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Transcranial magnetic stimulation: delays in visual supression due to luminance changes

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TRANSCRANIAL magnetic stimulation (TMS) was used to investigate the delays in visual processing time produced by changes in luminance. By administering a magnetic pulse over the occipital pole 80–140 ms after the onset of visual stimuli, we could suppress perception of a four-digit number within a 30 ms time window. Commensurate with previous studies of visual processing latencies, a drop in luminance from 3.52 logTd to 2.61 logTd delayed the peak of the suppression window by 8.9 ms, while a further drop from 2.61 logTD to 1.75 logTd delayed the peak by an additional 15.4 ms. This study validates the use of TMS as a psychophysical tool.

Key Words: Transcranial magnetic stimulation; Visual processing time; Luminance; Visual suppression

Introduction

Lowering the luminance of a target has previously been shown to delay visual processing of that stimulus. This delay has been attributed to increases in processing time at the level of the retina.[1] Measures previously used to assess this delay include reaction time, the Hess effect (an apparent spatial lag in the dimmer of two moving targets), the Pulfrich effect (apparent depth produced by dimming the image reaching one eye)[2,3] and electrophysiological recordings such as event related potentials.[4] We attempted to measure this delay using single-pulse transcranial magnetic stimulation (TMS).

TMS involves the application of a brief, focal magnetic pulse to neural tissue. The rapidly changing magnetic pulse can induce momentary eddy currents in this tissue which disrupt normal patterns of activity.[5] The application of TMS to the occipital lobe has previously been shown to interfere with visual recognition.[6] This effect is most pronounced if there is a brief delay between the presentation of the visual stimulus and the onset of the pulse, which must be administered within a specific time window. Presumably this is because the disruption is most effective when the pulse occurs after retinal signals have had sufficient time to arrive in visual cortex and before processing has been completed.

We reasoned that an increase in precortical visual processing time would be accompanied by a corresponding increase in the delay between the stimulus onset and the occurrence of suppression by the magnetic pulse. Therefore, dimming the target should increase this delay. Furthermore, we expected the delay in visual processing time produced by luminance changes to be a logarithmic function similar to those obtained in previous studies using more traditional methods of measurement, thereby demonstrating the viability of TMS as a technique for investigating the time course of sensory processes. In this regard, we were also interested in how the stimulus–pulse delays we obtained would reflect on the stage of processing at which the disruption of vision by TMS is effective.

Materials and Methods

Subjects: Two university students and two postdoctoral fellows served as subjects for the experiment with their understanding and consent. They ranged in age from 25 to 30 years old; three were males and one was female. None of the subjects reported a history of head trauma or other neurological disorders. The use of human subjects for this study was approved by the UC Davis Human Subjects Review Committee.

Apparatus: TMS was administered using a Caldwell MES-10 single pulse magneto-electric stimulator with a circular 9 cm Focalpoint coil. This device delivers 70 μs magnetic pulses with a peak magnetic flux of 2.3 Tesla. The timing of the stimulus presentations and triggering of the magnetic pulses was controlled by a PC computer. Visual stimuli were presented on a monitor 57 cm from the subject. Stimulus and background luminance levels were measured with a Photo Research Spectra spotmeter. Subjects wore an Electro-Cap with 10/20 system coordinates, but no electrodes.

Stimuli and procedure: The subject's task was to identify a random four-digit number which was presented foveally on the monitor screen. The magnetic coil was held flush against a subject's head over the occipital pole by an investigator. On each trial, subjects fixated on a 0.9° × 1.6° rectangular box at the center of the monitor screen and initiated stimulus presentations with a key press. Four-digit random numbers, with each digit subtending 0.5° × 0.3° were displayed within the box for 50 ms. The presentation was terminated with a pattern mask consisting of four asterisks at the same luminance as the numbers and it remained on until the subject responded. This mask was used to eliminate the possible confounding effects of visual persistence. The magnetic pulse was administered with a stimulus onset asynchrony (SOA) of 80–140 ms (a range established by pilot observations) following the appearance of the visual stimulus. This SOA was varied in 10 msec steps. Following the pulse, subjects were asked to verbally report or guess the number that had been presented. Accuracy rates were based on the number of digits correctly reported in the correct position. Suppression by magnetic stimulation disrupts visual processing so that the subject's accuracy drops. The subjective sense of the suppression reported by subjects ranges from a blurring of the numbers to seeing nothing where the numbers were supposed to be.

The numbers had a luminance of 1.13, 8.04 and 66.11 cd m^{-2} and were presented against a dark (0.05 cd m^{-2}) background. Interestingly, during our pilot observations we found that accuracy rates dropped not only with low luminance levels but also when the luminance of the stimuli exceeded 85 cd m^{-2}. The luminance levels we employed were selected to be as far apart as possible without producing a significant degradation in performance. Testing was conducted in a dark room and subjects were dark adapted. We assumed an 8 mm pupil size, yielding presumed retinal illumination levels of 1.75, 2.61, or 3.52 logTd. Because the background illumination was close to 0, the Michelson contrast of the numbers was always close to 1.

Subject accuracy rates in the absence of TMS were initially evaluated to ensure performance exceeded 75% at all three luminance levels. After the baseline performance measures were taken, 28 blocks of 12 trials were run. Within a block the SOA was held constant and there were four blocks at each of the seven SOAs. There were four presentations at each of the three luminance levels within each block. This gave us a total of 16 trials at each luminance for each SOA. The order of the blocks and the luminance levels within each block was randomized.

The optimum position of the coil's center with the stem of the coil parallel to the ground and the face of the coil flush against the subject's head was determined during preliminary testing with each subject, using the high luminance level and a 100 ms SOA. The location which produced the greatest suppression effect fell between 3.5 and 5.5 cm above the inion on the mid-sagittal line, in accord with previous findings.[6] We marked this location on the Electro-cap fitted over the subject's head to ensure consistent placement of the coil from trial to trial. The magnetic pulse power level was calibrated for each subject to produce an accuracy of 25% under the stated conditions. This power level ranged from 70% to 77%. Some subjects experienced the magnetic stimulation as a mild jolt due to contractions of the small muscles in the back of the head and neck. During our preliminary testing, stimulation 2 cm above the optimal coil location produced no suppression effect, discounting variables such as the sound of the coil, the jolt produced by the stimulation, or visual suppression due to eye blinks as the basis of the observed disruption of perception.

Results

Figure 1 shows the proportion of correct responses for the four subjects as a function of SOA for each of the three illumination levels. The visual disruption produced by the TMS can be seen as an inverted bell-shape at all three luminance levels for three of the four subjects. The width of the suppression effect, and presumably the duration of the disruption, is typically 20–30 ms. The peak of the suppression effect with the lowest luminance could not be established for subject JM because his performance had not started to recover at the 140 ms SOA. However, he shows the characteristic pattern of the other subjects at the two higher luminances. For all four subjects, lowering the luminance of the target delayed the window of visual disruption.

Figure 2 shows best fit Gaussian curves matched to data points of the group average from Figure 1. From the highest to lowest luminances, the means of these curves fall respectively at 100.2, 109.1 and 124.5 ms SOA. Thus, a drop in luminance from 3.52 logTd to 2.61 logTd delayed the maximum suppression window by 8.9 ms, while a further drop from 2.61 logTd to 1.75 logTd delayed the suppression by an additional 15.4 ms.

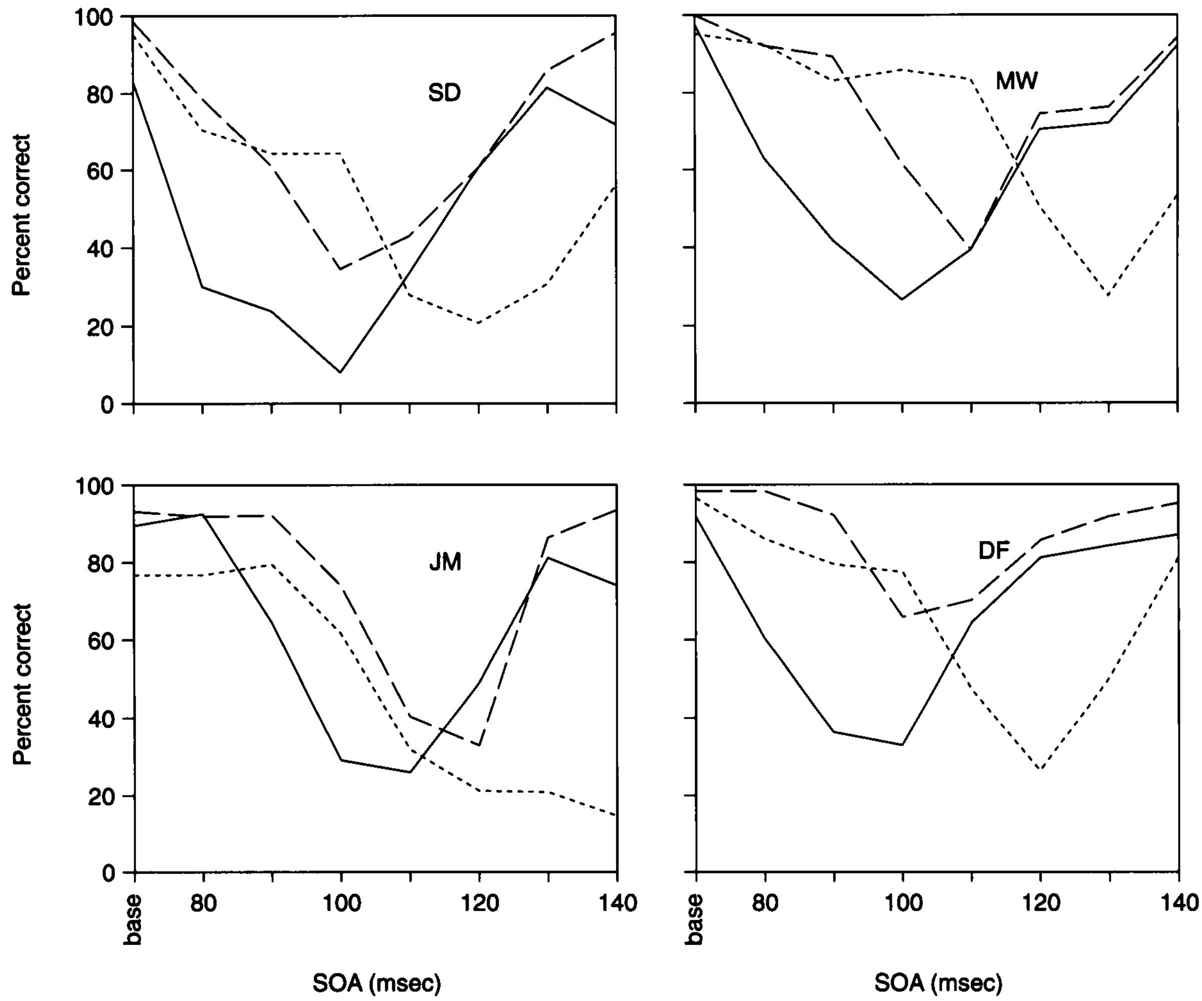

FIG. 1. Individual data on the effects of luminance on processing time. The dotted lines represent performance on target stimuli at the low luminance, 1.75 logTd. The dashed lines represent target stimuli at the medium luminance, 2.61 logTd. The solid lines represent target stimuli at the high luminance, 3.52 logTd.

In accord with the findings of our pilot study, overall performance declined at both the low and high luminances. Given the relatively small size of the visual stimuli, this may be explicable in terms of the retinal line spread function. In any case, the data clearly indicate a delay in visual processing time as the luminance is lowered. Furthermore, this delay appears to increase according to a function that is non-linear with respect to log luminance. Figure 3 shows a comparison of the normalized TMS data from this study with data for the same luminance range based on measurements of the Hess effect reported by Williams and Lit.[2]

Discussion

Transcranial magnetic stimulation is being used increasingly to investigate perceptual and cognitive processes through the *de facto* creation of local momentary `lesions' in specific cortical areas. Not only has stimulation over primary visual cortex been shown to disrupt visual perception,[6] but TMS over extrastriate cortex has been shown to be capable of abolishing motion perception,[7] while parietal TMS has been used to investigate interhemispheric inhibition.[8] Furthermore, repetitive TMS (rTMS) has been employed to induce a recall deficit by stimulating bilaterally over dorsolateral prefrontal cortex, and to induce visual extinction by stimulating over the parietal lobe.[9,10] However, very little work has been done to validate the use of TMS as a tool for making psychophysical measurements.

Since TMS has only been used for a short time on human subjects, a comment on the safety of this technique is warranted. Several studies have been published asserting the safety of single-pulse TMS.[11] One report on human subjects attempted to deal with long-term effects of TMS using single photon emis-

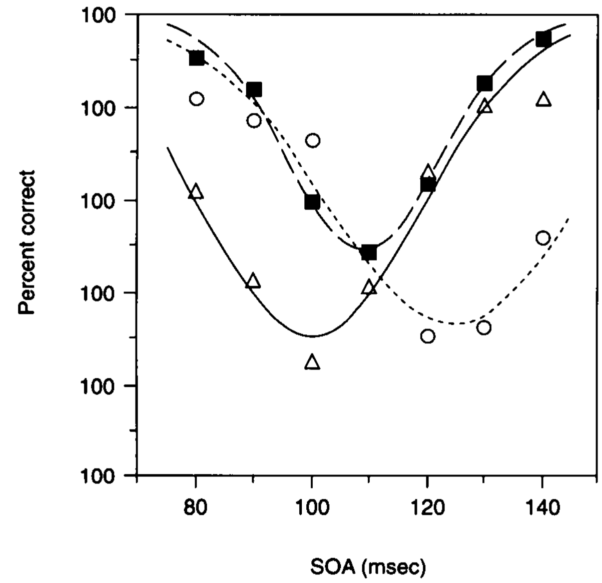

FIG. 2. Averaged group data showing the effect of luminance on processing time. Symbols depict averages for the four subjects, whereas lines are best fitting gaussian functions at each luminance. Gray triangles, filled squares, and unfilled circles represent data for high, medium and low luminances, respectively. The line patterns follow the same convention as the previous figure.

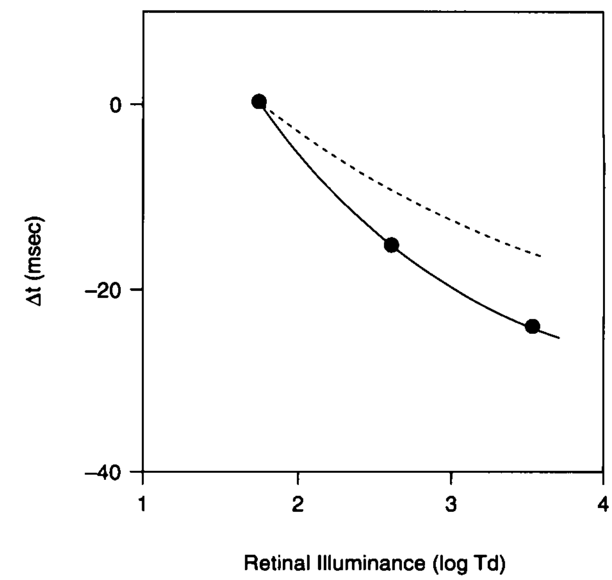

FIG. 3. Plot of visual latency *vs* retinal illumination. Symbols and solid line represent normalized data from the current study. Data was transformed by assigning a latency of zero to the lowest retinal luminance and fitting a function as described by Williams and Lit.[2] The dotted line represents the data for the same luminance range based on measurements of the Hess effect also reported by these authors. Assigning the latency associated with the lowest luminance to zero necessitates the use of negative Dts at higher luminances, this has been done to allow direct comparisons.

sion-computed tomography (SPECT) in a subject who had undergone several thousand stimulations over a long period of time. The regional cerebral blood flow patterns indicated no pathology.[12] Furthermore, a few animal studies have reported no changes in histological analysis of rat brains after magnetic brain stimulation.[13] The general use of TMS as a psychophysical tool will of course depend on continued evidence of its safety.

It has been argued that area V1 is the site of the disruption of perception by TMS, based on the placement of the coil and the geometry of its magnetic field.[6] This disruption is believed to occur because eddy currents induced by the magnetic stimulation elicits the discharge of EPSPs from visual cortical neurons and, indirectly, discharges IPSPs from inhibitory interneurons.[14] Moving the center of the coil slightly to the left or right of our optimal suppression location enabled our subjects to perceive the left or right digits of the number, respectively, with improved accuracy, while moving the coil's center the same distance rostrally or caudally enabled the subject to perceive the four numbers much more accurately. The effect of moving the coil therefore seems to be related to the topography of the geniculocalcarine projection system. However, area V1 may not necessarily be the sole site of disruption by TMS. In our study, the latency for a decrement in performance ranged from 80 to > 140 ms, depending on the luminance level, with the optimal SOA for visual disruption ranging from 100 ms to 140 ms. Investigations of signal processing time from the retina to visual cortex using ERPs[15] in humans or single cell recordings[16,17] in monkeys have found the signals reach visual striate cortex in 35–80 ms. Presumably, retinal signals arrive in cortex at comparable latencies in our subjects. Thus, the optimal effectiveness of TMS is occurring at some time after cortical processing has begun. Beckers and Zeki[7] reported in a TMS study that visual motion signals must reach V1 at or before 60 ms because magnetic stimulation over the occipital pole abolished motion perception with that delay between the onset of the visual stimulus and the pulse. In both their study and our study the target stimuli were similar in size and luminance, and in both cases the subject's response was self-paced. In addition, Beckers and Zeki used a control condition in which the subject had to identify the orientation of a Landolt `C' with similar size and luminance. In this condition, the optimal suppression effect due to TMS occurred at an SOA of 80 ms *vs* our optimal SOAs of 100–140 ms. An important distinction between the Beckers and Zeki study and ours is that their task involved the simple detection of motion or orientation, whereas our study involved the identification of digits, a more cognitively loaded task.

Maccabee *et al*[18] reported that in a task in which the subjects identified three random letters or linear spatial patterns, optimal suppression of the visual target by TMS occurred at an SOA of 80–100 ms, delays closer to but still shorter than the values we obtained. However, it was unclear what the luminance level was for their target stimuli, and luminance differences could account for the difference in SOA. Based on a another paradigm in which they presented two trigram stimuli separated in time and then unmasked the first presentation by suppressing the second presentation with TMS, they concluded that neural representation of the three letters and line patterns was conveyed from striate cortex to extrastriate cortex within 160 ms after the onset of the visual stimulus. The relatively long SOAs for the optimal suppression of letter and number identifications by TMS found in the Maccabee study and in ours suggests that some cortical processing must occur before TMS becomes effective, and this raises the possibility that this suppression may result from the disruption of neural processing in areas beyond V1. It is noteworthy that Nowak *et al*[17] found latencies as short as 80 ms in certain layers of V2. This result agrees with the latencies of our study and the concept that TMS could be disrupting extrastriate cortex.

The fact that the optimal SOA between the onset of the visual stimuli and the disruption of neural processing by TMS increases as the luminance of the stimuli decreased conforms with the premise that signals from low luminance stimuli arrive in cortex later than the signals from higher luminance stimuli. Furthermore, as illustrated in Figure 3, the delays for TMS suppression are a negatively accelerated function of log luminance, an outcome compatible with data from previous studies.

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Conclusion

The SOA data obtained in our study demonstrate that TMS can be a viable technique for investigating the time course of sensory processes. These results appear to be compatible with those of previous studies that have employed a variety of methods to assess the effect of luminance on the speed of visual processing, thereby validating TMS as a psychophysical measuring tool. They also serve to underscore the fact that in investigations using TMS stimulus luminance is a potential confounding variable which needs to be controlled.

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General Summary

Transcranial magnetic stimulation (TMS) has recently been used by investigators to study various perceptual and cognitive processes by stimulating cortical neural tissue with a rapidly changing magnetic field. However, very little work has been done to validate the use of TMS as a psychophysical tool to measure sensory processing. This study accomplishes this goal by investigating the changes in processing time of visual stimuli produced by changes in luminance. TMS applied over the occipital pole causes an imperception of visual stimuli within a small window of time. Commensurate with previous studies using traditional methods, our data on the latencies of this time window show that lowering the luminance of the target increases the latency, thereby validating the use of TMS as a psychophysical tool.