Chapter 3004 to be published in *Learning and Memory: A Comprehensive Reference, 3rd Edition*

Memory Modulation through Brain Stimulation

Nathan S. Rose[1], Justine Fragetta[1], & Robert M. G. Reinhart[2]

[1]Department of Psychology, University of Notre Dame

[2]Department of Psychological & Brain Sciences, Boston University

Address Correspondence to:

Nathan S. Rose

390 Corbett Family Hall

Notre Dame, IN 46656

nrose1@nd.edu

Abstract

Advancements in neuroscience, technology, and psychology have led to developments with various brain stimulation techniques for modulating memory. Findings from diverse methodologies are reviewed with a focus on transcranial magnetic or electrical stimulation. These offer numerous non-invasive approaches to target and modulate neurocognitive processes and brain networks that support memory encoding, consolidation, and retrieval. Research has shown enhancements, impairments, and null effects on memory in both healthy individuals and those with memory-related disorders. Methodological considerations are discussed to enhance research rigor and clinical applicability. Elucidating the impact of brain stimulation on memory provides valuable insights into cognition and neurological function, and will help shape future research and clinical practices.

Keywords: TMS, tDCS, tACS, working memory, long-term memory, Direct Cortical Stimulation, Deep Brain Stimulation, Optogenetics, Photobiomodulation, Transcranial Focused Ultrasound Stimulation

Key points/Objectives box:

- Brain stimulation methods help elucidate the neurocognitive processes and brain networks that support various forms of memory, and different stages of memory (encoding, storage, retrieval).
- Invasive methods, typically used on animals (who may share some but not all aspects of human cognition) or neurosurgical patients (with diseased or damaged brains), offer insights about neurocognitive mechanisms regarding the effects of stimulation on memory, but are limited by their generalizability and scalability for widespread adoption in humans.
- Noninvasive methods are relatively safe, cheap, and easy to administer for most people, and extensive research has shown some promising, though variable results for their ability to modulate memory.
- Definitive conclusions about the precise collection of parameters to use to enhance memory in a given individual or population are hindered by the vast parameter space of the numerous variables that can be manipulated.
- More rigorous research and sophisticated modeling is needed to explain and predict intra- and inter-individual variability within and between samples of people, and the variability in findings with protocols which show the gamut of enhancements, impairments, and null effects.
- Recommendations are provided to highlight important considerations that are needed to improve both research rigor, and the reproducibility and generalizability of findings, which are required for the development and adoption of effective translational applications to treat and enhance memory in both healthy individuals and those with memory-related disorders.

Chapter Outline

Introduction

Memory

Brain Stimulation

- **Invasive Brain Stimulation**
  - *Direct Cortical Stimulation*
  - *Deep Brain Stimulation*
  - *Optogenetics*
  - *A comment about invasive brain stimulation methods*
- **Noninvasive Brain Stimulation (NIBS)**
  - *Photobiomodulation*
  - *Transcranial Focused Ultrasound Stimulation*
- **Transcranial Magnetic Stimulation**
  - *TMS Protocols*
  - *Paired pulse TMS (ppTMS*
    - *Short Interval Cortical Inhibition*
    - *Intracortical Facilitation*
    - *Long-interval intracortical inhibition.*
  - *rTMS (repetitive or rhythmic TMS).*
  - *kilohertz Transcranial Magnetic Perturbation.*
  - *Offline Protocols*
  - *Online Protocols*
  - *TMS Summary*
- **Transcranial Electric Stimulation**
  - *Transcranial Direct Current Stimulation*
  - *Transcranial Alternating Current Stimulation*
  - *Transcranial Random Noise Stimulation*

Limitations of NIBS

- *Gaps in Literature*
- *Limited Spatial Resolution and Stimulation Depth*
- *Transient Effects*
- *Nonlinearity of Effects in NIBS*

NIBS Customization

- ***Personalized Stimulation***

Acknowledgments. We thank Joel Voss for helpful comments on the manuscript.

Glossary *(for a box after the first couple of introductory paragraphs)*

Direct cortical stimulation, DCS (direct "acute" electrical stimulation): invasive brain stimulation technique that accomplishes acute/sub-acute periods of electrical stimulation using temporarily implanted electrodes - either subdural grid electrodes which directly stimulate the surface of the cortex or depth electrodes that penetrate the brain and directly stimulate cortical and/or subcortical structures.

Deep brain stimulation, DBS (direct chronic electrical stimulation): invasive brain stimulation technique that accomplishes sustained periods of electrical stimulation using chronically implanted electrode systems with internalized current generators, potentially leading to long-term potentiation and/or neurogenesis.

Optogenetics: a revolutionary technique that cause specific cells (that are infected with viral vectors that change ion channels on cell membranes to become photosensitive) to be instantaneously depolarized (using channelrhodopsin) or hyperpolarized (using halorhodopsin) in response to specific light frequencies.

Photobiomodulation / Transcranial laser stimulation: noninvasive technique that involves the application of low-level laser or light-emitting diode (LED) energy to the scalp with the aim of modulating brain function.

Transcranial magnetic stimulation, TMS: non-invasive brain stimulation technique in which electrical pulses discharged through an insulated coil held to the scalp produce a strong, localized magnetic field that can cause neurons to fire in a focused brain region.

Transcranial static magnetic field stimulation, TSMS*:* noninvasive technique that applies a static magnetic field, using a permanent magnet (i.e. a magnet that does not require a power source) placed on the scalp, to modulate activity in the brain. TSMS does not involve the application of electrical or magnetic pulses, but relies on the direct interaction between the static magnetic field and neural tissue.

Transcranial direct-current stimulation, tDCS: non-invasive brain stimulation technique in which low levels of direct electrical current are passed between two or more electrodes attached directly to the scalp with the goal of modulating cortical excitability in underlying brain areas.

Transcranial alternating-current stimulation, tACS: noninvasive brain stimulation technique in which low levels of alternating electrical current are passed between two or more electrodes attached to the scalp with the goal of modulating cortical oscillations in underlying brain areas.

Transcranial random noise stimulation, tRNS: noninvasive brain stimulation technique in which low levels of alternating electrical current are passed between two or more electrodes at random amplitude and frequency with the goal of modulating cortical excitability.

Temporal interference stimulation: noninvasive brain stimulation technique for electrically stimulating neurons at depth. Multiple electric fields are delivered to the brain at frequencies too high to affect overlying cortical tissue. Deeper neurons can be targeted in the region where interference between the multiple fields create an electric field envelope.

Transcranial focused ultrasound stimulation, TFUS: noninvasive technique that uses focused ultrasound to target deep brain structures with high spatial resolution.

Introduction

Technological advances in brain stimulation methods have led to the ability to causally modulate memory functioning, with some technologies achieving approval for clinical applications/treatments by federal regulatory agencies, and some even reaching the marketplace for purchase and self-administration. Some examples that are described below (e.g., brain-computer interfaces to augment human memory) seem to be the stuff of science fiction, but they are very much a current reality. In this chapter we discuss some particularly "sci-fi" examples involving the real-time decoding of future memory failures and AI-triggered stimulation of memory networks to cause memory enhancements (e.g., Ezzyat et al., 2017; Kim et al., 2016; Suthana et al., 2012; Suthana & Fried, 2014).

What are the currently available technologies, and where might this field go in the future? In this chapter, we review current brain stimulation methods used to modulate memory, with an emphasis on noninvasive methods, particularly transcranial magnetic stimulation (TMS) and transcranial electrical stimulation (tES) protocols, primarily because this is our area of interest and expertise, but also because 1) these methods provide an extensive body of research to review, and 2) they represent some of the most accessible methods available for researchers, clinicians, and consumers to use. We provide reference to examples of relevant experimental literature, illustrate the methodological rigor required to conduct such experiments, and address the variable findings in brain stimulation research on memory.

Before doing so, it is important to note that, in order to effectively design an experiment or randomized clinical trial to study and test the effects of a stimulation protocol on memory, it is essential to consider the various types of memory representations and processes, and their neurocognitive substrates involved in the memory function that is to be modulated, because some, but not all of these representations, processes, and substrates may be modulated by the stimulation protocol. Therefore, we briefly review important concepts about different types of memory and different stages of memory processing to help ground the review regarding the effects of stimulation on memory.

We conclude that, when embarking on a brain stimulation study that attempts to modulate memories, it is important to develop clear, well-motivated research questions that are designed to advance theory and test theoretically motivated hypotheses about potentially effective treatment protocols. These questions and hypotheses should be informed by the extensive history of memory research on both animal models and humans, including lesion, neurophysiological recording, and behavioral/cognitive studies, as well computational models of memory and cognition. In addition to using such an informed approach, the quality of a brain stimulation study depends on a well-

operationalized experiment that rigorously tests the efficacy of stimulation with excellent control conditions. We argue that more basic and applied research is needed to 1) develop predictive models of both the neurocognitive processes that support ecologically valid forms of memory in the real world, and 2) elucidate the mechanisms of action regarding how these neurocognitive processes are manipulated by brain stimulation methods. This research is needed before there is widespread adoption of brain stimulation methods for modulating memory, particularly due to safety and ethical concerns.

Memory

Memory is multifaceted, consisting of declarative (short-term, working, episodic, and semantic memory) and nondeclarative (implicit and procedural) memory. Short term memory (STM) refers to the temporary storage of information, while working memory (WM) involves manipulation of that information. Episodic and semantic memory are forms of long-term memory (LTM), which involve the storage and recall of information over an extended period of time. Episodic memory relates to unique, personal experiences, while semantic memory relates to conceptual facts. Implicit and procedural memory are also forms of LTM, with implicit memory involving automatic, unconscious influences on behavior from prior experiences and procedural memory involving learned sequences of motor actions for performing skilled behaviors. While brain stimulation can be used to modulate various forms of memory, this chapter focuses on episodic and STM/WM, given their importance in higher order cognition, involvement in numerous clinical conditions, and the large body of relevant research.

Memory has multiple stages including encoding, storage (consisting of maintenance and consolidation), and retrieval. Memory encoding involves the initial sensory/perceptual acquisition of the representations and associations that compose a memory. This is followed by memory storage, which can involve active maintenance of encoded information in STM or WM if it is needed for ongoing cognition. Encoded memories--representations and their associations--are then consolidated into a more stable state that may be accessed over the long term via cue-driven retrieval processes. Retrieval involves explicit/declarative or implicit/nondeclarative access to stored information to influence behavior. The extent to which a prior experience can be vividly recollected in conscious awareness seems to depend on the nature of the encoding and maintenance operations that were conducted as well as the extent to which retrieval context encourages the mental reinstatement of the initial experience. When designing a study to modulate memory processes with brain stimulation it is crucial to be as clear as possible about the specific types of memory processes being affected and the timing of

stimulation relative to each stage (encoding, storage, and retrieval) because different forms of memory and different stages of memory involve distinct neurocognitive processes and networks brain regions.

While our understanding of memory representations and processes in the brain continues to be elucidated, researchers have identified several key structures and neurophysiological mechanisms involved in the formation, storage, and retrieval of memories. During the initial encoding of a memory, neurons in sensory cortex process input and transmit the information to other regions of the brain, such as the hippocampal complex in the medial temporal lobes (MTL), and the parietal and prefrontal cortex (PFC). These regions are largely implicated in LTM and WM. The synaptic connections between neurons can change in response to neuronal firing, through a process known as synaptic plasticity, via stimulation arising from either exogenous activity (e.g., caused by external stimulation from the environment) or endogenous activity (e.g., caused by internal stimulation within and between brain networks). Long-term potentiation (LTP) and long-term depression (LTD) are two forms of synaptic plasticity that are particularly important in memory processes. LTP involves the strengthening of synaptic connections after repeated activation, which leads to enhanced synaptic transmission. This process is thought to underlie the encoding and storage of memories in the brain. LTD involves the weakening of synaptic connections and is thought to refine and update existing memories. Memory processes are regulated by distributed neural networks that involve interactions between multiple brain regions, including the PFC, hippocampus, and sensory cortices. These networks exhibit changes in connectivity and activity patterns during memory encoding, storage, and retrieval, which reflect the coordinated processing of information across distributed brain regions.

Brain Stimulation

Brain stimulation refers to a wide variety of techniques used to modulate neural activity through direct/invasive or indirect/noninvasive means. While “brain stimulation” technically encompasses any technique that modulates brain and behavioral functioning [including the presentation of environmental stimuli (sights, sounds, etc.) or psychoactive drugs], the focus of this chapter is on technologies that apply stimuli (e.g., electrical, magnetic) to cause neurons to be more or less active. These techniques provide answers to a multitude of neural and behavioral research questions and have been used to treat a variety of clinical conditions. Brain stimulation has been used to successfully modulate memory in both healthy individuals and those experiencing cognitive changes associated with brain damage or diseases. While the precise effects of brain stimulation on memory are not fully understood, it is believed that

stimulation impacts behavior through modulation of neural dynamics (excitation or inhibition) and the potentiation or depression of synaptic plasticity and network connectivity.

At the cellular level, memory formation primarily relies on synaptic plasticity, the ability of synapses to strengthen or weaken in response to activity (Bailey et al., 2015; Bliss & Collingridge, 1993; Citri & Malenka, 2008). Brain stimulation is thought to modulate synaptic plasticity through mechanisms such as LTP and LTD, which, as already noted, involve changes in the efficacy of synaptic transmission, typically mediated by alterations in the number or function of neurotransmitter receptors at the synapse. It is generally thought that high-frequency stimulation induces LTP and strengthens synaptic connections, while low-frequency stimulation may induce LTD, leading to the weakening of synaptic connections (Staubli & Lynch, 1990). However, it's important to note that this is a simplified description of the relationship between frequency and excitation vs. inhibition and the relationship is nuanced.

Memory processes are also associated with specific patterns of neuronal firing, which are regulated by the integration of excitatory and inhibitory inputs at the cellular level (Izquierdo & Medina, 1997; Squire et al., 2015). Brain stimulation can modulate neuronal firing patterns by influencing the membrane potential and firing threshold of memory relevant neurons. Stimulation that depolarizes neuronal membranes can trigger action potentials, leading to the synchronous firing of neurons within a network (Siebner et al., 2022). This synchronized activity is thought to facilitate the encoding and consolidation of memories by strengthening synaptic connections and promoting the propagation of neural activity through distributed networks (Buzsáki & Draguhn, 2004). Conversely, stimulation that hyperpolarizes neuronal membranes can suppress neuronal firing, leading to the inhibition of synaptic transmission within a network. This inhibition may disrupt the encoding, consolidation or retrieval of memories by reducing the excitability of neurons and interfering with the generation of coherent neural representations. Brain stimulation can also modulate neurotransmitter release at the cellular level, thereby influencing synaptic transmission and neuronal excitability (Stagg & Nitsche, 2011). Direct electrical stimulation can evoke the release of neurotransmitters such as glutamate, GABA, dopamine, and acetylcholine, which play critical roles in regulating synaptic plasticity and neuronal activity and memory processes.

Invasive stimulation methods are invaluable in that they provide critical insight into memory processes by enabling precise modulation of relevant neural structures and circuits, and direct observation of resulting behavior. By applying targeted stimulation to specific brain regions involved in memory, researchers can induce or inhibit neural activity to reveal how stimulation alters neuronal firing patterns, neurotransmitter release, and network dynamics, thereby elucidating the cellular and

molecular underpinnings of memory encoding, consolidation, and retrieval. This approach allows for the identification of causal relationships between neural activity and memory functions, advancing our understanding of the precise neural mechanisms that support memory modulation.

One of the first documented (controlled) uses of brain stimulation to modulate memory in humans occurred in the mid-20th century when Walter Penfield (1938) applied direct electrical stimulation to the right superior temporal gyrus during an awake craniotomy of an epileptic patient.[1] This stimulation was intended to elicit an aura related to a childhood memory, which typically preceded the patient's seizures. Penfield was able to reproduce the patient's perceived aura through stimulation to the parietal cortex, and upon further cortical mapping, found that stimulation to the superior temporal gyrus caused the patient to report living through experiences that were not part of her usual symptoms (Sjöberg, 2023). Penfield described these results as an "experiential phenomenon" that led the patient to be aware of previous experience (Penfield, 1938), similar to the process known today as episodic retrieval (Sjöberg, 2023). While Walter Penfield's pioneering research marked a significant milestone in the exploration of memory modulation with brain stimulation, subsequent scrutiny has raised doubts as to whether the phenomena observed were truly indicative of memory recall (Sjöberg, 2023). For example, the "recovered memories" may have been an epiphenomenal illusion associated with the subjective experience of familiarity - the belief that a memory was recovered rather than stimulation causing true recollection of the experience (Sjöberg, 2023).

Advances in research methodologies afford greater confidence in the ability to isolate and study memory processes than previous (e.g., correlational) methods, but it is essential to acknowledge that uncertainty and variability still exist in brain stimulation research (Guerra et al., 2020). To address these challenges and encourage robust, reproducible findings, researchers should adhere to best practices in brain stimulation research. This includes rigorous experimental design with appropriate control conditions, adherence to established safety guidelines, knowledge of existing research and potential pitfalls, replication of findings across independent studies, and transparent reporting of methods and results. Additionally, interdisciplinary collaborations between neuroscientists, psychologists, and clinicians can enhance the interpretation and applications of memory-targeted brain stimulation. The goal of this chapter is to help introduce readers to various methods (their strengths and limitations) and

[1] For an interesting example of an early, relatively uncontrolled use of electrical stimulation that modulated memory, see the story of Benjamin Franklin's report of retrograde amnesia following electrical shock described in Finger & Zaromb (2006).

important conceptual and methodological considerations to take into account in order to address the challenges of brain stimulation approaches.

Invasive Brain Stimulation

Direct Cortical Stimulation

Direct cortical stimulation (DCS) is a neurosurgical procedure that involves delivering electrical impulses to the surface of the cortex, typically with two electrode tips or arrays containing strips or grids of electrodes (Jahangiri et al., 2020). DCS is commonly used to map brain functions (e.g., speech production, motor movements) and identify regions to avoid during surgery, but has also revealed interesting insights into memory functioning.

Alagapan et al. (2019) used multi-site DCS to simultaneously target multiple frontal and parietal brain regions known to be associated with WM processes. Researchers found that stimulation influenced neural dynamics and memory in a phase-dependent manner. “Anti-phase” stimulation, seeking to induce oscillations in two brain regions out of phase with each other, increased the difference in phases between EEG oscillations in different WM-related brain regions, while in-phase stimulation, seeking to induce synchronous oscillations in these regions, reduced phase lag and improved accuracy on a Sternberg WM task. DCS can also be applied in a closed-loop manner, where stimulation is adjusted in response to real-time measurements of neural activity. Ezzyat et al. (2018) used DCS to examine the role of the lateral temporal cortex (LTC) in memory encoding. Invasive neural recordings were made while neurosurgical patients studied and recalled lists of words. Machine learning algorithms could decode and classify patterns of brain activity associated with words that were subsequently remembered vs. forgotten. The classifiers were then used to trigger stimulation of the LTC when memory was predicted to fail in real time. Researchers found that this “closed-loop” stimulation to the LTC caused improved word recall. While this study provides an exciting example of the potential for DCS to enhance memory, the literature is complicated and variable. Full review of direct electrical stimulation on memory functioning is beyond the scope of this chapter. For further details, see Kucewicz et al. (2023).

Deep Brain Stimulation

Deep brain stimulation (DBS) involves the surgical implantation of electrodes in targeted brain regions and a neurostimulator (“pacemaker”) to deliver stimulation with the goal of regulating abnormal neural activity. The procedure was developed to treat various movement disorders and gained FDA

approval in 2002 (Gardner, 2013). The DBS neurostimulator is a battery-operated device that is typically implanted under the skin near the chest. The location of the electrode placement is determined by the condition being treated. While the mechanisms are not fully understood, DBS involves the generation of electric fields to stimulate neural elements (mainly axons) near the stimulation site (Vissani, Isaias & Mazzoni, 2020). The majority of current DBS systems use open-loop devices, where parameters are configured to provide constant stimulation regardless of fluctuations in ongoing neural activity (Vissani et al., 2020).

A promising new application for DBS is the ability to study and improve cognitive function, namely memory. By targeting subcortical brain regions involved in memory processes, DBS can alter neural activity, leading to enhanced or impaired memory function. For example, Zhang, Hu, Wu, Zhang,& Zhang (2015) studied the effects of DBS on memory in a rodent model of Alzheimer's disease (AD) and found that stimulation to the anterior nucleus of the thalamus resulted in improved memory relative to a control group. Geva-Sagiv et al. (2023) implemented a closed-loop real-time DBS protocol to alter memory consolidation during sleep in humans. They found that synchronizing stimulation to the active phases of endogenous slow waves in the medial temporal lobe (MTL) enhanced sleep spindles, increased brain-wide neural spiking activity to MTL slow waves, and improved coupling between MTL ripples and thalamocortical oscillations. This synchronized stimulation led to enhanced recognition memory, as evidenced by increased accuracy in a paired-associates task. Importantly, changes in memory accuracy were highly correlated with electrophysiological effects at the individual level. For a more comprehensive review on the use of DBS for memory modulation refer to Khan et al. (2019) and Mankin & Fried (2020).

Optogenetics

Optogenetic stimulation is an invasive neuromodulatory technique that uses light to control the activity of individual neurons. It involves genetically modifying neurons to express light-sensitive proteins called opsins, which are activated or inhibited in response to the presentation of specific wavelengths of light (Bansal, Shikha, & Zhang, 2023). The exquisite spatial and temporal precision of this technique is elucidating previously unrecognized molecular and cellular properties of specific neuronal subtypes associated with memory. For example, de Sousa et al. (2019) used optogenetic reactivation to examine the neural circuits involved in memory changes over prolonged periods, known as systems consolidation (Nadel et al., 2007; Squire et al., 2015; see also Yonelinas et al., 2019). Researchers selectively reactivated neural circuits associated with a contextual fear memory in the retrosplenial

cortex of mice and found that high frequency stimulation of these neural ensembles one day after learning produced a recent memory with features normally observed in consolidated memories. These results suggest that post-learning memory ensemble reactivation is a mechanism of systems consolidation, and that this process can be accelerated when stimulation occurs in an unconscious (asleep or anesthetized) state. For a review on the use of optogenetics in fear acquisition and consolidation, see section 4 of Borgomaneri et al., (2021).

Because gamma oscillations in the hippocampus have been linked to spatial memory and are altered in memory disorders such as AD, Etter et al. (2019) studied the effects of optogenetic gamma stimulation to the hippocampus in a mouse model of AD. They found that causing an increase in gamma oscillations during retrieval led to improved spatial memory, in spite of the presence of significant AD-related pathology. Similarly, Etter et al. (2023) used optogenetic frequency scrambling to dissociate the role of theta rhythms in spatiotemporal coding and working memory by disrupting these rhythms in the hippocampus. They found that frequency scrambling led to decreased episodic and WM retrieval, but did not affect spatiotemporal codes in the hippocampus (e.g., place cells), suggesting that theta oscillations play an essential role in memory, but not the coding of spatiotemporal representations per se.

While the potential for optogenetics to affect the encoding, consolidation, and retrieval (or reconsolidation or extinction, Borgomaneri et al., 2021) of specific memories might evoke thoughts of science fiction and ethically dubious scenarios, the first human trials involving optogenetics do not involve implanted optrodes; so far, optogenetic stimulation in humans has been used to modulate peripheral nerves to treat retinitis pigmentosa. Nonetheless, there is a current need for bioethicists to inform and guide policy for future applications. For a discussion of the memory-modifying potential of optogenetics, see Zawadzki and Adamczyk (2021; as well as associated commentary, e.g., Gilbert et al. 2021).

A comment about invasive brain stimulation methods

Investigating the effects of stimulation on animal models and neurosurgical patients can provide information about the neural mechanisms of memory with a degree of spatial and temporal precision that is difficult or impossible to attain with noninvasive methods. While these techniques are necessary for establishing proof-of-principle applications and underlying neural mechanisms, results may not generalize to neurotypical human brains. In order for brain stimulation methods to be accessible, scalable, and equitable for large numbers of people, noninvasive methods are necessary.

Noninvasive Brain Stimulation (NIBS)

Currently, the two most popular noninvasive brain stimulation (NIBS) techniques are transcranial magnetic stimulation (TMS) and transcranial electric stimulation (tES). Additionally, transcranial focused ultrasound stimulation (tFUS) and transcranial photobiomodulation are two relatively new and promising techniques for modulating metabolic processes in the brain that support memory functioning. Each of these techniques can be used to modulate neuronal activity with varying degrees of spatial specificity, and can have an inhibitory or facilitatory effect on more widespread brain and behavioral functioning. TMS uses rapidly changing electromagnetic fields to stimulate the underlying cortical surface, while tES involves the application of a weak electrical current. These differ from photobiomodulation and tFUS, which use light illumination and ultrasound waves to modulate neural activity, respectively.

The cognitive effects produced by TMS and TES depend on the propagation of the induced electromagnetic field, which is influenced by both external methodological factors (e.g. technical parameters used during stimulation) and internal factors such as individual cortical geometry and attentional and physiological states (Polania et al., 2018; Romei et al., 2016). The electric field alters neuronal excitability by modulating the activity of ion channels and altering the transmembrane potential. While NIBS can be used to temporarily and reversibly modulate memory performance, long-lasting effects are also observed following stimulation. Just as with endogenous brain activity following sensory and cognitive “stimulation”, and exogenous stimulation caused by invasive methods, LTP and LTD are, at the synaptic level, the physiological mechanisms responsible for the changes observed following NIBS (Polania, 2018). As introduced above in the opening section on memory, the terms LTP and LTD refer to the collection of cellular mechanisms through which synaptic connections are modified in response to activity patterns. These forms of synaptic plasticity represent the core mechanisms involved in learning and memory processes. The principles of LTP and LTD were initially revealed by invasive stimulation methods; it is now apparent that NIBS techniques can also induce changes in neuronal excitability and synaptic strength, which can lead to LTP- or LTD-like alterations in both synaptic plasticity processes and associated changes in memory. The induction of LTP or LTD depends on the electric field delivered by NIBS. This depends on multiple factors, including coil placement or electrode configuration and stimulation intensity, as well as individual differences in skull conductivity and cortical anatomy. Estimating the spatial distribution and intensity of the electric field is an essential step in developing a NIBS experiment.

Photobiomodulation

Photobiomodulation (PBM), also known as low level laser therapy is a form of NIBS that uses lasers (or LED lights) to stimulate cellular processes. PBM has been primarily used for tissue repair and pain relief and has recently gained attention for its applications in memory research. The metabolic effects following PBM can increase cerebral metabolic energy production, oxygen consumption, and blood flow in animals and humans (Zhao, 2022). It has also been suggested that PBM can increase ATP production, enhance neuroprotection and neurogenesis, modulate neurotransmitters, and provide anti-inflammatory effects (Zhao, 2022).

Alzheimer's disease (AD) is characterized by the accumulation of amyloid-beta (Aβ) plaques and neurofibrillary tangles (NFTs) in the brain, which is associated with cognitive deficits. Tao et al. (2021) administered PBM to an AD mouse model and found that 1070-nm light reduced the cerebral Aβ burden and mitigated recognition memory impairment. Chan et al. (2021) investigated the effects of PBM on memory in a sample of older adults with mild cognitive impairment (MCI). Individuals who received active PBM showed significant improvements on a visual memory task, which were accompanied by reduced hemodynamic responses (measured by functional near-infrared spectroscopy) in prefrontal cortex, as compared to a sham stimulation group. Based on these results, the authors suggested that PBM may lessen cognitive effort in tasks requiring high memory loads, potentially improving cognitive performance in individuals with MCI. In a sample of healthy older adults, Qu et al. (2022) studied the effects of repeated PBM on WM as compared to single sessions. They found that both repeated (7 days) and single PBM sessions significantly enhanced accuracy rates and reduced response times on a WM task, with repeated sessions showing greater improvements. These benefits persisted for at least three weeks post-intervention, suggesting potential as an intervention for memory decline in older individuals.

Transcranial Focused Ultrasound Stimulation

Transcranial focused ultrasound stimulation (tFUS) is a NIBS technique that uses focused ultrasound waves to modulate neural activity in specific brain regions. These waves can stimulate or inhibit neural activity, depending on factors such as ultrasound intensity, frequency, and duration. tFUS has gained attention in memory research due to its ability to penetrate the skull and reach deep cortical structures with high spatial precision.

Nicodemus et al. (2019) examined the effects of tFUS administered during sleep on cognitive and motor performance in a sample of participants with AD or Parkinson's disease (PD). They found that

stimulation to the hippocampus in AD and stimulation to the substantia nigra in PD led to improved motor function as well as improved memory in many patients, as evidenced by increased scores on the Repeatable Battery for Assessment of Neuropsychological Status and the Montreal Cognitive Assessment. While this preliminary study was encouraging, the research should be replicated and extended with larger sample sizes. Jeong et al. (2021) explored the effects of low-intensity hippocampal tFUS on the blood-brain barrier opening, regional cerebral metabolic rate of glucose (rCMRglu), and cognition in AD patients. Results showed no evidence of blood-brain barrier opening, but rCMRglu increased in the superior frontal gyrus, middle cingulate gyrus, and fusiform gyrus, and patients demonstrated mild cognitive improvement. These findings suggest potential therapeutic benefits of tFUS in AD.

Transcranial Magnetic Stimulation

TMS is a form of NIBS with relatively high spatial and temporal precision. Stimulation of cortical neurons is produced when a strong electric current is passed through a coil of insulated wiring, e.g., in a figure-of-eight shaped coil. The strong electrical current that is discharged generates a brief, high-intensity electromagnetic field maximally focused in the center of the coil. Basic principles of TMS have been covered in many excellent reviews (Pascual-Leone et al., 2000; Ziemann et al., 2008; Siebner et al., 2022). The focal magnetic pulse instantaneously passes through the scalp, skull, and meninges, and induces an electric field with positive and negative current flow. The electric field depolarizes neurons within 2-3 cm into the cortex (for a figure-of-eight coil; Deng et al., 2014; Hallett 2007; for details about "deep" TMS and an application to treat AD, see Bersani et al., 2013).

It is important to understand that only some neurons in the targeted area may be activated, the population of neurons consist of both excitatory and inhibitory cells, the activated neurons may or may not be task-relevant to ongoing cognitive processing, and not only will the neurons that are directly stimulated by TMS be activated, but so too may be neurons in distal brain regions that are structurally and functionally coupled with the stimulated neurons (Polania et al., 2018). Thus, elucidating the precise mechanisms of action of TMS on high-level cognition such as memory is complex. For a relatively recent consensus paper on what is stimulated by TMS, see Siebner et al. (2022).

That the modulation of cortical excitability also occurs in distal brain regions whose activity happens to be functionally connected with the targeted region of cortex at the time of stimulation provides a powerful noninvasive tool to modulate activity in deeper cortical and subcortical memory-related regions such as the hippocampal complex (Arulchelvan & Vanneste, 2023; Davis et al., 2017;

Wang et al., 2014). Critically, because it does not directly apply electrical current to the participant's head, TMS is typically well-tolerated and is safe for most people while they are awake and performing memory tasks. Safety guidelines concerning frequency and intensity limits, as well as restrictions on the series of pulses (train length), should be followed to minimize potential risks (for more information, see Rossi et al. (2021)). compared to other forms of NIBS, e.g., tES), TMS has relatively high temporal precision because pulses can be delivered and activate underlying cortex very rapidly (within microseconds). Indeed the timing and frequency with which pulses are applied, the time intervals between trains of pulses, as well as the shape and direction of the electromagnetic field are factors that strongly affect the causal modulation of brain activity in addition to the level of intensity and other factors (for review, see Valero-Cabré et al., 2017).

Full review of the mechanism of activation of TMS is beyond the scope of this chapter. However, it is important for researchers and clinicians to understand the complex and technical details of the mechanisms by which TMS can modulate brain activity in order to appreciate what can and cannot be inferred about its effects on memory processes and representations. For comprehensive reviews of the technical aspects of magnetic stimulators, and associated methodological concerns (Groppa et al., 2012), see Kammer et al. (2001) and Sauve and Crowther (2014).

As we discuss in more detail below, the selection of sham/control stimulation conditions in particular is very important for making strong causal inferences about the effects of active stimulation conditions. Criticism about the rigor and reproducibility of NIBS research may be largely due to suboptimal selection of sham/control conditions and other potential confounds. The literature selected for review consist primarily of studies with adequate control conditions. As recommended by Duecker and Sack (2015). for sham/control conditions, we advocate for the use of active stimulation applied either to brain regions that are not hypothesized to be involved in the memory process of interest when that process is hypothesized to be engaged by the participant at the particular timepoint in the task (e.g., encoding, maintenance, retrieval), or to the same brain region as the active stimulation condition, but at a different timepoint than when the targeted process is hypothesized to be engaged.

TMS Protocols

Single pulse TMS. Single pulse TMS with simultaneous neuroimaging provides a ping and record technique analogous to SONAR. See Figures 1 for an image of the experimental setup with NRI-guided TMS with simultaneous EEG, and Figure 2 for a graphical depiction of the analogy between SONAR and

pinging the brain with single pulses of TMS and recording the induced signals on simultaneous neuroimaging.

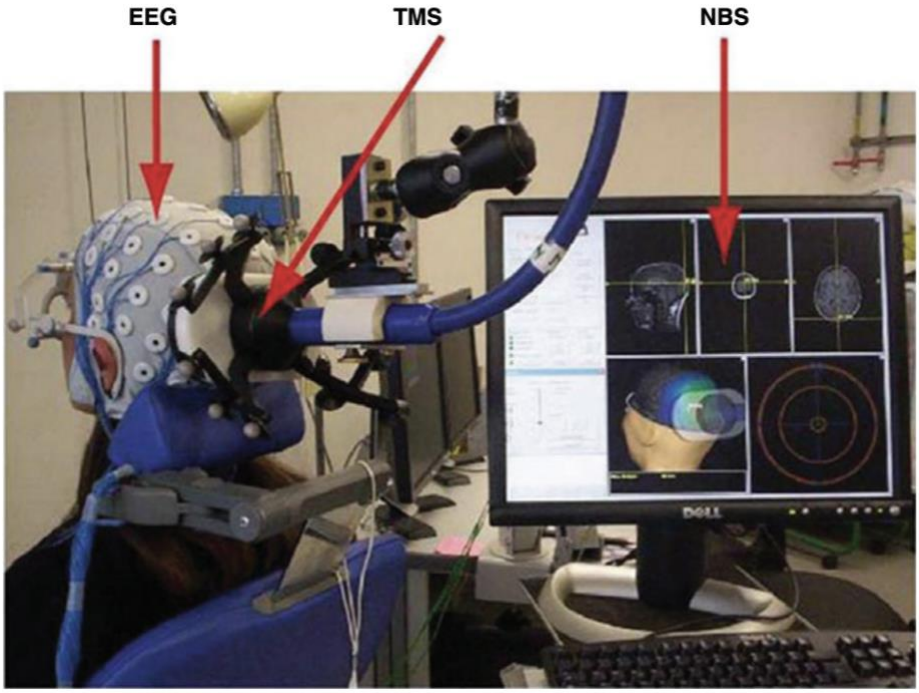

Figure 1. Example of simultaneous electroencephalography (EEG) and transcranial magnetic stimulation (TMS) setup with navigated brain stimulation (NBS). Reprinted with permission from Rosanova et al. (2012). Copyright 2012 Springer Nature

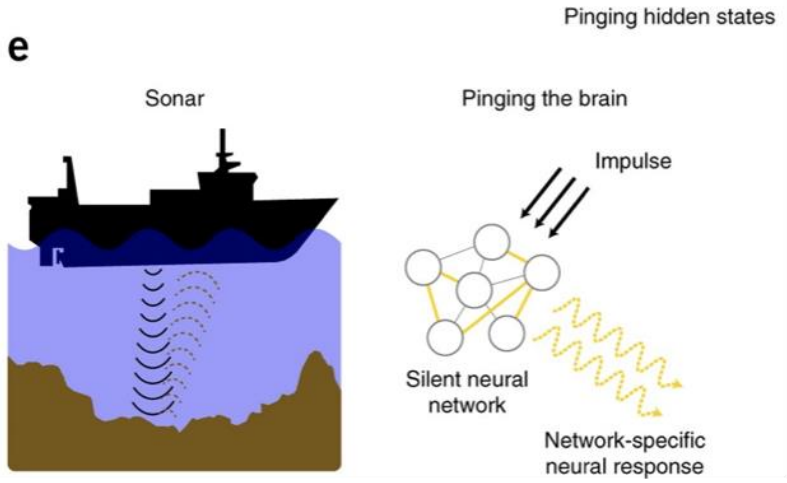

Figure 2. Graphical depiction of the analogy between SONAR and the use of noninvasive brain stimulation (e.g., from sensory or TMS pulses) with neuroimaging to ping the brain and record neuronal network responses to detect hidden or latent ("activity-silent") states of memory representations. Adapted with permission from Wolff et al. (2017). Copyright 2017 Springer Nature.

This was the approach used by Rose et al. (2016) to test the synaptic theory of WM. Briefly, if a memory is encoded and temporarily retained in WM via a distributed pattern of synaptic weights in a latent state that is "activity silent", then applying a nonspecific impulse to the network (such as a single pulse of TMS) should ping the network and the evoked neural activity recorded with simultaneous neuroimaging should reveal this latent representation. Multivariate pattern analysis (MVPA) of EEG data recorded while participants were performing a WM task provided evidence to support this idea. Applying spTMS to representation-related regions of parietal cortex during the WM retention period resulted in a 'reactivation' of the passively-retained, latent memory, as reflected by MVPA decoding evidence from TMS-evoked signals on EEG for the targeted stimulus category relative to the absent/control category on that trial. Replications and extensions of this experiment showed that this reactivation effect only occurred for items that were potentially relevant on that trial, and reactivating their representations resulted in elevated false alarms to recognition memory lure probes that matched the reactivated item. After a cue indicated that a passively retained item was no longer relevant on the trial, meaning the participant could drop the item from maintenance in WM, TMS no longer reactivated the neural representation and was no longer associated with elevated false alarm rates (Rose et al., 2016; see also Fulvio & Postle, 2020). Analyzing the TMS-evoked response on EEG revealed a unique role of beta-oscillations on the reactivation effect and the prioritization of memories held in WM (Rose et al., 2016; Fulvio, Haegens & Postle, 2024).

Paired pulse TMS (ppTMS). ppTMS protocols provide unique assessments given their ability to activate and measure relatively specific neural mechanisms at the synaptic level. Therefore, the insights that may be revealed by this form of stimulation are unique. This section provides examples of commonly used ppTMS protocols and how they have been reported to modulate memory.

Short Interval Cortical Inhibition (SICI) is a ppTMS protocol used to measure inhibitory neurophysiological dynamics. When ppTMS is applied to the motor cortex, with the first pulse as a conditioning stimulus, followed by a short (~3-5 millisecond) interval before a second, suprathreshold pulse, it leads to a suppression or reduction in the amplitude of motor evoked potentials (MEPs) (Duque et al. 2012). This suppression is believed to reflect the inhibitory interactions between GABA-A mediated interneurons in the stimulated layers of cortex. ppTMS with a 3 millisecond ISS to DLPFC of healthy young adults during episodic memory encoding has been found to interfere with subsequent recognition memory discrimination rates (Gagnon et al., 2010). A meta-analysis by Mimura et al. (2021) found that SICI is reduced in AD. Benussi et al. (2018) conducted a multicenter study using machine learning to diagnosis different dementias [AD, dementia with Lewy bodies (DLB), and frontotemporal dementia

(FTD)] from TMS-EEG measures including SICI and found high accuracy (89-92% sensitivity), especially when combined with other biomarkers. Thus, SICI appears to noninvasively measure GABA-A mediated inhibitory circuit dynamics that are implicated in memory disorders.

Intracortical Facilitation (ICF) is an additional neurophysiological measure that addresses cortical excitability. When measuring ICF, two TMS pulses are delivered to the motor cortex, but the interstimulus interval (ISI) between the conditioning and test pulses is longer than in SICI, typically ranging from 7 to 30 milliseconds. Additionally, in contrast to SICI, ICF enhances the amplitude of the MEPs elicited by the test pulse. ppTMS with a 15 millisecond ISI to DLPFC of healthy young adults during episodic memory encoding has been found to speed up hits on a subsequent recognition test (Gagnon et al., 2011). However there is insufficient research reporting evidence of ICF effects on memory to provide a strong conclusion at this time.

Long-interval intracortical inhibition (LICI)*, s*imilar to SICI and ICF, is a neurophysiological measure involving two TMS pulses. However, the ISI between test pulses is longer in LICI, usually from 50 to 200 milliseconds. The conditioning pulse is believed to activate GABA-B receptor-mediated mechanisms of inhibitory interneurons, and has been found to affect WM performance in middle-aged adults (Redondo-Camós et al., 2022). Rogasch and colleagues utilized a ppTMS LICI paradigm to assess the role of $GABA_B$-mediated cortical inhibition in the dorsolateral prefrontal cortex, and found that greater pre-synaptic inhibition in DLPFC is negatively related to individual differences in WM ability (Rogasch et al., 2015). Thus, ppTMS uniquely allowed for investigation of inhibitory states in the brain, and the role that intracortical inhibition has on WM.

rTMS (repetitive or rhythmic TMS). rTMS involves the application of repeated pulses over a period of time. Additionally, while the effects of TMS are temporary, the effects of rTMS are longer lasting and may induce neuroplastic changes in the brain. Frequency refers to the number of pulses delivered per second and is a key factor in entrainment, or the synchronization of endogenous brain oscillations to the frequency of an exogenous, rhythmic series of pulses (Thut et al., 2011). The frequency is motivated by the research question and targeted brain region. (For a comprehensive review on the use of entrainment for modulating human memory, see Hanslmayr, Axmacher, & Inman, 2019). rTMS can be delivered in a continuous or intermittent manner and, depending on the stimulation parameters, rTMS can either inhibit or enhance neural excitability, thereby enhancing or disrupting function. Although, it should be noted that this simplistic dichotomy of excitation/enhancement vs. inhibition/disruption is largely based on measuring effects of rTMS on motor cortex and motor function, and the effects of rTMS on regions more strongly associated with memory and various assessments of

memory appears to be more complex and nuanced. For a review on the effects of rTMS on memory modulation, refer to Phipps et al., 2021; Yeh & Rose, 2019.

Theta burst stimulation (TBS) is a form of rTMS that delivers bursts of high (gamma) frequency stimulation repeated at the theta frequency (5 Hz) to entrain neural oscillations in the targeted brain region and functionally connected networks. Typically, continuous theta burst (cTBS) produces inhibitory effects on cortical excitability, while intermittent TBS has facilitatory effects. Several studies have shown significant modulation of memory caused by TBS (see below), including some aimed at modulating the severity or persistence of emotional memories, which has translational implications for PTSD. Bovy et al. (2020) used cTBS and Yeh et al. (2021) used iTBS to assess the role of medial PFC in the encoding and subsequent consolidation of emotional (negative) memories. The preferential consolidation of negative memories was disrupted by cTBS and enhanced by iTBS. For systematic reviews and meta-analyses, see Lowe et a., (2018), Pabst et al. (2022), and Yeh & Rose, 2019).

kilohertz Transcranial Magnetic Perturbation. kilohertz Transcranial Magnetic Perturbation (kTMP) is a recently developed magnetic induction method that utilizes oscillating magnetic fields at very high (kilohertz) frequencies to modulate neural excitability (Labruna et al. 2024). While the effects of kTMP has only been investigated on motor cortex excitability, its ability to induce electro-magnetic fields in the cortex at sufficiently high intensities to modulate cortical excitability with dramatically reduced artifacts associated with muscle twitching and participant discomfort relative to TMS and TES (Labruna et al. 2024), suggests potential for this new NIBS method to noninvasively modulate memory. kTMP may have several methodological advantages over TMS and TES including the induction of stronger electrical field amplitudes with personalized (participant-specific) waveforms aligned to memory-relevant oscillation frequencies without uncomfortable scalp stimulation and associated artifacts on simultaneous neuroimaging (Labruna et al., 2024).

Offline Protocols

In an offline protocol, TMS is applied and then brain activity and/or behavior is measured subsequently to assess persisting effects of stimulation. This type of protocol has been used to investigate the role of the prefrontal cortex, specifically the right inferior frontal gyrus, in biasing selective attention and visual WM processes through top-down modulation of neural activity in posterior, visual cortex (Zanto et al., 2011). In this experiment, rTMS was used to perturb PFC function before participants performed a delayed-recognition task that required top-down attentional selection of to-be-remembered and to-be-ignored stimuli. The rTMS perturbation of PFC resulted in a diminished

difference between to-be-remembered and to-be-ignored stimuli in the perceptual processing during encoding and associated activity in posterior cortex. That rTMS was associated with a decrease in WM accuracy, with greater decreases for participants with stronger functional connectivity between the frontal and posterior regions is consistent with the idea that the PFC provides top-down modulation of posterior areas. These findings provide causal evidence in the healthy human brain for the role of the right IFJ in the top-down modulation of posterior brain activity and perceptual/encoding processes in the service of selective attention. For other examples of the offline "virtual lesion" approach to assess WM network interactions, see Feredoes et al. (2006, 2007), and Feredoes (2022) for review.

Offline TMS-fMRI studies have also provided opportunities to address research questions where purely correlational data are unable to disentangle the specific contributions of cortical regions, especially concerning their functional coupling with, and potential control over, other cortical regions (see Riddle et al., 2022 for a guide). For example, the frontal operculum had been repeatedly shown to be active during complex tasks requiring cognitive control, yet its mechanism of action had remained elusive until researchers used causal stimulation with simultaneous neuroimaging, namely TMS-fMRI. Higo et al. (2011) first showed that the frontal operculum regulated increases and decreases in activity of multiple occipitotemporal cortical areas during a selective (vs. a non-selective) attention task in which task performance depended on directing attention to different classes of stimuli held in memory. The causal dependency of these activity changes was then demonstrated: TMS-mediated interference of the frontal operculum specifically diminished top-down modulation of the occipitotemporal regions during the selective attention task, while having no effect on the non-selective bottom-up, stimulus-driven task in which a single stimulus was presented in isolation (Higo et al., 2011).

Another noteworthy study that utilized rTMS in conjunction with fMRI was conducted to investigate the causal roles of hypothesized oscillations from distinct brain region in supporting specific WM processes by assessing the effects of different frequencies of rTMS. Riddle et al. (2020) initially used fMRI to localized frontal and parietal regions of healthy young adults associated with the attentional prioritization of to-be-remembered items (e.g., an array of colored squares) that were cued as to-be-remembered target items after their presentation. In subsequent sessions, they applied theta burst or alpha rTMS to the left middle frontal gyrus or parietal cortex. Matching the frequency of TMS with the presumed brain oscillations in the targeted regions led to distinct effects on behavior (working memory capacity). The assumption was that theta burst stimulation increased frontal theta activity thought to be related to memory target prioritization and alpha stimulation decreased parietal alpha oscillations thought to be related to memory distractor suppression (for an update with concurrent TTMS-EEG, see

Riddle et al., 2024). This provides compelling evidence for the distinct roles of different oscillations from frontal and parietal cortex in different neurocognitive mechanisms that support memory functioning; however, even stronger inferences may be derived from direct observation of effects on simultaneously acquired neuroimaging data in online TMS studies.

Online Protocols

Numerous studies have demonstrated the efficacy of repetitive transcranial magnetic stimulation (rTMS) in enhancing memory function. A seminal study by Wang et al. (2014) reported that rTMS targeting the hippocampal network led to improved episodic memory performance. Because the hippocampus cannot be directly stimulated by TMS, the researchers first identified the cortical target (e.g., in each participant's angular gyrus) that could be stimulated with TMS which showed strong functional connectivity with the participant's hippocampal 'seed'. Beneficial effects of hippocampal-network targeted rTMS on episodic memory have been corroborated and expanded upon in subsequent research. Findings have revealed sustained memory benefits lasting from hours to weeks post-stimulation, along with increased connectivity within the hippocampal network and enhanced memory-related activity measured via fMRI (Freedberg et al. 2022; Hermiller et al. 2019; Warren et al. 2019). Online TMS-fMRI studies have reported that the underlying mechanism appears to involve the facilitation of hippocampal network activation during encoding (Hermiller et al., 2020; Hermiller & Voss, 2023) and the enhancement of associative binding of items to their context (Tambini et al., 2018).

For example, Hermiller et al. (2020) found that TBS that targeted the left hippocampal network using the procedure described above with simultaneously recorded fMRI immediately increased fMRI activity in the left hippocampus during the encoding of scenes, and also increased subsequent recollection of the scenes, but had no effect on a non-memory, numerical control task. Also, neither non-hippocampal network stimulation nor beta frequency stimulation affected hippocampal activity or recollection. Thus, 'closing the loop' by stimulating brain networks at frequencies hypothesized to be relevant for specific cognitive processes while simultaneously measuring the causal modulation of neural signals that reflect the hypothesized cognitive processes that underlie memory provide strong inferential support for theory advancement. For a systematic review and meta-analyses on the effects of TMS on episodic memory, see Yeh and Rose (2019). For reviews on the use of TMS for WM research, see Johnson, Feredoes, & Postle (2021) and Widhalm & Rose (2019).

Online TMS-EEG protocols are beneficial for exploring the neural mechanisms underlying memory representations and processes through the analysis of the TMS-evoked response (TMS-ER).

Analyzing TMS-ER through source localization of simultaneously recorded EEG enables the assessment of cortical excitability in stimulated brain regions and effective connectivity between them. Effective connectivity reflects the causal modulation of regions that are distant from the site of stimulation. The spread of TMS-induced activity can cause distant regions to be more or less active through its effects on the network of regions that are structurally and functionally coupled with the TMS-targeted site when it is stimulated (Rosanova et al., 2012). Additionally, phase locking analyses measure the extent to which TMS resets the phase of ongoing cortical oscillations (Casali et al., 2010). These analyses provide insights akin to traditional functional connectivity analyses but also reveal the causal nature and directionality of neural communication between distant sites. Relatedly, double- or multi-coil stimulation methods, that stimulate multiple regions and manipulate variables such as the order and timing of stimulation, offer further direct evidence of neuronal transmission timing and directionality within functionally coupled circuits (Wilhelm et al., 2016).

It is also important to note that the TMS-ER is influenced by the ongoing neural activity in the targeted brain region during stimulation, which makes it sensitive to endogenous factors such as the overall brain state related to the task situation and the participant's level of arousal (Johnson et al., 2012; Kundu et al., 2014). For example, engaging in a working memory task, as opposed to passive fixation, enhances the strength of electrical currents induced by TMS, expands the spatial extent of TMS-evoked activity in distant brain regions, and improves TMS's ability to reset ongoing cortical oscillations (Johnson et al., 2012). However, task performance has minimal impact on the dominant frequency of the TMS-ER, both locally and in distant brain areas (Johnson et al., 2012). Consequently, this method offers a robust means of assessing changes in cortical excitability and connectivity driven by individual and task-related variations in participants' cognitive states (Kundu et al., 2014).

Studies combining TMS with fMRI offer a unique approach to investigate causal connections among different brain regions involved in memory processes, particularly regarding connectivity between cortical and deeper cortical/sub-cortical areas (such as the hippocampus and thalamus) and between frontal and parietal cortical regions. Additionally, fMRI provides higher spatial resolution compared to EEG, making it valuable for studies focused on function, representation, or process localization. To distinguish between two hypothesized influences of the dorsolateral prefrontal cortex (DLPFC) on posterior areas during working memory maintenance—namely, maintaining memory targets or suppressing distractors—event-related TMS was utilized as a "physiological probe" to modulate the blood oxygen level-dependent (BOLD) response without affecting task performance (Feredoes et al., 2011). Results supported the 'target protection' hypothesis, revealing increased activity in category-

specific visual regions representing memory targets only in the presence of distractors following DLPFC stimulation (Feredoes et al., 2011). This elucidation of the DLPFC's role in target protection amidst distractors was facilitated by the combination of TMS-fMRI methods, enabling visualization of cortical activity alongside causal intervention. For further insights into the dynamic role of the prefrontal cortex in controlling posterior, representational regions, refer to exemplary studies by Zanto et al. (2013) and Lee & D'Esposito (2012).

TMS Summary

TMS with simultaneous neuroimaging are technologies with much promise for causally manipulating memory representations and/or processes in a non-invasive manner in the human brain. TMS must be understood as distinct from other forms of non-invasive brain stimulation for its utility to be appropriately evaluated. Its unique benefit arises from causing neurons to fire in specific areas of the cortex in awake, healthy humans, as well as it's potential for effectively treating memory related disorders (Weiler et al., 2020). It allows for high temporal precision, and the combination of TMS with various neuroimaging techniques can be used to uncover the neural activity that is time-locked to behavioral outcomes. The current review highlights several promising approaches (see also the excellent reviews by Feredoes, 2022, and Phipps et al., 2021), but also reveals a strong need for the extension and refinement of existing protocols for elucidating and enhancing the neural bases of memory encoding, maintenance, and retrieval.

As described in the sections below on both the limitations and nonlinearity of current research using NIBS to modulation memory, and some recommendations for memory experiments with NIBS, including a call for personal customization, researchers should strive towards the use of fMRI-guided neuro-navigation and personalized TMS protocols, as well as an informed choice of good active or sham/placebo control conditions. Such efforts should help to improve the establishment of replicable and meaningful manipulation of memory functioning. For example, systematic exploration of the parameters of TMS studies are needed to directly compare the effects of TMS on specific memory processes and representations when applied at different stimulation frequencies and intensities to different sites throughout the network of subregions (e.g., in frontal, parietal, temporal and sensory cortices) known to be associated with various aspects of task performance. Such an approach would propel the field forward in understanding of the variability in the effects of TMS for a given individual; however, the combinatorial permutation of manipulations needed to investigate such questions to fully

map the massive 'parameter space' makes this approach unfeasible for any single research laboratory to pursue.

Transcranial Electric Stimulation

Transcranial electric stimulation (tES) refers to a collection of techniques that use electrical current to impact neural excitability[2]. Noninvasive tES techniques, including transcranial direct current stimulation (tDCS), alternating current stimulation (tACS), and random noise stimulation (tRNS), apply low-intensity (~1-2 mA) current to modulate brain function. tDCS involves the application of constant direct current to modulate neuronal excitability by altering the resting membrane potential, while tACS applies an alternating sinusoidal current at specific frequencies to modulate neural oscillations by potentially synchronizing or entraining neuronal activity. tRNS utilizes random noise currents spanning a broad frequency range to enhance neural excitability through stochastic resonance, a phenomenon where the introduction of noise amplifies weak signals (e.g. previously subthresholded oscillations). See Figure 3 for a graphical depiction of the electrical current applied with tDCS, tACS, tRNS and the positive (anode) and negative (cathode) polarity of current. High-definition (HD) tES is a more recently developed technique that involves a multi-electrode montage, allowing for more precise stimulation than traditional tES. In comparison, HD-tES provides better control over the distribution and intensity of the electrical field by allowing for optimal electrode placement and current intensity.

[2] Electroconvulsive therapy (ECT) is an invasive form of electrical stimulation used to alleviate major depression, with significant improvement in ~80% of patients (psychiatry.org), with long-lasting adverse effects on memory (Lisanby et al., 2000). ECT has been shown to significantly disrupt recall of memories that are reactivated immediately prior to ECT treatment compared to control memories that were not reactivated (Kroes et al., 2014). Rodent studies support the idea that stimulation analogous to ECT can disrupt "reconsolidation" of reactivated memories (Misanin et al., 1968). One case report suggested that reactivating a patient's traumatic memory and then administering ECT led to both decreased recollection of their trauma memory and their PTSD symptoms associated with that trauma (Gahr et al., 2014). However, a randomized, controlled and blinded trial showed that, while ECT effectively reduced PTSD symptoms for at least 3 months, there was no additional benefit of reactivating traumatic memories prior to ECT relative to control memories (Tang et al., 2021).

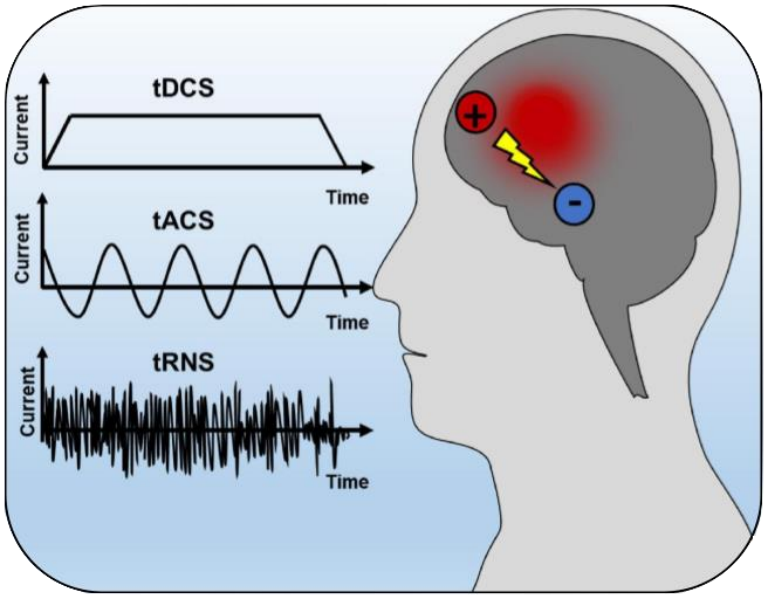

Figure 3. Graphical depiction of electrical current over time with tDCS, tACS, tRNS and the positive (anode) and negative (cathode) polarity of current. Source: https://www.neuroupclinic.com/.

When administering tES, the electrodes are placed on the scalp with a conductive paste or saline-soaked sponges and secured with tape or an elastic band. In HD-tES, multiple electrodes are placed in plastic holders filled with conductive gel and secured by an elastic cap. In both forms of tES, the current is generated by a battery-driven stimulator, which passes through the anode electrode(s) to the cathode electrode(s) and scalp in attempt to modulate the electrical potential in the underlying cortex. During stimulation a large portion of the electrical current is shunted by the scalp, skull, and meninges before it reaches the cortex. Unlike TMS, the current used in tES techniques is not powerful enough to elicit an action potential. Instead, these techniques can alter the response threshold of the stimulated neurons and change the likelihood that they will fire (Fertonani & Miniussi, 2017). The specific physiological and behavioral effects depend on the type of current (i.e., direct current vs. alternating current) and the timing of stimulation (online vs. offline). Additionally, because tES is incapable of directly causing neurons to fire, the intensity of the effects depends heavily on the physiological state (i.e., endogenous or ongoing neural activity) the target region (Woods, 2016).

In tDCS and tACS, the ramp-up and ramp-down procedures are important components of the stimulation protocol. These procedures help ensure participant comfort and minimize potential side effects. The ramp-up phase occurs at the beginning of the stimulation session and involves gradually increasing the electrical current from zero to the desired level over a specified period of time. The gradual increase in current intensity allows participants to acclimate to the sensation of stimulation and

minimizes discomfort at the electrode sites. Following completion of the ramp-up period, stimulation intensity remains constant at the desired level throughout the steady-state phase. The ramp-down phase occurs at the end of the stimulation session. During this phase, the intensity of the electrical current gradually decreases from the desired level back to zero to minimize potential abrupt changes in neural activity or bodily sensations. The ramp-up and ramp-down of current can also be applied in sham/placebo conditions so that the participant is blind as to whether they are in an active or sham stimulation condition.

Below the current state of knowledge about how various tES techniques have modulated memory are reviewed. Note that tES often faces criticism due to its largely variable literature and concerns over stimulation depth and specificity. Many researchers have challenged the proposed mechanisms of tES, using in-vivo studies in animals, epilepsy patients, and cadavers to show that a significant portion of the current in tES is attenuated by soft tissue and skull (Booth et al., 2022; Lafon et al., 2017; Liu et al., 2018). These results suggest that the induced electrical field reaching the brain is too weak to significantly affect neural activity (but see, Ozen et al., 2010; Vöröslakos et al., 2018). In response, it has been proposed that tES may work through more indirect mechanisms, such as either peripheral sensory afferents, (e.g. skin fibers) (Asamoah et al., 2019), or activation of the ascending reticular activating system and norepinephrine distribution by the locus coeruleus (van Boekholdt et al. 2021) (for reviews, see Horvath et al., 2015; Majdi et al., 2023).

To mitigate the variability observed in tES research, it is essential to establish and adhere to standardized protocols. Replication studies, transparent reporting, and data sharing can enhance reliability and reproducibility in the field. Additionally, elucidating the direct and indirect mechanisms of tES can further refine tES methodologies and improve their efficacy and consistency. This approach will help to clarify the true potential and limitations of tES in modulating brain function and memory. These issues should be kept in mind when critically reviewing the current evidence of tES effects on memory.

Transcranial Direct Current Stimulation

tDCS is a tES technique that delivers a direct current from one or more active electrodes (anode) to the reference electrode (cathode) in a constant, unidirectional manner. The potential difference between the two electrodes creates an electromotive force that pushes positively charged ions away from the anode and pulls them toward the cathode (Reinhart, Cosman, Fukuda, & Woodman, 2017). Anodal stimulation can depolarize the resting membrane potential and increase cortical excitability, potentially leading to enhanced memory. Conversely, cathodal stimulation causes a hyperpolarization of

the resting membrane potential and a reduction in cortical excitability, which can have a negative impact on memory. However, it is important to note that the propagation of the current is complex; it does not simply flow directly from anode to cathode or vice versa, and tES cannot selectively modulate the membrane potential of only excitatory or only inhibitory neurons. Intrinsic factors such cortical geometry or skull thickness and conductivity, as well as extrinsic factors such as electrode placement can affect the flow of the current.

Antonenko et al. (2019) administered anodal tDCS to the left temporoparietal cortex of older adults to modulate episodic memory and found that stimulation led to better performance on a paired-associates task using pictures and pseudowords compared to sham stimulation. fMRI results showed that hippocampo-temporoparietal functional connectivity was positively correlated with both initial memory performance and the magnitude of an individual's tDCS-induced enhancement. These results suggest that intrinsic network coupling determined individual responsiveness to stimulation, and may help explain the variability observed in the effects of tDCS. For a meta-analysis on the effect of tDCS on episodic memory in older adults, see Huo et al. (2021). For a systematic review and meta-analysis of tDCS to remediate age-related cognitive decline in healthy older adults, see Indahiastari et al. (2021).

There are many reports of significant modulation of WM from tDCS (for review, see Müller et al., 2022). Nissim et al. (2019) investigated the effects of single session in-scanner bilateral tDCS on functional connectivity of the network associated with WM in healthy older adults. The results showed a significant change in functional connectivity between the left DLPFC and left ventrolateral PFC (VLPFC) while applying 2 mA stimulation in the MRI scanner during an n-back task. In a subsequent study, researchers used individualized finite element models derived from older adults' MRI data to predict significant changes of functional connectivity related to tDCS application (Indahlastari et al., 2021). Individual head models comprising 11 tissue types were used to construct current density maps. Researchers found that the amount of current within the left DLPFC ROIs was positively correlated with changes in functional connectivity between left DLPFC and left VLPFC during active 2 mA stimulation. These results suggest that the amount of current within the left DLPFC may be important for eliciting functional connectivity changes between the left DLPFC and left VLPFC.

In a similar study, Vaqué-Alcázar et al. (2021) used baseline MRI characteristics to predict tDCS-induced episodic memory enhancement in older adults with subjective cognitive decline (SCD). Results showed that individuals with greater tDCS-induced effects on memory reconsolidation exhibited higher left temporal lobe thickness and greater intrinsic functional connectivity in the default-mode network.

These findings suggest that SCD participants with more preserved structural and functional integrity may experience greater benefits from stimulation.

Au et al. (2022) studied the effects of multisession tDCS over the left DLPFC in older adults, using an n-back WM task and a word learning LTM task. Researchers found robust effects on LTM, but mixed effects on WM that only emerged for individuals with lower baseline abilities. Despite the lack of an overall effect on n-back WM performance, researchers observed a strong effect on the subsequent incidental (LTM) recall of the stimuli used in the n-back task, suggesting that tDCS may exhibit more robust effects on LTM due to enhanced consolidation processes.

Ke et al. (2019) studied the effects of tDCS and WM training in young adults by administering HD stimulation to the left DLPFC during training on 5 consecutive days. They found that, compared to sham stimulation, higher learning rates of performance metrics during training were found when WM training was combined with active anodal stimulation. Additionally, these improvements transferred to a similar but untrained WM task. Further analysis revealed a negative relationship between training improvements and baseline performance, suggesting that tDCS may be used to facilitate WM training, perhaps especially so for those with lower WM abilities.

Jones, Johnson, and Berryhill (2020) studied the effects of frontoparietal tDCS paired with WM training in young adults over four days and found that active stimulation enhanced WM performance by modulating interactions between frontoparietal theta oscillations and gamma activity, as measured by pre- and post-training EEG. The increased phase-amplitude coupling (PAC) between the prefrontal stimulation site and temporo-parietal gamma activity was accompanied by behavioral improvements and was most effective when gamma occurred near the prefrontal theta peak. These results show that WM training paired with tDCS can lead to lasting behavioral changes by optimizing the oscillatory mechanisms of PFC control.

Overall, these studies suggest influences on WM and LTM through tDCS of frontoparietal and temporal regions, although some effects may be more likely to occur in individuals with poorer memory function. Interestingly, tDCS of these regions can produce network-level differences in functional connectivity and oscillatory synchronization, thereby producing downstream effects which may be important for memory. It should be noted that, while this section focused its review on studies that reported significant effects of tDCS on memory, numerous studies have failed to find any reliable effects of tDCS on memory (e.g., on prospective memory Rose et al., 2020; Ellis et al., 2020), as well as some failures to replicate effects. Some have suggested that variability in the e-field distribution contributes to variability in (prefrontal) tDCS effects on WM (Razza et al., 2024).

Transcranial Alternating Current Stimulation

tACS is a form of tES that applies a weak, oscillating electrical current to the scalp. This technique was developed to study the role of neural oscillations in behavior in a frequency-specific manner (Polania et al. 2021). For example, Abellaneda-Pérez (2020) studied the differential effects of tDCS and 6 Hz tACS on WM-related neural activity and resting-state connectivity. fMRI results showed tDCS increased functional connectivity particularly within the default-mode network (DMN), while tACS decreased connectivity. These patterns were observed during WM task performance and at rest. These results show how DMN mechanisms and its relationships with other systems can be externally modulated with tES. For a review and meta-analysis, see Grover et al., 2023.

tACS does not directly alter neuronal excitability, but it may be able to entrain underlying neuronal oscillations to the tACS-induced frequency (Aktürk et al., 2022; Helfrich et al., 2014; Witkowski et al., 2016, but see Vossen et al., 2015). Additionally, tACS can be used as a tool to investigate the role of synchronized oscillations between distinct brain regions and networks (Polania, 2018). This is an especially promising application, as memory dysfunction is often attributed to misaligned connectivity between brain regions that are normally synchronized when memory is functioning well. For example, Grover et al. (2022) examined the effects of HD-tACS on memory in older adults and observed that modulation of low-frequency oscillations in the parietal cortex improved WM, while modulation of high-frequency oscillations in the PFC led to improvements in LTM. The observed WM and LTM improvements lasted up to one month post-stimulation and were greater for individuals with lower baseline cognitive function.

Cheng et al. (2022) investigated the effects of HD-tACS on STM for unconscious perceptual content using a masked delayed target–probe discrimination task. Researchers found that entrainment of beta oscillations in bilateral visual areas enhanced memory for perceived stimuli, while alpha entrainment enhanced memory for unseen stimuli. These results suggest that β-rhythms facilitate conscious STM through attentional mechanisms, while α-rhythms aid unconscious processing by enhancing task-relevant information.

Benussi et al. (2022) applied gamma-frequency tACS over the precuneus to alter episodic memory and cholinergic transmission in adults with AD.[3] Dysfunction in the cholinergic neurotransmitter system is one of the contributing factors to cognitive impairments observed in AD. This stimulation

[3] Note that the precuneus encompasses the cortical surface of posterior parietal cortex (Cavanna & Trimble, 2006), and, therefore, it is sufficiently superficial to be stimulated by tES and TMS.

protocol led to significant improvements in memory for face-name associations and an auditory verbal learning task, as well as an increase in short latency afferent inhibition (an indirect measure of cholinergic transmission), relative to sham stimulation. For a recent review, see Manippa et al. (2024).

Reinhart and Nguyen (2019) showed that WM deficits in old age can result from misaligned connectivity between local and long-range circuits, manifesting as disrupted theta–gamma phase-amplitude coupling (PAC) in the temporal cortex, as well as disrupted theta phase synchronization across the frontotemporal cortex. The researchers developed a personalized HD-tACS procedure for targeting these mechanisms by matching the external current to the individual's normal resonance frequency determined first in a resting state EEG assessment. The results suggest that by customizing stimulation to individual network dynamics, it may be possible to influence functional connectivity, and enhance WM in older adults. For review, see Grover et al. (2023).

Together, these studies suggest that different facets of memory may be affected through modulation of different brain rhythms in distinct regions. While theta and gamma rhythms in frontoparietal networks may be modulated in order to improve memory maintenance and recall, alpha and beta rhythms in sensory regions may be modulated to change how information is perceived and encoded into STM. Moreover, longer-term, clinically relevant changes can also be induced using tACS potentially through the alteration of neuroplasticity and neural connectivity between brain regions.

Transcranial Random Noise Stimulation

Both tDCS and tRNS involve the application of a unidirectional current, but unlike tDCS, tRNS utilizes random noise currents (typically ranging from 0.1-640 Hz) to enhance neural excitability. The random noise currents in tRNS are not characterized by a specific waveform or frequency, such as the sinusoidal alternating currents used in tACS. Instead, tRNS applies electrical noise that encompasses a broad spectrum of frequencies, ranging from low to high frequencies. The proposed physiological mechanism of tRNS is an inflow of sodium leading to prolonged depolarization and apparent long-term potentiation (Fertonani & Miniussi, 2017). However, the specific physiological mechanisms leading to tRNS after-effects are not fully understood. One possible explanation is that these random noise currents enhance neural excitability and synaptic plasticity through stochastic resonance (see below), where the introduction of noise to a nonlinear system (e.g. the brain) enhances the detection or transmission of weak signals (e.g. oscillations) (Fertonani & Miniussi, 2017).

tRNS is a less commonly used form of tES for memory modulation, perhaps because it is difficult to draw definitive conclusions about its efficacy and mechanisms of action. Nonetheless, some notable

examples exist. Murphy et al (2020) compared the effects of tRNS and tDCS on WM performance and found that tRNS led to a more robust and consistent enhancement. Conversely, Brambilla et al. (2021) studied the effect of tRNS combined with cognitive training on WM performance in older adults. Researchers found that cognitive training improved memory performance, but tRNS did not. Penton et al. (2018) conducted three experiments using tRNS to target the ventrolateral prefrontal cortices (VLPFC) on a memory task with younger and older adults. In the first experiment, young adults memorized faces while receiving tRNS. Participants who received active tRNS outperformed those in the sham condition. However, in experiment two, this effect was not observed when tested on object memory. The third experiment sought to replicate the effects of experiment one using a within-subject design, and with the addition of older adult participants. Surprisingly, researchers found that active tRNS relative to sham tRNS reduced face memory performance in both younger and older adults. These findings demonstrate how sensitive tES effects are to subtle differences in experimental design and individual differences in participants.

Batelli et al. (2022) studied the effect of N-back WM training paired with tRNS on various untrained cognitive tasks. Participants were tested on three tasks within the same cognitive domain (including dual N-Back, Forward/Backward Digit Span, and Corsi short-term memory tasks) and three in a separate cognitive domain (Posner attention, Flanker inhibitory control and Raven fluid intelligence tasks). Results indicated that WM training coupled with tRNS led to improved performance in untrained tasks, particularly dual N-Back and Forward Digit Span tasks. These effects were only observed at the one-month follow-up, suggesting variability in the timing of transfer to untrained tasks.

Overall, existing work suggests some inconsistencies in the effectiveness of tRNS to modulate memory function, but these inconsistencies may be due to differences in experimental design and individual differences. With a better characterization of these factors and other important factors discussed below, the promise of tRNS as a potential tool for enhancing memory function can be rigorously explored.

Limitations of NIBS

Gaps in Literature

The use of NIBS techniques for memory modulation has several limitations, many of which are reflected in the existing gaps within the literature. One major concern is that the current literature lacks standardization in methodology across studies investigating NIBS for memory modulation. Variability in stimulation parameters (e.g., intensity, frequency, duration), target brain regions, and experimental

designs makes it challenging to compare results across studies and draw definitive conclusions about the efficacy of NIBS for memory modulation. Studies often employ different stimulation protocols without clear justification for their choices. In order to maximize the efficacy of NIBS interventions, standardized protocols based on systematic investigations into the effects of various parameters are necessary (for review, see Antal et al., 2022).

Limited understanding of the precise mechanisms involved in NIBS for memory modulation is another limiting factor. Memory is a complex process that involves numerous (likely nonlinear) interactions among localized neural circuits, distributed brain regions, and large-scale networks. While NIBS can modulate neural activity in specific brain regions, the current understanding of how these changes translate to behavior (memory enhancement or impairment) is incomplete. The precise neural mechanisms through which NIBS affects different aspects of memory, such as encoding, consolidation, and retrieval have not been fully elucidated. Collaborative efforts from various disciplines, (including neuroscience, psychology, clinical practice, and biomedical engineering), can lead to innovative approaches to address research gaps and facilitate the understanding of NIBS in memory research. The remainder of this chapter reviews important limitations and offers recommendations with the aim of improving the rigor and reproducibility of research using NIBS to modulate memory.

Limited Spatial Resolution and Stimulation Depth

The use of NIBS techniques such as TMS and tES for modulating memory present significant limitations related to both the spatial and temporal resolution of stimulation. While TMS offers more precise targeting than tES, the spatial resolution of both techniques is limited compared to invasive methods. In tES, the electric field is spatially diffuse, affects regions adjacent to the target region, and temporally extended. This lack of spatial specificity negatively impacts the ability to selectively target memory-related brain networks, warranting the use of HD-tES which offers more precise targeting. The lack of temporal specificity of tDCS and tRNS warrants the titration of tACS frequencies to known memory-relevant oscillations for the targeted brain region of the individual for more precise targeting.

Directly targeting deeper cortical structures is not currently possible with TMS or tES, but there are alternatives for noninvasively targeting subcortical regions. One approach involves using TMS or tES to target superficial cortical areas that are functionally coupled with deeper brain structures like the hippocampus (Arulchelvan & Vanneste, 2023). Targeting superficial cortical regions that are interconnected with these structures can indirectly influence their activity (e.g., Wang et al., 2014). An alternative approach for targeting deeper brain structures is the use of tFUS or temporal interference

stimulation. Unlike other noninvasive methods such as TMS and tES, tFUS and temporal interference stimulation have the advantage of deeper penetration, allowing for more direct modulation of deep brain regions (Grossman et al., 2017).

Transient Effects

The duration of effects on memory observed following NIBS is another significant concern. Many studies report immediate memory improvements following stimulation, but these effects may quickly dissipate and, therefore, have little functional consequence to memory in daily life. For example, whereas TMS-induced modulation of memory functioning may be observable early on in an experimental session, as practice effects or strategies for task performance develop, or as the deleterious effects of proactive interference and/or fatigue set in, the effects may disappear or change later in a session (e.g., Zanto et al., 2011). The transient nature of the effects limits the application of NIBS interventions for memory enhancement in the real world. The best way to address this limitation is to systematically investigate and adjust stimulation parameters (e.g. intensity, frequency, duration, timing, and number of sessions) and include long-term follow-up memory assessments to assess the duration and magnitude of memory benefits. Tailoring protocols based on individual characteristics could further enhance efficacy. Longitudinal assessments of memory performance over time are crucial for evaluating NIBS-induced effects and optimizing stimulation protocols for sustained memory-related benefits.

Nonlinear Effects

The highly variable effects of NIBS on memory may be more coherently viewed by considering nonlinear interactions between stimulation parameters (e.g., intensity, frequency, duration) and endogenous neural excitability (state-dependency) (Bradley et al., 2022). Stochastic resonance refers to a phenomenon observed in nonlinear systems where the addition of noise enhances the detection or transmission of weak signals. See Figure 4 for a graphical representation of the effect of adding either a small or large amount of random Gaussian noise to a weak image of Big Ben to either reveal or obscure the underlying signal in the image. In the context of NIBS, the introduction of noise can push neural signals closer to the threshold of detection. For example, after finding that stimulation applied at either the beginning or end of a WM retention period impaired or enhanced performance, respectively, Cattaneo et. al (2009) hypothesized that TMS may preferentially activate neurons in a low initial activation state (low firing rate). This hypothesis is supported by studies showing that spTMS to sensory

cortex can reactivate WM for weak representations of color (Silvanto et al., 2007), gratings (Jolij & Lamme, 2010), and motion (Rose et al., 2016; Silvanto & Cattaneo, 2010) and modeling work demonstrating that a neuron in a high initial activation state (i.e. firing strongly in response to a visual stimulus) can be less excitable in response to strong external stimulation than a neuron in a lower initial activation state (Siebner et al., 2009, 2022). Therefore, variable effects of NIBS on memory may be due to nonlinear responses as a function of brain states and stimulation intensities.

Figure 4. Images depicting the physical principle of 'stochastic resonance' and the effect that adding noise to a weak signal (left image) has on revealing an underlying signal (middle image), while adding too much noise (right image) can obscure the underlying signal. Figure adapted from Simonotto et al., 1997. Copyright 1997 American Physical Society

Recommendations for NIBS Studies

Personalization

The cognitive effects produced by NIBS depend on the technical parameters used during stimulation. Personalized stimulation intensity based on an individual's resting or active motor threshold has long been a hallmark of TMS research. An increasing focus of NIBS studies is how stimulation interacts with individual differences, and how personalized stimulation frequencies can lead to greater cognitive benefits (Romei Thut, & Silvanto, 2016). Customizing NIBS techniques to an individual's intrinsic neural frequency first requires identifying the individual's dominant neural oscillations, typically through EEG or MEG recordings. Once this frequency is determined, stimulation frequency for tACS or rTMS can be selected to modulate these oscillations.

Optimization of the stimulation protocol involves considerations of timing, duration, and intermittency to achieve desired neural and behavioral effects. Closed-loop designs can provide even

more personalization by dynamically adjusting stimulation parameters based on the individual's neural activity that is processed and analyzed in real time (e.g., Kahana et al., 2023).

Note that personalization also extends to adjusting stimulation targeting based on individual differences in structural and functional networks. Detailed prior knowledge of the anatomical, physiological, and functional properties of the targeted memory networks of each individual can be used to optimize stimulation targeting (Romei Thut, & Silvanto, 2016). Neuroimaging techniques such as MRI, fMRI, and diffusion tensor imaging (DTI) can be used to identify optimal stimulation targets based on individual brain anatomy and functional connectivity (Luber et al., 2022).

Neuroimaging and Neuronavigation

Targeting TMS based on a standardized or group-averaged structural MRI template or individually-tailored structural MRI scan (i.e., neuro-navigated TMS) is currently considered the gold standard in TMS administration. Incorporating diffusion-weighted imaging to identify the structural connectivity of white matter fiber tracts may be even more helpful to target memory networks in a personalized manner; targeting based on resting state functional MRI measures from resting state functional connectivity (e.g., Momi et al., 2021; Wang et al., 2014) and task-based analyses (e.g., Zanto et al., 2011) may be even superior for targeting, stimulating, and modulating memory networks.

Indeed, Sack and colleagues (2009) investigated issues related to the absence of neuronavigation in TMS by systematically comparing four TMS coil positioning approaches. After comparing individually tailored structural MRI-guided TMS neuronavigation, individually-tailored fMRI-guided TMS neuronavigation, standardized (MNI or Talairach), group-averaged functional MRI coordinates, or 10–20 EEG positionitiong, the targeting procedure that was found to produce the largest behavioral effect sizes and required the smallest number of participants to reveal a statistically reliable behavioral effect was individually-tailored fMRI-guided TMS neuronavigation (Sack et al., 2009). In contrast, targeting based on the location of standardized (10-20) EEG electrode positioning yielded the smallest behavioral effect size due to variability between subjects, and required ~10x the number of subjects (as compared to individual fMRI-guided TMS) to reveal a statistically significant behavioral effect (Sack et al., 2009; see also Ahdab et al., 2010).

Real-time neuroimaging with stimulation

Real-time neuroimaging analyses coupled with simultaneous brain stimulation show promise in enhancing the efficacy of brain stimulation by reducing inter- and intra-individual variability. With real-

time analyses, TMS pulses or tACS can be timed to be synchronized (in or out of phase) with an ongoing, task-relevant brain oscillation. For example, real-time EEG analysis with phase-triggered TMS aligned the timing of TMS pulse delivery to depressed patients' ongoing brain oscillations has been shown to enhance WM (Zrenner et al., 2020; other examples include Alekseichuk et al., 2016; de Lara et al., 2018; for review, see Abubaker et al., 2021). Note that NIBS can also be paired with adaptive cognitive training to maximize an individual's memory improvement. For a systematic review and meta-analysis on the efficacy of combining cognitive training and NIBS, see Poppe et al. (2023).

Several studies have applied simultaneous TMS during fMRI scanning to observe the effects of TMS on activity in targeted and coupled regions (Feredoes et al., 2011; Hawco et al. 2017; Hermiller et al. 2020; Riddle et al., 2021; for review, see Mizutani-Tiebel et al., 2022). For example, Hermiller et al. (2020) administered TMS to a region of individual's lateral parietal cortex that was found to be functionally coupled with their hippocampal network during a resting state scan; after TMS, the left hippocampus showed elevated activity during encoding of scenes and enhanced subsequent memory relative to controls.

Machine Learning

Electric-Field Modeling, Individual brain anatomy is a primary determinant of current distribution in NIBS (Antonenko et al., 2019). Electric field (E-field) modeling is a computational technique used to estimate the amount of stimulation that reaches the cortical target. This process involves segmenting an individual's structural MRI scan into different tissue types to simulate the propagation of the E-field (Van Hoornweder et al., 2023).

E-Field modeling holds significant promise in tailoring NIBS techniques for memory modulation by allowing researchers and clinicians to precisely target brain regions implicated in memory processes. Through E-field modeling, researchers can explore novel stimulation montages, identify optimal stimulation targets, and establish dose-response relationships specific to memory modulation. Moreover, by correlating E-field model predictions with neurophysiological and behavioral outcomes, researchers can elucidate the mechanisms underlying NIBS-induced memory enhancement, paving the way for more effective and targeted interventions in clinical and cognitive enhancement settings. For a review on the use of E-Field modeling and WM improvement, refer to Wischnewski, Mantell and Opitz (2021).

Decoding. The use of machine learning algorithms to decode multivariate patterns of brain activity from neuroimaging data associated with memory representations and processes provide

powerful insights about the nature of memories--how their representations change over time or as a function of cognitive processing. Targeting TMS and TES to memory-relevant regions identified by such multivariate pattern (decoding) analyses may provide even more informative insights regarding memory modulation than traditional univariate analyses, e.g., of rest or task evoked fMRI data. For example, Rose et al. (2016) had healthy young adults perform a WM task in the fMRI scanner that required remembering a single face, word, or direction of motion and applied whole brain searchlight decoding analyses to identify regions selectively involved in the delay period retention of each category for each participant. These stimulus specific retention 'nodes' were targeted with delay period TMS in a subsequent WM task that involved switching attention between faces, words, or directions of motion during delay periods. Single pulses of TMS were found to reactivate multivariate patterns associated with the retention of items that appeared to be passively retained from WM, and this memory specific reactivation effect was larger when TMS targeted the corresponding region of cortex that of the passively retained memory item (i.e., targeting the 'face' region when a face was passively retained). For reviews and a meta-analysis of the effects of noninvasive brain stimulation on WM, see Brunoni & Vanderhasselt (2014) and Widhalm & Rose (2019). For another example of using brain decoding for TMS targeting, see Lapate et al. (2024).

Designing NIBS experiments for Modulating Memory

Given the increasing popularity of NIBS in memory research, it is valuable for researchers to have extensive knowledge of the behavioral and theoretical literature, as well as the technical skills and knowledge to conduct a proper experiment. Parameters such as electrode or coil placement and stimulation intensity, duration, and frequency should be carefully developed and empirically-based. Proper control conditions are also necessary to substantiate research findings. In addition to adequate background knowledge, technical skills, and control conditions, it's vital to consider the ethical concerns that may arise in NIBS research (Molero-Chamizo et al., 2020). While this section focuses on designing a TMS or TES study for memory modulation, most recommendations are relevant for other forms of brain stimulation as well.

Preliminary Investigation. The first step in a well-designed experiment is to conduct an extensive review of the relevant literature. This is essential for developing an understanding of the theoretical framework and methodology relevant to the research question. Following literature review, pilot studies should be conducted to optimize the experimental protocol before data collection.

Task Design. The task should be selected based on its relevance to the stage of memory processing or type of memory in question. Free recall, recognition, and spatial memory tasks are examples of common tasks in memory research. Additionally, it's important to adjust task difficulty to suit the population being studied. Tasks should be challenging enough to detect stimulation-induced changes in memory performance, but not so difficult that participants cannot perform the task. Selecting appropriate outcome measures (e.g. accuracy or reaction time) to assess memory performance is another crucial aspect of experimental design. Additionally, tasks should be counterbalanced when possible, to account for learning and interference effects.

Stimulation Target. The coil placement or electrode configuration in a NIBS study should be based on the research question and theoretical framework. Targeted regions should modulate and measure the effects of stimulation on both domain-specific sensory/representational regions that are implicated in a particular memory process and more domain-general memory related processes (Cabeza et al., 2008, 2011; Ciaramelli et al., 2008). Structures commonly targeted in memory research are the PFC and parietal cortex, often to indirectly target the MTL. The lateralization of cognitive processes must also be considered when determining the stimulation target. The coil placement or electrode montage can be guided by the international 10-20 system for EEG electrode placement, but it should be emphasized that using the 10-20 system does not guarantee that stimulation is reaching the intended target, due to anatomical differences. For this reason, personalized stimulation protocols (e.g. neuro-navigated NIBS and current flow modeling) are ideal. It is also important to acknowledge that noninvasively stimulating superficial targets (within 2-3 cm of the surface of the cortex) may also modulate distant regions or networks that are structurally or functionally connected during stimulation (Luber et al., 2022).

Stimulation Intensity. While increasing stimulation intensity can lead to greater effects on performance, this is not necessarily the case. Additionally, higher intensity stimulation can cause itching or discomfort on the scalp. These issues can be mitigated by adapting high-frequency stimulation intensity to the participant's individual sensory threshold (Zaehle, 2010). As discussed earlier, in TMS, the most common way to determine stimulation intensity is to test individual motor or phosphene threshold and titrate based on those results. However, researchers should acknowledge and address the fact that motor cortex excitability is not necessarily the same as cortical excitability everywhere else in the brain (Deblieck et al. 2008).

Stimulation Duration. The after-effects produced by NIBS depend heavily on stimulation duration. For example, in tES, after-effects are typically observed following 10-20 minutes of

stimulation. Stimulating for a longer, continuous duration is not known to increase after-effects while intermittent stimulation in the 15-20 minute range has produced the greatest results (Monte-Silva et al., 2013). The temporal dynamics of memory processes should be considered in a NIBS study and stimulation duration should be tailored accordingly. For example, stimulation can be applied during encoding to enhance or disrupt memory formations, or during retrieval to facilitate or prevent access to stored information. Stimulation can also be delivered in repeated sessions over time to explore lasting effects on memory.

Stimulation Frequency, The frequency of stimulation is primarily relevant when designing a tACS, tRNS or rTMS experiment. As discussed above, one factor that complicates frequency-specific stimulation is individual differences in the peak or dominant frequency of memory relevant oscillations. For example, the peak frequency of the theta oscillation may be closer to 4hz for one individual, but closer to 8 Hz for another (Veniero, 2019). Haphazardly selecting and applying the same (e.g., 6 Hz) frequency for all participants may cause oscillations to speed up for some but slow down for others, thereby causing counteracting effects for group analyses. For this reason, a well-designed NIBS experiment using entrainment should first collect M/EEG data to determine each individual's dominant frequency and either adjust stimulation frequency accordingly or systematically compare the effects of different frequencies across individuals.

Online vs. Offline Effects. Online studies refer to those in which the participant completes the behavioral task during stimulation, while offline stimulation involves completing the behavioral task separately (Thair, 2017). The rationale for using online vs. offline stimulation in tES is rarely reported, and may depend on other parameters in the study. For example, online stimulation may be more common when experimental time is limited (Thair, 2017). Conversely, if EEG is recorded in the study, offline stimulation would be more appropriate as stimulation obscures the signal. Studies directly measuring the effects of online vs. offline tES are still needed, but growing evidence suggests that offline effects are generally stronger (Sandrini et al., 2020). In TMS, the use of offline vs online stimulation protocols depend on the particular phase of the learning and remembering process that is to be affected. Pairing stimulation during encoding, maintenance/consolidation, or retrieval is likely to require different targets, which will have different outcomes on learning and memory.

Adequate Control Conditions. To verify that NIBS has an effect on behavior, active stimulation must be compared with sham stimulation (placebo) as the control. In tDCS and tACS, the control condition should be identical to the stimulation condition and include a very brief ramp-up period to provide a sensation of stimulation without any cognitive effects. Popular sham conditions in TMS include

angling the coil 45-90 degrees away from the participant's head or using a specific sham coil that produces no stimulation. Although this mimics the auditory clicks present in active stimulation conditions, this does not include comparable somatosensory stimulation (for recommendations on disentangling TMS-evoked signals from sensory-evoked signals, see Rocchi et al., 2021; Rogasch et al., 2027; Trapp et al., 2024).

Duecker and Sack (2015) claimed that typical sham TMS approaches are insufficient control conditions. They argue that, in order to make claims about behavioral and/or physiological consequences of stimulation (of a particular brain region at a particular point in time during task execution), it is necessary to show that the same effects do not occur when stimulating another brain region at the same time point, or the same region at a different time point. For this reason, NIBS studies should strive to have such active control condition in order to make causal claims. The choice of active control site should be carefully considered and driven by solid theoretical justification. For example (and as a cautionary warning), the vertex has commonly been used as a control site in TMS research, under the assumption that it has relatively little influence over the on-going processes that would be involved in most tasks. However, it was shown that TMS to the vertex evokes widespread BOLD deactivations across the brain – especially in areas associated with the default mode network, which are known to be important for attention and memory functioning (Jung et al., 2016).

Transparency. In addition to having good control/sham stimulation conditions, is essential for NIBS research to maintaining transparency in order to both advance understanding of memory and develop effective therapeutic interventions. Preregistration of study protocols and analysis plans can help prevent selective reporting of results and hypothesizing after results are known. This helps address the “file drawer” problem--the tendency of researchers to publish studies with positive results while leaving null results unpublished in the “file drawer"--thereby reducing publication bias, and increasing the transparency and reproducibility of research. Platforms such as Open Science Framework provide opportunities to preregister studies. Additionally, Editors and Journals should facilitate the publication of negative or null findings, and researchers should openly share raw data and experimental materials to allow other researchers to replicate or extend studies.

Conclusion

In conclusion, research on the modulation of memory with brain stimulation has provided promising avenues for understanding and potentially enhancing human memory functions. NIBS techniques such as TMS and TES enable scientists to use noninvasive, relatively low-cost methods to

help reveal dynamic neurocognitive, context-dependent processes that support memory encoding, consolidation, and retrieval. High-powered, well-controlled, and rigorously designed studies exploring the effects of brain stimulation on memory will continue to reveal intriguing insights about the role of specific brain regions and networks of regions in memory processing. Findings have important implications for understanding and treating memory-related disorders. As research in this field continues to advance, and the vast parameter space is more fully mapped out, further discoveries are expected to pave the way for innovative, personalized applications to enhance memory function and improve cognitive in general.

References

Abellaneda-Pérez, K., Vaqué-Alcázar, L., Perellón-Alfonso, R., Bargalló, N., Kuo, M. F., Pascual-Leone, A., ... & Bartrés-Faz, D. (2020). Differential tDCS and tACS effects on working memory-related neural activity and resting-state connectivity. Frontiers in neuroscience, 13, 497934.

Abubaker, M., Al Qasem, W., & Kvašňák, E. (2021). Working memory and cross-frequency coupling of neuronal oscillations. Frontiers in psychology, 12, 756661.

Ahdab, R., Ayache, S. S., Brugières, P., Goujon, C., & Lefaucheur, J. P. (2010). Comparison of "standard" and "navigated" procedures of TMS coil positioning over motor, premotor and prefrontal targets in patients with chronic pain and depression. Neurophysiologie Clinique/Clinical Neurophysiology, 40(1), 27-36.

Alagapan, S., Riddle, J., Huang, W. A., Hadar, E., Shin, H. W., & Fröhlich, F. (2019). Network-targeted, multi-site direct cortical stimulation enhances working memory by modulating phase lag of low-frequency oscillations. Cell reports, 29(9), 2590-2598.

Alekseichuk, I., Diers, K., Paulus, W., & Antal, A. (2016). Transcranial electrical stimulation of the occipital cortex during visual perception modifies the magnitude of BOLD activity: a combined tES–fMRI approach. Neuroimage, 140, 110-117.

Aktürk, T., de Graaf, T. A., Güntekin, B., Hanoğlu, L., & Sack, A. T. (2022). Enhancing memory capacity by experimentally slowing theta frequency oscillations using combined EEG-tACS. Scientific Reports, 12(1), 14199.

Antal, A., Luber, B., Brem, A. K., Bikson, M., Brunoni, A. R., Kadosh, R. C., ... & Paulus, W. (2022). Non-invasive brain stimulation and neuroenhancement. Clinical neurophysiology practice, 7, 146-165.

Antonenko, D., Thielscher, A., Saturnino, G. B., Aydin, S., Ittermann, B., Grittner, U., & Flöel, A. (2019). Towards precise brain stimulation: Is electric field simulation related to neuromodulation?. Brain stimulation, 12(5), 1159-1168.

Arulchelvan, E., & Vanneste, S. (2023). Promising neurostimulation routes for targeting the hippocampus to improve episodic memory: A review. Brain Research, 148457.

Asamoah, B., Khatoun, A., & Mc Laughlin, M. (2019). tACS motor system effects can be caused by transcutaneous stimulation of peripheral nerves. Nature communications, 10(1), 266.

Au, J., Smith-Peirce, R. N., Carbone, E., Moon, A., Evans, M., Jonides, J., & Jaeggi, S. M. (2022). Effects of multisession prefrontal transcranial direct current stimulation on long-term memory and working memory in older adults. Journal of cognitive neuroscience, 34(6), 1015-1037.

Bailey, C. H., Kandel, E. R., & Harris, K. M. (2015). Structural components of synaptic plasticity and memory consolidation. Cold Spring Harbor perspectives in biology, 7(7), a021758.

Benussi, A., Alberici, A., Ferrari, C., Cantoni, V., Dell'Era, V., Turrone, R., ... & Borroni, B. (2018). The impact of transcranial magnetic stimulation on diagnostic confidence in patients with Alzheimer disease. Alzheimer's research & therapy, 10, 1-10.

Benussi, A., Cantoni, V., Grassi, M., Brechet, L., Michel, C. M., Datta, A., ... & Borroni, B. (2022). Increasing brain gamma activity improves episodic memory and restores cholinergic dysfunction in Alzheimer's disease. Annals of Neurology, 92(2), 322-334.

Bansal, A., Shikha, S., & Zhang, Y. (2023). Towards translational optogenetics. Nature Biomedical Engineering, 7(4), 349-369.

Battelli, L., Pergher, V., Min, O., Gardiner, L., Van Hulle, M., & Santarnecchi, E. (2022). Delayed long term impact of working memory training coupled with tRNS on near-and far-transfer cognitive tasks. Journal of Vision, 22(14), 4286-4286.

Bersani, F. S., Minichino, A., Enticott, P. G., Mazzarini, L., Khan, N., Antonacci, G., ... & Biondi, M. (2013). Deep transcranial magnetic stimulation as a treatment for psychiatric disorders: a comprehensive review. European Psychiatry, 28(1), 30-39.

Borgomaneri, S., Battaglia, S., Sciamanna, G., Tortora, F., & Laricchiuta, D. (2021). Memories are not written in stone: Re-writing fear memories by means of non-invasive brain stimulation and optogenetic manipulations. Neuroscience & Biobehavioral Reviews, 127, 334-352.

Booth, S. J., Taylor, J. R., Brown, L. J., & Pobric, G. (2022). The effects of transcranial alternating current stimulation on memory performance in healthy adults: A systematic review. Cortex, 147, 112-139.

Bovy, L., Berkers, R. M., Pottkämper, J. C., Varatheeswaran, R., Fernández, G., Tendolkar, I., & Dresler, M. (2020). Transcranial magnetic stimulation of the medial prefrontal cortex decreases emotional memory schemas. Cerebral Cortex, 30(6), 3608-3616.

Bradley, C., Nydam, A. S., Dux, P. E., & Mattingley, J. B. (2022). State-dependent effects of neural stimulation on brain function and cognition. Nature Reviews Neuroscience, 23(8), 459-475.

Brambilla, M., Dinkelbach, L., Bigler, A., Zokaei, N., & Brem, A. K. (2021). The effect of transcranial random noise stimulation on cognitive training outcome in healthy aging. Frontiers in neurology, 12, 625359.

Brunoni, A. R., & Vanderhasselt, M. A. (2014). Working memory improvement with non-invasive brain stimulation of the dorsolateral prefrontal cortex: a systematic review and meta-analysis. Brain and cognition, 86, 1-9.

Buzsáki G, Draguhn A. 2004. Neuronal oscillations in cortical networks. Science, 304(5679):1926-9. doi: 10.1126/science.1099745. PMID: 15218136.

Cabeza, R., Ciaramelli, E., Olson, I. R., & Moscovitch, M. (2008). The parietal cortex and episodic memory: an attentional account. Nature reviews neuroscience, 9(8), 613-625.

Cabeza, R., Mazuz, Y. S., Stokes, J., Kragel, J. E., Woldorff, M. G., Ciaramelli, E., ... & Moscovitch, M. (2011). Overlapping parietal activity in memory and perception: evidence for the attention to memory model. Journal of cognitive neuroscience, 23(11), 3209-3217.

Casali, A. G., Casarotto, S., Rosanova, M., Mariotti, M., & Massimini, M. (2010). General indices to characterize the electrical response of the cerebral cortex to TMS. Neuroimage, 49(2), 1459-1468.

Casali, A. G., Gosseries, O., Rosanova, M., Boly, M., Sarasso, S., Casali, K. R., ... & Massimini, M. (2013). A theoretically based index of consciousness independent of sensory processing and behavior. Science translational medicine, 5(198), 198ra105-198ra105.

Cattaneo, Z., Vecchi, T., Pascual-Leone, A., & Silvanto, J. (2009). Contrasting early visual cortical activation states causally involved in visual imagery and short-term memory. European Journal of Neuroscience, 30(7), 1393–1400.

Cavanna, A. E., & Trimble, M. R. (2006). The precuneus: a review of its functional anatomy and behavioural correlates. Brain, 129(3), 564-583.

Chan, M. M., Yau, S. S., & Han, Y. M. (2021). The neurobiology of prefrontal transcranial direct current stimulation (tDCS) in promoting brain plasticity: A systematic review and meta-analyses of human and rodent studies. Neuroscience & Biobehavioral Reviews, 125, 392-416.

Cheng, P., Grover, S., Wen, W., Sankaranarayanan, S., Davies, S., Fragetta, J., ... & Reinhart, R. M. (2022). Dissociable rhythmic mechanisms enhance memory for conscious and nonconscious perceptual contents. Proceedings of the National Academy of Sciences, 119(44), e2211147119.

Ciaramelli, E., Grady, C. L., & Moscovitch, M. (2008). Top-down and bottom-up attention to memory: a hypothesis (AtoM) on the role of the posterior parietal cortex in memory retrieval. Neuropsychologia, 46(7), 1828-1851.

Citri, A., & Malenka, R. C. (2008). Synaptic plasticity: multiple forms, functions, and mechanisms. Neuropsychopharmacology, 33(1), 18-41.

Davis, S. W., Luber, B., Murphy, D. L., Lisanby, S. H., & Cabeza, R. (2017). Frequency-specific neuromodulation of local and distant connectivity in aging and episodic memory function. Human brain mapping, 38(12), 5987-6004.

de Lara, G. A., Alekseichuk, I., Turi, Z., Lehr, A., Antal, A., & Paulus, W. (2018). Perturbation of theta-gamma coupling at the temporal lobe hinders verbal declarative memory. Brain stimulation, 11(3), 509-517.

de Sousa, A. F., Cowansage, K. K., Zutshi, I., Cardozo, L. M., Yoo, E. J., Leutgeb, S., & Mayford, M. (2019). Optogenetic reactivation of memory ensembles in the retrosplenial cortex induces systems consolidation. Proceedings of the National Academy of Sciences, 116(17), 8576-8581.

Deblieck, C., Thompson, B., Iacoboni, M., & Wu, A. D. (2008). Correlation between motor and phosphene thresholds: a transcranial magnetic stimulation study (Vol. 29, No. 6, pp. 662-670). Hoboken: Wiley Subscription Services, Inc., A Wiley Company.

Deng ZD, Lisanby SH, Peterchev AV. Coil design considerations for deep transcranial magnetic stimulation. Clin Neurophysiol. 2014 Jun;125(6):1202-12. doi: 10.1016/j.clinph.2013.11.038. Epub 2013 Dec 22. PMID: 24411523; PMCID: PMC4020988.

Duecker, F., & Sack, A. T. (2015). Rethinking the role of sham TMS. Frontiers in psychology, 6, 210.

Duque, J., Labruna, L., Verset, S., Olivier, E., & Ivry, R. B. (2012). Dissociating the role of prefrontal and premotor cortices in controlling inhibitory mechanisms during motor preparation. Journal of Neuroscience, 32(3), 806-816.

Ellis, D. M.; Veloria, G. K. G.; Arnett, C. R.; Vogel, A. E.; Pitães, M., & Brewer, G. A. (under review). No Evidence for Enhancing Prospective Memory with Anodal Transcranial Direct Current Stimulation across Dorsolateral Prefrontal Cortex. Journal of Cognitive Enhancement.

Etter, G., van der Veldt, S., Manseau, F., Zarrinkoub, I., Trillaud-Doppia, E., & Williams, S. (2019). Optogenetic gamma stimulation rescues memory impairments in an Alzheimer's disease mouse model. Nature communications, 10(1), 5322.

Etter, G., van der Veldt, S., Choi, J., & Williams, S. (2023). Optogenetic frequency scrambling of hippocampal theta oscillations dissociates working memory retrieval from hippocampal spatiotemporal codes. Nature communications, 14(1), 410.

Ezzyat, Y., Kragel, J. E., Burke, J. F., Levy, D. F., Lyalenko, A., Wanda, P., ... & Kahana, M. J. (2017). Direct brain stimulation modulates encoding states and memory performance in humans. Current biology, 27(9), 1251-1258.

Ezzyat, Y., Wanda, P. A., Levy, D. F., Kadel, A., Aka, A., Pedisich, I., ... & Kahana, M. J. (2018). Closed-loop stimulation of temporal cortex rescues functional networks and improves memory. Nature communications, 9(1), 365.

Feredoes, E., Tononi, G., & Postle, B. R. (2006). Direct evidence for a prefrontal contribution to the control of proactive interference in verbal working memory. Proceedings of the National Academy of Sciences, 103(51), 19530-19534.

Feredoes, E., Tononi, G., & Postle, B. R. (2007). The neural bases of the short-term storage of verbal information are anatomically variable across individuals. Journal of Neuroscience, 27(41), 11003-11008.

Feredoes, E., Heinen, K., Weiskopf, N., Ruff, C., & Driver, J. (2011). Causal evidence for frontal involvement in memory target maintenance by posterior brain areas during distracter interference of visual working memory. Proceedings of the National Academy of Sciences, 108(42), 17510-17515.

Feredoes, E. (2022). Developments in transcranial magnetic stimulation to study human cognition. Journal of Cognitive Neuroscience, 35(1), 6-10.

Fertonani, A., & Miniussi, C. (2017). Transcranial electrical stimulation: what we know and do not know about mechanisms. The Neuroscientist, 23(2), 109-123.

Finger S, Zaromb F. Benjamin Franklin and shock-induced amnesia. Am Psychol. 2006 Apr;61(3):240-8. doi: 10.1037/0003-066X.61.3.240. PMID: 16594840.

Freedberg, M. V., Reeves, J. A., Fioriti, C. M., Murillo, J., & Wassermann, E. M. (2022). Reproducing the effect of hippocampal network-targeted transcranial magnetic stimulation on episodic memory. Behavioural brain research, 419, 113707.

Fulvio, J. M., & Postle, B. R. (2020). Cognitive control, not time, determines the status of items in working memory. Journal of Cognition, 3(1).

Fulvio, J. M., Haegens, S., & Postle, B. R. (2024). Single-pulse Transcranial-magnetic Stimulation Affects Working-memory Performance via Posterior Beta-band Oscillations. Journal of Cognitive Neuroscience, 1-20.

Gagnon, G., Blanchet, S., Grondin, S., & Schneider, C. (2010). Paired-pulse transcranial magnetic stimulation over the dorsolateral prefrontal cortex interferes with episodic encoding and retrieval for both verbal and non-verbal materials. Brain Research, 1344, 148-158.

Gagnon, G., Schneider, C., Grondin, S., & Blanchet, S. (2011). Enhancement of episodic memory in young and healthy adults: a paired-pulse TMS study on encoding and retrieval performance. Neuroscience Letters, 488(2), 138-142.

Gahr, M., Schönfeldt-Lecuona, C., Spitzer, M., & Graf, H. (2014). Electroconvulsive therapy and posttraumatic stress disorder: first experience with conversation-based reactivation of traumatic memory contents and subsequent ECT-mediated impairment of reconsolidation. The Journal of neuropsychiatry and clinical neurosciences, 26(3), E38-E3

Gardner, J. (2013). A history of deep brain stimulation: Technological innovation and the role of clinical assessment tools. Social studies of science, 43(5), 707-728.

Geva-Sagiv, M., Mankin, E. A., Eliashiv, D., Epstein, S., Cherry, N., Kalender, G., ... & Fried, I. (2023). Augmenting hippocampal–prefrontal neuronal synchrony during sleep enhances memory consolidation in humans. Nature neuroscience, 26(6), 1100-1110.

Gilbert, F., Harris, A. R., & Kidd, M. (2021). Burnt in your memory or burnt memory? Ethical issues with optogenetics for memory modification. AJOB neuroscience, 12(1), 22-24.

Groppa, S., Muthuraman, M., Otto, B., Deuschl, G., Siebner, H. R., & Raethjen, J. (2013). Subcortical substrates of TMS induced modulation of the cortico-cortical connectivity. Brain stimulation, 6(2), 138-146.

Grossman, N., Bono, D., Dedic, N., Kodandaramaiah, S. B., Rudenko, A., Suk, H. J., ... & Boyden, E. S. (2017). Noninvasive deep brain stimulation via temporally interfering electric fields. cell, 169(6), 1029-1041.

Grover, S., Wen, W., Viswanathan, V., Gill, C. T., & Reinhart, R. M. (2022). Long-lasting, dissociable improvements in working memory and long-term memory in older adults with repetitive neuromodulation. Nature neuroscience, 25(9), 1237-1246.

Grover, S., Fayzullina, R., Bullard, B. M., Levina, V., & Reinhart, R. M. (2023). A meta-analysis suggests that tACS improves cognition in healthy, aging, and psychiatric populations. Science translational medicine, 15(697), eabo2044.

Guerra, A., López-Alonso, V., Cheeran, B., & Suppa, A. (2020). Variability in non-invasive brain stimulation studies: Reasons and results. Neuroscience letters, 719, 133330. https://doi.org/10.1016/j.neulet.2017.12.058

Hallett, M. (2007). Transcranial magnetic stimulation: a primer. Neuron, 55(2), 187-199.

Hanslmayr, S., Axmacher, N., & Inman, C. S. (2019). Modulating human memory via entrainment of brain oscillations. Trends in neurosciences, 42(7), 485-499.

Hawco, C., Armony, J. L., Daskalakis, Z. J., Berlim, M. T., Chakravarty, M. M., Pike, G. B., & Lepage, M. (2017). Differing time of onset of concurrent TMS-fMRI during associative memory encoding: a measure of dynamic connectivity. Frontiers in human neuroscience, 11, 404.

Helfrich, R. F., Schneider, T. R., Rach, S., Trautmann-Lengsfeld, S. A., Engel, A. K., & Herrmann, C. S. (2014). Entrainment of brain oscillations by transcranial alternating current stimulation. Current biology, 24(3), 333-339.

Hermiller, M. S., Karp, E., Nilakantan, A. S., & Voss, J. L. (2019). Episodic memory improvements due to noninvasive stimulation targeting the cortical–hippocampal network: a replication and extension experiment. Brain and Behavior, 9(12), e01393.

Hermiller, M. S., Chen, Y. F., Parrish, T. B., & Voss, J. L. (2020). Evidence for immediate enhancement of hippocampal memory encoding by network-targeted theta-burst stimulation during concurrent fMRI. Journal of Neuroscience, 40(37), 7155-7168.

Hermiller, M. S., & Voss, J. L. (2023). Downstream hippocampal memory response during concurrent theta-burst TMS-fMRI. Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation, 16(1), 178.

Higo, T., Mars, R. B., Boorman, E. D., Buch, E. R., & Rushworth, M. F. (2011). Distributed and causal influence of frontal operculum in task control. Proceedings of the National Academy of Sciences, 108(10), 4230-4235.

Horvath, J. C., Forte, J. D., & Carter, O. (2015). Evidence that transcranial direct current stimulation (tDCS) generates little-to-no reliable neurophysiologic effect beyond MEP amplitude modulation in healthy human subjects: a systematic review. Neuropsychologia, 66, 213-236.

Huo, L., Zhu, X., Zheng, Z., Ma, J., Ma, Z., Gui, W., & Li, J. (2021). Effects of transcranial direct current stimulation on episodic memory in older adults: a meta-analysis. The Journals of Gerontology: Series B, 76(4), 692-702.

Indahlastari, A., Albizu, A., Kraft, J. N., O'Shea, A., Nissim, N. R., Dunn, A. L., ... & Woods, A. J. (2021). Individualized tDCS modeling predicts functional connectivity changes within the working memory network in older adults. Brain stimulation, 14(5), 1205-1215.

Izquierdo I, Medina JH. (1997). Memory formation: the sequence of biochemical events in the hippocampus and its connection to activity in other brain structures. Neurobiol Learn Mem. 68(3):285-316. doi: 10.1006/nlme.1997.3799. PMID: 9398590.

Jahangiri, F. R., Dobariya, A., Kruse, A., Kalyta, O., & Moorman, J. D. (2020). Mapping of the motor cortex. Cureus, 12(9).

Jeong, H., Im, J. J., Park, J. S., Na, S. H., Lee, W., Yoo, S. S., ... & Chung, Y. A. (2021). A pilot clinical study of low-intensity transcranial focused ultrasound in Alzheimer's disease. Ultrasonography, 40(4), 512.

Johnson, J. S., Kundu, B., Casali, A. G., & Postle, B. R. (2012). Task-dependent changes in cortical excitability and effective connectivity: a combined TMS-EEG study. Journal of neurophysiology, 107(9), 2383-2392.

Johnson, J.S., Feredoes, E., & Postle, B.R. (2021). 'TMS in working memory research', in Eric M. Wassermann, and others (eds), The Oxford Handbook of Transcranial Stimulation: Second Edition, 2nd edn, Oxford Handbooks (2024; online edn, Oxford Academic, 10 Feb. 2021), https://doi.org/10.1093/oxfordhb/9780198832256.013.34

Jolij, J., & Lamme, V. A. (2010). Transcranial magnetic stimulation-induced 'visual echoes' are generated in early visual cortex. Neuroscience letters, 484(3), 178-181.

Jones, K. T., Johnson, E. L., & Berryhill, M. E. (2020). Frontoparietal theta-gamma interactions track working memory enhancement with training and tDCS. Neuroimage, 211, 116615.

Jung, J., Bungert, A., Bowtell, R., & Jackson, S. R. (2016). Vertex stimulation as a control site for transcranial magnetic stimulation: a concurrent TMS/fMRI study. Brain stimulation, 9(1), 58-64.

Kahana, M. J., Ezzyat, Y., Wanda, P. A., Solomon, E. A., Adamovich-Zeitlin, R., Lega, B. C., ... & Diaz-Arrastia, R. R. (2023). Biomarker-guided neuromodulation aids memory in traumatic brain injury. Brain stimulation, 16(4), 1086-1093.

Kammer, T., Beck, S., Erb, M., & Grodd, W. (2001). The influence of current direction on phosphene thresholds evoked by transcranial magnetic stimulation. Clinical Neurophysiology, 112(11), 2015-2021.

Ke, Y., Wang, N., Du, J., Kong, L., Liu, S., Xu, M., ... & Ming, D. (2019). The effects of transcranial direct current stimulation (tDCS) on working memory training in healthy young adults. Frontiers in human neuroscience, 13, 19.

Khan, I. S., D'Agostino, E. N., Calnan, D. R., Lee, J. E., & Aronson, J. P. (2019). Deep brain stimulation for memory modulation: a new frontier. World neurosurgery, 126, 638-646.

Kim, K., Ekstrom, A. D., & Tandon, N. (2016). A network approach for modulating memory processes via direct and indirect brain stimulation: toward a causal approach for the neural basis of memory. Neurobiology of learning and memory, 134, 162-177.

Kroes, M. C., Tendolkar, I., Van Wingen, G. A., Van Waarde, J. A., Strange, B. A., & Fernández, G. (2014). An electroconvulsive therapy procedure impairs reconsolidation of episodic memories in humans. Nature neuroscience, 17(2), 204-206.

Kucewicz, M. T., Worrell, G. A., & Axmacher, N. (2023). Direct electrical brain stimulation of human memory: lessons learnt and future perspectives. Brain, 146(6), 2214-2226.

Kundu, B., Johnson, J. S., & Postle, B. R. (2014). Trait-like differences in underlying oscillatory state predict individual differences in the TMS-evoked response. Brain stimulation, 7(2), 234-242.

Labruna, L., Merrick, C., Peterchev, A. V., Inglis, B., Ivry, R. B., & Sheltraw, D. (2024). Kilohertz Transcranial Magnetic Perturbation (kTMP): A New Non-invasive Method to Modulate Cortical Excitability. eLife13:RP92088; https://doi.org/10.7554/eLife.92088.1

Lafon, B., Henin, S., Huang, Y., Friedman, D., Melloni, L., Thesen, T., ... & A. Liu, A. (2017). Low frequency transcranial electrical stimulation does not entrain sleep rhythms measured by human intracranial recordings. Nature communications, 8(1), 1199.

Lapate, R., Heckner, M., Phan, A., Tambini, A., & D'Esposito, M. (2024). Information-based TMS to mid-lateral prefrontal cortex disrupts action goals during emotional processing. Nature Communications, 15(1), 4294.

Lee, T. G., & D'Esposito, M. (2012). The dynamic nature of top-down signals originating from prefrontal cortex: a combined fMRI–TMS study. Journal of Neuroscience, 32(44), 15458-15466.

Lisanby, S. H., Maddox, J. H., Prudic, J., Devanand, D. P., & Sackeim, H. A. (2000). The effects of electroconvulsive therapy on memory of autobiographical and public events. Archives of general psychiatry, 57(6), 581-590.

Liu, A., Vöröslakos, M., Kronberg, G., Henin, S., Krause, M. R., Huang, Y., ... & Buzsáki, G. (2018). Immediate neurophysiological effects of transcranial electrical stimulation. Nature communications, 9(1), 5092.

Lowe, C. J., Manocchio, F., Safati, A. B., & Hall, P. A. (2018). The effects of theta burst stimulation (TBS) targeting the prefrontal cortex on executive functioning: a systematic review and meta-analysis. Neuropsychologia, 111, 344-359.

Luber, B., Davis, S. W., Deng, Z. D., Murphy, D., Martella, A., Peterchev, A. V., & Lisanby, S. H. (2022). Using diffusion tensor imaging to effectively target TMS to deep brain structures. Neuroimage, 249, 118863.

Majdi, A., Asamoah, B., & Mc Laughlin, M. (2023). Reinterpreting published tDCS results in terms of a cranial and cervical nerve co-stimulation mechanism. Frontiers in Human Neuroscience, 17, 1101490.

Manippa, V., Palmisano, A., Nitsche, M. A., Filardi, M., Vilella, D., Logroscino, G., & Rivolta, D. (2024). Cognitive and neuropathophysiological outcomes of gamma-tACS in dementia: a systematic review. Neuropsychology Review, 34(1), 338-361.

Mankin, E. A., & Fried, I. (2020). Modulation of human memory by deep brain stimulation of the entorhinal-hippocampal circuitry. Neuron, 106(2), 218-235.

Mimura, Y., Nishida, H., Nakajima, S., Tsugawa, S., Morita, S., Yoshida, K., ... & Noda, Y. (2021). Neurophysiological biomarkers using transcranial magnetic stimulation in Alzheimer's disease and mild cognitive impairment: A systematic review and meta-analysis. Neuroscience & Biobehavioral Reviews, 121, 47-59.

Misanin, J. R., Miller, R. R., & Lewis, D. J. (1968). Retrograde amnesia produced by electroconvulsive shock after reactivation of a consolidated memory trace. Science, 160(3827), 554-555.

Mizutani-Tiebel, Y., Tik, M., Chang, K. Y., Padberg, F., Soldini, A., Wilkinson, Z., ... & Keeser, D. (2022). Concurrent TMS-fMRI: technical challenges, developments, and overview of previous studies. Frontiers in Psychiatry, 13, 825205.

Molero-Chamizo, A., Sánchez, M. Á. S., Riquel, R. M., Gutiérrez Lérida, C., & Rivera-Urbina, G. N. (2020). Regulation and ethics of transcranial electrical stimulation: a general view. Neurophysiology, 52, 234-238.

Momi, D., Griffiths, J., & Wang, Z. (2021). Modelling large-scale brain network dynamics underlying the TMS-EEG evoked response. Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation, 14(6), 1714.

Monte-Silva, K., Kuo, M. F., Hessenthaler, S., Fresnoza, S., Liebetanz, D., Paulus, W., & Nitsche, M. A. (2013). Induction of late LTP-like plasticity in the human motor cortex by repeated non-invasive brain stimulation. Brain stimulation, 6(3), 424-432.

Müller, D., Habel, U., Brodkin, E. S., & Weidler, C. (2022). High-definition transcranial direct current stimulation (HD-tDCS) for the enhancement of working memory–A systematic review and meta-analysis of healthy adults. Brain stimulation, 15(6), 1475-1485.

Murphy, O. W., Hoy, K. E., Wong, D., Bailey, N. W., Fitzgerald, P. B., & Segrave, R. A. (2020). Transcranial random noise stimulation is more effective than transcranial direct current stimulation for enhancing working memory in healthy individuals: Behavioural and electrophysiological evidence. Brain stimulation, 13(5), 1370-1380.

Nadel, L., Winocur, G., Ryan, L., & Moscovitch, M. (2007). Systems consolidation and hippocampus: two views. Debates in Neuroscience, 1, 55-66.

Nicodemus, N. E., Becerra, S., Kuhn, T. P., Packham, H. R., Duncan, J., Mahdavi, K., ... & Jordan, S. (2019). Focused transcranial ultrasound for treatment of neurodegenerative dementia. Alzheimer's & Dementia: Translational Research & Clinical Interventions, 5, 374-381.

Nissim, N. R., O'Shea, A., Indahlastari, A., Kraft, J. N., von Mering, O., Aksu, S., ... & Woods, A. J. (2019). Effects of transcranial direct current stimulation paired with cognitive training on functional connectivity of the working memory network in older adults. Frontiers in aging neuroscience, 11, 340.

Ozen S, Sirota A, Belluscio MA, Anastassiou CA, Stark E, Koch C, Buzsáki G. Transcranial electric stimulation entrains cortical neuronal populations in rats. J Neurosci. 2010 Aug 25;30(34):11476-85. doi: 10.1523/JNEUROSCI.5252-09.2010. PMID: 20739569; PMCID: PMC2937280.

Pabst, A., Proksch, S., Mede, B., Comstock, D. C., Ross, J. M., & Balasubramaniam, R. (2022). A systematic review and meta-analysis of the efficacy of intermittent theta burst stimulation (iTBS) on cognitive enhancement. Neuroscience & Biobehavioral Reviews, 135, 104587.

Pascual-Leone, A., Walsh, V., & Rothwell, J. (2000). Transcranial magnetic stimulation in cognitive neuroscience–virtual lesion, chronometry, and functional connectivity. Current opinion in neurobiology, 10(2), 232-237.

Penton, T., Bate, S., Dalrymple, K. A., Reed, T., Kelly, M., Godovich, S., ... & Banissy, M. J. (2018). Using high frequency transcranial random noise stimulation to modulate face memory performance in younger and older adults: Lessons learnt from mixed findings. Frontiers in Neuroscience, 12, 422658.

*Phipps, C. J., Murman, D. L., & Warren, D. E. (2021). Stimulating memory: reviewing interventions using repetitive transcranial magnetic stimulation to enhance or restore memory abilities. Brain Sciences, 11(10), 1283.

An excellent review of studies examining the effects of TMS on memory with discussion of important methodological and related issues.

Penfield, W. (1938). The cerebral cortex in man: I. The cerebral cortex and consciousness. Archives of Neurology & Psychiatry, 40(3), 417-442.

Polanía, R., Nitsche, M. A., & Ruff, C. C. (2018). Studying and modifying brain function with non-invasive brain stimulation. Nature neuroscience, 21(2), 174-187.

Polania, R., Kuo, M. F., & Nitsche, M. A. (2021). Physiology of transcranial direct and alternating current stimulation. Transcranial Direct Current Stimulation in Neuropsychiatric Disorders: Clinical Principles and Management, 29-47.

Poppe, A., Ritter, F. D., Bais, L., Pustejovsky, J. E., van Tol, M. J., Ćurčić-Blake, B., ... & van Der Meer, L. (2023). The efficacy of combining cognitive training and noninvasive brain stimulation: A transdiagnostic systematic review and meta-analysis. Psychological Bulletin.

Qu, X., Li, L., Zhou, X., Dong, Q., Liu, H., Liu, H., ... & Niu, H. (2022). Repeated transcranial photobiomodulation improves working memory of healthy older adults: behavioral outcomes of poststimulation including a three-week follow-up. Neurophotonics, 9(3), 035005-035005.

Razza, L. B., De Smet, S., Van Hoornweder, S., De Witte, S., Luethi, M. S., Baeken, C., ... & Vanderhasselt, M. A. (2024). Investigating the variability of prefrontal tDCS effects on working memory: An individual E-field distribution study. Cortex, 172, 38-48.

Reinhart, R. M., Cosman, J. D., Fukuda, K., & Woodman, G. F. (2017). Using transcranial direct-current stimulation (tDCS) to understand cognitive processing. Attention, Perception, & Psychophysics, 79, 3-23.

Reinhart, R. M., & Nguyen, J. A. (2019). Working memory revived in older adults by synchronizing rhythmic brain circuits. Nature neuroscience, 22(5), 820-827.

Redondo-Camós, M., Cattaneo, G., Alviarez-Schulze, V., Delgado-Gallén, S., España-Irla, G., Solana-Sanchez, J., ... & Bartres-Faz, D. (2022). Long-interval intracortical inhibition in primary motor cortex related to working memory in middle-aged adults. Frontiers in psychology, 13, 998062.

Riddle, J., Scimeca, J. M., Pagnotta, M. F., Inglis, B., Sheltraw, D., Muse-Fisher, C., & D'Esposito, M. (2022). A guide for concurrent TMS-fMRI to investigate functional brain networks. Frontiers in Human Neuroscience, 16, 1050605.

Riddle, J., Scimeca, J. M., Cellier, D., Dhanani, S., & D'Esposito, M. (2020). Causal evidence for a role of theta and alpha oscillations in the control of working memory. Current Biology, 30(9), 1748-1754.

Riddle, J., McPherson, T., Sheikh, A., Shin, H., Hadar, E., & Frohlich, F. (2024). Internal Representations Are Prioritized by Frontoparietal Theta Connectivity and Suppressed by alpha Oscillation Dynamics: Evidence from Concurrent Transcranial Magnetic Stimulation EEG and Invasive EEG. Journal of Neuroscience, 44(15).

Rocchi, L., Di Santo, A., Brown, K., Ibánez, J., Casula, E., Rawji, V., ... & Rothwell, J. (2021). Disentangling EEG responses to TMS due to cortical and peripheral activations. Brain stimulation, 14(1), 4-18.

Rogasch, N. C., Daskalakis, Z. J., & Fitzgerald, P. B. (2015). Cortical inhibition of distinct mechanisms in the dorsolateral prefrontal cortex is related to working memory performance: A TMS–EEG study. Cortex, 64, 68-77.

Rogasch, N. C., Sullivan, C., Thomson, R. H., Rose, N. S., Bailey, N. W., Fitzgerald, P. B., … Hernandez-Pavon, J. C. (2017). Analysing concurrent transcranial magnetic stimulation and electroencephalographic data: A review and introduction to the open-source TESA software. NeuroImage, 147, 934–951.

Romei, V., Thut, G., & Silvanto, J. (2016). Information-based approaches of noninvasive transcranial brain stimulation. Trends in Neurosciences, 39(11), 782-795.

Rosanova, M., Casarotto, S., Pigorini, A., Canali, P., Casali, A. G., & Massimini, M. (2012). Combining transcranial magnetic stimulation with electroencephalography to study human cortical excitability and effective connectivity. Neuronal network analysis: concepts and experimental approaches, 435-457.

Rose, N. S., LaRocque, J. J., Riggall, A. C., Gosseries, O., Starrett, M. J., Meyering, E. E., & Postle, B. R. (2016). Reactivation of latent working memories with transcranial magnetic stimulation. Science, 354(6316), 1136-1139.

Rose, Thomson, & Kliegel. 2020. No effect of transcranial direct-current stimulation to dorsolateral prefrontal cortex on naturalistic prospective memory in healthy young and older adults. Journal of Cognitive Enhancement.

Rossi, S., Antal, A., Bestmann, S., Bikson, M., Brewer, C., Brockmöller, J., ... & Hallett, M. (2021). Safety and recommendations for TMS use in healthy subjects and patient populations, with updates on training, ethical and regulatory issues: Expert Guidelines. Clinical Neurophysiology, 132(1), 269-306.

Sauvé, W. M., & Crowther, L. J. (2014). The science of transcranial magnetic stimulation. Psychiatric Annals, 44(6), 279-283.

Sack, A. T., Kadosh, R. C., Schuhmann, T., Moerel, M., Walsh, V., & Goebel, R. (2009). Optimizing functional accuracy of TMS in cognitive studies: a comparison of methods. Journal of cognitive neuroscience, 21(2), 207-221.

Sandrini, M., Xu, B., Volochayev, R., Awosika, O., Wang, W. T., Butman, J. A., & Cohen, L. G. (2020). Transcranial direct current stimulation facilitates response inhibition through dynamic modulation of the fronto-basal ganglia network. Brain stimulation, 13(1), 96-104.

Silvanto, J., & Cattaneo, Z. (2010). Transcranial magnetic stimulation reveals the content of visual short-term memory in the visual cortex. Neuroimage, 50(4), 1683-1689.

Simonotto, E., Riani, M., Seife, C., Roberts, M., Twitty, J., & Moss, F. (1997). Visual perception of stochastic resonance. Physical review letters, 78(6), 1186.

Siebner, H. R., Funke, K., Aberra, A. S., Antal, A., Bestmann, S., Chen, R., ... & Ugawa, Y. (2022). Transcranial magnetic stimulation of the brain: What is stimulated?–a consensus and critical position paper. Clinical Neurophysiology, 140, 59-97.

Siebner, H. R., Hartwigsen, G., Kassuba, T., & Rothwell, J. C. (2009). How does transcranial magnetic stimulation modify neuronal activity in the brain? – Implications for studies of cognition. Cortex, 45, 1035–1042.

Silvanto, J., Muggleton, N. G., Cowey, A., & Walsh, V. (2007). Neural adaptation reveals state-dependent effects of transcranial magnetic stimulation. European Journal of Neuroscience, 25(6), 1874–1881.

Sjöberg, R. L. (2023). Brain stimulation and elicited memories. Acta Neurochirurgica, 165(10), 2737-2745.

Staubli, U., & Lynch, G. (1990). Stable depression of potentiated synaptic responses in the hippocampus with 1–5 Hz stimulation. Brain research, 513(1), 113-118.

Squire, L. R., Genzel, L., Wixted, J. T., & Morris, R. G. (2015). Memory consolidation. Cold Spring Harbor perspectives in biology, 7(8), a021766.

Suthana, N., & Fried, I. (2014). Deep brain stimulation for enhancement of learning and memory. Neuroimage, 85, 996-1002.

Suthana, N., Haneef, Z., Stern, J., Mukamel, R., Behnke, E., Knowlton, B., & Fried, I. (2012). Memory enhancement and deep-brain stimulation of the entorhinal area. New England Journal of Medicine, 366(6), 502-510.

Stagg CJ, Nitsche MA. 2011. Physiological basis of transcranial direct current stimulation. Neuroscientist, 17(1):37-53. doi: 10.1177/1073858410386614. PMID: 21343407.

Tambini, A., Nee, D. E., & D'Esposito, M. (2018). Hippocampal-targeted theta-burst stimulation enhances associative memory formation. Journal of cognitive neuroscience, 30(10), 1452-1472.

Tang, V. M., Trought, K., Gicas, K. M., Kozak, M., Josselyn, S. A., Daskalakis, Z. J., ... & Wong, A. H. (2021). Electroconvulsive therapy with a memory reactivation intervention for post-traumatic stress disorder: A randomized controlled trial. Brain Stimulation, 14(3), 635-642.

Tao, L., Liu, Q., Zhang, F., Fu, Y., Zhu, X., Weng, X., ... & Wei, X. (2021). Microglia modulation with 1070-nm light attenuates Aβ burden and cognitive impairment in Alzheimer's disease mouse model. Light: Science & Applications, 10(1), 179.

Thair, H., Holloway, A. L., Newport, R., & Smith, A. D. (2017). Transcranial direct current stimulation (tDCS): a beginner's guide for design and implementation. Frontiers in neuroscience, 11, 641.

Thut, G., Veniero, D., Romei, V., Miniussi, C., Schyns, P., & Gross, J. (2011). Rhythmic TMS causes local entrainment of natural oscillatory signatures. Current biology, 21(14), 1176-1185.

Trapp, N. T., Tsang, E. W., Bruss, J., Russo, S., Gander, P. E., Berger, J. I., ... & Boes, A. D. (2024). TMS-associated auditory evoked potentials can be effectively masked: Evidence from intracranial EEG. Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation, 17(3), 616-618.

Valero-Cabré, A., Amengual, J. L., Stengel, C., Pascual-Leone, A., & Coubard, O. A. (2017). Transcranial magnetic stimulation in basic and clinical neuroscience: A comprehensive review of fundamental principles and novel insights. Neuroscience & Biobehavioral Reviews, 83, 381-404.

van Boekholdt, L., Kerstens, S., Khatoun, A., Asamoah, B., & Mc Laughlin, M. (2021). tDCS peripheral nerve stimulation: a neglected mode of action?. Molecular psychiatry, 26(2), 456-461.

Van Hoornweder, S., Nuyts, M., Frieske, J., Verstraelen, S., Meesen, R. L., & Caulfield, K. A. (2023). A systematic review and large-scale tES and TMS electric field modeling study reveals how

outcome measure selection alters results in a person-and montage-specific manner. BioRxiv, 2023-02.

Vaqué-Alcázar, L., Mulet-Pons, L., Abellaneda-Pérez, K., Solé-Padullés, C., Cabello-Toscano, M., Macià, D., ... & Bartrés-Faz, D. (2021). tDCS-induced memory reconsolidation effects and its associations with structural and functional MRI substrates in subjective cognitive decline. Frontiers in Aging Neuroscience, 13, 695232.

Veniero, D., Strüber, D., Thut, G., & Herrmann, C. S. (2019). Noninvasive brain stimulation techniques can modulate cognitive processing. Organizational Research Methods, 22(1), 116-147.

Vissani, M., Isaias, I. U., & Mazzoni, A. (2020). Deep brain stimulation: a review of the open neural engineering challenges. Journal of neural engineering, 17(5), 051002.

Vöröslakos, M., Takeuchi, Y., Brinyiczki, K., Zombori, T., Oliva, A., Fernández-Ruiz, A., ... & Berényi, A. (2018). Direct effects of transcranial electric stimulation on brain circuits in rats and humans. Nature communications, 9(1), 483.

Vossen, A., Gross, J., & Thut, G. (2015). Alpha power increase after transcranial alternating current stimulation at alpha frequency (α-tACS) reflects plastic changes rather than entrainment. Brain stimulation, 8(3), 499-508.

Wang, J. X., Rogers, L. M., Gross, E. Z., Ryals, A. J., Dokucu, M. E., Brandstatt, K. L., ... & Voss, J. L. (2014). Targeted enhancement of cortical-hippocampal brain networks and associative memory. Science, 345(6200), 1054-1057.

Warren, K. N., Hermiller, M. S., Nilakantan, A. S., & Voss, J. L. (2019). Stimulating the hippocampal posterior-medial network enhances task-dependent connectivity and memory. elife, 8, e49458.

Weiler M, Stieger KC, Long JM, Rapp PR. Transcranial Magnetic Stimulation in Alzheimer's Disease: Are We Ready?(external link) eNeuro. 2020;7(1).

Widhalm, M. L., & Rose, N. S. (2019). How can transcranial magnetic stimulation be used to causally manipulate memory representations in the human brain?. Wiley Interdisciplinary Reviews: Cognitive Science, 10(1), e1469.

Wischnewski M, Mantell KE, Opitz A. 2021. Identifying regions in prefrontal cortex related to working memory improvement: A novel meta-analytic method using electric field modeling. Neurosci Biobehav Rev;130:147-161. doi: 10.1016/j.neubiorev.2021.08.017. Epub 2021 Aug 18. PMID: 34418436; PMCID: PMC8511213.

Witkowski, M., Garcia-Cossio, E., Chander, B. S., Braun, C., Birbaumer, N., Robinson, S. E., & Soekadar, S. R. (2016). Mapping entrained brain oscillations during transcranial alternating current stimulation (tACS). Neuroimage, 140, 89-98.

Wilhelm, E., Quoilin, C., Petitjean, C., & Duque, J. (2016). A double-coil TMS method to assess corticospinal excitability changes at a near-simultaneous time in the two hands during movement preparation. Frontiers in Human Neuroscience, 10, 88.

Wolff, M. J., Jochim, J., Akyürek, E. G., & Stokes, M. G. (2017). Dynamic hidden states underlying working-memory-guided behavior. Nature neuroscience, 20(6), 864-871.

Woods, A. J., Antal, A., Bikson, M., Boggio, P. S., Brunoni, A. R., Celnik, P., ... & Nitsche, M. A. (2016). A technical guide to tDCS, and related non-invasive brain stimulation tools. Clinical neurophysiology, 127(2), 1031-1048.

Yeh, N., & Rose, N. S. (2019). How can transcranial magnetic stimulation be used to modulate episodic memory?: a systematic review and meta-analysis. Frontiers in Psychology, 10, 423829.

Yonelinas, A. P., Ranganath, C., Ekstrom, A. D., & Wiltgen, B. J. (2019). A contextual binding theory of episodic memory: systems consolidation reconsidered. Nature Reviews Neuroscience, 20(6), 364-375.

Zawadzki, P., & Adamczyk, A. K. (2021). Personality and authenticity in light of the memory-modifying potential of optogenetics. AJOB neuroscience, 12(1), 3-21.

Zaehle, T., Rach, S., & Herrmann, C. S. (2010). Transcranial alternating current stimulation enhances individual alpha activity in human EEG. PloS one, 5(11), e13766.

Zanto, T. P., Rubens, M. T., Thangavel, A., & Gazzaley, A. (2011). Causal role of the prefrontal cortex in top-down modulation of visual processing and working memory. Nature neuroscience, 14(5), 656-661.

Zanto, T. P., Chadick, J. Z., Satris, G., & Gazzaley, A. (2013). Rapid functional reorganization in human cortex following neural perturbation. Journal of Neuroscience, 33(41), 16268-16274.

Zhang, C., Hu, W. H., Wu, D. L., Zhang, K., & Zhang, J. G. (2015). Behavioral effects of deep brain stimulation of the anterior nucleus of thalamus, entorhinal cortex and fornix in a rat model of Alzheimer's disease. Chinese Medical Journal, 128(9), 1190-1195.

Zhao, C., Li, D., Kong, Y., Liu, H., Hu, Y., Niu, H., ... & Song, Y. (2022). Transcranial photobiomodulation enhances visual working memory capacity in humans. Science Advances, 8(48), eabq3211.

Ziemann, U. (2008). Pharmacology of TMS measures. The Oxford Handbook of Transcranial Stimulation, 2008, 135-151.

Zrenner, B., Zrenner, C., Gordon, P. C., Belardinelli, P., McDermott, E. J., Soekadar, S. R., ... & Müller-Dahlhaus, F. (2020). Brain oscillation-synchronized stimulation of the left dorsolateral prefrontal cortex in depression using real-time EEG-triggered TMS. Brain stimulation, 13(1), 197-205.