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Research Report

The influence of rTMS over the right dorsolateral prefrontal cortex on top-down attentional processes

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ABSTRACT

Repetitive Transcranial Magnetic Stimulation (rTMS) provides a unique opportunity to study causal relationships between activity in the dorsolateral prefrontal cortex (DLPFC) and executive functioning, by modulating brain activity in SHAM controlled designs. We devised a new Stroop task paradigm in which subjects must engage in both strategic and automatic attentional processes. In the current experiment, we manipulated subjects' expectancies for incongruent stimuli. Previous research demonstrated that when subjects have a high level of expectancy that a stimulus will be incongruent, they are able to strategically adjust the relative influence of word reading on color naming. The effect of high frequency (HF) rTMS on Stroop performance of 20 right-handed healthy female volunteers was tested using a double blind within subjects design by counterbalanced crossover sham (placebo) and active rTMS over the right DLPFC. Since mood remained unchanged after rTMS, the Stroop data could be evaluated independent of mood changes. Only in the high expectancy condition, we found a decreased response time to both congruent and incongruent trials on the Stroop task performance after HF rTMS. The SHAM placebo condition yielded no effects. We conclude that high frequency stimulation over the right DLPFC has an effect on top-down attentional processes by modulating the attentional set.

1. Introduction

Repetitive Transcranial Magnetic Stimulation (rTMS) has been used as a non-invasive tool for stimulating the human cerebral cortex and, as a result, becomes a heuristic technique of neuronal depolarizing and altering underlying cortical physiology. This technique is capable of transiently disrupting local processing in neural networks in the brain. High-frequency rTMS (above 1 Hz) evokes increased excitability of the stimulated cortical region, an activation pattern that lasts for hours after stimulation (Muller et al., 2000; Wasserman and Lisanby, 2001; Pascual-Leone et al., 1994). rTMS provides a unique opportunity to study causal relationships between focal brain function and behavior. It can provide more insight into the workings of the neural circuits involved in executive functioning, by modulating brain activity in SHAM controlled designs (Moser et al., 2002).

A well-studied behavioral paradigm of controlled attention selection is the Stroop task (Stroop, 1935). The principle is that word reading – a highly automatic ability – interferes with

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color naming when a color–word noun, e.g. the word "RED" is printed in green and the task is to name the word's printed color. The Stroop interference is characterized by a slower response in naming these incongruent words as compared to color-congruent words. Studies using functional neuroimaging techniques have linked Stroop task performance to activity in the dorsolateral prefrontal cortex (DLPFC) (Hadland et al., 2001).

Neuropsychological and neuroimaging studies revealed that the DLPFC implements top-down attentional control (Milham et al., 2003). Specific lateralized involvement of the DLPFC in cognitive control is becoming a latest source of debate. Although top-down attentional processes are commonly associated to the left DLPFC (MacDonald et al., 2000), recent research revealed an essential role of the right DLPFC in task preparation (Vanderhasselt et al., 2006b, Brass and Von Cramon, 2004; Dreher et al., 2000; Sohn et al., 2000) and conflict predicting in cued switching tasks (Liston et al., 2006).

We are aware of only one study to date in which the standard color word Stroop performance has been compared before and after HF-rTMS over the DLPFC, while mood was kept under control (Vanderhasselt et al., 2006a). The latter might be essential since mood has an important influence on executive functioning (Bechara and Damasio, 2005). Results demonstrated the involvement of the left DLPFC in implementing top-down attentional set. To our knowledge, analogous research regarding rTMS over the right DLPFC has not yet been reported. The aim of the present study is to investigate the role of the right DLPFC in imposing top-down attentional set. We constructed a novel behavioral Stroop paradigm, based on former research (Carter et al., 1999; MacDonald et al., 2000), to unambiguously activate top-down attentional processes, which have been associated to activity in the DLPFC (Milham et al., 2003).

In our new paradigm, before the onset of each trial, subjects must keep in mind, or actively maintain, the instruction. This task cue can have two different dimensions, namely the instruction to read the word (automatic process) and the instruction to name the color of the word (strategic process) (MacDonald et al., 2000). In addition, subjects perform the Stroop task under the conditions "high expectancy" and "no expectancy" for incongruent stimuli by blocked manipulation of the frequency of incongruent trials (Carter et al., 1999). Top-down attentional processes will particularly be activated when strategic processes are engaged (after instruction "color") *and* when expectancy for incongruent trials is high (anticipation for the upcoming event is possible in high expectancy blocks). These processes, associated to the DLPFC (Carter et al., 1999), facilitate a high degree of top-down control whereby the tendency to read the word should be overcome and conflict associated with responding to incongruent stimuli should be reduced. Therefore, we hypothesize that HF-rTMS over the right DLPFC will cause faster reaction time to incongruent trials after the instruction "color" in "high expectancy" blocks compared to the "no expectancy" blocks. More specific, if HF-rTMS over the right DLPFC improves the attentional set, the strategic processes that are particularly involved in the abovementioned condition will be facilitated and reaction time on incongruent trials will decrease. After the "word reading" instruction, we expect no effects since in this condition no attentional control over automatic responses is required. Effects in this condition would suggest general speeding effects of rTMS unrelated to the attentional set.

To our knowledge, attentional orientating combined with HF rTMS over the right DLPFC to investigate the influence on top-down attentional control, has not yet been performed. Comparable rTMS research where the influence of mood was taken under control is currently very scarce. In one former similar study (Vanderhasselt et al., 2006a), a regular Stroop paradigm was used after left DLPFC stimulation. However, a shortcoming of the regular Stroop task is that there is ambiguity regarding response selection and the attended strategic processes. The Stroop task we used in the present study is more specific and unambiguously referring to strategic processes since an instruction and an expectancy condition were used. Given these variations between both Stroop paradigms, attentional outcomes of HF-rTMS over the right DLPFC and left DLPFC cannot be completely compared. To additionally control for shortcomings in earlier rTMS research, we used a sham-controlled condition, a long time interval between stimulation sessions, a large homogenous sample, stimulation of one single region per session in order to exclude interaction effects with the previous stimulation, structural magnetic resonance imaging (MRI) to determine the exact target of stimulation and a large number of pulses at high stimulation intensity (Baeken et al., 2006). Since some gender differences in attentional processing have been demonstrated (e.g. Roalf et al., 2006) and for reasons of homogeneity, we only included female volunteers to investigate the role of the right DLPC in top-down attentional processing.

2. Results

2.1. *Mood effects*

Changes of mood were analyzed using repeated measures ANOVA for each VAS scale with stimulation (rTMS-SHAM) and time (pre–post1–post2) as within-factors and mood scores evaluated with the VAS as dependent variable. The significance level was set at $p<0.05$. No significant interaction effects between time and stimulation were found. Therefore, we conclude that there were no mood changes caused by right prefrontal HF-rTMS between baseline and immediately after stimulation and after the second Stroop task.

2.2. *Reaction time congruent and incongruent trials*

Statistical analysis was performed using repeated measures ANOVA's. Latencies more than 2.3 standard deviations beyond each participant's mean were removed. Using this criterion, a total of 43 trials (0.7%) was excluded from the analysis, no more than three per participant. The significance level was set at $p<0.05$. The basic design was a $2\times2\times2\times2\times2$ factorial design with stimulation condition (rTMS-SHAM), time (pre-post), expectancy (high expectancy-no expectancy) and type of trial (congruent-incongruent) as within-factors and the order of stimulation as between factor.