Neural Oscillation Modulation of Working Memory: Based on Neural Entrainment

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Abstract

Research on the neural oscillation mechanisms of working memory constitutes a prominent focus in the current field of memory studies. The fundamental question remains: Are neural oscillations merely epiphenomenal concomitants of working memory processes, or do they directly participate in and regulate working memory processing? Existing research has revealed that neural oscillatory activity within the brain gradually becomes phase-synchronized with external rhythmic stimulation under its driving influence—a phenomenon termed "neural oscillation entrainment." Intervention studies employing repetitive Transcranial Magnetic Stimulation (rTMS) and transcranial Alternating Current Stimulation (tACS) capitalize on this phenomenon to deliver rhythmic magnetic or electrical stimulation to localized brain regions, thereby modulating neural oscillatory activity in specific frequency bands, cross-frequency neural oscillation coupling, or inter-regional neural oscillation phase synchronization during working memory processes. These approaches provide relatively direct causal evidence for the involvement of neural oscillations in working memory processing. Future research should consider adopting a brain network perspective, regulating neural oscillatory activity across multiple brain regions to further examine its influence on working memory. Additionally, it is essential to explore and optimize rTMS/tACS stimulation protocols for working memory modulation, supplemented by objective electroencephalographic recordings, to enhance the validity and reproducibility of such studies, ultimately achieving the goal of improving working memory capacity.

Full Text

Preamble

Neural Oscillation Entrainment in Working Memory: A Review of Entrainment-Based Modulation

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Abstract: The neural oscillatory mechanisms of working memory (WM) represent a major focus in contemporary memory research. A fundamental question remains unresolved: Are neural oscillations merely epiphenomenal to WM processes, or do they directly participate in and regulate WM processing? Recent studies have revealed that brain oscillatory activity can be driven by external rhythmic stimuli, gradually synchronizing with the phase of the external rhythm—a phenomenon termed “neural oscillatory entrainment.”Based on this principle, repetitive transcranial magnetic stimulation (rTMS) and transcranial alternating current stimulation (tACS) interventions have been employed to modulate neural oscillations in specific frequency bands, cross-frequency coupling, and inter-regional phase synchronization during WM tasks, providing relatively direct causal evidence for the role of neural oscillations in WM processing. Future research should adopt a network-level perspective to modulate oscillatory activity across multiple brain regions and further investigate how neural oscillations influence WM. Additionally, it is crucial to explore and optimize rTMS/tACS protocols for WM modulation, supplemented with objective EEG recordings to enhance the validity and reproducibility of such studies, ultimately aiming to improve WM capacity.

Keywords: working memory, neural oscillation entrainment, rTMS, tACS

Working memory (WM) is a core component of higher-order cognitive functions, temporarily storing and manipulating discrete information to guide ongoing or forthcoming cognitive behavior (Baddeley, 2010). The neural mechanisms underlying WM have long captivated researchers, with two critical questions at the forefront: Which brain regions are involved in WM, and when and how do these regions participate in WM processes? Regarding the first question, numerous functional magnetic resonance imaging (fMRI) studies have consistently demonstrated that WM tasks differentially activate the dorsolateral prefrontal cortex (DLPFC), parietal lobe, and occipital lobe, establishing associations between regional activation and WM performance (Ambrose et al., 2016; Christophel et al., 2018; Ester et al., 2009, 2015; Gayet et al., 2017; Xu & Chun, 2006). Meanwhile, non-invasive brain stimulation (NIBS) techniques, such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), can transiently disrupt neural activity in targeted brain regions through temporally precise magnetic or electrical stimulation, enabling causal inferences about the relationship between specific neural activations and WM tasks (Arciniega et al., 2018; Berryhill et al., 2019; Röhner et al., 2018; Silvanto & Soto, 2012). However, due to fMRI’ s imaging principles (which emphasize task-evoked regional activation) and limited temporal resolution, such studies primarily highlight the importance of brain region activation while remaining unable to capture the dynamic evolution of neural activity within specific regions or the temporal dynamics of inter-regional synchronization during WM processes, thus precluding deeper investigation into the second question.

In parallel, electrophysiological research using magnetoencephalography (MEG) and electroencephalography (EEG) offers excellent temporal resolution, allowing researchers to address this gap by examining neural oscillatory phenomena during WM. WM tasks engage large neuronal ensembles, and neural oscillations reflect the sustained, rhythmic activity of these ensembles, enabling efficient information exchange between different neuronal populations (Bosman et al., 2012; Buzsáki et al., 2012). Oscillatory frequencies are categorized from slow to fast as delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (13–30 Hz), and gamma oscillations. Gamma oscillations are further subdivided into low-frequency (30–70 Hz) and high-frequency (70–150 Hz) bands. Extensive EEG and MEG research has demonstrated that both local oscillatory activity and inter-regional coupling (brain networks) are intimately linked to WM processing (Bonnefond & Jensen, 2012; Honkanen et al., 2015; Roux & Uhlhaas, 2014). For instance, gamma oscillations in frontal and specific visual cortices are associated with the maintenance of object feature information, while theta-gamma coupling in the left temporal lobe reflects the precision of visual memory representations. These findings partially elucidate how and when different brain regions support WM processing, yet they raise a more fundamental question: Are neural oscillations merely concomitant phenomena of WM processing, or do they directly participate in and regulate this process?

To address this question, researchers can modulate neural oscillations in local or inter-regional networks, disrupt specific network nodes, and thereby establish causal links between brain regions, neural oscillations, and WM behavior. Recent discoveries indicate that neural oscillations can be regulated through "neural oscillatory entrainment," wherein external rhythmic stimuli interact with endogenous oscillations in specific brain regions until synchronization occurs, thereby modulating internal neural activity (Thut et al., 2011). External rhythmic stimuli include perceptual inputs (e.g., rhythmic sounds or images) and rhythmic NIBS. While rhythmic perceptual stimuli can drive oscillations in sensory cortices (Garcia et al., 2017; Spaak et al., 2014), rhythmic NIBS techniques such as rTMS and tACS more selectively induce oscillatory activity in targeted regions and frequency bands, making them widely applied in studies investigating the specific roles of neural oscillations in WM (Reinhart & Nguyen, 2019; Vosskuhl et al., 2018).

This review focuses on recent studies employing rhythmic NIBS to modulate WM-related neural oscillations. We first introduce the principles and methods of rhythmic NIBS modulation. Subsequently, based on established roles of different frequency bands in WM, we systematically review evidence from rhythmic NIBS studies that modulate neural oscillations to influence WM capacity, providing causal evidence to address whether neural oscillations directly participate in WM processing and inspiring future research directions. Finally, we discuss limitations and potential improvements in rhythmic NIBS intervention studies for WM.

2.1 Principles of Neural Oscillation Entrainment

The fundamental principle of neural oscillation entrainment is that external rhythmic stimuli can induce synchronized neural oscillations in corresponding brain regions, producing phase locking between internal oscillations and external rhythms to achieve synchronization (Lakatos et al., 2019). During entrainment, neural activity in the stimulated region undergoes two primary changes: first, the phase of endogenous oscillations becomes increasingly synchronized with the phase of the external stimulus; second, this phase synchronization leads to increased oscillatory amplitude at the stimulation frequency. According to the model proposed by Hanslmayr et al. (2019), neuronal ensembles initially reside in a baseline state. Upon rhythmic stimulation presentation, the frequency and phase of neuronal activity gradually shift toward those of the external stimulus, entering a build-up phase of rhythmic synchronization. Finally, when the phase difference between brain oscillations and the external rhythm reaches zero, synchronization is maximal (fully entrained) and oscillatory amplitude peaks. Following stimulus offset, synchronization does not immediately dissipate but persists for several cycles, generating an "entrainment echo" before slowly returning to baseline.

2.2 Methods for Implementing Neural Oscillation Entrainment

Neural oscillation entrainment can be achieved through rhythmic NIBS, primarily rTMS and tACS. TMS employs transient high-intensity pulsed magnetic fields that penetrate the skull, inducing electrical currents in cortical tissue to stimulate neuronal activity. rTMS can modulate rhythmic oscillatory activity in neuronal ensembles (Vosskuhl et al., 2018). A representative study of rTMS-induced entrainment was conducted by Thut et al. (2011), who applied 10 Hz alpha-rTMS to the parietal cortex while simultaneously recording EEG. Compared to control conditions, alpha-rTMS significantly induced synchronized alpha oscillations in the stimulated region, with amplitude increasing as internal alpha oscillations gradually synchronized with the external rTMS phase. The study controlled for potential auditory confounds by employing a sham condition in which the TMS coil was angled 45° away from the scalp, preventing direct magnetic stimulation. This work provided compelling evidence for rhythmic rTMS-induced entrainment and offered valuable methodological guidance for future rTMS experiments.

The other rhythmic NIBS technique, tACS, delivers weak rhythmic alternating current through scalp electrodes to induce oscillations at the same frequency in neuronal ensembles (Antal & Paulus, 2013). Direct evidence for tACS-induced entrainment comes from Helfrich et al. (2014), who applied 10 Hz alpha-tACS to the posterior parieto-occipital cortex. Compared to sham stimulation, the stimulated region's alpha oscillations progressively synchronized with the tACS phase, and alpha power increased (Helfrich et al., 2014). Subsequent studies have confirmed tACS-induced entrainment across various cognitive tasks (Chander et al., 2016; Voss et al., 2014; Witkowski et al., 2016).

3 Evidence from NIBS Studies Modulating WM via Oscillation Entrainment

Leveraging the phenomenon of neural oscillatory entrainment, an increasing number of researchers have employed NIBS to investigate specific mechanisms linking brain oscillations to WM. Notably, only some of these studies have directly measured entrainment effects induced by rhythmic NIBS, as summarized in Table 1 . Below, we detail evidence from rhythmic NIBS studies organized by oscillatory frequency band (from slow to fast) involved in WM.

3.1.1 The Role of Frontal and Parietal Theta Oscillations in WM

Frontal theta oscillations are associated with cognitive resource demands and allocation during WM. Jensen et al. (2002) first observed enhanced frontal theta oscillations during sequential encoding and maintenance of letters, exhibiting a memory load effect, leading to the proposal that frontal theta reflects resource allocation. Similarly, Griesmayr et al. (2010) found that frontal theta activity, particularly in the dorsolateral prefrontal cortex (DLPFC), was more pronounced during WM maintenance when participants performed letter reordering tasks compared to simple memory tasks. These findings suggest that the prefrontal cortex may not directly store memory information but rather participates in information processing and cognitive resource allocation to support maintenance. Beynel et al. (2019) applied theta-rTMS to the left DLPFC either before encoding or during maintenance in a delayed letter-ordering task, finding significantly improved WM accuracy under high-demand conditions compared to sham stimulation. Additionally, a recent rTMS study demonstrated that theta-rTMS (versus non-rhythmic rTMS) delivered to the left DLPFC during maintenance enhanced WM capacity for right visual field targets in a paradigm containing both targets and distractors, indicating that frontal theta oscillations regulate the allocation of cognitive resources to prioritize target processing (Riddle et al., 2020). Recent research has also linked frontal theta oscillations to novelty detection during WM retrieval (Liang et al., 2017), though causal evidence for this relationship remains to be established.

Parietal theta oscillations play crucial roles in both information storage and manipulation in WM, as evidenced by increased theta amplitude during maintenance with higher memory loads and task demands (Palva & Palva, 2011; Sauseng et al., 2010). Jaušovec et al. (2014) applied theta-tACS to the left parietal (P3 electrode), right parietal (P4), and left frontal (F3) cortices during WM span tests. Compared to sham stimulation, parietal stimulation significantly improved WM storage capacity, with the most pronounced effect following left parietal stimulation, whereas frontal stimulation showed no such effect. These results implicate parietal theta oscillations in WM storage and updating (Jaušovec et al., 2014; Jaušovec & Jaušovec, 2014). Recent work has further linked parietal theta oscillations to information manipulation. Albouy et al. (2017) employed theta-rTMS (versus non-rhythmic rTMS) over the left intraparietal sulcus (IPS) during maintenance of an auditory WM task requiring note reordering. Theta-rTMS significantly improved memory accuracy, and concurrent EEG recordings revealed enhanced theta power in the IPS and increased theta phase synchronization between the left IPS and right DLPFC, with these enhancements correlating positively with behavioral performance (Albouy et al., 2017). This study establishes a causal relationship between IPS theta oscillations and auditory WM manipulation.

However, some researchers argue that IPS theta oscillations do not directly mediate WM manipulation. Griffiths and Kumar (2017) propose that theta-rTMS over the IPS enhances theta phase synchronization between the DLPFC and IPS, facilitating frontoparietal information transfer and strengthening prefrontal control over parietal regions, thereby improving WM manipulation performance (Albouy et al., 2017; Griffiths & Kumar, 2017). Similarly, Li et al. (2017) applied theta-rTMS to the superior parietal lobule (SPL) during maintenance in a Sternberg task while recording EEG. Theta-rTMS enhanced both parietal theta power and frontoparietal theta phase synchronization, leading to significant improvements in WM accuracy (Li et al., 2017). These findings suggest that modulating oscillations in any node of the frontoparietal network may affect oscillatory activity in other network nodes, underscoring the need for cautious interpretation of results and highlighting the importance of concurrent EEG recordings. They also inspire researchers to interpret NIBS effects from a network perspective rather than focusing solely on local changes.

3.1.2 The Role of Theta Oscillation Synchronization Between Frontoparietal and Frontotemporal Regions

Beyond single brain regions, researchers have extensively investigated how different brain regions coordinate and integrate memory information during WM. Previous studies have shown that theta phase synchronization between frontoparietal and temporoparietal regions can integrate information across multiple brain areas to support WM processing and storage (Daume et al., 2017; Fell & Axmacher, 2011; Fries, 2015; Payne & Kounios, 2009). For example, the strength of theta phase coupling between frontal and parietal cortices correlates with WM load (Payne & Kounios, 2009), manipulation difficulty (Sauseng et al., 2005), and predicts individual WM capacity (Kopp et al., 2006). Consequently, numerous studies have used tACS to modulate theta phase synchronization between different brain regions within functional networks and examined its impact on WM capacity (Alekseichuk et al., 2017; Polanía et al., 2012; Tseng et al., 2018). Polanía et al. (2012) applied theta-tACS (6 Hz) simultaneously to frontal (F3) and parietal (P3) regions with either desynchronized (180° phase difference) or synchronized (0° phase difference) phases. Participants receiving synchronized stimulation exhibited shorter WM response times compared to those receiving desynchronized stimulation. Similarly, Alekseichuk et al. (2017) found that desynchronized theta-tACS over frontal and parietal cortices in a visuospatial WM task reduced theta phase connectivity between these regions, decreasing WM capacity (hit rate minus false alarm rate) and increasing response times.

Furthermore, processing real-world objects primarily involves the ventral visual pathway, including temporal cortex. According to top-down WM control mechanisms, temporal processing and representation of real objects are under prefrontal regulation, which may be implemented through theta phase synchronization between frontal and temporal regions (Daume et al., 2017; Fell & Axmacher, 2011). A recent MEG study in older adults revealed weaker theta synchronization between prefrontal and temporal cortices compared to younger adults, which researchers hypothesized contributes to age-related WM deficits. Building on this, high-precision theta-tACS was applied simultaneously to frontal and temporal cortices with phase differences of 0° (synchronized) or 180° (desynchronized). Only the 0° phase condition enhanced frontotemporal theta phase synchronization and improved WM performance (response time and accuracy) in older adults (Reinhart & Nguyen, 2019), demonstrating the functional significance of frontotemporal theta phase synchronization for interregional information transfer in WM.

3.2 Modulating WM via Alpha Oscillation Entrainment

Parieto-occipital alpha oscillations are closely associated with the ability to suppress distracting information during WM (Bonnefond & Jensen, 2012; Jensen et al., 2002; Klimesch et al., 2007; Rihs et al., 2007; Van Dijk et al., 2010). Sauseng et al. (2009) employed a bilateral visual field WM paradigm and observed a clear alpha lateralization effect during maintenance, with alpha power increasing in brain regions involved in distractor suppression and scaling with the number of distractors. To investigate the causal role of alpha oscillations in distractor suppression, they applied alpha-rTMS (10 Hz) to the right parietal cortex (P4 electrode) during maintenance. Alpha-rTMS (compared to 15 Hz rTMS) delivered to the hemisphere ipsilateral to the memory array (i.e., involved in distractor suppression) significantly improved WM capacity, whereas stimulation of the contralateral hemisphere (i.e., involved in target processing) impaired capacity, thereby validating the distractor suppression function of parieto-occipital alpha oscillations during WM maintenance. Similar results have been obtained in aging research (Borghini et al., 2018; Grande et al., 2017). For instance, Borghini et al. (2018) hypothesized that age-related cognitive decline (e.g., reduced WM accuracy) might stem from impaired distractor suppression. Using a WM task with retro-cues and distracting information, they found that alpha-tACS over the right parietal cortex (P4) in older adults (compared to sham) significantly enhanced distractor suppression and improved memory accuracy (Borghini et al., 2018). However, these studies selected stimulation sites based primarily on the P4 EEG electrode position, which covers variable brain regions across individuals, limiting the establishment of causal links between specific brain areas and WM.

Given prior findings highlighting the IPS as a critical region for WM storage (These & Thus, 2004; Todd & Marois, 2005; Xu & Chun, 2006) and showing load-dependent alpha activity in the IPS during maintenance (Grimault et al., 2009), many researchers have used fMRI to precisely localize stimulation targets when investigating the role of IPS alpha oscillations in distractor suppression. Emrich et al. (2017) applied 10 Hz alpha-rTMS to the left IPS during maintenance in a delayed-match task and found improved WM capacity, but only in participants with lower baseline capacity (Stephen et al., 2017). Additionally, Riddle et al. (2020) demonstrated that alpha-rTMS over the left IPS (compared to non-rhythmic rTMS) significantly enhanced distractor suppression and increased WM capacity, establishing the frequency- and region-specificity of IPS alpha oscillations in distractor suppression (Riddle et al., 2020).

3.3 Modulating WM via Gamma Oscillation Entrainment

Gamma oscillations (>30 Hz) are associated with the maintenance of object information representations in visual WM (Milner, 1974). Howard et al. (2003) recorded intracranial signals during a Sternberg task and observed significant gamma activity in occipital, temporal, and frontal lobes that increased with memory load. Scalp EEG and MEG studies have similarly shown that frontal gamma activity is modulated by the number and complexity of memory representations, exhibiting load effects and correlating significantly with WM capacity (Honkanen et al., 2015; Roux & Uhlhaas, 2014). Based on these findings, Hoy et al. (2015) applied gamma-tACS to the left DLPFC (F3 electrode) and found improved WM performance under high memory load. However, Santarnecchi et al. (2015) using identical gamma-tACS over the left frontal cortex (F3) found no significant effect on WM performance (Santarnecchi et al., 2016). Similarly, Pahor and Jaušovec (2018) applied gamma-tACS to bilateral frontal cortices (F3 and F4) without observing significant WM changes compared to sham stimulation (Pahor & Jaušovec, 2018). These discrepancies may arise because tACS effects are sensitive to task difficulty and individual differences; Santarnecchi et al. did not manipulate task difficulty (e.g., memory set size), while Pahor and Jaušovec found no entrainment effect in concurrent EEG recordings. Furthermore, Tseng et al. applied 180° out-of-phase gamma-tACS simultaneously to left parietal and temporal cortices and found improved visual WM discriminability, suggesting that gamma-mediated information exchange between temporal and parietal cortices during WM involves a 180° phase lag, though this effect was significant only in individuals with poorer WM capacity (Tseng et al., 2016). Future studies should therefore carefully adjust task difficulty, participant grouping, improve targeting precision, and incorporate concurrent EEG monitoring.

3.4 Modulating WM via Cross-Frequency Coupling Entrainment

Beyond single-frequency oscillations, cross-frequency coupling (CFC) between different frequency bands also plays a vital role in WM (Siebenhühner et al., 2016). Lower-frequency oscillations (theta, alpha, beta) often co-occur with higher-frequency gamma oscillations, with high-frequency activity reflecting local encoding and representation of external information (Jensen et al., 2007) and low-frequency oscillations mediating inter-regional information transfer (Daume et al., 2017). Modulating CFC can thus reveal its specific functions in WM.

3.4.1 Theta-Gamma Coupling in WM Frontoparietal theta-gamma coupling is implicated in WM encoding and storage (Fuentemilla et al., 2010; Rutishauser et al., 2010; Sauseng et al., 2019). According to the theta-gamma coupling model, individual gamma cycles represent neural representations of single memory items, while a single theta cycle can embed multiple gamma sub-cycles. Consequently, more gamma sub-cycles nested within a theta cycle correspond to greater representational capacity (Lisman & Jensen, 2013). If entrainment can lengthen theta cycles, the number of nested gamma sub-cycles should increase, thereby enhancing memory capacity. Recent tACS findings support this hypothesis: Bender et al. (2019), Vosskuhl et al. (2015), and Wolinski et al. (2018) applied low-frequency (4 Hz) and high-frequency (7 Hz) theta-tACS to the right IPS during spatial WM tasks, finding that lower-frequency theta-tACS significantly improved WM capacity. Unfortunately, these studies did not provide concurrent EEG evidence.

The theta-gamma model further posits that gamma sub-cycles nested at theta peaks (neuronal excitatory states) enable optimal encoding efficiency (Lisman & Jensen, 2013). Alekseichuk et al. (2016) combined tACS-EEG in a spatial WM task, comparing single-frequency theta (6 Hz) tACS with theta-gamma compound tACS (gamma sub-cycles nested at theta peaks or troughs) over the left prefrontal cortex (PFC). Both single-frequency and peak-nested compound tACS improved WM discriminability, with the compound stimulation showing superior effects, whereas trough-nested compound tACS showed no benefit (Alekseichuk et al., 2016). Resting-state EEG revealed enhanced theta phase synchronization between the left PFC and other brain regions following peak-nested compound tACS. However, due to scalp EEG’ s limited sensitivity to high-frequency gamma activity, whether compound tACS successfully induced matching neural oscillation patterns at the stimulation site remains uncertain; future studies could employ MEG to address this limitation. Nevertheless, this work provides novel approaches for simulating natural brain oscillation patterns with tACS and for investigating causal relationships between CFC and cognitive functions.

3.4.2 Alpha-Gamma Coupling in WM Posterior parieto-occipital alpha-gamma coupling is associated with gating external information processing, suppressing task-irrelevant distractors from entering visual encoding and memory storage (Bonnefond & Jensen, 2013, 2015; Jokisch & Jensen, 2007). The alpha-gamma coupling model proposes that multiple gamma sub-cycles are nested within alpha troughs; shortening alpha cycles reduces gamma sub-cycle number, thereby suppressing WM representations (Bonnefond & Jensen, 2013). Thus, increased alpha-gamma coupling strength reflects enhanced distractor suppression. For example, Bonnefond et al. (2015) used a Sternberg WM task with strong and weak distractor conditions during maintenance, observing significant alpha-gamma coupling in posterior parieto-occipital cortex before distractor onset that increased with distractor strength (Bonnefond & Jensen, 2015). Conversely, when task-relevant information entered the memory system for further processing, alpha-gamma coupling decreased (Tzvi et al., 2018). Previous studies have also shown that alpha-rTMS over the SPL during maintenance enhanced both alpha power and alpha-gamma coupling, with both changes correlating negatively with WM performance (Hamidi et al., 2009). These findings suggest that alpha-frequency NIBS can modulate not only alpha oscillations but also alpha-gamma coupling. Additionally, research has shown that individual alpha peak frequency (IAF) varies across participants (Klimesch et al., 2003), suggesting that tailoring NIBS frequency to individual IAF may offer a promising approach for modulating alpha-gamma coupling.

3.4.3 Beta-Gamma Coupling in WM Beta-gamma coupling is considered fundamental for integrating and maintaining visual information in WM (Bullmore & Sporns, 2009; Siebenhühner et al., 2016). Laminar recordings in prefrontal cortex have revealed coupling between deep-layer (layers 5–6) beta oscillations and superficial-layer (layers 2–3) gamma oscillations (Bastos et al., 2018; Miller et al., 2018). Specifically, during WM encoding and maintenance, beta-gamma coupling in deep prefrontal layers decreases, allowing gamma power to increase; when information processing is unnecessary, beta-gamma coupling strengthens and gamma power is suppressed (Miller et al., 2018). Bastos et al. (2018) similarly observed reduced beta-gamma coupling strength during WM maintenance, indirectly supporting this model (Miller et al., 2018). However, few studies have used rhythmic NIBS to modulate beta-gamma oscillations across cortical layers in single brain regions, representing a valuable future direction.

Regarding superficial cortical layers, no studies have identified local or inter-regional beta-gamma coupling related to WM tasks, nor have NIBS interventions targeted this phenomenon, leaving it to be explored. Considering beta oscillations alone, some studies have found that parietal beta amplitude decreases with increasing memory load in object WM (Lundqvist et al., 2011) and temporal beta amplitude decreases with load in spatial WM (Proskovec et al., 2018). Additionally, frontal beta amplitude decreases during memory encoding (Hanslmayr et al., 2011), reflecting an inhibitory function. Hanslmayr et al. (2014) applied beta-rTMS to the inferior frontal gyrus during encoding, which, as expected, significantly impaired memory encoding. Concurrent EEG recordings confirmed successful beta entrainment, with participants showing the greatest beta amplitude enhancement exhibiting the poorest memory performance (Hanslmayr et al., 2014). Other studies have observed sustained beta phase coupling between visual and frontoparietal cortices during WM maintenance, with IPS beta phase coupling strength increasing with memory load (Palva et al., 2010). Future research should therefore attempt to modulate beta oscillations in specific brain regions to examine their impact on WM performance and explore whether beta-gamma coupling can be regulated through single-frequency beta interventions.

4 Summary and Outlook

In summary, rhythmic NIBS interventions can induce neural oscillation entrainment in stimulated brain regions, affecting memory performance and providing relatively direct causal evidence that neural oscillatory activity indeed participates in regulating WM processing. However, it is important to note that the causal relationships established through NIBS exhibit greater variability than those from lesion studies. In lesion research, damage to specific brain regions produces temporary or permanent cognitive changes (Corrigan & Hammond, 2013), yielding more direct and definitive causal relationships between brain regions and cognitive functions with high reproducibility. In contrast, NIBS studies show that identical stimulation protocols applied to different brain regions or tasks produce varying effects on WM performance (Jaušovec & Jaušovec, 2014; Pahor & Jaušovec, 2018). Future research should therefore address several key considerations to enhance validity and reproducibility.

4.1 Comparison of rTMS and tACS

Both rhythmic rTMS and tACS can induce oscillatory activity at the target frequency in stimulated regions, with concurrent EEG providing evidence of entrainment (Witkowski et al., 2016). However, the techniques have distinct advantages. First, navigator-equipped rTMS offers higher spatial precision, as it can integrate individual structural MRI for accurate targeting, whereas conventional non-navigated rTMS and tACS typically rely on EEG 10–20 electrode positions. Research indicates that EEG-based targeting is less effective than MRI-based approaches (Sack et al., 2008). Second, rTMS provides higher temporal precision, often targeting specific task phases (e.g., a 500 ms window during WM maintenance) to investigate neural mechanisms of particular cognitive stages, such as parietal theta regulation of maintenance. In contrast, tACS is typically applied before or throughout the entire task (usually ~20 minutes) to examine relationships between local oscillations and cognitive functions (Helfrich et al., 2014; Witkowski et al., 2016). Third, tACS induces more frequency-specific entrainment, as the sinusoidal current is strictly confined to the preset frequency without activating other bands (Herrmann et al., 2013). rTMS-EEG studies show that rhythmic rTMS pulses can induce target-frequency oscillations but also generate artifacts at other frequencies (Thut et al., 2011), requiring careful discrimination of entrainment effects. Fourth, tACS offers greater flexibility in modulating inter-regional phase synchronization. While rhythmic rTMS can enhance functional connectivity by promoting phase synchronization between the target region and other areas at the same frequency (Albouy et al., 2017), dual-anode tACS can simultaneously deliver synchronized (0°) or desynchronized (180°) stimulation to two regions to strengthen or disrupt functional connectivity (Violante et al., 2017). Moreover, tACS can deliver customized theta-gamma compound rhythms to directly modulate cross-frequency coupling (Alekseichuk et al., 2016). Fifth, tACS produces minimal tactile sensation and noise, making it more suitable for cognitive intervention studies in children and older adults (Antal et al., 2017). Finally, tACS uses electrical current without magnetic fields, enabling concurrent fMRI measurement (Bächinger et al., 2017).

Task Selection

NIBS studies of neural oscillation modulation are typically embedded within specific experimental tasks, making results highly task-dependent. For instance, rhythmic stimulus presentation (visual or auditory) can itself induce neural oscillations at matching frequencies, so task effects on endogenous oscillations must be considered and controlled. Additionally, interactions between NIBS and task demands influence outcomes: rTMS interference effects are more pronounced in high-difficulty tasks but minimal in simple tasks (Barr et al., 2013), with similar findings in tACS studies (Hoy et al., 2015; Violante et al., 2017). Experimental designs must therefore carefully control task difficulty and include appropriate control conditions.

Individual Differences

First, individual peak frequencies of resting-state or task-related EEG oscillations must be considered, as individual alpha frequency (IAF) typically varies between 8–12 Hz. Defining NIBS frequency based on individual IAF may enhance modulation efficacy (Klimesch et al., 2003). Second, baseline activity in target brain regions influences NIBS effects. fMRI studies show that participants with high DLPFC activation exhibit significant behavioral changes after rTMS, whereas those with low activation are unaffected (Sligte et al., 2011). Moreover, activation sites vary across individuals, so targeting based on individual fMRI activation can improve NIBS efficacy (Sack et al., 2008). Third, regarding cognitive ability, NIBS interventions can improve WM performance in low-capacity individuals but not in high-capacity groups (Hsu et al., 2014). Finally, entrainment effects themselves show individual variability; for instance, Hamidi et al. (2009) found no group-level alpha entrainment, but at the individual level, stronger alpha entrainment correlated with poorer WM performance (Hamidi et al., 2009), necessitating careful analysis and interpretation.

Rigorous Stimulation Protocol Design

NIBS efficacy is influenced by target selection methods, intensity, duration, coil shape, and orientation. Four targeting approaches exist, ranked by effectiveness: (1) individual fMRI activation-based, (2) group fMRI activation-based, (3) individual structural MRI-based, and (4) EEG 10–20 system-based (Sack et al., 2008). Researchers should select the optimal method based on available resources. Additionally, when using theta burst stimulation (TBS) over motor cortex, doubling stimulation duration can reverse the expected effects of continuous TBS (cTBS, normally inhibitory) and intermittent TBS (iTBS, normally facilitatory) (Gamboa et al., 2010). TMS coil orientation parallel to the target gyrus also optimizes stimulation effects (Thut et al., 2011). Given individual variability in cortical excitability responses to NIBS, protocols should be individualized, such as by measuring motor thresholds before intervention.

Control Group Design and Concurrent EEG Monitoring

To establish frequency specificity, studies should include control conditions using alternative frequencies or non-rhythmic stimulation. Enhancing NIBS efficacy also requires EEG acquisition before, during, and after intervention. Pre-intervention resting-state/task EEG can extract individual oscillatory characteristics to guide NIBS frequency selection. Concurrent and post-intervention EEG can provide evidence of entrainment and reveal whole-brain network changes, establishing correlations between NIBS-induced oscillatory/network changes and behavioral outcomes to further strengthen causal arguments. Given that brain activity is dynamically changing, optimizing the integration of NIBS with EEG and brain-computer interfaces to enable real-time adjustment of stimulation protocols based on brain state represents an important future direction.

Finally, beyond improving modulation efficiency, current WM research predominantly targets local brain regions, yet interpretations remain ambiguous. For example, when tACS applied to a specific node in a memory network improves WM, it is unclear whether this reflects node-specific activation or current spread to connected regions. As theoretical frameworks increasingly conceptualize memory as a network rather than isolated centers (Watrous et al., 2013; Winocur & Moscovitch, 2011), effective memory modulation should adopt a network perspective to promote interactions among multiple brain nodes rather than simple local stimulation.

Moreover, regarding how rhythmic NIBS interacts with endogenous oscillations to produce entrainment, current understanding relies primarily on simple computational models and indirect neuronal measurements. The critical question of how NIBS affects neuronal activity remains unresolved. Future research should therefore combine single-cell recordings, electrical stimulation, and computational modeling to better understand how entrainment influences neuronal populations.

Note: Figure translations are in progress. See original paper for figures.