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Contextual influence of TMS on the latency of saccades and vergence

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Abstract

This study examines the effects of TMS of the right PPC on the latency of saccades and vergence alone or combined and the role of experimental design. Two designs were used: pure blocks with exclusively no-TMS or TMS trials; mixed blocks in which no-TMS and TMS trials were interleaved; a control study with TMS of the primary motor cortex (pure blocks) was also conducted and showed no effects on latencies. In contrast, in the experiment with TMS of the PPC latencies for TMS trials increased relative to no-TMS trials for almost all eye movements (isolated saccades, convergence, divergence, and for saccade and divergence components of combined eye movements). However, such increase was significant for pure blocks only. In mixed blocks no difference between TMS and no-TMS was found mainly because the latency of no-TMS trials increased relative to corresponding latencies in pure blocks. A second study centered on isolated convergence and divergence confirmed the interaction between block-design and TMS effects, and showed significant TMS/no-TMS differences only for the pure design and for a design in which the rate of TMS trials was high (75%). Again, the absence of difference was due to increase of latency for no-TMS trials in mixed blocks with low rates of TMS trials (50% or 25%), but also to decreased effects for the TMS trials themselves. We conclude that latency of all eye movements, saccades and vergence is highly influenced by the context. Such a contextual factor is the number of TMS versus no-TMS trials within a block; low numbers of TMS trials (50% or less) increases baseline latencies. The design of mixed blocks with 50% or less of TMS trials should not be recommended as it underestimates the direct effects of TMS on cortical processing. In fact, the majority of TMS studies on eye movements do use paradigms with high rates of TMS trials (75% or more). Our study confirms the validity of such paradigms.

Keywords: TMS; rPPC; Eye movements; Experimental design; Contextual influence

Transcranial magnetic stimulation is a powerful tool of cognitive neuroscience allowing to examine the involvement of different cortical areas in the preparation of different types of movements. In the field of oculomotor physiology it has been used to study cerebral control of various types of saccades, visually guided or memory-guided. Several studies have shown that TMS of the right PPC increases the latency of visually guided saccades by about 20–30 ms [1,3]. Similar effects have been found for memory-guided saccades [5]. Vergence eye movements allow to adjust the angle of visual axis to the distance of the object in space; they are essential for single binocular vision and also important for depth vision and stereopsis. Kapoula and coworkers [3,4] reported latency increases due to TMS over the right PPC for saccades, vergence and for both components of combined saccade-vergence movements; combined movements being the most frequent movements we make in natural conditions. Thus, the right parietal cortex is instrumental for the initiation of all types of eye movements in 3D space. The mechanism underlying this latency prolongation could be related to the connection between parietal cortex and superior colliculus (SC). The TMS could interfere with excitatory signal the PPC should relay on the SC thereby lengthening the latency

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of eye movements. Such signal could be related to fixation disengagement [13].

In most studies [1,3,5] trials with TMS and trials without TMS were done in separate blocks (pure blocks) or in blocks with high rates of TMS (>80%). Another experimental design, widely used in other fields of human physiology is the mixed block design, in which stimulus trials (whatever the stimulus is) and control trials are interleaved. The goal of the present study is to verify whether an experimental design in which TMS and no-TMS trials are interleaved within the same block could provide different results relative to design where the two types of trials are run in separate blocks. The first study showed significant effects of TMS but also significant interaction between TMS and block design. The TMS/no-TMS differences were significant in the pure block design only. A second experiment examines further the effect of experimental design only for convergence and divergence movements. In this experiment, in different blocks the probability of TMS varied from 0% (no-TMS), to 25%, 50%, 75% or 100%.

Nine healthy adult subjects participated in the experiments. Five subjects performed the experiment 1, their ages ranged from 26 to 46 years (mean 36.6 ± 5.7). Other four subjects performed experiment 2, their ages ranged from 29 to 48 years (mean 37.5 ± 9.0). All subjects had normal or corrected-to-normal vision. Binocular vision was assessed with the TNO test of stereoacuity; all individual scores were normal, 60 s of arc or better. Each subject gave informed consent to participate in the study. This investigation was approved by the local ethics committee and consistent with the Declaration of Helsinki.

A single-pulse TMS was applied by a MagStim 200 magnetic stimulator with a figure-of-eight coil (each wing 70 mm diameter) allowing focal stimulation [2]. The right PPC was stimulated by placing the coil 3 cm posteriorly and 3 cm laterally to the vertex. This criterion was also used in prior studies [3,5]. The coil was placed down to the scalp with its handle oriented backward and 45° rightward relative to the midline [9]. The rPPC was stimulated at 60–80% of total stimulator output i.e. well above motor threshold; such capacity has been used by other studiers [8]. The occurrence of blinks was monitored online by observing eye movement traces; the capacity of the stimulator was thus adjusted for individual subjects to avoid blinks. The rising time of the TMS pulse was 5 μs, the decay lasting 160 μs, and a click occurred simultaneously with the stimulation discharge.

For the trials without TMS in mixed blocks, a sound simulating the click of the TMS was produced by a speaker located behind the subject in his median plane 30 cm over the top of his head. For pure blocks without TMS the TMS stimulator was switched on but the coil was placed 30 cm over the head of the subject and oriented towards the ceiling. Thus, acoustic events were similar for all trials, TMS or no-TMS in pure or in mixed blocks.

In experiment 1, the visual display consisted of three LEDs placed at an isovergence circle at 20 cm, and other three LEDs placed at a circle at a distance of 150 cm; the three LEDs at each circle were placed at the center and at ±20°. The required mean vergence angle for fixating any of the far LEDs was 2.3° and 17° for the LEDs at the near circle.

In experiment 2, we used three LEDs along the median plane, for the initial fixation the LED at 70 cm, for convergence the LED at 40 cm, and for divergence the LED at 150 cm.

In a dark room, the subject was seated in an adapted chair with chin rest and forehead. The subject viewed binocularly and faced the display of the LEDs. The display was placed at eye level to avoid vertical eye movements; all LEDs were highly visible as only one LED was illuminated at a time.

In order to elicit short-latency reflexive eye movements, we used the gap paradigm described below. Each trial started by lighting a fixation LED at the center of one of the circles (at 150 cm or 20 cm in experiment 1, and at 70 cm in experiment 2). After a 2.5-s fixation period the central LED was turned off; following a gap of 200 ms a target-LED was turned on for 2 s. TMS was delivered at 90 ms after target onset; for no-TMS trials the acoustic click was also delivered at 90 ms after target onset. When the target-LED was on the center of the other circle it called for a pure vergence eye movement, along the median plane. When it was at the same circle it called for a pure saccade, and when it was lateral and on the other circle the required eye movement was a combined saccade and vergence eye movement.

In experiment 1, all target LEDs for saccades were at 20°. All targets along the median plane required a change in ocular vergence of 15°; similarly, combined movements required a saccade of 20° and a vergence of 15°. In one block, 20 trials for each type of eye movement (saccade, vergence and combined movements) were interleaved randomly, i.e. a total of 60 trials. Two pure blocks without TMS, two blocks with TMS, and 4 mixed blocks (TMS trials at 50%) were performed.

A control study was performed for four of the subjects: one pure TMS block of 60 trials was run in which TMS was delivered 90 ms after target onset on the primary motor cortex; the coil was placed on the vertex with the handle oriented backward.

In experiment 2, fixation point was at 70 cm and targets along the median plane were at 150 cm or 40 cm, and required a change in ocular divergence (2.7°) and convergence (3.6°). In a block of 64 trials, 32 trials of convergence and 32 trials of divergence were interleaved randomly. One pure block without TMS and one block with TMS were run; mixed blocks were also performed with TMS probability of 25% (condition TMS25, 4 blocks), of 50% (TMS50, 2 blocks), of 75% (TMS75, 4 blocks). In the conditions pure blocks and TMS50, there were in total 64 trials with TMS and 64 trials without TMS (32 for convergence and 32 for divergence). In condition TMS25, there were 64 TMS trials and 192 no-TMS trials; in condition TMS75 there were 192 TMS trials and 64 no-TMS trials. Thus, in all conditions there was a minimum of 64 TMS trials.