



## Journal Club

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## Complex Interactions between Distinct Theta Oscillatory Patterns during Sleep Deprivation

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Review of Snipes et al.

The characteristics (e.g., amplitude and peak frequency) of cortical oscillations captured by scalp EEG offer important insights regarding the neural mechanisms of cognitive behaviors. However, the specific neural mechanisms associated with cortical oscillatory characteristics at particular frequency bands remain elusive (Wang, 2010). The frontal-midline theta (fmTheta) and sleep deprivation theta (sdTheta) are two different cortical oscillatory patterns within the theta frequency band (4–8 Hz) that are of scientific interest.

Previous studies have shown that fmTheta and sdTheta are associated with different physiological states, and originate from different brain regions through different molecular mechanisms. When well-rested individuals perform vigilant attention and working memory tasks (Ishii et al., 2014), the increase in the amplitude of theta oscillations detected by EEG electrodes is restricted to the frontal midline region and is known as the fmTheta (Cavanagh and Frank, 2014). Studies have shown that fmTheta is generated by the GABAergic pacemaker neurons

in the medial septum that recruit hippocampal principal cells through long-range projections (Zutshi et al., 2018). In response to the medial septal input, the intrinsic hippocampal oscillators further generate accelerated oscillations (Zutshi et al., 2018) and recruit the medial prefrontal cortical neurons through excitatory projections (O'Neill et al., 2013). In contrast, when sleep-deprived individuals continuously engage in cognitive tasks under sleep pressure (Siclari and Tononi, 2017), an increase in the amplitude of theta oscillations is detected in a broader frontocentral area that extends beyond the brain regions where fmTheta is detected (Brown et al., 2012). This pattern is referred to as sdTheta, and it is associated with the accumulation of adenosine at the synapses and extracellular space of cortical glutamatergic and GABAergic neurons (Hudson et al., 2020). The accumulation of adenosine modulates the theta-oscillating excitatory input from the brainstem reticular formation to the septum (Palchykova et al., 2010) and regulates acetylcholine release (Fredholm et al., 2005) that alters the theta oscillations generated by the cholinergic basal forebrain neurons (Lee et al., 2005). However, previous studies have not directly compared the cortical EEG signals recorded when different tasks are performed under different conditions, so how fmTheta and sdTheta change between well-rested and

sleep-deprived conditions and across different cognitive tasks remains unclear. Therefore, Snipes et al. (2022) designed a study aimed to delineate the relative fmTheta and sdTheta contributions to oscillatory activity recorded with high-density EEG (Snipes et al., 2022) during different tasks.

Snipes et al. (2022) extended our current understanding of fmTheta and sdTheta by comparing cortical theta amplitude and peak frequency patterns measured in well-rested and sleep-deprived individuals performing a variety of vigilant attention (Psychomotor Vigilance Task, Lateralized Attention Task, Game, and Music Listening) and working memory (Short Term Memory, and Tongue-Twister Reading) tasks. Two major analyses were conducted to distinguish between fmTheta and sdTheta. First, topographical analysis was used to compare the distribution of theta power spectral density measured by different scalp electrodes. Second, beamformer source localization analysis was conducted to identify the major brain regions contributing to the cortical theta signals. Consistent with previous studies that recorded cortical theta power during cognitive tasks (e.g., Ishii et al., 2014), results from the Short Term Memory task confirmed that fmTheta power was only evident in frontal midline electrodes, with the signals originating from more restricted brain regions encompassing the

Received Jan. 8, 2023; revised Mar. 20, 2023; accepted Mar. 24, 2023.

The authors declare no competing financial interests.

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<https://doi.org/10.1523/JNEUROSCI.0043-23.2023>

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medial prefrontal and anterior cingulate cortices. In contrast, the authors further showed that sdTheta power recorded during Short Term Memory task was evident in frontocentral electrodes, with the signals originating from widespread brain regions encompassing the middle and superior frontal gyri, cuneus, insula, and temporal poles.

Interestingly, sleep pressure only impaired participants' performance in vigilant attention but not working memory tasks, which also contributed to task-specific manifestations of fmTheta and sdTheta characteristics. For instance, sleep pressure impaired participants' behavioral performance in both the Psychomotor Vigilance Task and Lateralized Attention Task, which was accompanied with amplitude increases in both fmTheta and sdTheta. In contrast, sleep pressure did not impair participants' behavioral performance in working memory tasks with different cognitive load, while fmTheta amplitude exhibited load-dependent decreases and sdTheta exhibited load-independent increases.

These results confirm that fmTheta and sdTheta are distinct oscillatory patterns generated from different brain regions that coexist when participants perform cognitive tasks under sleep pressure. Importantly, Snipes et al. (2022) suggest that the relative contributions of fmTheta and sdTheta modulate successful cognitive task performance, whereas others have suggested that fmTheta and sdTheta play different roles in modulating cognitive behaviors (Scheeringa et al., 2009; Hudson et al., 2020). A previous neuroimaging study demonstrated that maintaining the same level of working memory task performance under sleep pressure requires our brain to adopt a top-down compensatory recruitment mechanism by increasing activation of the cognitive control network (Drummond et al., 2005), indicated by a decrease in fmTheta amplitude (Scheeringa et al., 2009). Furthermore, an increase in sdTheta amplitude with increasing sleep pressure is believed to impede an individual's ability to discriminate competing incoming stimuli, which results in impaired cognitive processing (Palchykova et al., 2010; Hudson et al., 2020). Hence, findings of Snipes et al. (2022) may reflect the deployment of top-down cognitive control (indicated by a decreased fmTheta) to counteract the effects of sleep pressure (indicated by an increased sdTheta) on these circuits, thus allowing performance to be maintained in working memory tasks when one is sleep-deprived. In the same vein, impaired performance in vigilant

attention tasks could be attributed to the failure in cognitive control deployment (indicated by an increased fmTheta). Future studies should further examine the relationship between fmTheta and sdTheta to reveal what these signals can tell us about the underlying compensation mechanisms for cognitive functioning under sleep pressure.

The work by Snipes et al. (2022) also highlights three important future study directions. First, it is worthwhile to further investigate the modulating effects of time allowed for information processing on cognitive tasks. In line with Slama et al. (2018), Snipes et al. (2022) did not find working memory impairment under sleep pressure, which was in contrast to some other studies involving participants that performed similar visual working memory tasks (Choo et al., 2005; Lythe et al., 2012). Comparing task designs reveals that participants' performance was only impaired in studies with shorter duration of stimulus presentation for working memory encoding [Lythe et al. (2012): 1000 ms; Choo et al. (2005): 500 ms], but not when stimuli were presented for longer periods [Slama et al. (2018): 1750 ms; Snipes et al. (2022): 2000 ms]. Because Snipes et al. (2022) did not vary the time allowed for the Short Term Memory task, it remains unanswered how the relative contributions of fmTheta and sdTheta to the overall cortical EEG patterns when the time for encoding and retrieving visual information is varied. Second, the neural mechanism underlying task-dependent sdTheta amplitude change could be further explored. When comparing the sdTheta across vigilant attention tasks, the increase of sdTheta amplitude is greater in Psychomotor Vigilance Task and Lateralized Attention Task than that observed in Music Listening and Game tasks. In contrast to Psychomotor Vigilance Task and Lateralized Attention Task, Music Listening and Game tasks do not involve the presence of visual stimuli that require rapid ( $\leq 500$  ms poststimulus onset) and accurate responses (i.e., target signals), which has been operationalized as having higher cognitive demand on individuals (Hudson et al., 2020). Given that cognitive demand has been shown to mediate synaptic transmissions and consequently affect information processing (Williamson et al., 2015), the greater increase of sdTheta amplitude observed in cognitively demanding vigilant attention tasks might be attributable to greater adenosine accumulation at the synapses within the task-relevant neuronal

populations. Third, interindividual variabilities of the relative fmTheta and sdTheta contributions to cortical EEG could be further examined. Psychomotor Vigilance Task and Lateralized Attention Task behavioral data demonstrated that some individuals performed better than others in maintaining vigilant attention under sleep pressure, and this was accompanied by increased interindividual variability in cortical theta peak frequencies. It has been shown that a positive shift of theta peak frequency predicts better cognitive control ability in well-rested individuals (Senoussi et al., 2022), and that this reflects a higher rate of neuronal computation for processing more information according to environmental changes (Kropff et al., 2021). To examine how interindividual variability in theta peak frequencies modulates performance on the vigilant attention task under sleep pressure, future studies could examine the association between changes in theta peak frequency and changes in behavioral performance from well-rested to sleep-deprived conditions. By taking this association into account, we may be able to delineate the intricate relationships between fmTheta, sdTheta, the averaged scalp EEG theta-band signal, and behavioral changes associated with sleep pressure.

In conclusion, Snipes et al. (2022) highlight the complex interactions between two theta oscillatory patterns (i.e., fmTheta and sdTheta) when participants perform vigilant attention and working memory tasks during well-rested and sleep-deprived conditions. This study reveals that the relative contribution of fmTheta and sdTheta to cortical EEG signals is task-specific, which may be modulated by the time allowed for information processing on cognitive tasks, cognitive demand of different tasks, and interindividual variabilities in the ability to deploy cognitive control under sleep-deprived condition. Careful delineations of different band-specific oscillatory characteristics captured by EEG further deepen our understanding regarding the neural mechanisms underlying cognitive behaviors in different physiological states.

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