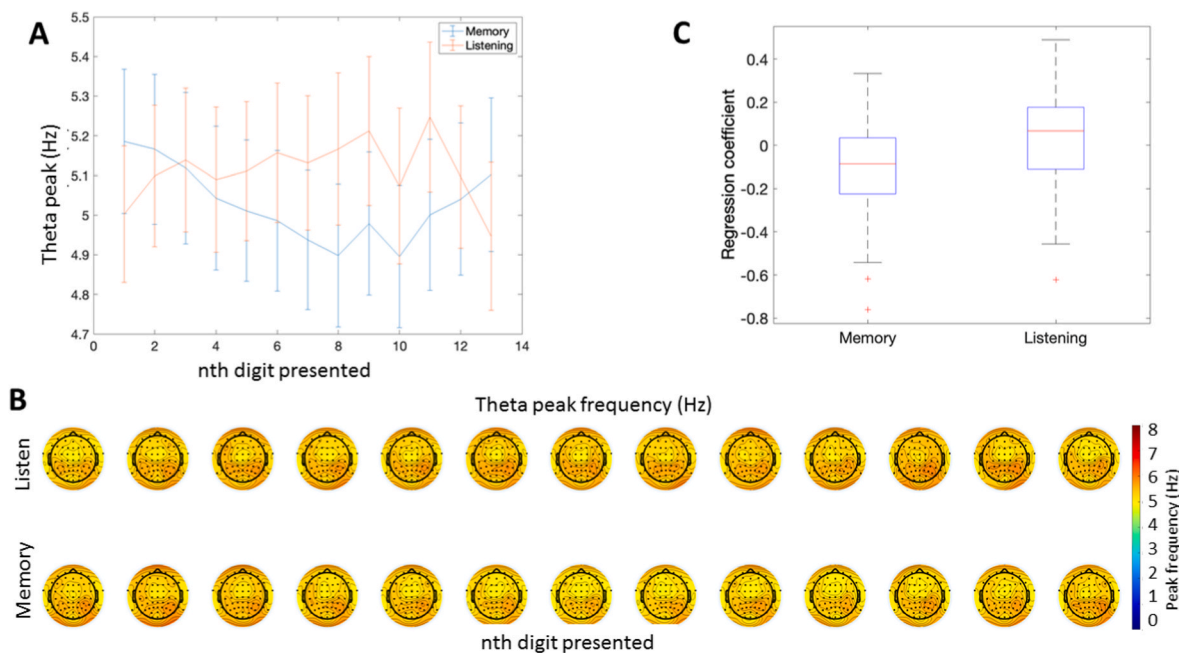

Fig. 4. *Frontal midline theta peak frequency – cognitive load relationship. Panel A shows the mean ± SD of the FMT peak frequency across subjects at each nth digit presented both during Memory and Listening condition. Panel B shows the average peak theta frequency at each nth digit presented both during Listening and Memory condition. Panel C shows the distribution of regression coefficients between FMT peak frequency and the nth digit presented in the two conditions.*

studies should confirm its reliability. However, as the S50 was highly correlated with the MS, which was earlier found to be a highly reliable measure (Woods et al., 2011), the assumption is that S50 is another promising candidate to reliably measure the memory capacity.

Grand average power-spectra of the frontal channels showed increased theta power during the Memory condition as expected. The power spectra also showed prominent alpha peak that can be observed equally high during listening and memory condition, and it is likely to be

connected to stimulus processing as suggested by earlier studies (Vijayan and Kopell, 2012; Barne et al., 2020). Regarding the resting-state theta and task-behavior relationship, there have been few studies that argued that one can predict the performance based on resting state EEG (Kamiński et al., 2011). These assumptions rely on the theta gamma code, i.e. the number of elements that can be stored in our short-term memory is determined by the number of gamma cycles that can fit into one theta cycle (Lisman and Jensen, 2013). However, a
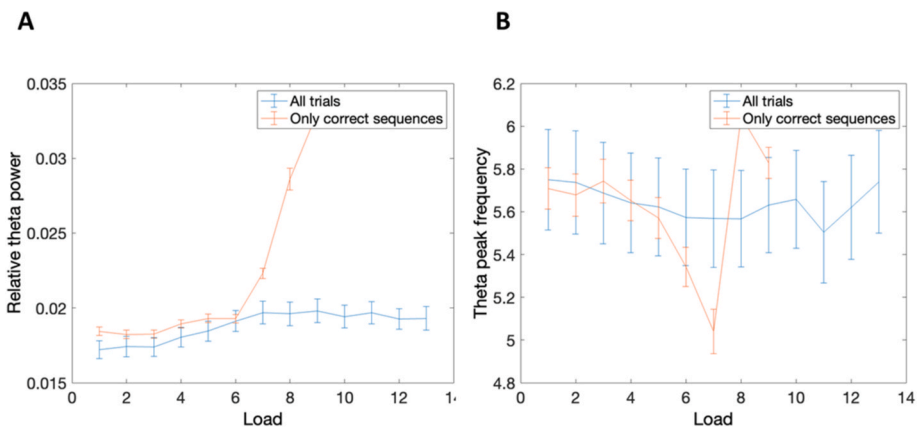
Fig. 5. *Frontal midline theta – load relationship in correct sequences vs all trials. Panel A shows the relationship between FMT power and load in the correct sequences and the sequences that contained both correct and incorrect trials. Panel B shows the relationship between FMT peak frequency and load in the correct sequences and the sequences that contained both correct and incorrect trials.*
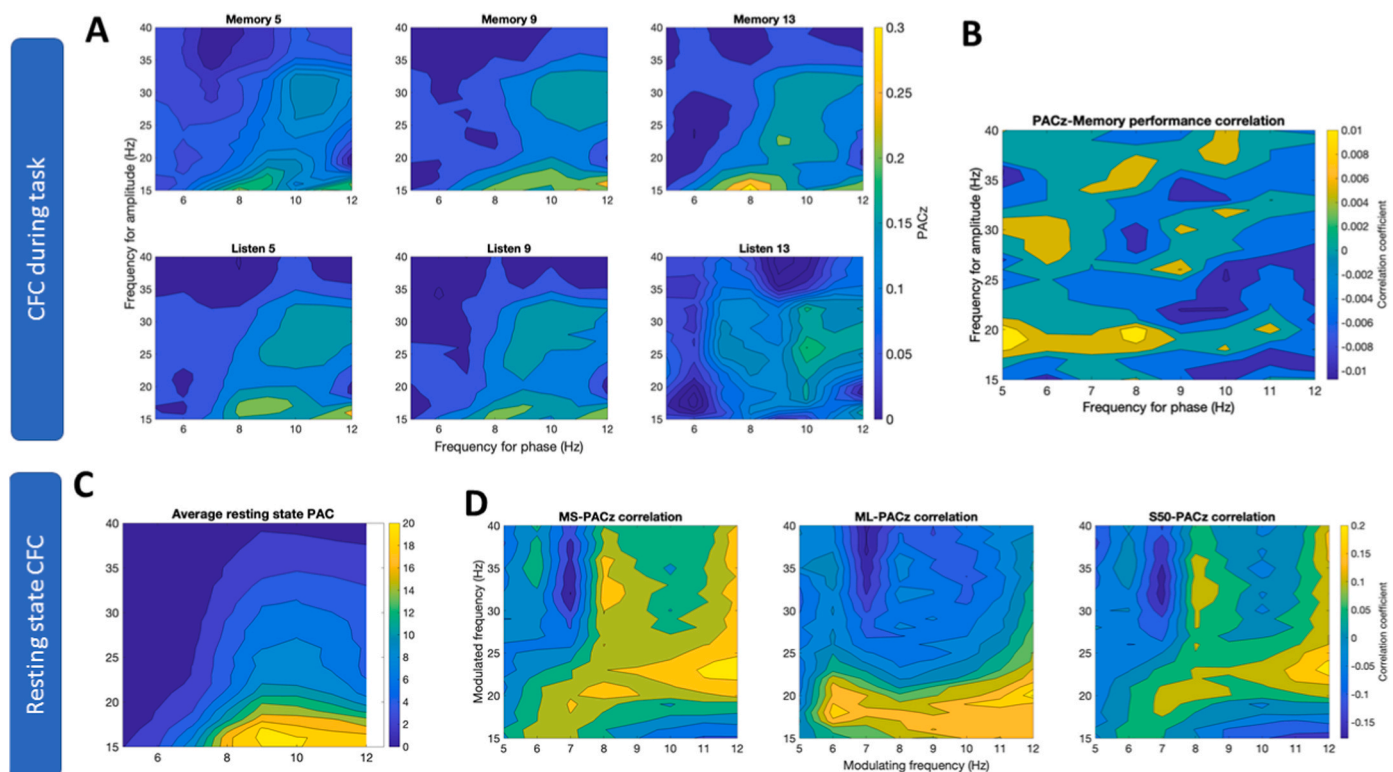
Fig. 6. *Comodulograms in different conditions and their correlation with memory performance. Panel A shows the mean comodulograms for each Load/Task conditions across subjects. Panel B shows the correlation coefficients between the strength of PACz and S50. Panel C shows the average comodulogram during resting state, and panel D shows the correlation between different behavioural measures and the cross-frequency coupling during resting state.*

recent publication by (Malenínská et al., 2021) failed to replicate the relationship between resting state theta cycle length and short-term memory. The current paper also confirms that there is no relationship between resting state theta activity and short-term memory performance, possibly because theta oscillations are not a static property of our brain but rather an observation of a dynamically modulated network (Cavanagh and Frank, 2014; Sauseng et al., 2010).

The existence of theta-gamma code however is evident from measures during various tasks. Numerous studies reported increased frontal midline theta power during memory task (Jensen and Tesche, 2002; Kahana et al., 2001) as well as increased gamma power (Gruber et al., 2004; Herrmann et al., 2004). However, as reviewed by Cavanagh et al. (Cavanagh and Frank, 2014), theta not only emerges during memory

encoding but rather in situations where there is a need for top-down cognitive control. The results of this paper further support this model, as there has been no relationship between the recall accuracy and FMT but the increased FMT power followed the increased memory load.

There was also a negative relationship between the peak of the FMT frequency and the memory load. Thus, the increased need to store more items in our short-term memory resulted in the slowing of the theta oscillations, which is reasonable following the model of theta-gamma code. Providing empirical support for this model, previous studies demonstrate that a greater memory load results in an increased average theta period, leading to lower frequency oscillations Axmacher et al. (2010); Moran et al. (2010)(Senoussi et al., 2022),

This paper also shows that both FMT power and peak frequency both

show a saturation curve, that further supports the assumption that the short-term memory capacity is determined by both the capacity of modulation of FMT power and peak frequency. Furthermore, assuming that the plateau of the theta power and theta peak frequency is deterministic to short term memory capacity, increasing it by external stimulation or via biofeedback could improve short term memory capacity. Indeed, studies suggest that both tACS theta stimulation (Vosskuhl et al., 2015), and TMS over frontal channels (Riddle et al., 2020), as well as biofeedback protocols (Jeddi and Nazari, 2013; Pop-Jordanova and Chakalaroska, 2008) could increase the memory capacity by modulating theta oscillations.

Interestingly, this paper shows that the FMT power keeps increasing with cognitive load within the correctly recalled sequences opposed to the sequences that contains both correct and incorrect recalls. While the assumption for the theta peak frequency was the opposite, here the theta peak frequency seems to return to higher frequency after it reaches an inflection point. Despite the discrepancy of the two results, there are three possibilities that provide explanation of this effect: (1) The cognitive load of the encoded sequences does not modulate the peak frequency, but rather the theta power, (2)The rebound at higher load to higher frequency at >7 load could be because the participants at this point were merely guessing while they were still trying to retrieve the current digit, and hence trying to access more attentional resources (that's what would the increasing power reflect) (3) There is a biological and a mathematical limitation to the modulation of the frequency: the biological one lies on the cellular properties of the given cell-assemblies that produce the theta oscillations, while the mathematical one is simply due to the frequency resolution of the FFT (in our 2-sec window case its 0.5 Hz). Either way these findings need further investigation with more suited task-design.

Regarding the cross-frequency coupling this paper shows that there is a clear coupling during resting state between alpha phase and beta power, however, there was no relationship between the resting state coupling strength and the behavioural performance during the upcoming digit span task. This indicates that the alpha beta cross frequency coupling in resting state is not deterministic for memory performance, but for perhaps other mechanisms such as motor timing (Gwon and Ahn, 2021; Kononowicz et al., 2020; Grabot et al., 2019).In general the coupling strength during the memory task was low and its correlation with the memory performance or memory load was not significant, even when different methods were applied to avoid the pitfalls of the cross-frequency coupling analysis. This negative result is in contrary to other studies that found increased theta-gamma coupling during different memory tasks (for review see (Abubaker et al., 2021)) However, all studies listed in the review and found increased theta-gamma coupling used invasive measures (such as ECoG, iEEG, etc), and therefore the coupling strength could be solely sensitive for LFP-measures. Indeed, EEG has a limitation measuring higher frequency components through the skull as it works as a low-pass filter. Altogether, given the impressive amount of evidence, the existence of the theta gamma coupling is undoubtful, however there are two remaining questions, that needs further investigation: (1) Is theta gamma coupling correlates with memory performance or rather with memory/cognitive load and (2) Perhaps measuring the theta-gamma phase amplitude coupling is more appropriate in LFP-recordings and EEG-recodings are not sensitive enough.

In conclusion, this paper introduced a novel measurement, the S50, that is the memory load at which the recall accuracy is 50% calculated by fitting sigmoid function of the accuracy of the nth digit presented in the digit span task. It also confirms that resting state theta is not associated with memory capacity and that the power and the peak frequency of the frontal midline theta is modulated by the memory load during short-term memory but not the recall accuracy.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ynirp.2022.100124.

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