Title: Transcranial magnetic stimulation of the occipital cortex interferes with foot movements in blind individuals

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Abstract

Research in blind individuals has shown that after visual loss, the occipital cortex can be reorganized and repurposed for nonvisual perception and cognitive functions. No studies, however, have directly examined its involvement in motor production. Here we show that a rhythmic foot movement performed by acquired blind participants can be disrupted by transcranial magnetic stimulation (TMS) to their primary and secondary visual cortex (V1/V2). This disruptive effect of TMS was absent for both sighted and congenitally blind participants. These results suggest that the visual cortex of blind individuals is involved in motor production, but its involvement requires prior visual experience. Our finding indicates that functional repurposing of the visual cortex may not be restricted to perception and cognitive functions, but extended to motor function. The reorganization of the visuomotor network, which has been developed before visual loss, may allow motor function to emerge from the visual cortex of blind individuals.

Introduction

Sensory loss can lead to dramatic plasticity of the cerebral cortex (Merabet et al., 2005, Merabet and Pascual-Leone, 2010). There is accumulating evidence for cross-modal plasticity after visual loss, where the visual cortex is reorganized to participate in the process of remaining sensory modalities. For example, the visual cortex of blind individuals responds to auditory (Kujala et al., 1995, Weeks et al., 2000, Amadeo et al., 2019, Vetter et al., 2020) and tactile stimuli (Sadato et al., 1996, Cohen et al., 1997, Burton et al., 2002, Pietrini et al., 2004, Ptito et al., 2008). This cross-modal plasticity has been regarded as the neural underpinnings driving blind individuals' superior ability over sighted individuals in nonvisual perception like sound localization and tactile spatial discrimination (Lessard et al., 1998, Roder et al., 1999, Goldreich and Kanics, 2003, Voss et al., 2004). Furthermore, research suggests that the visual cortex can also be reorganized to contribute to higher cognitive processes like verbal memory, language processing, or mathematical processing (Amedi et al., 2003, Amedi et al., 2004, Bedny et al., 2011, Kanjlia et al., 2016). Thus, it is well accepted that the visual cortex of blind individuals takes a more prominent role in nonvisual perception and cognitive functions than in sighted individuals.

However, no studies to date have examined whether the visual cortex of blind individuals is involved in motor production, which is one of the essential brain functions. To examine this question, we applied transcranial magnetic stimulation (TMS) to the occipital cortex of acquired blind participants, including the primary and secondary visual cortex (V1/V2),

while they performed a rhythmic and alternating foot movement. We show that TMS of the occipital cortex increases the variability of the foot movements in the acquired blind participants but not in sighted controls. We also show that this TMS effect is absent in congenitally blind individuals. Our results suggest that the visual cortex of blind individuals is involved in motor production, but the involvement requires prior visual experience.

Results

Twelve acquired blind participants, including six athletes (see Methods), and twelve age-matched sighted participants, took part in the main experiment (see Table 1 for the participant characteristics). Blindfolded participants made rhythmic movements of alternating dorsiflexion and plantar flexion of the feet (Fig. 1 A) without any sound cue. The participants were instructed to keep their movement frequency (1 Hz) as constant as possible. We selected this rhythmic and alternating lower limb movement because it requires no visuomotor coordination. We also emphasize that it characterizes locomotion, one of the most common daily activities shared between blind and sighted individuals.

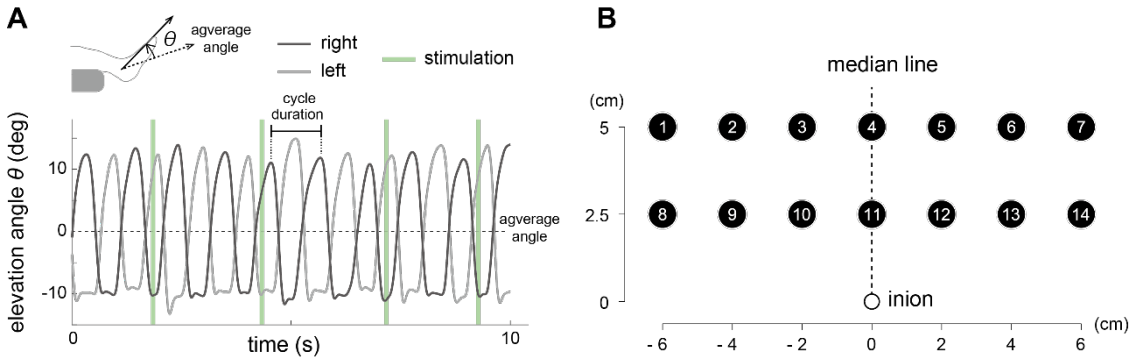

Fig 1. The experiment and stimulation sites: A) The rhythmic foot movement of a representative participant for a 10-s period is shown by the elevation angle, θ of right foot (dark gray line) and left foot (light gray line). For each foot, θ is defined as the angle relative to the average angle (dashed line). Thus, θ = 0 indicates the average angle. Each vertical line (light green) indicates the timing of a single transcranial magnetic stimulation (TMS) pulse delivered with at random. The cycle durations for each foot were used to calculate the CV (see Methods). B) Fourteen stimulation sites arranged in a 2 × 7 grid were identified for each participant using the inion and the median line as a reference point and line (see Methods). Stimulation site #11 corresponds to pV1/V2.

Table 1. Characteristics of the participants.

Participant #	Group	Age (y)	Onset of blindness (y)	Cause of blindness	TMS intensity (%)
1	BL^{A}	26	2	retinoblastoma	80
2	BL^{A}	27	14	retinal choroidal degeneration	75
3	BL^{A}	39	20	morning glory anomaly	85
4	BL^{A}	28	23	uveitis	90
5	BL^{A}	20	1	retinoblastoma	75
6	BL^{A}	40	25	retinitis pigmentosa	85
7	BL^{NA}	25	14	chorioretinal atrophy	70
8	BL^{NA}	25	5	glaucoma	65
9	BL^{NA}	42	17	uveitis + glaucoma	70
10	BL^{NA}	19	2	behcet's disease	100
11	BL^{NA}	20	3	retinal cell death	75
12	BL^{NA}	19	15	glaucoma	55
13	SI	22	-	-	85
14	SI	22	-	-	85
15	SI	23	-	-	95
16	SI	22	-	-	90
17	SI	34	-	-	70
18	SI	35	-	-	85
19	SI	40	-	-	80
20	SI	26	-	-	75
21	SI	23	-	-	70
22	SI	27	-	-	100
23	SI	20	-	-	95
24	SI	39	-	-	85
25	CBL	29	birth	unknown	80
26	CBL	40	birth	cataract	95
27	CBL	36	birth	anophthalmia + persistent fetal vasculature	60
28	CBL	32	birth	amaurosis	75

BL, acquired blind; SI, sighted; CBL, congenitally blind; y, year. Superscripts A and NA

indicate athlete and non-athlete acquired blind participants, respectively.

During the movement, 20 single TMS pulses were applied to one of 14 stimulation sites over the occipital cortex (Fig. 1B) with 2–4 s inter-stimulus intervals (see Methods for details). The intensity of TMS used in the experiment was comparable between the acquired blind (77.083 ± 11.968% of the maximum stimulator output) and sighted (84.583 ± 9.643%) participants (unpaired t-test: $t[22] = 1.691$, $p = 0.105$ without correction). In addition, control trials (no-stimulation trial) were conducted in which the participants performed the same movements without TMS. TMS did not induce an immediate effect such as muscle twitching or movement stop. Thus, the effects of TMS on the rhythmic foot movement were evaluated by quantifying the variability of the movement frequency with the coefficient of variation (CV) of the cycle duration (Fig. 1A, see Methods for details). As our main target area is the early visual cortex, the results we show in the main text are limited to stimulation site #11 (see Fig. 1B), which corresponds to the putative V1/V2 (pV1/V2). The supplementary information (see Fig. S1) report the averaged data over all stimulation sites, covering broader visual areas.

We first confirmed that both groups of participants successfully performed the instructed movement. The movement frequency averaged over all the stimulation, and no-stimulation trials was 0.942 ± 0.168 Hz and 0.968 ± 0.163 Hz for the acquired blind and sighted participants, respectively. Importantly, no significant difference was found between the two groups (unpaired t-test: $t[22] = 0.381$, $p = 0.707$ without correction).

We, however, found distinct group differences in the TMS effects on movement performance movement performance. TMS to stimulation site #11 (pV1/V2) affected the foot movements in the acquired blind participants (blue bars in Fig. 2) but not in the sighted participants (red bars). Compared to the non-stimulation trial, TMS to stimulation site # 11 increased the CV in the acquired blind participants (paired t-test: $t[11] = 3.838$, $p = 0.006$ with Bonferroni correction for multiple comparisons) but not in the sighted participants ($t[11] = 1.766$, $p = 0.105$ without correction). This result suggests that TMS to pV1/V2 interfered with motor production only in the acquired blind participants. We obtained the same result when analyzing the average data over all stimulation sites (Fig. S1).

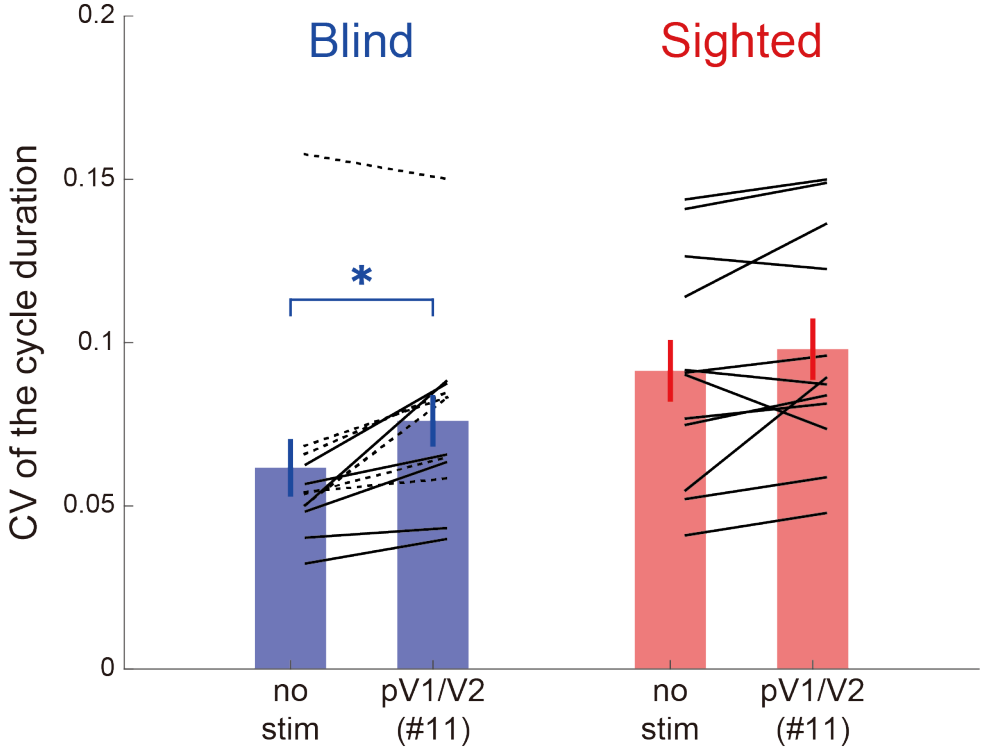

Fig. 2. CV of the cycle duration for the acquired blind (blue) and sighted (red) participants. The CV was compared between the no-stimulation trial (no stim) and the stimulation trial in which TMS was applied over pV1/V2 (#11). Each line represents data from an individual participant. For the acquired blind participants, solid black lines and dashed lines indicate subgroups of athletes (BL^{A}) and nonathletes (BL^{NA}), respectively. Bars and error bars indicate the mean and standard errors, respectively. The asterisk indicates $p < 0.05$.

This increase in the CV (stimulation site # 11) of the acquired blind participants was not correlated with their age ($r = -0.321$, $p = 0.309$), their age at onset of visual loss ($r = -0.455$, $p = 0.138$), or the duration of visual loss ($r = 0.197$, $p = 0.540$). Moreover, the increase in CV did not differ between the subgroups of athlete (BL^{A} in Table 1, black solid lines in Fig. 2 left) and nonathlete (BL^{NA}, dashed lines) acquired blind participants (unpaired t-test: $t[10] = 0.512$, $p = 0.620$ without correction).

The group comparison in the no-stimulation trial showed a smaller CV in the acquired blind participants than the sighted participants (unpaired t-test: $t[22] = 2.20$, $p = 0.037$) (Fig. 2). This suggests that the acquired blind participants exhibited a better ability for temporal control of the foot movement than the sighted participants.

Finally, we performed an additional experiment with four congenitally blind participants. We utilized the same procedure as in the main experiment. In contrast to the acquired blind participants, none of the congenitally blind participants showed any clear increase in the CV when TMS was applied to stimulation site #11 (pV1/V2) (Fig. 3). We again obtained the same result when analyzing the average data over all stimulation sites (Fig. S2).

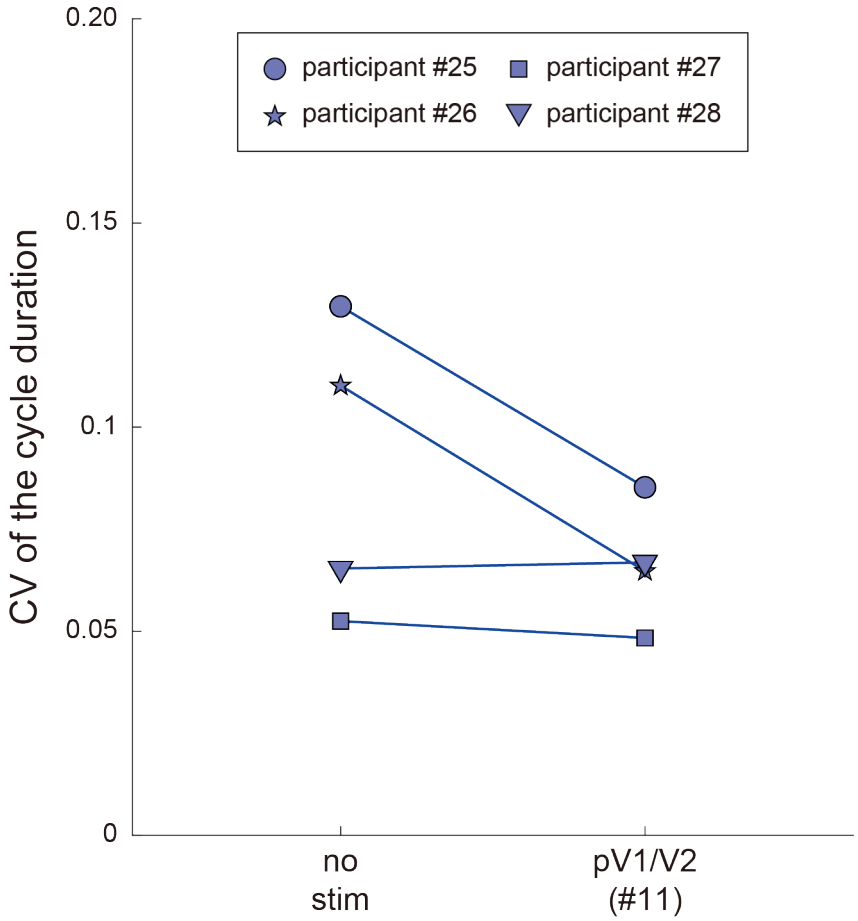

Fig. 3. CV of the cycle duration for congenitally blind participants. The CV for each participant was compared between the no-stimulation trial (no stim) and the stimulation trial in which TMS was applied over pV1/V2 (#11). Each line represents data from an individual participant. In contrast to the result of the acquired blind participants (Fig. 2), TMS of pV1/V2 did not induced an evident increase relative to the no-stimulation trial in all of the participants.

Discussion

Our results showed that TMS of the occipital cortex, including pV1/V2, interfered with a foot movement task in the acquired blind participants but not in the sighted controls. However, the TMS effect was absent in the congenitally blind participants. These results suggest that the visual cortex of acquired blind individuals is involved in motor production. Numerous studies have reported that the visual cortex of blind individuals is reorganized to participate in nonvisual perception and cognitive functions (Merabet and Pascual-Leone, 2010, Fine and Park, 2018, Castaldi et al., 2020). On the other hand, the current research provides the first neurobehavioral evidence suggesting that the visual cortex of blind individuals is further reorganized to participate in motor production.

We first discuss a possible confounder for our results. One may argue that the performance deterioration (i.e., increase in the CV) found only in the acquired blind participants may be mainly caused by sensory side effects of TMS, such as tactile (pain) sensation or a clicking sound (Duecker and Sack, 2015). However, this would be unlikely. We carefully calibrated the TMS intensity for each participant so that TMS did not induce pain (see Methods). In addition, no participant reported any nociceptive feelings, including pain or noisy sounds, during the experiment. Importantly, the TMS intensity used in the experiment did not differ between the groups of participants (see Results and Table 1). Therefore, the subjective and objective intensity of the sensory side effects was similar between the groups. We thus argue that the difference of the TMS effect on motor performance between the acquired blind and sighted participants can be attributed to differences in the neural processing of their visual cortex during the movement task, rather than from sensory side effects of TMS.

In contrast to the results from the acquired blind participants, the movement performance of the congenitally blind participants was not deteriorated by TMS of the occipital cortex (Fig. 3). Although we should be cautious due to the limited sample size of only four, this observation suggests that visual experience before visual loss is essential for motor function to emerge from the visual cortex. Even small amounts of prior visual experience seems sufficient for the visual cortex plasticity to occur. Our sample of acquired blind participants covered a broad range of onset of blindness: five early-blind (age < 6), three intermediate-blind ($6 \leq$ age ≤ 16), and four late-blind participants (age > 16) (Voss, 2013, Fine and Park, 2018). Irrespective of the age at onset, all the participants except for one late-blind participant (# 9) showed increases in their CV (Fig. 2). This observation leads us to suggest a possible mechanism behind the visual cortex plasticity. The visuomotor

experience may develop neural connections between the visual cortex and other brain regions related to motor production during the early development stages (Attinger et al., 2017). Such neural connections may contribute to motor control of visually-guided movements in sighted individuals, as suggested by a recent study (Gallivan et al., 2019). When one loses vision, the pre-existing neural connections may be enhanced and repurposed (Merabet et al., 2005, Merabet and Pascual-Leone, 2010) for motor control of nonvisually-guided movements like the motor task used in the present study.

It is well accepted that the cross-modal plasticity of the visual cortex depends on visual experience before visual loss and nonvisual experience after visual loss (Singh et al., 2018, Castaldi et al., 2020). However, we found no reliable relationship between the CV increase and age, the age at onset of visual loss, the duration of visual loss, or motor experience (i.e., sports athlete or not). Therefore, the degree of visual cortex plasticity and its effects on motor behavior may not be determined merely by a single factor of experience.

Although the current study cannot identify the exact roles of the visual cortex of the blind participants in their motor production, we consider three possible roles from the computational understanding of motor control (Scott, 2004). The first potential role is motor command generation. We believe this is unlikely given our results. If the visual cortex played a role in motor command generation, we should have observed immediate effects of TMS, such as muscle twitching or movement stop. However, we did not observe any such effects. The second potential role is nonvisual feedback processing. After visual loss, cross-modal plasticity allows the visual cortex to participate in the process of nonvisual sensory modalities (Pascual-Leone et al., 2005, Merabet and Pascual-Leone, 2010). Therefore, it is possible that the visual cortex contributes to the processing of online nonvisual sensory (probably proprioceptive) feedback of the body state (i.e., position, velocity, or movement phase information of the foot). The third potential role is sensory prediction–predicting sensory consequences of motor commands–which is utilized together with online sensory feedback, to estimate the body state for motor control (Wolpert and Flanagan, 2001, Shadmehr et al., 2010). Recent studies in both sighted mice and humans have provided growing evidence supporting the role of the visual cortex in predicting the visual consequence of movements (e.g., optical flow) (Keller et al., 2012, Saleem et al., 2013, Attinger et al., 2017, Leinweber et al., 2017, Buaron et al., 2020). If visual loss triggers the neural connections for visual sensory prediction to be repurposed for nonvisual sensory prediction, the visual cortex could

become an essential element of the brain network for nonvisual sensory prediction. In fact, our previous study in blind individuals have suggested possible involvement of visual association area in motor prediction (imagery) (Amemiya et al., 2021). Further studies are, however, needed to identify the specific role of the visual cortex.

Finally, the acquired blind participants showed better baseline (i.e., nonstimulation trial) performance than sighted participants, suggesting a remarkable temporal precision of motor control. A large body of studies have reported that blind individuals showed greater nonvisual perceptual or cognitive performance compared to sighted individuals (Lessard et al., 1998, Roder et al., 1999, Goldreich and Kanics, 2003, Voss et al., 2004, Tinti et al., 2006, Fortin et al., 2008, Lewald, 2013). Some of these studies showed a relationship between their superior performance and the reorganization of the visual cortex (Sadato et al., 2002, Amedi et al., 2003, Gougoux et al., 2005). Supporting these previous findings, we speculate that the superior motor performance observed in our acquired blind participants may also be based on the reorganization of the visual cortex.

Before the conclusion, we would like to note two methodological limitations of our study. First, we determined stimulation sites (see Methods for additional information) without using an individual anatomy-based navigation system guided by magnetic resonance imaging (Amedi et al., 2004). Thus, some between-participant differences may exist in the anatomical locations of stimulation sites. We, however, focused on the V1/V2 and the corresponding stimulation site (#11) was determined based on the well-established external anatomical landmark (2.5 cm above inion; Salminen-Vaparanta et al., 2012, Cowey and Walsh, 2000). Therefore, we claim that we stimulated V1/V2 when TMS was applied to stimulation site #11. As for the other stimulation sites, our methodology limits us to exactly identify the corresponding anatomical locations for each participant. To mitigate the effect of the between-participant differences in anatomical locations, we analyzed the averaged CV over all stimulation sites. This may reflect the overall trend of the TMS effect over early- and higher-order visual cortices. Further studies are required to determine whether specific higher-order visual areas like V3, V4, or V5 are involved in motor production.

Second, we cannot deny the concern regarding implicit side effects of TMS. As already mentioned, none of the participants explicitly claimed nociceptive feeling during the experiment. The possibility, however, remains that a TMS-induced tactile sensation or a TMS clicking sound implicitly affected the movement performance only in acquired blind

participants. To address this concern, further studies are required on the implicit attention of blind individuals to TMS-induced nonvisual sensations.

In conclusion, our study is the first that provides neurobehavioral evidence that the visual cortex of blind individuals contributes to motor production. We also provide evidence that prior visual experience is essential for motor function to emerge from the visual cortex after visual loss. Our findings indicate that the plasticity of the human brain after sensory loss is more flexible than previously thought; functional repurposing of the lower sensory cortices may not be restricted to perception and cognitive functions but extended to motor function. This plasticity may help blind individuals navigate or interact with the ever-changing and diverse environment around us without vision.

Methods

Participants

Twelve acquired blind, who lost vision after birth (BL in Table 1), and twelve age-matched sighted (SI) individuals with normal or corrected-to-normal vision participated in the main experiment. Four congenitally blind individuals, who had never experienced vision (CBL), participated in an additional experiment. All participants healthy male volunteers without a history of cognitive impairment or psychiatric disorders. They all presented no contraindications to TMS as assessed using a screening questionnaire in compliance with the guidelines for non-invasive magnetic brain stimulation in research applications. Six acquired blind participants were current or former members of the Japanese national blind football team (BL^{A} in Table 1). The remaining six acquired blind participants (BL^{NA}) were blind individuals from the general population. All the sighted participants were from the general population. We selected the sample size (n = 12 per group) for the main experiment based on previous works that examined the effect of TMS on motor tasks (Foltys et al., 2001, Orban de Xivry et al., 2011a, Orban de Xivry et al., 2011b, Mawase et al., 2017). The experiment was approved by the ethics committee of the National Institute of Information and Communications Technology and was conducted according to the Declaration of Helsinki. All participants gave their written informed consent prior to participating in the experiment and were naïve to the purpose of the study.

Apparatus

All participants wore eye patches and an eye mask to eliminate any possible visual stimuli, which were worn on from ~ 30 min before the experiment begun until the end of the

experiment. They were also instructed to close their eyes through the experiment. They sat in a comfortable reclining chair with their heads on a chinrest and legs extended on a leg rest. The height and location of the chinrest and the leg rest were adjusted for each participant to allow them to comfortably make the rhythmic movements of alternating dorsiflexion and plantar flexion of their feet. The elevation angles of the first metatarsals of both feet from the horizontal plane was recorded using an electromagnetic position sensor (Micro Sensor 1.8 Extra Flex, Polhemus Liberty, Burlington, VT). The obtained data were digitized with a temporal sampling ratio of 240 Hz and then low-pass filtered with a cutoff frequency of 5 Hz.

Electromyographic (EMG) activity was recorded at 2,000 Hz utilizing surface electrodes from the medial and lateral heads of the gastrocnemius and tibialis anterior of both legs using wireless EMG sensors (Wave Plus Wireless EMG, Cometa, Bareggio, Italy). This EMG recording was performed to test the possibility that TMS stimulation of the occipital cortex may elicit a muscle twitch. However, as we did not observe any twitch, the EMG data are not reported in this study.

TMS stimulation was applied using a 70 mm figure-eight coil and a Magstim Rapid Transcranial Magnetic Stimulator (Magstim Company, Spring Gardens, UK). The maximum stimulator output was 2.1 T. TMS pulse delivery was controlled by an in-house program running on MATLAB, version R2013b (The MathWorks, Natick, MA).

TMS protocol

The stimulation sites for each participant were identified using an elastic swimming cap with 14 (2 × 7) position markers (Fig. 1B). The marker positions were determined on the cap worn by a male individual with an average head size for Japanese men (head circumference: ~ 57 cm; Kouchi and Mochimaru, 2008) who did not participate in the experiment. The markers were placed at inion, 2.5 cm (stimulation site #11), and 5 cm (stimulation site #4) dorsal from the inion on the median line (nasion-to-inion line through the vertex), and 2, 4, and 6 cm right and left away from the median line at the same level as stimulation sites #4 and #11. For each participant, the same swimming cap was placed on the head as follows: 1) the inion mark was placed at the participant's inion, 2) stimulation sites #4 and #11 were aligned on the participant's median line, and 3) stimulation site #11 was placed 2.5 cm dorsal from the inion to target V1/V2 (Fig. 1A) (Cowey and Walsh, 2000, Salminen-Vaparanta et al., 2012).

The stimulation intensity for each participant was subsequently determined using the highest value not inducing pain on the scalp (Table 1). We applied single TMS pulses to each stimulation site in order from stimulation site #1 to # 14. For stimulation site #1, stimulation was first applied with 100% intensity of the stimulator output, and the intensity was decreased by 5% steps until the participant reported not feeling pain. Then, we moved to the following stimulation sites, starting each stimulation with the highest intensity of stimulation that did not result in pain at the previous stimulation site. In each participant, the intensity determined at stimulation site #14 was used as the stimulation intensity for the experiment.

Task procedure

We performed the main (12 acquired blind participants and 12 sighted participants) and additional (4 congenitally blind participants) experiments with the following task procedure. Blindfolded participants sat in the chair and made rhythmic movements of alternating dorsiflexion and plantar flexion of the feet without any sound cue. To keep the movement frequency as constant as possible, the participants practiced the movements with a sound of 1 Hz for ~2 min twice: once before the determination process of stimulation intensity and once before starting the experiment. Then, they were instructed to maintain the trained movement frequency throughout the experiment.

In the experiment, the participants performed the movements during the following three types of trials. On stimulation trials, the 20 single TMS stimulations were applied to one of the 14 stimulation sites with 2–4 s inter-stimulus intervals (drawn from a uniform random distribution). The TMS coil was held tangentially to the scalp. The trial started 3 s before the first stimulation and ended 3 s after the last stimulation. The duration of each trial was between 56.34 and 70.26 s. On sham trials, a fake coil was placed over stimulation site #11, while 20 single TMS pulses were delivered in the air with another coil near the fake coil. Thus, the participant could feel the clicking sound coming from the fake coil on the scalp. The duration of the sham trials followed the TMS pulse delivery protocol used in the stimulation trials. On no-stimulation trials, no coil was placed on the scalp, and TMS pulses were not generated. The duration of no-stimulation trials was set to 50 s.

Participants completed two blocks of 15 trials with 14 stimulation trials (once for each of 14 stimulation sites) and one sham trial. The trial order was pseudorandomized in each block. Each of two no-stimulation trials was performed before the first block and after

the second block. Thus, the participants completed a total of 32 trials in the experiment.

Data analysis

As we could not any immediate effect of TMS on rhythmic foot movements such as muscle twitching and movement stop, we examined the effects of TMS on movement by evaluating the variability of the movement frequency. For each foot in each trial, we identified the duration of each movement cycle, which was defined as the time between the peaks of the dorsiflexion (Fig. 1A and see details in the next paragraph), and calculated the CV. Then, the CV for each stimulation site was obtained as the average of the four CV values for left and right feet in two stimulation trials (first and second blocks). Similarly, the CV for the no-stimulation trials was calculated as control. For stimulation site #14 of participant #23 (Table 1), we utilized the data only from the second block to calculate the CV due to the lack of the first block data (recording error). For stimulation site # 5 of participant #20, we excluded the second block data of the left foot because the foot posture largely changed during the trial. We note that sham trials were excluded from the analysis because almost all the participants (25 out of 28 participants) noticed the lack of stimulation and/or felt something going wrong during the trials. Therefore, the data were likely to be biased by this surprising effect. The main interest of our analysis was in data at stimulation site #11, which was inferred to be V1/V2 (see TMS protocol) (Fig. 2). The other stimulation sites may cover broad visual areas, including not only early visual areas (V1/V2) but also higher-order visual areas (V3, V4, and V5) according to the literature (Cowey and Walsh, 2000, Pascual-Leone and Walsh, 2001, Salminen-Vaparanta et al., 2012, Amemiya et al., 2017). To look at the overall trend of the TMS effect over early and higher-order visual cortices, we analyzed the averaged CV over all stimulation sites, which is reported in a Supplementary figure (Fig. S1).

We identified the peaks of the dorsiflexion (Fig. 1A) for each foot of each trial as follows (See Data availability). First, we calculated the time average of the elevation angle and subtracted it from the entire time series to obtain the relative angle data (θ in Fig. 1A). Then, we identified the crossing times where θ changed from negative to positive. Finally, we identified the point of maximum value between each of the two consecutive crossing times and defined it as the peak.

Statistical analysis

We conducted statistical analyses for the results of the main experiment as follows. For each group, we examined differences in the CV between the no-stimulation trial and

stimulation site #11 (pV1/V2) using a two-tailed paired Student's t-test (Fig. 2). The same test was done for the averaged CV over all stimulation sites (Fig. S1). We reported the statistical p-value after Bonferroni correction for multiple comparisons (i.e., multiplied by two because we analyzed the two groups) for the significant results. As only the acquired blind participants showed a significant increase in the CV for stimulation site #11, we performed correlation analyses to examine the relationship of the CV increase with their age, age at onset of visual loss, and duration of visual loss. Besides, to check the relationship between the CV increase and their sport experience, we performed a sub-group comparison between athlete (BL^{A} in Table 1) and non-athlete acquired blind participants (BL^{NA}). Finally, we compared the baseline performance (i.e., CV in no-stimulation trial) between the acquired blind participants and the sighted participants. For the correlation analyses, we report Pearson's correlation coefficients and statistical p-values for the test of no correlation. For the sub-group and group comparisons, we used two-tailed unpaired Student's t-test. The analyses were conducted in MATLAB version R2018b (The MathWorks, Natick, MA). All data are presented as mean ± standard deviation. Because of its limited sample size, we could not perform statistical test for the congenitally blind participants and thus, qualitatively compared their TMS effect on CV with that of the acquired blind participants.

Data availability

Data and codes to reproduce Figs. 2, 3, S1, and S2 and the related analyses are available from https://github.com/ikegami244/Blind-TMS. The code to identify the peaks is also available from the same repository.

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SUPPLEMENTARY INFORMATION

Supplementary figures

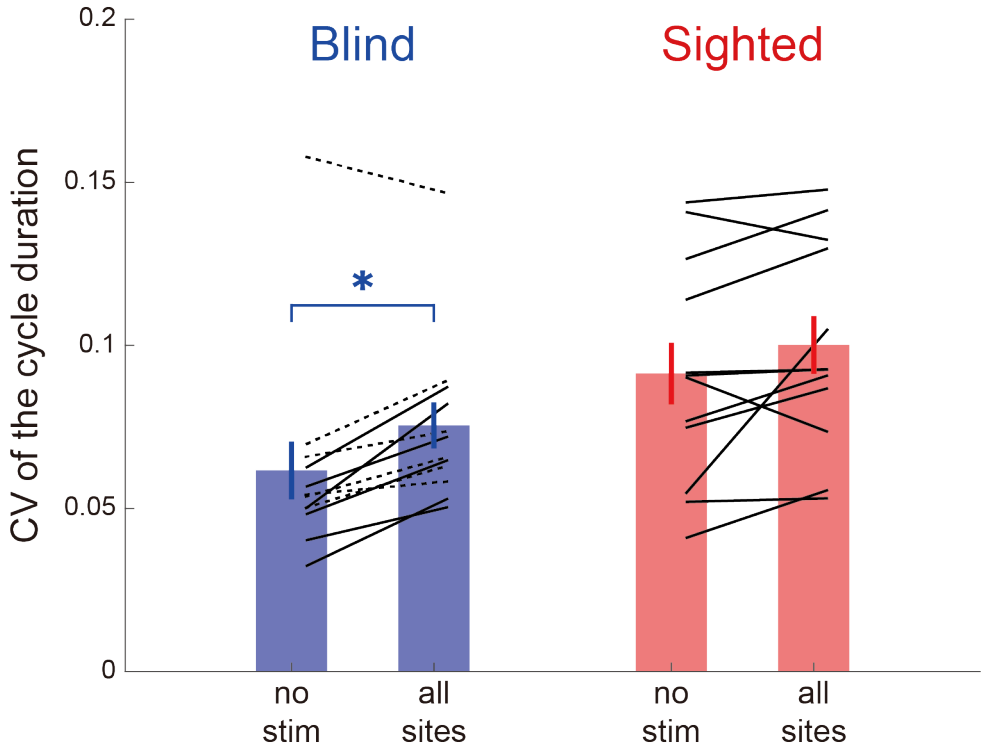

Fig. S1. CV of the cycle duration for the acquired blind (blue) and sighted (red) participants. The averaged CV over all stimulation sites (all sites) were compared with the CV in the no-stimulation trial (no stim). Each line represents data from an individual participant. For the acquired blind participants, solid black lines and dashed lines indicate the subgroups of athletes (B^{LA}) and nonathletes (BL^{NA}), respectively. Bars and error bars indicate the mean and standard errors, respectively. The asterisk indicates $p < 0.05$. Compared to the no-stimulation trial, the averaged CV reliably increased only in the acquired blind participants (paired Student's t-test: $t(11) = 4.358$, $p = 0.002$ with Bonferroni correction for multiple comparisons) but not the sighted controls ($t(11) = 1.821$, $p = 0.096$ without correction).

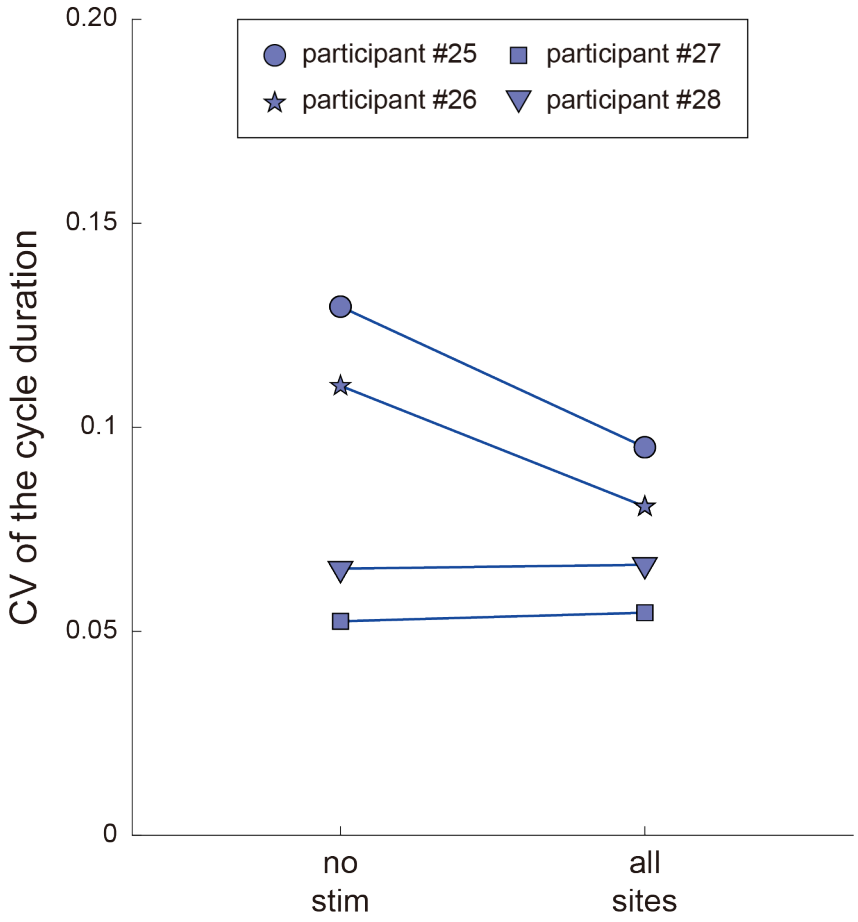

Fig. S2. CV of the cycle duration for congenitally blind participants. The CV in the no-stimulation trial (no stim) and the averaged CV over all stimulation sites (all sites) were plotted for each participant. Each line represents data from an individual participant. In contrast to the result of the acquired blind participants (Fig. S1), TMS did not induce an evident increase relative to the no-stimulation trial (no stim) in all the participants.