Neurosci Bull June 1, 2013, 29(3): 381–389. http://www.neurosci.cn
DOI: 10.1007/s12264-013-1309-z

·Review·

Dorsolateral prefrontal cortex, working memory and episodic memory processes: insight through transcranial magnetic stimulation techniques

Michela Balconi

Laboratory of Cognitive Psychology, Department of Psychology, Catholic University of Sacred Heart, Milan, Italy

Corresponding author: Michela Balconi. E-mail: michela.balconi@unicatt.it

The ability to recall and recognize facts we experienced in the past is based on a complex mechanism in which several cerebral regions are implicated. Neuroimaging and lesion studies agree in identifying the frontal lobe as a crucial structure for memory processes, and in particular for working memory and episodic memory and their relationships. Furthermore, with the introduction of transcranial magnetic stimulation (TMS) a new way was proposed to investigate the relationships between brain correlates, memory functions and behavior. The aim of this review is to present the main findings that have emerged from experiments which used the TMS technique for memory analysis. They mainly focused on the role of the dorsolateral prefrontal cortex in memory process. Furthermore, we present state-of-the-art evidence supporting a possible use of TMS in the clinic. Specifically we focus on the treatment of memory deficits in depression and anxiety disorders.

Keywords: transcranial magnetic stimulation; dorsolateral prefrontal cortex; memory; working memory; anxiety; depression

Introduction

Human memory can be defined not only as the ability to correctly or erroneously recall events of the past but also the capacity to generate knowledge fundamental to the evaluation of the world in which we live. Like several cognitive functions, memory processes may be differentiated into several components characterized by specific ways of functioning and the involvement of different cortical areas. Moscovitch[1] proposed a model of memory that has four essential components:

—a non-frontal neocortical component that mediates item-specific performance in implicit tests of memory;

—a modular medial temporal/hippocampal component that mediates the encoding, storage, and retrieval of explicit (specifically episodic) memory tasks that are associative/cue dependent;

—a basal ganglia component that mediates performance on sensorimotor, procedural tests of memory;

—a central system component based on the frontal lobe that mediates performance on explicit tests requiring the use of cognitive strategies.

Neuropsychological and neuroimaging evidence confirms that the frontal lobes play a crucial role in memory processes[2-4]. Furthermore, one study on patients with lesions of the prefrontal cortex (PFC) reported a specific cognitive profile characterized by memory impairment[5]. In particular, several studies seem to converge towards the idea that the PFC, specifically the dorsolateral prefrontal cortex (DLPFC), is crucial in working memory (WM) and episodic memory processes[5]. This important relationship is explored in the present review, to underline the specificity the DLPFC has for this memory ability.

WM is the ability to temporarily maintain and manipulate information. Episodic memory is a long-term memory system that receives and stores information about specific events and their temporal-spatial relationships. It consists of the ability to recall specific events that happened in the past[6]. Since Tulving[6] defines episodic memory as a complex system, he identifies two main temporal components: the perception of the event (the encoding phase) and the private awareness or explicit recall of the event on a later occasion (the retrieval phase).

It is interesting to note that both neuroimaging and clinical evidence show that the same area (the DLPFC) is crucial for WM and episodic memory, suggesting a correlation and interaction between them. In fact, an important component of the WM has been discovered: the episodic buffer. This component consists of a multimodal loop in which phonological and visual information from WM converges with information from long-term memory, promoting the storage process of the new material[7]. It has been hypothesized that the frontal areas are crucial in the functioning of the episodic buffer[8]. Further evidence is provided by Blumenfeld[9] who reported how the DLPFC contributes to the formation of episodic memory through its role in WM organization: increased activation of the DLPFC during tasks requiring the organization of information and the necessity to manage their relationships promotes the strengthening of inter-item association with a resulting enhancement of long-term episodic memory formation[9].

Therefore the implication of the DLPFC in memory processes could be related to these “convergence” functions, which allow, by using an episodic buffer, the use of old information (episodic memories) to better operate on new information (WM). Moreover, an adjunctive factor that was shown to modulate DLPFC activity in memory processes is the asymmetric specificity of the DLPFC as a function of different processing phases, that is the encoding or the retrieval phase. Thus, the debate is still open about the possible asymmetry of activation of the DLPFC during memory processes. The HERA (hemispheric encoding/retrieval asymmetry) model[6] states that there is an hemispheric asymmetry in the encoding and retrieval processes of episodic memory that sees a higher involvement of the left PFC in the encoding phase and a stronger involvement of the right PFC in the retrieval phase.

However several studies partially refuted this hypothesis, since they found a bilateral involvement of the DLPFC in both the encoding[10,11] and retrieval phases[11]. Different models tried to explain these contrasting data. For example the MEM (multiple entry, modular memory system) model[12] assumes that encoding and retrieval processes need to be considered as made by the same perceptual and reflective components and that the latter are associated with a particular activation of the right PFC. In conditions in which the cognitive demand is low, reflective processes (with the exclusive involvement of the right PFC) are sufficient to perform the task, but when the demands grow in complexity, additional aid from the left PFC may be useful.

The relevance of the complexity of the task is underlined also by the CARA (cortical asymmetry of reflective activity) model[13] that affirms that heuristic reflective processes, mediated by the right PFC, are sufficient to perform simple episodic memory tasks, while more systematic processes, mediated by the left PFC, are engaged when episodic memory test demands are high.

The purpose of this article is to review studies focusing on the involvement of the DLPFC in WM and episodic memory, taking into account the lateralization effect related to the encoding and retrieval phases, through a particular technique: transcranial magnetic stimulation (TMS). TMS was previously used to study the significance of specific cortical modules with respect to some cognitive functions, such as language, attention, and memory. Thus, the “perturbation” of these cortical modules induced by TMS may causally explain the role they play in the implicated cognitive functions. We also aim to suggest future research directions in investigations of the role of the DLPFC in memory processes with the TMS method and its potential applications in the clinic. Our review is divided into three main sections: first, we briefly describe the TMS technique and illustrate the main TMS protocols used in memory investigation. Second, we review TMS studies focusing on the role of the DLPFC in WM and episodic memory. Finally, we report and discuss the potential clinical application of TMS of the DLPFC for the treatment of neuronal and psychiatric disorders, such as anxiety and depression.

The TMS Technique

Almost 30 years ago, when TMS was introduced, a new way to investigate brain-behavior relationships was born. TMS, a non-invasive tool for the magnetic stimulation of neuronal tissue based on Faraday’s principle of electromagnetic induction, allows us to investigate the relationship between cortical activity and behavior. Before TMS, the ‘lesion approach’ ruled the world of neuroscience and clinical neuropsychology. Functional neuroimaging methods such as fMRI help us to identify changes in brain activity correlated with cognitive performance beyond pathology. However they often leave unclear whether such activations are necessary (in term of causality) for specific cognitive functions or only associated with them. Nowadays, the TMS paradigm, thought of as the creation of a "perturbation", offers a unique opportunity to interact directly with the functioning of a cortical area during the execution of a cognitive task. This has made TMS such a useful tool for investigating the causal relationships between cortical areas and behavior in normal and pathological cases[14].

At the beginning, TMS was almost exclusively applied to spinal roots, and cranial and peripheral nerves[15]. Recently, it has become an important tool in the study of cognition, neurological and psychiatric disorders, neuroplasticity, and recovery[16]. Different TMS protocols may be applied to the investigation of cortical involvement in different cognitive functions. These protocols are the outcome of the interaction of two main parameters:

—strength of stimulation, defined as percentage of the maximum stimulator output;

—the frequency of stimulation (the number of pulses delivered in 1 s).

A specific stimulation modality, that is repetitive TMS (rTMS), which uses repetitive stimulation within a specific time interval, may be applied at low frequency (no more than 1 Hz) or high frequency (>1 Hz). In general, lower frequencies (~1 Hz) are thought to suppress cortical excitability, while high-frequency rTMS may result in a temporary increase of cortical excitability. Depending on the stimulation frequency, inhibitory or facilitatory effects have been observed at the behavioral level. It has been hypothesized that the physiological mechanisms of these after-effects may be connected to long-term potentiation and long-term depression of cortical synapses although this is still unclear.

The efficacy of TMS in cortical modulation has been demonstrated in several studies: in a review of 51 experiments with an overall sample of 650 participants the authors reported robust effects of ~1 h duration on a cerebral physiologic index (EEG) after a single session of TMS[17]. However, it is important to point out that so far no study has measured the EEG after-effects induced by multiple session of rTMS. In any case, there are exciting prospects for the use of TMS as a tool to promote changes of brain activity and consequent behavioral improvements, although, at present, these are generally short-lived.

TMS Studies on DLPFC in Memory Processes

In this section, we discuss specific findings from TMS studies that we consider especially relevant to the understanding of the role of the DLPFC in WM and episodic memory.

WM and TMS

Although WM is accessible to the innovation of TMS, few studies have investigated this aspect of memory processes. Furthermore, the studies had different aims and paradigms. The first group of relevant studies[18-22] aimed to verify the hypothesis that the DLPFC plays a crucial role in WM by using the TMS technique. All the studies agree in finding that the DLPFC is involved in the performance of WM tasks, in particular those tasks in which the manipulation of information is required. These important findings confirmed the relevant role of the DLPFC not only in information processing but also in the operations that are necessary to manipulate information. More recently, other studies followed this line of research and replicated the data that emerged from previous studies: for example Osaka showed the crucial role of the left DLPFC in WM[23] and Preston[24] showed that the DLPFC is crucial for neural efficacy (defined as the ratio between accuracy and response time). The contribution to specific "types" of WM was investigated by Mull *et al.*[25], who found an important distinction between the important role that the left DLPFC plays in response to a verbal task (sequential-letter) and the right DLPFC which is not directly implicated in this task. Moreover, Mottaghy and others[20-22] investigated the chronometry of the DLPFC involvement in WM and reported how TMS really interferes with the WM task if applied later than 180 ms after the stimulus onset. In fact, they found that the processing of information in WM follows a flow from posterior to anterior regions, and from right to left hemisphere within the PFC[20]. An interesting study by Hadland[26] explored the relationship between response selection and WM function within the DLPFC, by separating response tasks that require or do not require WM. Finally, some important studies analyzed the relationship between the PFC and sensory information processing. These studies demonstrated that the PFC improves WM maintenance[27], with better performance and improved WM performance by the DLPFC pathway[28].

Thus, these studies focused on the “specificity” of the DLPFC for WM processes that are related to specific tasks or specific operations supported by WM.

Episodic Memory and TMS

In this section, we review findings that emerged from studies that investigated the issue of the neural correlates of episodic memory using TMS techniques. Two main branches of research tried to explain the hemispheric specialization of frontal structures: the first branch affirms that the different involvement of the right and left DLPFC is determined by the nature of the material processed. In particular, the left DLPFC is supposed to be crucial for the encoding/retrieval of verbal information, while the right DLPFC seems to manage the encoding/retrieval of non-verbal material. The other branch, instead, states that the crucial involvement of the left/right frontal structures is associated with the process in action rather that the nature of the material processed. Following this latter perspective, and in particular the HERA model[6], the left DLPFC is fundamental for encoding processes and the right DLPFC for retrieval processes. The debate on this issue is still open and several authors continue to investigate this controversial field. For example, Gagnon in two experimental studies[29, 30] using both verbal and non-verbal stimuli, observed how in the encoding phase only TMS stimulation of the left DLPFC was able to interfere with both accuracy and response times. In the retrieval phase, instead, stimulation of the right DLPFC was able to affect the accuracy and the response times of the memory performance. The interesting results from these two studies were that they did not report differences either for accuracy or for response time in the encoding/retrieval between verbal and non-verbal material. Also, Rossi *et al.*[31] in a study with pictorial information, reported that the left DLPFC is involved in encoding operations while the right DLPFC is crucial for retrieval, providing evidence for the idea that even with non-verbal material the left DLPFC is implicated in encoding while the right DLPFC is involved in the retrieval phase. Further evidence for the crucial role of the left DLPFC was provided by Innocenti *et al.*[32] who investigated the asymmetry of the DLPFC in encoding through a paradigm that differentiates between deep (semantic) and shallow (perceptual) encoding. They found that the left but not the right DLPFC is involved during encoding for both semantic and phonological strategies, since rTMS affects response times at retrieval for both the encoding conditions. Furthermore, stimulation of the left DLPFC at encoding seems to erase the positive effect of the deep encoding on the shallow encoding during retrieval performance. Hence, it looks like the involvement of the DLPFC is generally associated with the encoding process but it seems also to be strictly connected to the way in which we encode material. In effect, Manenti *et al.*[33] focused attention on the effect that the use of strategies during memory recall may have on behavioral performance and which areas are implicated in this process. They first found a bilateral involvement of the DLPFC during the memory retrieval process. Furthermore, they observed how hemispherical specialization is associated with the use of cognitive strategies: when they stimulated the right DLPFC in participants who reported the use of some strategies, they found a change in their ability to successfully recall information, while TMS of the left DLPFC did not affect their performance. In addition, left, but not right, DLPFC TMS interferes with memory processes only in those participants who do not use cognitive strategies. Moreover, different strategy types may determine a different involvement of the DLPFC: the dual-coding theory[34] claims that in the encoding phase the use of strategies based on a verbal code requires selective and predominant activation of the left PFC, while the right hemisphere is particularly involved in managing strategies based on images. Hence, the dual-coding model is able to explain the bilateral DLPFC involvement in episodic encoding, since participants may use a mixture of verbal and non-verbal strategies.

However, Sandrini *et al.*[10] reported that the involvement of the DLPFC is only connected with the processing of unrelated stimuli (word-pairs). When they stimulated the DLPFC of normal participants in a task in which they were required to recognize related and unrelated word-pairs, only the performance of the new (unrelated) word-pairs was affected by TMS. The supposition that the DLPFC is particularly involved in the processing of novel information is confirmed also by ERP[35] and behavioral studies[36].

On the other hand, several authors[37] reported that the right DLPFC, but not the left, contributes to the encoding of visual-object associations[38] and the left but not the right DLPFC plays a crucial role in the encoding of verbal material[36, 37], supporting the theories of material specificity.

Although the studies confirming this material-specific point of view provide controversial evidence, factors specifically related to the stimulus, beyond their verbal/nonverbal nature, may determine the different involvement of the DLPFC in episodic memory processes. For example, emotional content may modulate the cortical asymmetry. Several studies provide evidence for the hypothesis called the "valence model", which states that withdrawal-related emotions are located in the right hemisphere whereas approach-related emotions are biased to the left hemisphere[36,38]. Focusing on the TMS technique, Balconi *et al.*[39,40] found an increased facilitation of the retrieval of positive emotional cues (in terms of reduced response times) under stimulation of the left DLPFC during the retrieval phase. On the contrary, the memory performance relative to negative information was not influenced by left frontal stimulation.

Potential Applications in the Clinic: Mood Disorders and Memories

The efficacy of TMS on cortical modulation has been demonstrated by several studies. Since these preliminary studies, the possibility of applying neurostimulation techniques to rehabilitation is gaining ground among both clinicians and researchers. However, this approach needs to be carefully evaluated by experimental studies, since clinical trials conducted so far seem to suggest a promising future but they are far from reaching a conclusion on the efficacy of TMS. In this section, we aim to present the current state of the debate surrounding the possibility of introducing TMS techniques in the treatment of depression and anxiety disorders, with particular attention to the rehabilitation of the memory deficits associated with these clinical profiles. In particular, we focus on those studies that investigate the efficacy of TMS of the DLPFC in potentiating memory performance and in resolving clinical symptoms.

The idea of introducing TMS to treat anxiety and mood disorders emerged when researchers realized that the stimulation of specific areas may interfere with the evaluation and regulation of emotions. In particular, several studies identified the DLPFC as a crucial area in emotion monitoring, since it seems to manage the cognitive control over emotional stimuli and emotional behavior. Many neuropsychological models were proposed to explain anxiety and depression, taking into account the role of the PFC (among other cerebral areas such as the amygdala, hippocampus, and thalamus) in the etiology of these pathologies.

However, different hypotheses have been suggested to explain the fundamental involvement of this cortical region. Similar to the debate about WM and episodic memory, the evidence for hemispheric specialization is controversial and different models have been proposed. We tried to support some evidence related to the direct incidence by left/right hemisphere in processing emotional cues. Second, the overview furnished here underlines the possible rehabilitative applications of neuromodulation techniques, considering the direct effect that TMS may have when applied to the PFC with respect to WM performance in patients.

Bishop[41] suggested that the PFC could serve emotional regulation through its role in the mechanism of inhibition: the frontal structures act to control (through a top-down mechanism) the pre-attentive emotional processes of the amygdala[42,43]. Consequently, an increased state of anxiety, even in sub-clinical healthy participants, induces a reduced involvement of prefrontal control resuting in the inability to ignore emotional but irrelevant information. The ability to suppress this automatic processing would be specifically impaired in subjects with anxiety disorder[44].

In addition, Tucker *et al.*[42] suggested that anxiety may be explained by dysfunctional hyperactivity of the left hemisphere. This hypothesis has been supported by EEG studies[43] and neuroimaging experiments (e.g.,[44]). Contrasting data that emerged in subsequent years led Heller[45] to conclude that anxiety is associated with greater right-hemisphere activity. Besides Heller's experimental studies on perceptual hemispatial bias[45], evidence for this hypothesis was provided by neuroimaging studies on the mechanism of functioning of anti-anxiety medications that reduce anxiety symptoms and limit the metabolism of the right hemisphere[46]. In line with this model, recently the "valence" model has been proposed to explain the relationship between anxiety and emotional information processing. As noted above, this model supposes specialization of the right hemisphere for withdrawal-related emotions and of the left hemisphere for approach-related emotions[47,48]. Since anxiety seems to be associated with dysfunctional right-hemispheric activity with increased activation, the valence model is able to explain the bias towards withdrawal-related emotions and the processing of aversive conditions[49,50]. Consequently, the bias for negative stimuli leads to the characteristic hyper-vigilant attention to negative information and to unbalanced processing of negative/positive stimuli[51]. Finally, it is interesting to note that Davidson's model may be useful to conceptualize both depression and anxiety, since they manifest a similar pattern of anterior activity characterized by interhemispheric imbalance[51,52].

Concerning depression, Pascual-Leone and colleagues were the first to apply TMS in the psychiatric field and they found that rTMS applied over the left medial PFC increases sadness in healthy participants[53]. Since 1993, when TMS was used for the first time with therapeutic intent in depression, mood disorder continues to be the most commonly studied psychiatric pathology. The studies that tested the efficacy of TMS identified the DLPFC as the area of main interest for different reasons: the DLPFC is reported to be involved in mood regulation, and lesion and neuroimaging studies show that left PFC dysfunction is physiologically linked to primary and secondary depression[51,52].

Several reviews on these issues have been published in recent years but they drew different conclusions. Gross and colleagues[54] in a meta-analysis study showed how recent clinical trials of rTMS on depression (both high-frequency stimulation of the left DLPFC and low-frequency stimulation of the right DLPFC) induced a greater effect than in the initial studies (e.g.[55]). They suggested that the recent evidence for the antidepressant effects of TMS over the left/right DLPFC may be due to the development of new paradigms of stimulation (such as more rTMS sessions, or study designs with larger sample sizes) able to optimize the therapeutic potential of TMS. In fact, in a recent review investigating the efficacy of TMS in treating mood disorders, a clear statistical superiority of the treatment over placebo effects emerged, although small clinical effects have been reported[54].

In this regard, we suggest that a critical review should take into account several potential limitations due to different factors, such as a duration of treatment (<2/4 weeks) that may be inadequate to determine changes in behavior and clinical profile. Only a few studies have reported the results of longer periods of stimulation and they suggest that a longer course of rTMS may be crucial for optimal therapeutic outcomes.

Although in 2008 TMS was approved by the U.S. Food and Drug Administration for the treatment of depressed subjects who do not primarily respond to antidepressant medication, its use as a therapy is still controversial specifically for anxiety disorders, as there are not yet sufficient studies to surely affirm that the treatment works. However, what emerged from the first studies is that mainly obsessive-compulsive disorder seems to benefit from rTMS treatment, while the published and unpublished data for panic disorder and post-traumatic stress disorder are controversial[16].

But what about memory functions? We have collected evidence for the crucial role of the DLPFC in memory functions. Moreover, we considered evidence that TMS treatment applied to the DLPFC should affect not only mood regulation but also the memory-related symptoms. Several studies showed how memory functions are affected in depression, specifically WM[56] and the encoding and retrieval of episodic memory[57]. Also, in anxiety disorders these memory processes seem to be deficient[58].

However, TMS is a potentially useful tool in the treatment of these symptoms. Our recent work found that TMS of the left DLPFC, in participants with high levels of anxiety, facilitates the retrieval of positive, but not of negative, emotional cues (reduced response times and increased accuracy), while in participants with low levels of anxiety performance is not affected (data in press). Furthermore, the performance of participants with high anxiety without TMS is characterized by a positive bias towards negative information, creating an imbalance between the retrieved positive/negative information, which decreases with TMS of the left DLPFC. Unfortunately, no other study has been implemented on mood and anxiety disorders. However, studies on other pathologies involving the dysfunction of frontal structures (e.g. Alzheimer syndrome) seem to show benefits from treatment based on the TMS technique in terms of memory[59].

Thus, future integration is necessary to confirm (or refute) the real potential of neuromodulation for WM functions in the treatment of anxiety, and mainly, depression. More specifically, a wider debate should include consideration of the variety of stimulation techniques and the modification of stimulus parameters (such as TMS or rTMS).

Conclusions

The aim of this review was to present data emerging from studies using the TMS technique to investigate the role of the DLPFC in memory processes. All the studies agree in attributing to the DLPFC a crucial role in WM and episodic memory. To summarize the main function the DLPFC in both WM and episodic memory it was suggested the DLPFC allows the use of old information (episodic memories) to better operate on new information (WM) by activating an episodic buffer.

However, some main points remain to be elucidated, such as the specific functions that left *versus* right DLPFC have in the encoding and retrieval phases of the memory process. In this regard, the debate about a possible asymmetric contribution by frontal structures in the encoding/retrieval phases remains open. We present different models and data supporting a possible lateralization effect.

In addition, the hypothesis that specific characteristics of the stimuli may interfere with these memory processes is emerging in TMS studies: the emotional valence of the processed material seems to strongly modulate the DLPFC activity. This hypothesis is acquiring more and more importance in both the experimental and clinical fields. In fact, it provides us an explanatory model of emotion processing and emotional dysregulation, and allows us to better conceptualize such “emotional syndromes” as mood and anxiety disorders.

Furthermore, the “valence model” combined with the TMS technique provides a potentially useful tool for the treatment of mood and anxiety disorders with specific reference to the impairment of emotional memories. To support this potential, it was shown that TMS applied to the frontal lobe should be able to improve the cognitive control of emotional information and to restore the bias toward negative stimuli, which is characteristic of depression and anxiety disorders. However, so far, few studies have investigated how TMS may impact on memory performance in order to restore the negative/positive imbalance both in processing information and managing emotions.

Received date: 2012-07-16; Accepted date: 2012-11-02

REFERENCES

[1] Moscovitch, A. Neuropsychology of Memory. 2nd ed. New York: Guilford Press, 1992: 5–22.

[2] Brenda Milner MP. Behavioural effects of frontal-lobe lesions in man. Trends Neurosci 1984, 7: 403–407.

[3] Petrides M. Frontal Lobes and Memory. 2nd ed. New York: Elsevier Science Publishers, 1989: 75–90.

[4] Fletcher PC, Shallice T, Frith CD, Frackowiak RS, Dolan RJ. The functional roles of prefrontal cortex in episodic memory. II. Retrieval. Brain 1998, 121 (Pt 7): 1249–1256.

[5] Curtis CE, D'Esposito M. Persistent activity in the prefrontal cortex during working memory. Trends Cogn Sci 2003, 7: 415–423.

[6] Tulving E. Précis of Elements of episodic memory. Behav Brain Sci 1984, 7: 223–268.

[7] Baddeley A. The episodic buffer: a new component of working memory? Trends Cogn Sci 2000, 4: 417–423.

[8] Papagno C. Neuropsicologia della Memoria [Neuropsychology of Memory]. Bologna: Il Mulino, 2010.

[9] Blumenfeld RS, Ranganath C. Dorsolateral prefrontal cortex promotes long-term memory formation through its role in working memory organization. J Neurosci 2006, 26: 916–925.

[10] Sandrini M, Cappa SF, Rossi S, Rossini PM, Miniussi C. The role of prefrontal cortex in verbal episodic memory: rTMS evidence. J Cogn Neurosci 2003, 15: 855–861.

[11] Schmidt D, Krause BJ, Mottaghy FM, Halsband U, Herzog H, Tellmann L*, et al.* Brain systems engaged in encoding and retrieval of word-pair associates independent of their imagery content or presentation modalities. Neuropsychologia 2002, 40: 457–470.

[12] Johnson MK, Multhaup KS. The Handbook of Emotion and Memory: Current Research and Theory. Hillsdale: Erlbaum Associates, 1992: 33–66.

[13] Nolde SF, Johnson MK, Raye CL. The role of prefrontal cortex during tests of episodic memory. Trends Cogn Sci 1998, 2: 399–406.

[14] Miniussi C, Ruzzoli M, Walsh V. The mechanism of transcranial magnetic stimulation in cognition. Cortex 2010, 46: 128–130.

[15] Chen R, Classen J, Gerloff C, Celnik P, Wassermann EM, Hallett M*, et al.* Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation. Neurology 1997, 48: 1398–1403.

[16] George MS, Padberg F, Schlaepfer TE, O'Reardon JP, Fitzgerald PB, Nahas ZH*, et al.* Controversy: Repetitive transcranial magnetic stimulation or transcranial direct current stimulation shows efficacy in treating psychiatric diseases (depression, mania, schizophrenia, obsessive-complusive disorder, panic, posttraumatic stress disorder). Brain Stimul 2009, 2: 14–21.

[17] Thut G, Pascual-Leone A. A review of combined TMS-EEG studies to characterize lasting effects of repetitive TMS and assess their usefulness in cognitive and clinical neuroscience. Brain Topogr 2010, 22: 219–232.

[18] Pascual-Leone A, Hallett M. Induction of errors in a delayed response task by repetitive transcranial magnetic stimulation of the dorsolateral prefrontal cortex. Neuroreport 1994, 5: 2517–2520.

[19] Jahanshahi M, Profice P, Brown RG, Ridding MC, Dirnberger G, Rothwell JC. The effects of transcranial magnetic stimulation over the dorsolateral prefrontal cortex on suppression of habitual counting during random number generation. Brain 1998, 121 (Pt 8): 1533–1544.

[20] Mottaghy FM, Krause BJ, Kemna LJ, Topper R, Tellmann L, Beu M, *et al.* Modulation of the neuronal circuitry subserving working memory in healthy human subjects by repetitive transcranial magnetic stimulation. Neurosci Lett 2000, 280: 167–170.

[21] Mottaghy FM, Gangitano M, Krause BJ, Pascual-Leone A. Chronometry of parietal and prefrontal activations in verbal working memory revealed by transcranial magnetic stimulation. Neuroimage 2003, 18: 565–575.

[22] Postle BR, Ferrarelli F, Hamidi M, Feredoes E, Massimini M, Peterson M, *et al.* Repetitive transcranial magnetic stimulation dissociates working memory manipulation from retention functions in the prefrontal, but not posterior parietal, cortex. J Cogn Neurosci 2006, 18: 1712–1722.

[23] Osaka N, Otsuka Y, Hirose N, Ikeda T, Mima T, Fukuyama H, *et al.* Transcranial magnetic stimulation (TMS) applied to left dorsolateral prefrontal cortex disrupts verbal working memory performance in humans. Neurosci Lett 2007, 418: 232–235.

[24] Preston G, Anderson E, Silva C, Goldberg T, Wassermann EM. Effects of 10 Hz rTMS on the neural efficiency of working memory. J Cogn Neurosci 2010, 22: 447–456.

[25] Mull BR, Seyal M. Transcranial magnetic stimulation of left prefrontal cortex impairs working memory. Clin Neurophysiol 2001, 112: 1672–1675.

[26] Hadland KA, Rushworth MF, Passingham RE, Jahanshahi M, Rothwell JC. Interference with performance of a response selection task that has no working memory component: an rTMS comparison of the dorsolateral prefrontal and medial frontal cortex. J Cogn Neurosci 2001, 13: 1097–1108.

[27] Chao LL, Knight RT. Contribution of human prefrontal cortex to delay performance. J Cogn Neurosci 1998, 10: 167–177.

[28] Hannula H, Neuvonen T, Savolainen P, Hiltunen J, Ma YY, Antila H, *et al.* Increasing top-down suppression from prefrontal cortex facilitates tactile working memory. Neuroimage 2010, 49: 1091–1098.

[29] Gagnon G, Blanchet S, Grondin S, Schneider C. Paired-pulse transcranial magnetic stimulation over the dorsolateral prefrontal cortex interferes with episodic encoding and retrieval for both verbal and non-verbal materials. Brain Res 2010, 1344: 148–158.

[30] Gagnon G, Schneider C, Grondin S, Blanchet S. Enhancement of episodic memory in young and healthy adults: a paired-pulse TMS study on encoding and retrieval performance. Neurosci Lett 2011, 488: 138–142.

[31] Rossi S, Cappa SF, Babiloni C, Pasqualetti P, Miniussi C, Carducci F, *et al.* Prefrontal [correction of Prefontal] cortex in long-term memory: an "interference" approach using magnetic stimulation. Nat Neurosci 2001, 4: 948–952.

[32] Innocenti I, Giovannelli F, Cincotta M, Feurra M, Polizzotto NR, Bianco G, *et al.* Event-related rTMS at encoding affects differently deep and shallow memory traces. Neuroimage 2010, 53: 325–330.

[33] Manenti R, Tettamanti M, Cotelli M, Miniussi C, Cappa SF. The neural bases of word encoding and retrieval: A fMRI-guided transcranial magnetic stimulation study. Brain Topogr 2010, 22: 318–332.

[34] Paivio A. Dual coding theory: Retrospect and current status. Can J Psychol 1991, 45: 255–287.

[35] Kishiyama MM, Yonelinas AP, Knight RT. Novelty enhancements in memory are dependent on lateral prefrontal cortex. J Neurosci 2009, 29: 8114–8118.

[36] Skrdlantova L, Horacek J, Dockery C, Lukavsky J, Kopecek M, Preiss M, *et al.* The influence of low-frequency left prefrontal repetitive transcranial magnetic stimulation on memory for words but not for faces. Physiol Res 2005, 54: 123–128.

[37] Floel A, Poeppel D, Buffalo EA, Braun A, Wu CW, Seo HJ, *et al.* Prefrontal cortex asymmetry for memory encoding of words and abstract shapes. Cereb Cortex 2004, 14: 404–409.

[38] Epstein CM, Sekino M, Yamaguchi K, Kamiya S, Ueno S. Asymmetries of prefrontal cortex in human episodic memory: effects of transcranial magnetic stimulation on learning abstract patterns. Neurosci Lett 2002, 320: 5–8.

[39] Balconi M, Ferrari C. Emotional memory retrieval. rTMS stimulation on left DLPFC increases the positive memories. Brain Imaging Behav 2012, 6: 454–461.

[40] Balconi M, Ferrari C. rTMS stimulation on left DLPFC increases the correct recognition of memories for emotional target and distractor words. Cogn Affect Behav Neurosci 2012, 12: 589–598.

[41] Bishop S, Duncan J, Brett M, Lawrence AD. Prefrontal cortical function and anxiety: controlling attention to threat-related stimuli. Nat Neurosci 2004, 7: 184–188.

[42] Tucker DM, Antes JR, Stenslie CE, Barnhardt TM. Anxiety and lateral cerebral function. J Abnorm Psychol 1978, 87: 380–383.

[43] Carter WR, Johnson MC, Borkovec TD. Worry: An electrocortical analysis. Adv Behav Res Ther 1986, 4: 193–204.

[44] Baxter LR Jr, Schwartz JM, Phelps ME, Mazziotta JC, Guze BH, Selin CE, *et al.* Reduction of prefrontal cortex glucose metabolism common to three types of depression. Arch Gen Psychiatry 1989, 46: 243–250.

[45] Heller W, Etienne MA, Miller GA. Patterns of perceptual asymmetry in depression and anxiety: implications for neuropsychological models of emotion and psychopathology. J Abnorm Psychol 1995, 104: 327–333.

[46] Buchsbaum MS, Wu J, Haier R, Hazlett E, Ball R, Katz M*, et al.* Positron emission tomography assessment of effects of benzodiazepines on regional glucose metabolic rate in patients with anxiety disorder. Life Sci 1987, 40: 2393–2400.

[47] Balconi M, Brambilla E, Falbo L. Appetitive vs. defensive responses to emotional cues. Autonomic measures and brain oscillation modulation. Brain Res 2009, 1296: 72–84.

[48] Davidson RJ, Irwin W. The functional neuroanatomy of emotion and affective style. Trends Cogn Sci 1999, 3: 11–21.

[49] Zwanzger P, Fallgatter AJ, Zavorotnyy M, Padberg F. Anxiolytic effects of transcranial magnetic stimulation--an alternative treatment option in anxiety disorders? J Neural Transm 2009, 116: 767–775.

[50] van Honk J, Tuiten A, Verbaten R, van den Hout M, Koppeschaar H, Thijssen J*, et al.* Correlations among salivary testosterone, mood, and selective attention to threat in humans. Horm Behav 1999, 36: 17–24.

[51] Bench CJ, Frackowiak RS, Dolan RJ. Changes in regional cerebral blood flow on recovery from depression. Psychol Med 1995, 25: 247–261.

[52] Drevets WC. Functional anatomical abnormalities in limbic and prefrontal cortical structures in major depression. Prog Brain Res 2000, 126: 413–431.

[53] Pascual-Leone A, Catala MD, Pascual-Leone Pascual A. Lateralized effect of rapid-rate transcranial magnetic stimulation of the prefrontal cortex on mood. Neurology 1996, 46: 499–502.

[54] Gross M, Nakamura L, Pascual-Leone A, Fregni F. Has repetitive transcranial magnetic stimulation (rTMS) treatment for depression improved? A systematic review and meta-analysis comparing the recent vs. the earlier rTMS studies. Acta Psychiatr Scand 2007, 116: 165–173.

[55] Martin JL, Barbanoj MJ, Schlaepfer TE, Thompson E, Perez V, Kulisevsky J. Repetitive transcranial magnetic stimulation for the treatment of depression. Systematic review and meta-analysis. Br J Psychiatry 2003, 182: 480–491.

[56] Weiland-Fiedler P, Erickson K, Waldeck T, Luckenbaugh DA, Pike D, Bonne O*, et al.* Evidence for continuing neuropsychological impairments in depression. J Affect Disord 2004, 82: 253–258.

[57] Brand AN, Jolles J, Gispen-de Wied C. Recall and recognition memory deficits in depression. J Affect Disord 1992, 25: 77–86.

[58] Airaksinen E, Larsson M, Forsell Y. Neuropsychological functions in anxiety disorders in population-based samples: evidence of episodic memory dysfunction. J Psychiatr Res 2005, 39: 207–214.

[59] Sole-Padulles C, Bartres-Faz D, Junque C, Clemente IC, Molinuevo JL, Bargallo N*, et al.* Repetitive transcranial magnetic stimulation effects on brain function and cognition among elders with memory dysfunction. A randomized sham-controlled study. Cereb Cortex 2006, 16: 1487–1493.