



# Are recognition deficits following occipital lobe TMS explained by raised detection thresholds?

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**Abstract**—It is known that transcranial magnetic stimulation (TMS) administered over the occipital pole suppresses recognition of visual objects. Our aim was to ascertain whether this suppression can be interpreted as a change in visual contrast threshold. Four subjects detected the orientation of an U-shaped hook flashed for 21 ms. Under control conditions, mean contrast threshold was found at 0.88 log units Weber contrast. Thresholds were raised if TMS was applied 40–200 ms after the visual stimulus. Maximum elevation was 1.67 log units under TMS at 120 ms stimulus onset asynchrony. This phenomenon can be interpreted as a reduction in signal-to-noise ratio of the visual stimuli by TMS, which can be compensated for by increasing the contrast of the stimuli. © 1998 Elsevier Science Ltd. All rights reserved.

**Key Words:** transcranial magnetic stimulation; visual object recognition; contrast threshold; visual suppression; Weber contrast; signal-to-noise ratio.

## Introduction

Since the first description by Amassian *et al.* [1], transcranial magnetic stimulation (TMS) has often been shown to disturb visual object recognition when applied on the visual cortex [2, 5–9, 12, 14]. All these studies agree that there is a time window of 60–120 ms stimulus onset asynchrony (SOA) in which a magnetic pulse causes a considerable decrease in the accuracy of an object recognition task.

The effect of TMS on the visual cortex has always been interpreted as a transient lesion precisely defined in both time and localization. However, the mechanism underlying this disturbance of information processing remains unclear. Amassian *et al.* [1] postulated that, analogous to inhibitory phenomena related to magnetic stimulation of the motor cortex, an inhibitory postsynaptic potential component evoked by the magnetic pulse via polysynaptic circuits causes the suppression of visual perception.

To further characterize the influence of TMS on visual object recognition, we investigated the modulation of

contrast thresholds for object recognition by means of psychophysical procedures [3, 16]. The main question was whether suppression of perception was due to disruption of higher or lower level processes.

## Materials and Methods

### Subjects

The authors and two healthy subjects with no previous knowledge of the experiments were examined. They had a monocular Snellen acuity of 20/20 or better and no neurological history. The experiments were approved by the ethics committee of the Medical Faculty, University of Tübingen (No 3/96). Written informed consent was obtained.

### Apparatus

Visual stimuli were generated on a VSG 2/3 graphic board (Cambridge Research Systems, Rochester, UK), controlled by a PC and by software developed in Delphi (Borland, Scotts Valley, CA, USA). The frame rate was 100 Hz. Luminance levels were measured with a Photometer (Minolta LS 100, Osaka, Japan). Magnetic stimulation was administered using the MagPro stimulator (Dantec, Skovlunde, Denmark) with a circular 12 cm coil. Single pulses were applied in the biphasic mode with an intensity of 70% of maximal output. The trigger generated by the VSG board was directly synchronized to the frames. The coil was fixed on a tripod consisting of two right-

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angled frames orthogonal to each other. These could be rotated around the subject's head in the pitch and yaw axis. The subject sat in a comfortable chair in a darkened, light-shielded room. The head was supported by a forehead and chin rest. The subject focused on the stimulus monitor (Liyama Vision Master Pro, 21, Kitaowaribe, Japan) at a distance of 57 cm.

### Stimuli and experiments

Subjects were instructed to press a button on a custom-made keypad connected to the VSG board to run each separate trial. A fixation point of  $0.14^\circ \times 0.14^\circ$  ( $4 \times 4$  pixels) with a luminance of  $0.25 \text{ cd/m}^2$  was presented for 500 ms. To avoid forward masking effects, it was separated from the visual target by a 500 ms gap (dark screen, background luminance  $0.0125 \text{ cd/m}^2$ ). A stimulus was then flashed centrally in luminances varying from 0.041 to  $4.42 \text{ cd/m}^2$ . The stimulus was a U-shape subtending a square of  $0.42^\circ \times 0.42^\circ$  ( $12 \times 12$  pixel) with an opening of  $0.14^\circ \times 0.28^\circ$  ( $4 \times 8$  pixel) pointing in one of the four directions; up, down, right or left. Duration of the stimulus was three frames, resulting in a real presentation duration of 21 ms, as measured with a photomultiplier. A dark screen terminated each trial. In a four alternative forced choice (4AFC) design, subjects were instructed to indicate the direction of the U-shape by pressing one of four corresponding buttons on the keyboard.

The subjects were given five minutes to adapt to the background luminance of the screen. Then, in a control condition without TMS, thresholds of contrast sensitivity were obtained by the method of constant stimuli. Twenty trials were randomly presented in each of 11 different luminances ( $0.041\text{--}0.25 \text{ cd/m}^2$ ). Additionally, thresholds were measured twice by an adaptive up-down transformed-response (UDTR) staircase method with a 2:1 rule (down after two correct answers and up after one mistake) and a stepsize of about  $0.02 \text{ cd/m}^2$ . It was terminated after 15 reversals. The resulting luminance, calculated as the mean of the 15 reversals, marks the threshold at 78% correct responses ( $P = 0.25 + (1 - 0.25) * 0.5^{1/2}$ ) [18]. To avoid fatigue in these near-threshold experiments, 10% of the trials were randomly presented with a luminance onefold to threefold stepsize above the level of the actual staircase procedure. Weber contrast was calculated as  $\log_{10}((L - L_0)/L_0)$ , with  $L$  = luminance of the visual stimulus and  $L_0$  = luminance of the background screen.

The magnetic coil was positioned with the lower edge on theinion. The handle was oriented upwards, and face B of the coil oriented to the head. In a test session [14], the location causing a maximal suppression effect on the U-shape ( $0.25 \text{ cd/m}^2$ ) was determined at 120 ms SOA. With regard to the position of the lower edge, this location was 0.5–2 cm below theinion. Subjects were requested not to move their heads for the rest of the session. At a stimulus intensity of 70% only mild stimulation of the facial nerve occurred in all subjects but no apparent stimulation of nuchal muscles was achieved.

Three different types of experiments were then performed in a randomized order. (i) Thresholds were determined in two subjects by the method of constant stimuli with triggered TMS at a SOA of 120 ms. Each contrast value was tested 20 times. (ii) Using the UDTR method, contrast thresholds at 78% were measured with triggered TMS. Five different SOAs (40–200 ms in steps of 40 ms) were chosen in a random order. (iii) Extinction of visual object recognition was measured in three subjects with U-shapes at constant luminances and triggered TMS at SOAs which varied from 40–200 ms in steps of 20 ms and a SOA of 400 ms. Twelve presentations per SOA were randomly interleaved. The total sum of magnetic stimuli applied on the visual cortex was from about 800 to 1600 in each subject. Frequency of magnetic stimuli depended on the speed of answers, but could not exceed 0.5 Hz.

Contrast thresholds in the absence of TMS were measured

alternatively with experiments with extensive application of TMS, either by the method of constant stimuli or by the UDTR method.

### Results

The shape of the contrast threshold functions for the recognition of the orientation of the visual object, determined by the method of constant stimuli, is demonstrated for two subjects in Fig. 1. Under control conditions, mean threshold at 78% correct answers was 0.95 log units Weber contrast in subject HN and 1.07 log units in subject TK. These values are comparable to the light-difference sensitivity values with short exposure times used by Aulhorn *et al.* [3]. The control measurements in the absence

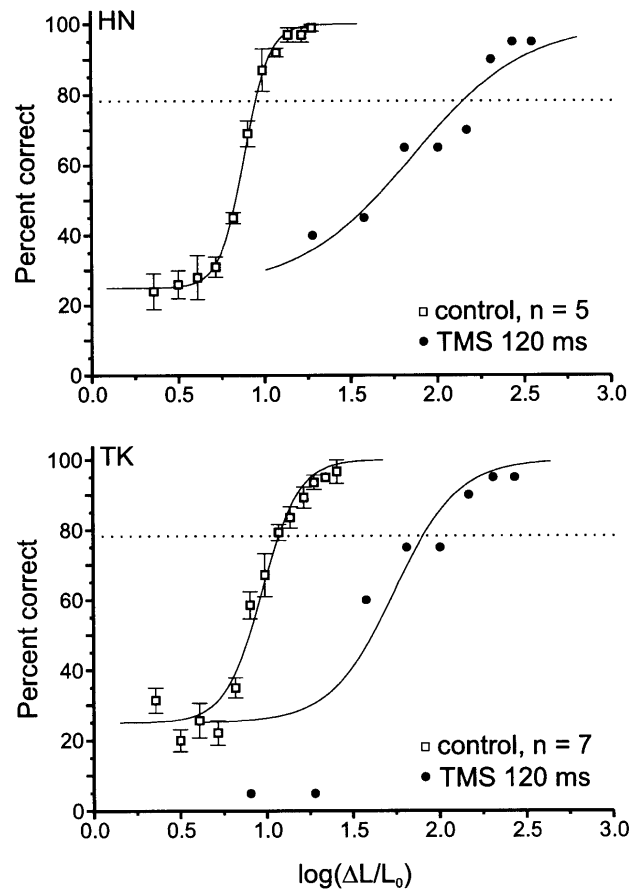


Fig. 1. Contrast sensitivity measured by the method of constant stimuli. Individual data from two subjects are given in log units Weber contrast. Squares represent values of several control measurements (mean  $\pm$  SEM) in the absence of TMS. Circles represent the values of a single experiment under TMS with a constant SOA of 120 ms. Twenty trials were performed for each of the different contrast values. Boltzmann fits with fixed first and final values (25 and 100%) were shown. The dotted line shows the threshold level at 78% correct answers to render data comparable to values given in Fig. 2. Note that numbers of repetition in the control measurements are given individually in the legends of the graphs.

of TMS were repeated several times (see Fig. 1, legends in the graph) at the beginning and during the whole course of the investigation. No systematic shift of threshold was observed in the control measurements which alternated with the experimental tasks with extensive magnetic stimulation.

TMS with a fixed SOA of 120 ms shifted threshold functions to higher contrast values in both subjects (HN: 2.15 log units, TK: 1.91 log units, each at 78% correct answers). Compared with the control condition, steepness of threshold function under TMS was only slightly flattened in one subject and more distinctly flattened in the other subject.

In order to reduce the number of magnetic stimuli required to determine contrast threshold function, we applied the adaptive UDTR-method. In Fig. 2, individual

data (top, four subjects) and mean values (bottom) of contrast thresholds are shown.

In the control condition without TMS, contrast threshold varied interindividually between 0.78 and 1.1 log units (mean  $0.88 \pm 0.04$ ), comparable to the data in Fig. 1. In all subjects, TMS raised contrast thresholds in a bell-shaped manner by increasing SOA from 40–200 ms. Maximal elevations of contrast thresholds (from 1.25 up to 2.25 log units) were found at 120 ms SOA (three subjects) or 160 ms SOA (one subject). Mean at 120 ms SOA was  $1.67 \pm 0.23$  while mean at 160 ms SOA was  $1.44 \pm 0.04$ . Stimulation at a SOA of 200 ms shifted contrast thresholds back to lower values in the range of 1.00–1.28 log units (mean  $1.10 \pm 0.04$ ), which is still higher than values in the control condition. In two subjects (JS and HN) a remarkable difference in threshold shifts was obtained in the two independent runs, but the trend of increasing and decreasing threshold shift with increasing SOA was still obtained. This modulation of contrast threshold was statistically significant. Analysis of variance with SOA and repetition as within factors ( $6 \times 2$ ) revealed a significant main effect of SOA,  $F(1,5) = 8.12$ ,  $P < 0.001$ , but no significant main effect of repetition. Significance levels of *post-hoc* comparisons are indicated in Fig. 2 (bottom).

In all three subjects we measured extinction of recognition of the visual object under TMS with various SOAs and different contrast values (Fig. 3). The contrast values were individually chosen to obtain a large range of extinction effects.

In all subjects, variation of SOA resulted in a typical inverse bell-shaped modulation of the number of correct answers. Regarding the highest contrast values (squares) subjects answered without error at short SOAs from 40 to 100 ms. A remarkable extinction of visual object recognition (41%–75%) occurred only at SOA of 120 ms in all subjects. At longer SOAs (180, 200, and 400 ms) subjects answered again without error. Lowering the contrast of the object presented resulted in an increase of errors in all subjects and an enlargement of the time window instrumental in disturbing recognition. The maximum of the bell-shaped function shifted slightly from about 120 to about 140 ms SOA. In subject TK the lowest contrast value investigated (1.07 log units) resulted in the loss of the bell-shaped modulation whereas TMS at SOAs from 40 to 180 ms diminished answer rates to chance level. This contrast value was the threshold level in the control experiments for this subject. Answer rates reached this threshold with TMS at 200 and 400 ms SOA.

During the test stimulation at the beginning of the experiment all subjects reported visual sensations induced by TMS. They were mainly situated bilaterally in the lower visual hemifield and were described as large “blobs” or contours without any apparent color but with the sensation of a different brightness. The “blobs” remained visible during the whole experiment, but a shift in attention to the visual targets reduced the perception of the visual sensations during the experimental tasks.

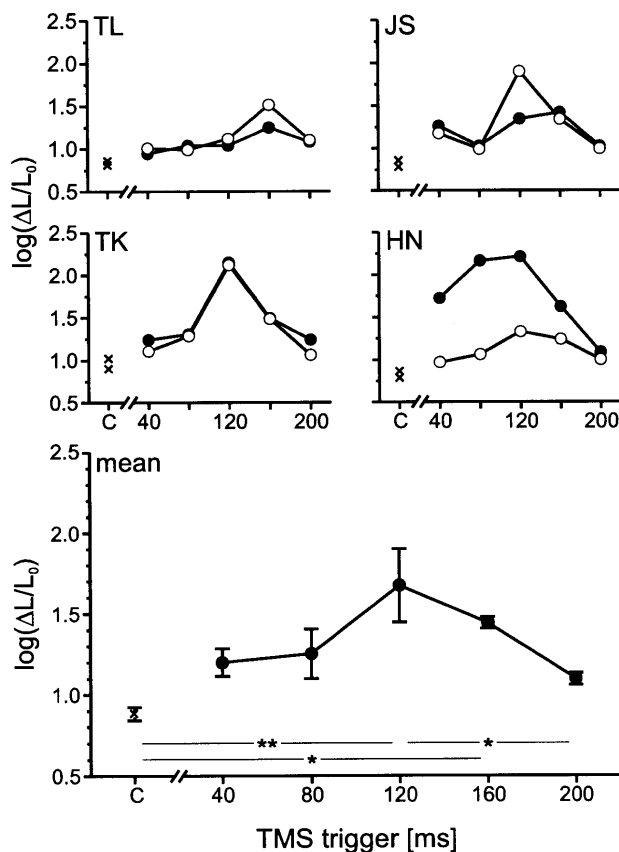


Fig. 2. Shift of contrast sensitivity threshold under various SOA. Weber contrast values of threshold at 78% correct answers are presented in log units, measured by the adaptive UDTR-method with a 2:1 rule. Top: individual data from two runs in each of the four subjects. Dots represent the first run, circles the second run. Bottom: mean values ( $\pm$  SEM) from the four subjects. On the abscissa the SOA between visual stimulus and the TMS pulse is given. Note the crosses representing the control measurements in the absence of TMS. The two-way ANOVA revealed a significant main effect on SOA ( $F(1,5) = 8.12$ ,  $P < 0.001$ ). Three significant differences were found by *post hoc* comparisons (Sheffé), as indicated in the bottom graph. \* $P < 0.05$ ; \*\* $P < 0.005$ .

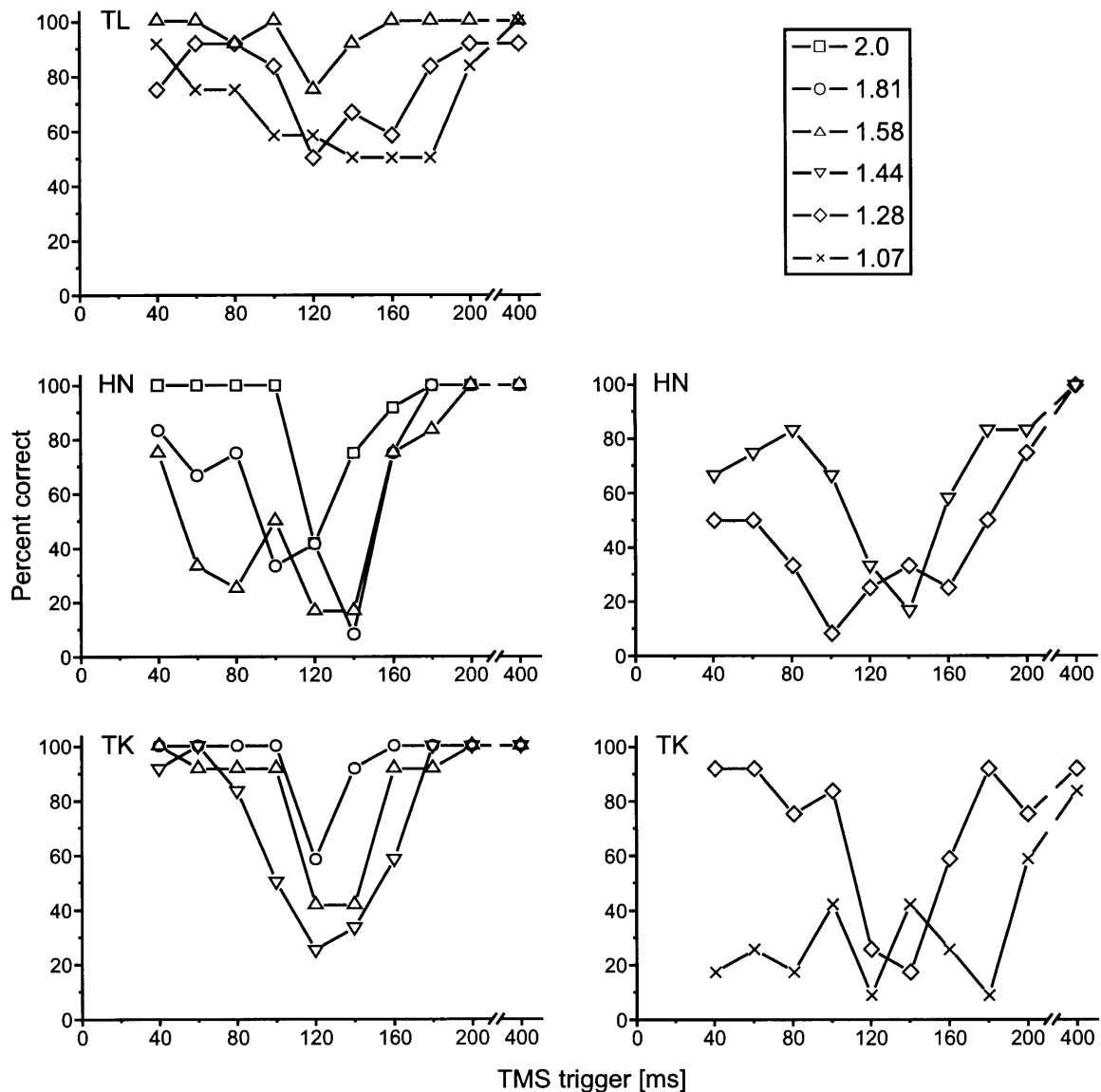


Fig. 3. Suppression of visual perception. Individual data of three subjects are given. In subject TL, three different contrast values, given in log units Weber contrast in the legend, were investigated. In subjects HN and TK, five different contrast values were measured and presented in two different graphs, left and right. Note that contrast values varied for different individuals.

## Discussion

In addition to the observation that TMS reduces accuracy [6–8, 14] or completely disrupts [1, 5, 9, 12] information processing in the visual cortex, our results demonstrate that the effects of TMS in an object recognition task may merely reflect a shift of threshold towards higher contrast levels (Fig. 1). The disturbance of object recognition caused by TMS can invariably be overcome by increasing the contrast of the objects. The amount of this contrast shift depends on the SOA between the visual stimulus and the magnetic pulse (Fig. 2). With the restriction of the limited number of SOAs measured we found that the modulation of contrast thresholds is just the inversion of the bell-shaped function revealed in the extinction experiment (Fig. 3). In other

words, the amount of extinction of a visual stimulus at a certain SOA depends on the amount of threshold shift caused by the magnetic pulse. Enhancement of contrast, then, reduces the extinction effect of TMS, firstly by narrowing the time window in which TMS is effective and secondly by reducing the error rates (Fig. 3). As can be concluded from the data given in Fig. 1, further enhancement of contrast beyond the contrast levels used in the extinction experiment (Fig. 3) would have completely overcome the extinction effect of TMS.

Masur *et al.* [12] were the first to find that the SOA of the magnetic pulse inducing the most effective extinction (maximum in the bell-shaped function) varied with regard to its dependence on the luminance of the visual stimulus. In normal subjects, reducing the brightness of the stimuli shifted the most effective SOA from about 70 to about

90 ms. In a recent study, Miller *et al.* [14] systematically replicated the effect of luminance of the visual stimuli on the SOA. Unlike Masur *et al.*, who used a gray filter maintaining contrast level, Miller *et al.* changed luminance of the stimuli on the same background luminance, thus varying contrast levels from 3.12 to 1.33 log units Weber contrast. Most effective SOA changed from about 100 to 125 ms. Both authors consider that transmission time of the visual signal from the retina to the visual cortex depends on the brightness of the visual stimuli [19]. Although our measurements (Fig. 3) were performed with a smaller contrast range from 1.07 to 2.0 log units, we found a tendency of SOA variation similar to those described earlier. In our study, TMS was most effective in suppressing object recognition at SOAs of 120–140 ms. These SOAs are 20–60 ms longer than SOA of maximal extinction in all previous experiments described [1, 5–9, 12, 14]. A plausible explanation for this long SOA is the low luminance level chosen in our experiment. We would anticipate that a raised luminance level would result in shorter SOAs for the maximal extinction effect of TMS as well as for maximal shift of contrast threshold.

Interestingly, Miller *et al.* [14] reported that increasing contrast of the targets above 3.12 log units in test experiments increased rather than decreased error rates. This conflicts with our finding that, at each TMS interval, a contrast level could be detected which overcomes the disruption of visual processing. A reason for this discrepancy could be that we did not use a pattern mask in order to terminate information processing after the flash. In a pilot experiment with backward masking we found interactions between the masking effect of TMS and a visual mask comparable to Miller *et al.* at high contrast levels. We subsequently flashed our target on a blank screen, avoiding visual forward and backward masking.

We shall consider the intraindividual and inter-individual differences in contrast threshold shift (Fig. 2). In our experience, the critical point is the position of the coil in relation to the skull. In the test session, changes of only a few mm of the coil position resulted in remarkable changes in suppression effects of TMS. The most plausible explanation for intraindividual changes is then, that subjects could not maintain their exact head positions, in relation to the coil over the whole range of the experiment. We have no evidence that intraindividual differences are based on systematic changes in cortical processing induced either by learning effects or by influence of TMS for two reasons. (i) Repetition of contrast threshold measurements without TMS interleaved to the experiments with TMS did not reveal any systematic change in contrast thresholds in any of the subjects. (ii) Comparing run one and run two of the UDTR-experiment (Fig. 2) revealed that contrast threshold changes were raised in two subjects while in the third subject no change occurred and in the fourth changes in contrast threshold were reduced. The lack of a systematic, long-lasting threshold shift under extensive TMS (up to 1600 stimuli applied in blocks of 100–200, maximal frequency

0.5 Hz) confirms the safety of TMS applied at low repetition rates [15, 17]. Interindividual differences are probably related to anatomical variations, which results in different parts of the visual cortex, being reached by TMS [11].

What is the underlying neurophysiological effect of contrast threshold modulation? As pointed out by Amassian *et al.* [1], we might expect a magnetic pulse to induce both an excitatory as well as an inhibitory effect on cortical neurons. They suggested that suppression of perception might be due to an inhibitory process of the excitation induced by the visual stimulus. In general, suppression of perception is due to a reduction of signal-to-noise ratio [4]. This means that TMS might reduce the retinal signal, increase the noise, or both. The “blobs” the subjects observed have to be interpreted as phosphenes [10, 11, 13], i.e. an additional signal generated in the visual cortex. With respect to the visual signal from the retina, the cortical phosphenes are to be considered as noise, and it seems likely that the increase in contrast threshold is a result of a rise in the noise level. This interpretation is strongly supported by our finding that, at each SOA tested, the disruption of information processing induced by TMS could be overcome by increasing visual contrast, i.e. the strength of the retinal signal. On the other hand, a linear increase of noise would shift contrast thresholds without changing the slope of the contrast threshold function. This is not the case here (Fig. 1). Besides elevation of the noise level, a reduction of the retinal signal may therefore also account for the effect of TMS on the visual cortex.

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