Original Research

Functional inhibition of the human middle temporal cortex affects non-visual motion perception: a repetitive transcranial magnetic stimulation study during tactile speed discrimination

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Abstract

The visual motion-responsive middle temporal complex (hMT+) is activated during tactile and aural motion discrimination in both sighted and congenitally blind individuals, suggesting a supramodal organization of this area. Specifically, non-visual motion processing has been found to activate the more anterior portion of the hMT+. In the present study, repetitive transcranial magnetic stimulation (rTMS) was used to determine whether this more anterior portion of hMT+ truly plays a functional role in tactile motion processing. Sixteen blindfolded, young, healthy volunteers were asked to detect changes in the rotation velocity of a random Braille-like dot pattern by using the index or middle finger of their right hand. rTMS was applied for 600 ms (10 Hz, 110% motor threshold), 200 ms after the stimulus onset with a figure-of-eight coil over either the anterior portion of hMT+ or a midline parieto-occipital site (as a control). Accuracy and reaction times were significantly impaired only when TMS was applied on hMT+, but not on the control area. These results indicate that the recruitment of hMT+ is necessary for tactile motion processing, and thus corroborate the hypothesis of a 'supramodal' functional organization for this sensory motion processing area.

Keywords: hMT+, tactile motion, TMS, supramodality

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Introduction

In humans, visual perception of motion activates a specific circuit of the temporo-occipital cortical regions that classically includes the middle temporal complex, hMT+.[1–3] This motion-responsive extrastriate area is also activated during apparent and illusory motion, and mental imagery of movement.[3–6] Furthermore, hMT+ responds to the perception of auditory or tactile motion in sighted,[7–9] as well as in congenitally blind, individuals.[8,10,11] These latter findings indicate that hMT+ also processes non-visual sensory inputs of motion and that visual experience is not a prerequisite for the development of the functional organization of this motion-responsive area. These results extend to hMT+ the supramodal functional organization demonstrated in other 'visual' ventral and dorsal extrastriate cortical areas that process perceptual information independently from the sensory modality through which such information is acquired.[12–17]

Visual experience, however, leads to a functional segregation of the motion-responsive hMT+ into a more anterior portion, corresponding to the middle superior temporal cortex, that responds to both visual and tactile motion, and a more posterior portion that is involved only in the processing of visual motion.[8,11,18,19]

Whether the neural response in hMT+ associated with non-visual motion stimuli is truly related to a causative role or rather is merely an epiphenomenon remains to be determined. Transcranial magnetic stimulation (TMS) provides a unique method to interfere with neuronal function in specific brain regions and assess the consequent effects

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on behavioral performance.[20–22] Indeed, the application of either single-pulse or repetitive TMS (rTMS) on area hMT+ resulted in impaired processing of visual moving stimuli.[23–25] Specifically, TMS-associated decrease in performance occurs between 130 and 150 ms following stimulus onset with single-pulse TMS during processing of visual moving stimuli,[26] or 200 ms with rTMS during visual discrimination of stimulus speed.[27]

Although TMS in the tactile domain has been used mainly to alter neural activity in the somatosensory cortex and to modulate cutaneous perception and sensorimotor transformations,[28] a small number of functional studies have applied TMS to extrastriate temporo-occipital regions to investigate sensory processing through touch, mainly in blind individuals. For instance, disrupting function of the occipital cortex using TMS interferes with tactile discrimination in both sighted and congenitally blind subjects,[29,30] while tactile sensations have been reported in early blind individuals following stimulation of the entire occipital cortex using single-pulse TMS.[31]

The present study was designed to examine whether the functional activation of hMT+ found in response to non-visual motion stimulation is required for processing tactile motion information, or is merely an epiphenomenon with no functional role. The first case would be in line with the hypothesis of a supramodal organization of this cortical area, whereas the second one would suggest that non-visual motion stimuli are actually processed elsewhere. Specifically, we applied rTMS on hMT+ during a tactile task that required subjects to discriminate speed changes of a moving Braille-like dot pattern. The stimulation site for hMT+ was chosen to induce transient interference of neural activity in the more anterior portion that has been shown to be activated in response also to non-visual motion-perception, as explained above.[9,18,19]

Materials and methods

Subjects

Sixteen healthy volunteers (seven men, mean age $\pm$ SD $=$ 23 $\pm$ 2 y; range: 20–28 y) were enrolled into the study. All of them were right-handed, according to the Edinburgh Handedness Inventory[32] (range: 71–100%). All participants were free of any medical, neurological or psychiatric disorder, had no contraindications to rTMS[33,34] and were not taking any medication. All participants gave their written informed consent after the study procedures and the risks involved had been explained, and received a reimbursement for participating to the study. The whole experimental protocol was approved by the Ethics Committee of IRCCS Fatebenefratelli, Brescia, Italy.

Experimental procedure

Participants were seated in a quiet room with their head placed on a chin rest. A cylinder covered by a grid of Braille-like plastic dots that could be rotated at different speeds by an engine system was enclosed in a polystyrene box with an aperture on the upper part to allow participants to insert the finger to be stimulated and to comfortably rest the other fingers on a support (see Figure 1). Participants were blindfolded while they touched the cylinder with either the index or the medium finger (alternatively, between blocks) of their right dominant hand; a pink noise at 50 dB was used to mask the sounds associated with the changes in the rotation speed of the engine. Participants were instructed to focus their attention on the tactile stimulation, and to press the keyboard spacebar with their left hand whenever they detected a change in the rotation velocity of the grid under their finger.

The cylinder was placed horizontally along its major axis in front of the subjects (Figure 1). The cylinder surface was made of a regular grid of plastic dots (diameter 0.5 mm, height 0.5 mm, density 0.8/cm^2). The cylinder rotated outwardly at five different speeds by means of an electric engine connected to a computer through a controller, which received impulses from the parallel port and translated them into variations in the power passed to the engine. The five cylinder speeds were set to regularly increase from 0.42 up to 0.62 rounds per second. The five velocities were coupled to obtain four velocity gaps, which were randomly presented in an increasing and decreasing way (i.e. passing from a slower to a faster speed, or *vice versa*). After starting, the flow of the speed change sequence continued with no interruption until the 40th trial, following a predetermined (but different between blocks) sequence. The disposition of velocities in couples produced a total of 20 different gaps separated into four levels on the basis of the distance between the two speeds, ranging from one (e.g. speed 3 versus speed

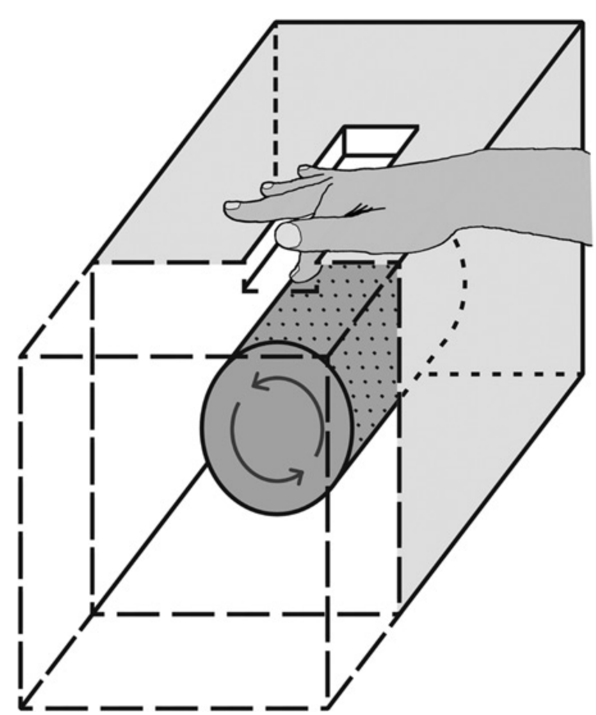

Figure 1 A representation of the experimental setting: the rotating cylinder was completely contained within a polystyrene box. Participants inserted one finger into the fissure, directly over the rotating surface of the cylinder

4) up to four (e.g. speed 1 versus speed 5). The number of stimuli for the largest gaps was repeated to obtain an equal number of stimulations (eight) for each category. Moreover, eight catch trials (with no speed changes) were included in each block. Thus, a total of $32 + 8 = 40$ trials were presented at five interstimulus intervals ranging from 4000 up to 6000 ms (different by 500 ms). Blocks lasted four minutes each, and were presented interleaved with a pause of five minutes.

rTMS protocol

Repetitive TMS was applied using a Magstim Super Rapid magnetic stimulator and a figure-of-eight coil (double 70 mm) (Magstim Company Limited, Whitland, UK). Before the experiment, individual active motor excitability thresholds of stimulation were determined by applying a single TMS pulse on the left motor cortex to induce a muscular contraction in the contralateral hand. The threshold was defined as the minimum intensity that induced a visible contraction in the tested hand on at least five out of 10 trials. The stimulation intensity used during the experiment was set at 110% of each subject's threshold. The mean stimulation intensity (as a percentage of the maximum machine output) was 52% (range 47–59%). During the experiment, rTMS was delivered starting 200 ms after any 'trial onset' (i.e. at the change of speed) using a train of seven pulses with a frequency of 10 Hz (i.e. lasting a total of 600 ms), which is within safety guidelines for rTMS.[33] The stimulation interval was chosen in order to cover the temporal window including both the stimulus arrival and its early processing in the sensorial areas. Participants tolerated the rTMS procedure well, and did not report any adverse effects or complaints.

The targeted stimulation sites were either the anterior portion of the left hMT+ in the experimental condition or an interhemispheric site (Talairach coordinates[35] $X = 0$, $Y = -76$, $Z = 30$; POz, according to the 10–20 nomenclature) during the control condition (Figure 2). The control condition was included to rule out any generic effects due to the interference arising from non-specific rTMS effects or the procedure itself.

The stimulation site for the anterior portion of hMT+ was chosen accordingly to the local maxima that was previously identified in those regions that responded significantly during tactile motion perception in sighted volunteers (Talairach coordinates $X = -49$, $Y = -62$, $Z = 5$[8]), and consistently reported in the literature.[18,19] These sites were localized on the subject's scalp using the SofTaxic Evolution Navigator system (www.emsmedical.net). The SofTaxic Navigator system permits the computation of an estimated volume of magnetic resonance imaging (MRI) of the subject's head to guide TMS coil positioning. The estimated volumes of MRI are automatically calculated by the means of a warping procedure, through the operation of a generic MRI volume (template) on the basis of a set of points digitized from the subject's scalp. With respect to using the individual subject's MRI for the coil localization on the target area, the mean error of the estimated MRI obtained with the above procedure was 2.11 (SD: ± 2.04) mm. This error is comparable to the spatial resolution of TMS on the cerebral cortex and to the individual average variability of hMT+ location.[7]

During the experiment, participant heads were stabilized on a chinrest, while the coil was fixed by means of an articulated mechanical holding arm (Manfrotto Magic arm with two clamps, www.manfrotto.com) and a heavy duty tripod for all conditions. This arm allowed maximum flexibility for positioning the coil at the desired location, and for selecting the appropriate orientation and providing maximum stability once fully positioned.

For hMT+ stimulation, the coil was placed tangential to the scalp with the handle pointing 45° off the midsagittal axis of the subject's head. In contrast, in the control condition the handle was parallel to the midsagittal axis, pointing anteriorly.

Participants were presented with five blocks (one practice and four experimental); both rTMS site (control-TMS, hMT+ -TMS) and Finger (index, middle) were randomized. The first block was always without TMS in order to familiarize the participants with the task. Trial administration, consisting of the transmission of the impulses through the parallel port, and the measurement of accuracy and reaction time (RT) were controlled by Presentation® (Neurobehavioural Systems Inc., Albany, CA, USA).

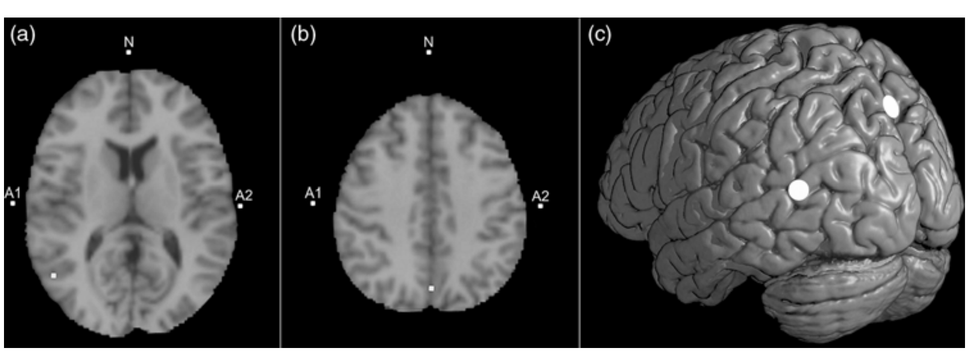

Figure 2 Locations of the stimulated sites on the cerebral cortex: (a) experimental site (left hMT+, transverse slice at $Z = 5$) and (b) control site (interhemispheric sulcus, transverse slice at $Z = 30$) as identified using the SofTaxic system. (c) View of a three-dimensional brain reconstruction showing the localization of the two stimulation sites

Statistical analysis

A series of repeated measures analysis of variances was carried out on the percent values of correct responses and the mean RT, considering the following independent within-subjects variables: Gap (4 levels, ranging from 1 to 4, determined by the distances between the speeds), Speed direction (acceleration versus deceleration), Finger (index versus middle) and rTMS site (control TMS or hMT+ TMS). The Gap 0 level was a repetition of the last speed with no change in speed direction, and thus was not included in the analyses. To avoid empty cells, missing data were estimated through a series of multiple linear regressions,[36] given that the go/no-go paradigm implies to collect a response only whenever a change was detected. Control and hMT+ conditions resulted in a total of about 10% and 20% of missing values, respectively. Statistical analyses were done by means of Statistical Package for Social Science (SPSS) statistical software (SPSS Inc, Chicago, IL, USA).

Results

The analysis of accuracy showed a significant main effect for the Gap (i.e. greater accuracy for larger gaps in speed changes; $F_{3,13} = 220.5$, $P < 0.01$, $\eta^2 = 0.94$), Speed direction (i.e. greater accuracy for decelerations of speed; $F_{1,15} = 28.3$, $P < 0.01$, $\eta^2 = 0.65$) and TMS site ($F_{1,15} = 18.3$, $P < 0.05$, $\eta^2 = 0.55$) factors. Moreover, the interactions Gap × Speed direction (i.e. more accurate for decelerations of speed at narrower gaps in speed changes) and Gap× TMS site were also significant ($F_{3,13} = 4.119$, $P < 0.05$, $\eta^2 = 0.22$ and $F_{3,13} = 4.164$, $P < 0.05$, $\eta^2 = 0.22$, respectively), as shown in Table 1 and Figure 3a. No significant finger effect ($F_{3,13} = 0.1$, $P <$ NS, $\eta^2 = 0.01$) or interactions were found for accuracy. Overall, accuracy was significantly impaired when rTMS was applied over hMT+ as compared with the control cortical site, and the greatest reductions in performance were seen with the smaller (i.e. the most difficult) gaps in speed changes.

In the RT analysis, the Gap ($F_{3,13} = 28.4$, $P < 0.01$, $\eta^2 = 0.66$; Table 1) and TMS site ($F_{1,15} = 5.1$, $P < 0.05$, $\eta^2 = 0.25$) factors also were significant, consistent with the accuracy analysis results. Furthermore the TMS site factor showed a significant interaction with Speed direction ($F_{1,15} = 7.138$, $P < 0.05$, $\eta^2 = 0.33$), as the TMS-mediated interference had a greater behavioral effect when subjects had to detect an acceleration of speed (Figure 3b), and the highest increases in RT were found for the smaller (i.e. the most difficult) gaps in speed changes. No significant finger effect ($F_{3,13} = 0.7$, $P <$ NS, $\eta^2 = 0.05$) or interactions were found for RT.

Discussion

This experiment was designed to determine whether the activation in the 'visual' area hMT+ found in response to tactile motion stimuli reflects a true functional role of this area during non-visual motion perception or is merely an epiphenomenon. Multiple functional MRI (fMRI) studies have demonstrated that hMT+ responds to both tactile

Table 1 Percentage of correct responses (upper part of the table) and reaction times (lower part of the table) separated for Gap factor, indicating the values for the two levels of Speed direction and for the two levels of TMS (left part of the tables) and the respective means (right part)

Gap	Deceleration		Acceleration		Mean for TMS		Mean for Speed direction		Grand mean
	Control TMS	hMT+ TMS	Control TMS	hMT+ TMS	Deceleration	Acceleration	Control TMS	hMT+ TMS	
Accuracy									
0	–	–	–	–	–	–	3.1% (3.9)	1.8% (1.9)	3.5% (1.5)
1	26.6% (4.1)	15.6% (3.5)*	15.6% (3.5)	10.2% (3.1)	21.1% (3.2)	12.9% (2.9)*	21.1% (3.3)	12.9% (2.8)*	17.0% (2.8)
2	81.3% (5.0)	60.2% (7.1)*	66.4% (6.2)	39.1% (6.6)*	70.7% (5.2)	52.7% (5.4)*	73.8% (5.0)	49.6% (6.1)*	61.7% (4.9)
3	93.0% (3.0)	79.7% (6.9)*	87.5% (4.6)	75.8% (6.6)	86.3% (4.6)	81.6% (4.7)	90.2% (3.3)	77.7% (6.5)*	84.0% (4.4)
4	97.7% (1.7)	91.4% (4.2)	89.1% (3.9)	81.3% (6.4)	94.5% (2.5)	85.2% (4.3)*	93.4% (2.4)	86.3% (5.1)	89.8% (3.2)
Mean	74.6% (2.6)	61.7% (4.6)*	64.7% (3.6)	51.6% (4.7)*	68.2% (3.3)	58.1% (3.8)*	69.6% (2.8)	56.6% (4.5)*	63.1% (3.4)
Reaction times									
1	1667 (190)	1771 (244)	1418 (90)	1758 (157)*	1718 (204)	1587 (111)	1542 (122)	1764 (190)	1653 (150)
2	1197 (108)	1285 (163)	1235 (132)	1683 (191)*	1241 (129)	1458 (148)*	1215 (104)	1483 (163)*	1349 (131)
3	1021 (112)	1150 (140)	1148 (94)	1294 (165)	1085 (117)	1220 (121)*	1084 (98)	1222 (146)	1153 (115)
4	1044 (116)	1082 (167)	1043 (101)	1178 (134)	1063 (134)	1110 (110)	1043 (102)	1129 (139)	1086 (114)
Mean	1232 (113)	1322 (162)	1211 (87)	1478 (149)*	1277 (135)	1344 (111)	1221 (97)	1400 (152)*	1310 (122)

hMT+, middle temporal complex; TMS, transcranial magnetic stimulation
Standard error means are in parentheses
*Significant *post hoc* comparisons (Bonferroni with alpha = 0.05) for each comparison

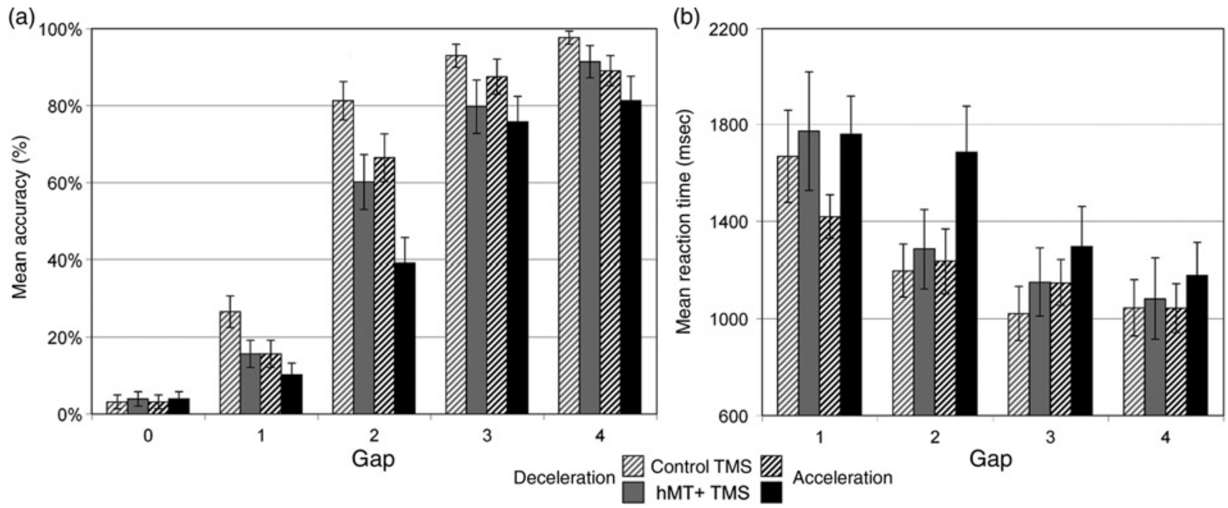

Figure 3 Average accuracy (a) and reaction time (b) values for TMS crossed with Speed direction are represented as a function of Gap (±SEs). Bars representing experimental stimulation are shown with full color, while control stimulation bars are shown with stripes filling. Accelerating speed direction is represented in black, while grey indicates decelerating speed direction. hMT+, middle temporal complex; TMS, transcranial magnetic stimulation

and auditory discrimination of motion,[7–11] and have consistently indicated a functional localization of non-visual motion processing in the more anterior part of hMT+.[8,11,18,19] Furthermore, neural activation of this cortical area in response to either tactile or aural motion perception has also been demonstrated in congenitally blind individuals, thus showing that the involvement of hMT+ in non-visual motion detection cannot be justified simply by visual imagery, but rather represents a supramodal functional organization within hMT+.[7–11] A similar supramodal functional organization has been shown both in the ventral and in the dorsal 'visual' cortical pathways during object recognition and spatial discrimination,[12–14,37] and in other prefrontal and parietal cortical areas subserving higher-order cognitive functions, such as mental imagery, working memory and action recognition.[16,17,37]

To verify the study's hypothesis, we used rTMS to modulate neuronal activity in the more anterior part of hMT+ during a tactile motion discrimination task. We reasoned that if hMT+ activity during tactile discrimination of motion is simply an epiphenomenon, then rTMS on hMT+ cortex should have no effect on the individual performance in detecting velocity changes. On the contrary, if activity in hMT+ reflects a true functional role in discriminating tactile motion, then we should observe an impairment in task performance when rTMS is applied to hMT+ cortex as compared with when it is applied to the control cortical site.

rTMS applied to the more anterior part of hMT+ (Talairach coordinates $X = -49$, $Y = -62$, $Z = 5$) produced a significant impairment (decreased accuracy and increased RTs) in the subject's ability to detect changes in the velocity of the rotating dotted grid by the tactile modality as compared with rTMS on the task-unrelated cortical control site. To our knowledge, this is the first TMS-related evidence that corroborates the hypothesis of a modality-independent representation of motion in hMT+ by demonstrating a functional role of this cortical area during a non-visual task, specifically, during a tactile speed motion detection task.

These findings are in agreement with and extend to the tactile domain previous experiments using TMS over the hMT+ cortical area during visual motion and visual speed discrimination tasks.[23,26,27,38–42] As previously reported, both psychophysical and brain functional features are similarly associated with touch and vision in motion discrimination.[23,43–45] The overlap in the timing of rTMS stimulation in our tactile task with the visual experimental setting in the study by McKeefry and collaborators[27] further supports this correspondence between tactile and visual discrimination of motion and speed.

As expected, rTMS effects on tactile discrimination of velocity changes were more pronounced when the task was more difficult (i.e. with narrower gaps of rotating speed changes). The acceleration/deceleration direction of the velocity changes showed a significant interaction with the Gap factor, as participants were generally more accurate when detecting a deceleration rather than an acceleration in speed, primarily with the narrower and more demanding gaps of rotating speed changes. Moreover, the TMS-mediated effect on RT was greater when subjects had to detect an acceleration of speed. While we know that the ability to scale tactile speed motion is critically dependent on the surface structure, that is, it is higher with textured than smoother surfaces,[43] we have no information regarding the importance of speed direction of the stimuli at either a psychophysical or a neural level (e.g. central encoding of acceleration/deceleration signals). In the visual domain, a study with a pattern of moving dots showed that the subjective perception of velocities was underestimated more after accelerations than after decelerations,[46] likely because of distinctive speed-dependent adaptation mechanisms in hMT+.[47] Thus, the results of the present study are consistent with, and extend to the tactile modality, the hypothesized adaptation of the perceptual system to accelerating but not to decelerating speeds, so that decelerating changes become more salient to the subject.

In the present study, we did not include a visual task component to examine the effects of rTMS on hMT+

during visual discrimination of motion in the same subjects, as many studies had already demonstrated that TMS application over hMT+ results in an impaired performance during visual perception of moving stimuli.[23–27,38–42] However, in light of the recent fMRI findings indicating the functional segregation within hMT+ discussed above – a more anterior part that responds to both visual and tactile motion, and a more posterior part that responds to visual motion only[8,11,18,19] – it would be of interest to compare the effects of selective disruptions of neural activity in these two subareas while subjects perform a combination of visual and tactile motion detection tasks. Given the results reported here, this would be the optimal paradigm to verify the distinctive functional role of the two hMT+ subregions. According to the functional imaging data discussed above and the results of the present study, we would expect that rTMS over the anterior (as shown here) but not the posterior part of hMT+ would disrupt tactile motion perception while visual motion detection would be affected by rTMS over the whole hMT+. Moreover, a similar rTMS study should be conducted in congenitally blind individuals to investigate to which extent the topographical functional organization within hMT+ develops in the absence of visual experience.[8,10] Finally, given that auditory motion has also been found to engage the hMT+ both in sighted and in congenitally blind individuals,[11] a future study should include an auditory motion task as well.

Another limitation of this study is the lack of functional localizers in the individual subjects to ensure that the TMS stimulation site may not overlap, even in part, with neighbor supramodal or multisensory areas in the lateral occipital cortex (LOtv),[12,13] or in the multisensory superior temporal sulcus (STSms).[48] It should be kept in mind, however, that the localization of the anterior portion of hMT+ used as the site for TMS stimulation (Talairach coordinates x: -49, y: -62, z: 5[8]) is sufficiently distant from the more dorsal and anterior STSms center-of-mass (x: -44, y: -35, z: 13[48]) and the more ventral LOtv localization (x: -45 ± 5, y: -62 ± 6, z: -9 ± 3[12]), to be clearly distinguished by using, as we did here, the individual subject morphological MRI scan for the coil localization on the target area (estimated mean error is 2.11 ± 2.04 mm). Furthermore, as detailed in the Materials and methods, while the individual average variability for hMT+ location[7] adds a certain amount of error, this has been estimated to be smaller than the amplitude of the magnetic field produced by TMS.[49]

In conclusion, the results of the present rTMS study provide direct evidence that hMT+ plays a functional role in tactile motion discrimination tasks, as tactile motion perception is significantly impaired when neural activity in hMT+ is disrupted by rTMS. Thus, the activation revealed in hMT+ by previous functional brain imaging studies during tactile motion processing indicates that the functional organization of this cortical area is not merely visual in nature.

Author contributions: All authors participated in the experimental design, analysis of the data and their interpretation and reviewed each version of the manuscript. ER, LS, DaB, TV and PP conceived the original proposal; DeB and CM performed the protocol experiments and collected the data; ER, DeB, PP and CM co-wrote the paper. PP and CM equally contributed to this work.

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