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Research report

Allocentric coding in ventral and dorsal routes during real-time reaching: Evidence from imaging-guided multi-site brain stimulation

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H I G H L I G H T S

- We examine contributions of ventral and dorsal neural areas in allocentric reaching.
- We use imaging-guided multi-site patterned transcranial magnetic stimulation.
- cTBS over lateral occipital cortex and angular gyrus affects reaching time.
- The results support the updated perception-action model (Milner and Goodale, 2008).

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Recent evidence has revealed an advantage for movements to last target positions in a structured visual display, suggesting a mediating role of allocentric, in addition to egocentric, information in goal-directed reaching. This notion is accommodated by the recently updated perception-action model (Milner and Goodale, 2008), which postulates functional roles of ventral and dorsal neural areas in allocentric coding. In the present study, we used imaging-guided multi-site continuous theta burst stimulation (cTBS) over regions of the ventral and dorsal processing streams to unravel their functional contribution on visually guided reaching in two display conditions: the “egocentric” condition where the target appeared in an empty display and the “allocentric” condition where the target appeared in a structured display with placeholders marking possible target locations. Cortical sites for cTBS were identified individually for each participant via coregistration with magnetic resonance scans. Results indicated that cTBS in the egocentric condition did not affect movement time, but cTBS in the allocentric condition modulated movement time contingent on stimulation site and target position. In particular, cTBS over the lateral occipital cortex (part of the ventral stream) and over the angular gyrus (part of the dorsal stream) eliminated the last-target advantage by slowing down reaching to the salient last target position. cTBS over the superior parietal occipital cortex did not affect the last-target advantage. These outcomes provide the first causal evidence for allocentric coding in ventral and dorsal routes during real-time reaching, thereby supporting the updated perception-action model.

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1. Introduction

Reaching for objects in space is essential for effective interaction with the environment. The position of an object in space and thus the motor program for reaching this object can be coded with respect to one's own body (the egocentric reference frame) or

relative to contextual features and other objects (the allocentric frame) (for a review, see Ref. [7]). More than 50 years ago, Fitts [18] was the first to examine systematically the effects of target distance and target size on the speed and accuracy of goal-directed reaching. Fitts discovered a lawful relationship between movement time (MT) and the difficulty of the movement: $MT = a + b \log_2(2D/W)$ (D = distance to be moved, W = target width). This mathematical formula—known as Fitts' law—reliably accounts for MT of target-directed movements in a variety of tasks (e.g., moving a joystick, moving a foot or the head) (for a review, see Ref. [37]).

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Despite the success of Fitts' law, it should be noted that it is largely based on experiments with "isolated" targets that provide a single focus of visual salience. That is, typically, participants move their hand to a single target in an otherwise empty field. In daily life, however, visual scenes are often cluttered, containing many potential target objects, which need to be discriminated: for instance, picking one specific coin from a wallet or hitting one specific key on a keyboard. Importantly, cluttered environments may place greater and qualitatively different demands on visuomotor control processes than "empty" or sparse environments, since non-target objects may act as distracters or obstacles that can compete for selective motor action (e.g., [9,47]).

We recently provided a clear demonstration that a simple perceptual manipulation can produce a striking violation of Fitts' law [2]. In this study, participants reached for a target that could appear in one of seven horizontally aligned locations to the right of the home (start) position on a touch screen. In the control (no-placeholder) condition, the target appeared in a blank field, and MTs for all seven targets conformed to Fitts' law, showing increases in MT for targets further away. In the experimental (placeholder) condition, empty placeholder boxes were continuously visible, marking all seven potential target locations. The target was presented by coloring in one of these placeholder boxes. In this placeholder condition, MTs for the first six locations again followed Fitts' law but, surprisingly, MT to the last target was shorter than that to the second last target. In other words, in a structured visual array, reaching movements to the last target are completed faster than movements to the second last target, without loss of accuracy. Since the first report of this *last-target advantage*, several successful replications of our own and other groups have testified its robustness [4,5,40].

Based on this demonstrated violation of Fitts' law in the placeholder condition, we speculated that rapid aimed hand movements can be influenced by allocentric information, rather than exclusively by egocentric information. By this view, the linear array of placeholders forms a "Gestalt" figure that provides an allocentric frame of reference, with faster spatial processing of the last target because it appears in a perceptually *salient* position. End or outmost positions are salient because they are the natural spatial anchors that define an organizational structure [41]. The importance of salient landmarks in the visual display for reaching has also been emphasized by Obhi and Goodale [36] who demonstrated that the presence of a visual background facilitates movement planning by stabilizing the target location.

Although this novel view that egocentric and allocentric coding conjointly mediate the planning and execution of goal-directed action is gaining support in the literature (e.g., [46,27,8,20]), it seemingly stands in contrast to the original perception-action model as proposed by Milner and Goodale [33,34]. These authors followed up on the earlier established anatomical distinction between a ventral and dorsal visual pathway in the brain [49] by proposing a functional specialization. The *ventral stream* projects to the inferior-temporal cortex and processes allocentric information to support visual identification and recognition of objects (vision-for-perception; e.g., [16]). The *dorsal stream*, on the other hand, projects upwards to the posterior parietal cortex and processes egocentric information to govern goal-directed movements to target objects (vision-for-action; e.g., [6]). Clearly, the finding of the last-target advantage for reaching in structured visual displays does not accord with this strict dichotomy, because it demonstrates the influence of allocentric information in goal-directed action. In line with this and other observations, Milner and Goodale [35] recently clarified and refined their model, stating that both streams may contribute to action, but in different ways. The role of the ventral system is to select and identify the goal object (the target) and to plan an adequate action towards it. This planning in the ventral stream is

assumed to be quite abstract and general—for instance, it chooses the most adequate hand to use and its posture. The dorsal stream, on the other hand, implements the chosen action by detailed programming and online control operations.

Furthermore, Milner and Goodale [35] now assume that the spatial context surrounding the target is processed by both ventral and dorsal systems. According to the updated perception-action model, both the ventral and dorsal streams need to focus on a target object in performing their key visual roles, and both should deal with other potentially conflicting visual information in the display. This conceptualization suggests that goal-directed actions are visually co-determined by complementary processing of allo- and egocentric information, but how exactly this is accomplished and what the respective ventral and dorsal contributions are remains unclear.

In the present study, we used imaging-guided multi-site continuous theta burst stimulation (cTBS) over regions of the ventral and dorsal processing stream during visually-guided real time reaching movements in order to unravel their functional contribution on reaching performance in egocentric (placeholders absent) and allocentric (placeholders present) conditions. Within the ventral stream, we delivered cTBS to the lateral occipital cortex (LOC). Its role in the (allocentric) coding of visual information for perception is undisputed (e.g., [23]). Moreover, LOC also has been implicated in the coding of movements in allocentric task conditions (i.e., copying; [45,44]). Within the dorsal stream, we applied cTBS to two different areas: the superior parietal occipital cortex (SPOC) and the angular gyrus (AG), which have been suggested to play specific functional roles in reaching, respectively the encoding of reach locations and the encoding of reach movements [51], both of which may involve allocentric coding. We used our placeholder paradigm, and in particular the last-target advantage, to test the updated perception-action model's hypothesis that dorsal regions encode target location not only in egocentric but also in allocentric coordinates. Empirical evidence for allocentric coding would be provided by a cTBS-induced disruption of Fitts' law violation in the placeholder condition, that is, a disruption of the faster movements to the last target position, which represents a salient allocentric landmark. In other words, cTBS over regions that process allocentric information was expected to eliminate the last-target advantage.

2. Methods

2.1. Participants

Sixteen paid, right-handed volunteers recruited from Maastricht University participated in this study (mean age = 23.5 years; range: 21–35 years; 10 female). All had normal or corrected-to-normal vision and no history of neurological or psychiatric disorders. They received medical approval for participation and gave their written informed consent in accordance with the Declaration of Helsinki after being introduced to the procedure. The study was approved by the local Medical Ethical Committee.

2.2. Stimuli and apparatus

Participants made rapid aimed hand movements to one of five possible targets that were linearly arrayed at increasing distances from the start position (see Fig. 1A) on a 19 inch LCD ELO touch monitor (response time 5 ms, accuracy 0.29 mm). Viewing distance and head position was fixed with a chin rest at 37 cm. There were two display conditions. In the placeholder condition, the potential target positions were indicated by empty placeholder boxes (each 10 × 10 mm, separated by 5 mm) that were continuously visible; the target signal was presented by coloring in one of these placeholders green. In the no-placeholder condition, there were no

Fig. 1. (A) Schematic overview of the start and target positions. Participants executed rapid hand movements in the horizontal direction from the start box to one of the five target boxes (each 10×10 mm, boxes separated by 5 mm) either with the other boxes present (placeholder condition) or with the other boxes absent (no-placeholder condition). The target box numbers were not present in the display. Not drawn to scale; (B) Stimulation sites of a typical subject. AG = angular gyrus (dorsal stream), SPOC = superior parietal occipital cortex (dorsal stream), LOC = lateral occipital cortex (ventral stream). These stimulation sites were restricted to the left hemisphere.

placeholders, and the green target appeared by itself. The start box was also 10×10 mm.

2.3. Procedure and experimental design

At the beginning of each trial, participants contacted the start box with the right index finger, prompting the target stimulus to appear immediately (and the start box to disappear). Participants were instructed to move their finger as quickly as possible to the target while maintaining endpoint accuracy. The target stimulus disappeared 250 ms after the end of the movement. After an additional 500 ms the start box appeared again, signaling the start of the next trial.

Participants were evaluated in 6 separate sessions on 6 separate days. In the first session, we obtained anatomical brain measurements of all participants using magnetic resonance imaging (MRI). In the following 5 sessions, participants performed the reaching task under five different cTBS conditions on separate days: Control (no stimulation), Sham, AG, SPOC and LOC. The order of these conditions was counterbalanced. On each day, participants first performed 15 practice trials (3 for each target) in each of the two placeholder conditions, after which cTBS was applied. Following cTBS, participants performed 80 test trials (16 for each target position) in each of the two placeholder conditions (with or without placeholders). The order of the two placeholder conditions was

counterbalanced, whereas the order of target position within a block of 80 test trials was random.

2.4. Neuronavigation and localization of brain sites

A high-resolution anatomical image was obtained from each participant in a 3-T magnetic resonance scanner (Siemens). The T1-weighted data set was acquired with the help of a magnetization prepared rapid acquisition gradient echo sequence or a T1-weighted structural scan with an isotropic resolution of 1 mm using a modified driven equilibrium Fourier transform sequence with optimized contrast for GM and WM and imaging parameters. Data were analyzed using BrainVoyager QX 1.8. Surface reconstruction was performed in order to recover the exact spatial structure of the cortical sheet and to improve the visualization of the anatomical gyrification. The stimulation sites were localised using frameless stereotaxy (BrainVoyager TMS Neuronavigator, [43]). This TMS neuronavigation system enabled us to account for inter-individual differences in anatomical brain structures while stimulating.

The cTBS coil was neuronavigated to one of four specific anatomical areas in the left hemisphere of each participant, that is, contralateral to the reaching arm (see Fig. 1B): (a) the superior parietal occipital cortex (SPOC), located along the medial surface of the parietal lobe, medial to the intraparietal sulcus, anterior to the parieto-occipital sulcus, and posterior to the subparietal sulcus [51]; (b) the angular gyrus (AG), located in the inferior parietal lobule and close to the posterior part of the adjoining intraparietal sulcus [51]; (c) the lateral occipital cortex (LOC), located slightly inferior and posterior to the junction of the inferior temporal sulcus and the lateral occipital sulcus [13]; and (d) a sham location, located midway between LOC and AG and posterior to AG. The average Talairach coordinates of the stimulated sites were (mean $\pm$ SE; x, y, z, respectively): SPOC -8.9 ± 0.8 , -79.6 ± 1.3 , 38.5 ± 1.6 ; AG -44.2 ± 1.4 , -70.0 ± 1.5 , 29.4 ± 2.0 ; LOC -45.5 ± 1.0 , -73.6 ± 1.7 , -1.9 ± 1.2 ; Sham -43.5 ± 1.1 , -73.5 ± 1.7 , 12.6 ± 1.4 . For the sham condition a placebo TMS coil was used with the same mechanical outline and clicking sound during discharge but equipped with a magnetic shield that reduced the effective magnetic field by approximately 80%. Otherwise the procedure was identical to the active stimulation conditions.

2.5. Continuous theta burst stimulation (cTBS)

The cTBS protocol consisted of a continuous 40 s train of 600 stimuli; short bursts (3 stimuli) of 50 Hz rTMS repeated at a rate in the theta range (5 Hz) (MagVenture x100 stimulator, MC-B70). This protocol produces an inhibitory effect temporarily suppressing local cortical excitability for up to 60 min [24]. Intensity was set at 80% of the resting motor threshold, ranging from 21 to 37 (SD = 5) of maximum stimulator output. Individual motor thresholds were determined as the intensity at which the stimulation of the left motor cortex with single-pulse TMS resulted in a visible movement of the contralateral thumb in 50% of the trials. Note, cTBS is an “offline” TMS technique that was delivered before, and not during, the execution of the motor task. The reasons for choosing cTBS instead of repetitive TMS were twofold: shorter stimulation times (40 s) and longer effect durations (e.g., [24,48]).

2.6. Analysis

Trials on which the movement endpoint deviated more than 10 mm from the target's center, as well as trials with movement times shorter than 200 ms or longer than 1200 ms, were considered outliers and were excluded from all analyses (0.22%). Furthermore, data from two participants were excluded from all analyses to ensure homogeneous task performance because their mean MT was

more than two standard deviations above the average MT across participants.

We derived two measures of response time: reaction time (RT), measured from target onset to release of the start box, and movement time (MT), measured from release of the start box to contact with the target area on the touch screen. Furthermore, we derived three measures of response (end-point) accuracy in the horizontal dimension: absolute error (AE), defined as the mean of the absolute deviations of the target's center; constant error (CE), defined as the signed deviation from the target's center; negative values reflect undershoots, positive values reflect overshoots; and variable error (VE), defined as the standard deviation of the movement endpoints.

Preliminary analyses revealed no significant differences between the Control and Sham conditions as a function of Placeholder Condition and Target Location (all dependent variables; all p -values $>.05$). Hence, to increase statistical power, we combined the data across these two conditions (from here on called: Combined Control condition). We conducted a cTBS Condition (Combined Control, AG, SPOC, LOC) $\times$ Placeholder Condition (placeholders present or absent) $\times$ Target Location (5 levels) repeated measures univariate analysis of variance (ANOVA) on mean MT, AE, CE, VE, and RT. Whenever sphericity was violated, we reported the Huynh–Feldt corrected p -values of the degrees of freedom. Importantly, since MT (in defining the last-target advantage) was the key dependent variable, we used planned comparisons directed at the difference in MT to Targets 4 (second-last target) and 5 (last target) to test the hypothesis that cTBS applied to ventral and dorsal sites would eliminate the last-target advantage relative to the Combined Control condition with placeholders present.

3. Results

For MT, all main effects were significant (all $p < .02$). The three-way interaction approached significance, ($F(12,156) = 1.66$, $p = .082$; $\eta_p^2 = .113$), suggesting that the effects of cTBS for placeholder and no-placeholder conditions diverged, as can be seen in Fig. 2A and B, which show mean MT for displays with and without placeholders as a function of cTBS condition and Target Location. To further investigate this pattern, we calculated separate two-way ANOVAs for the placeholder and no-placeholder condition. For the no-placeholder condition (see Fig. 2A), a cTBS (Combined Control, AG, SPOC, LOC) $\times$ Target Location (5 levels) repeated measures ANOVA revealed no significant effect involving the factor cTBS (all $p > .1$). This finding indicates that cTBS in the no-placeholder condition did not influence MT, suggesting that egocentric coding was spared. The significant main effect of Target Location, $F(4, 52) = 89.91$, $p < .001$, $\eta_p^2 = .874$, reflected robust increases in MT with each additional increase in movement distance, which accords with Fitts' law.

In contrast, for displays with placeholders, there was a significant interaction between cTBS and Target Location, $F(12, 156) = 2.26$, $p < .05$, $\eta_p^2 = .148$, which demonstrates a differential effect of cTBS on MT contingent on cTBS stimulation site and Target Location. This interaction is shown in Fig. 2B. Tests on the simple main effects of the factor cTBS indicated, for all target locations, substantially longer MTs in the LOC condition compared to the other TMS conditions, which did not differ significantly from each other. This outcome suggests that, with placeholders present, TMS over LOC interfered with allocentric coding of target location. Importantly, to test the influence of cTBS on the last-target advantage in the placeholder condition, we performed a one-way repeated measures ANOVA on the MT difference scores between the last target (Target 5) and second-last target (Target 4) as a function of cTBS condition (see box in Fig. 2B). In effect, this analysis provides a test of the effect of cTBS on the slope of the line connecting MT for Targets 4 and 5. This analysis revealed a significant pattern of

differential cTBS effects, namely decrements in MT for the last target (relative to the second-last target) for cTBS over SPOC (-13 ms) and CONTROL (-3 ms) but increments in MT for the last target (relative to the second-last target) for cTBS over LOC ($+28$ ms) and AG ($+16$ ms), $F(3, 39) = 5.25$, $p < .05$, $\eta_p^2 = .288$. Planned comparisons on these MT difference scores revealed that LOC ($F(1, 13) = 5.29$, $p < .05$) and AG ($F(1, 13) = 6.62$, $p < .05$) deviated significantly from Combined Control, SPOC did not ($F(1, 13) = 3.35$, $p > .05$). In contrast, in the no-placeholder condition, cTBS did not affect the slope of the function relating MT for last and second-last targets targets, $F(3, 39) = .71$, $p > .5$. In sum, with placeholders present, cTBS over LOC and AG eliminated, and even reversed, the MT benefit for the last target observed in the CONTROL and SPOC conditions. This pattern of differential MTs for last and second-last targets as a function of cTBS condition confirms the spatial status (i.e., saliency) of the last target in structured visual displays, and, importantly, suggests allocentric coding of target locations by LOC (ventral stream) and AG (dorsal stream).

Overall, the movements were very accurate with a mean AE of 2.30 mm. The presence of placeholders improved endpoint accuracy (2.20 vs. 2.40 mm, for the placeholder and no-placeholder conditions, respectively; $F(1,13) = 21.07$, $p < .001$, $\eta_p^2 = .618$). Furthermore, distant targets were touched more accurately than near targets (2.67, 2.31, 2.43, 2.14, and 1.97 mm for Targets 1–5, respectively; $F(4, 52) = 22.31$, $p < .001$, $\eta_p^2 = .632$). This effect of Target Position was weaker with than without placeholders, suggesting that the presence of placeholders attenuated the effect of movement distance ($F(4, 52) = 4.91$, $p < .01$, $\eta_p^2 = .274$; without placeholders: 2.91, 2.43, 2.55, 2.16, and 1.97 mm for Targets 1–5, respectively; with placeholders: 2.42, 2.19, 2.30, 2.12, and 1.97 mm, for Targets 1–5, respectively). There were no significant effects of cTBS on AE (all $p > .3$).

The ANOVA on CE yielded a significant main effect of Target Location, $F(4, 52) = 57.12$, $p < .001$, $\eta_p^2 = .815$, confirming a range effect, that is, stronger overshoots for near than distant targets (2.08, 1.49, 1.45, 0.68, and 0.63 mm for Targets 1–5, respectively). This effect was qualified by a significant interaction with Placeholder Condition, $F(4, 52) = 13.12$, $p < .001$, $\eta_p^2 = .502$, indicating an attenuation of the range effect for first and last targets with placeholders present (without placeholders: 2.46, 1.57, 1.49, 0.69, and 0.46 mm for Targets 1–5, respectively; with placeholders: 1.69, 1.41, 1.41, 0.66, and 0.79 mm, for Targets 1–5, respectively). Furthermore, cTBS Condition interacted with Placeholder Condition, $F(3, 39) = 3.07$, $p < .05$, $\eta_p^2 = .191$. This interaction reflected a modulating effect of cTBS for conditions without placeholders, $F(3, 39) = 3.11$, $p = .037$; $\eta_p^2 = .193$, see Fig. 2C, but not for conditions with placeholders, $F(3, 39) < 1$, $p > .9$; $\eta_p^2 = .030$, see Fig. 2D. In particular, without placeholders, the CE in the AG condition was smaller than the CE in all other three conditions (1.07, 1.32, 1.45 and 1.50 mm for AG, combined CONTROL, SPOC and LOC, respectively). This effect was independent of target position ($p > .9$; see Fig. 2C), suggesting a general bias for less overshoot, that is shorter movements, in the AG condition without placeholders.

The ANOVA on VE as a measure of movement consistency revealed two main effects, which were not qualified by higher-order interactions (all $p > .13$). The main effect of Placeholder, $F(1, 13) = 16.51$, $p = .001$, $\eta_p^2 = .559$, reflected a smaller VE for displays with than without placeholders (2.19 vs. 2.34 mm, respectively), indicating that the placeholders constrained the dispersion of the movement endpoints. The main effect of Target Location, $F(4, 52) = 4.22$, $p = .01$, $\eta_p^2 = .245$, revealed greater VE for target positions 3 and 4 than for the other positions (2.14, 2.22, 2.37, 2.48, and 2.21 mm, for positions 1, 2, 3, 4, and 5, respectively).

The ANOVA on RT revealed no significant effects (all $p > .12$; mean RT = 270 ms).

Fig. 2. Mean performance indices for the no-placeholders and placeholders condition as a function of target position (1 is closest to the start position) and cTBS condition: (A and B) movement time (ms); (C and D) constant error (mm). Error bars show standard error of the mean. The box in subgraph (B) reflects the planned comparisons executed to test the influence of cTBS on the last target advantage. AG = angulargyrus (dorsal stream), SPOC = superiorparietal occipital cortex (dorsal stream), LOC = lateral occipital cortex (ventral stream).

4. Discussion

Recent evidence suggests that goal-directed actions are visually co-determined by complementary processing of allo- and egocentric information. Subsequently, according to the updated perception-action model [35], both the ventral and dorsal streams need to focus on a target object in performing their primary visual roles, and both are sensitive to other visual information present in the display. In the present study, we used imaging-guided cTBS over regions of the ventral (LOC) and dorsal (SPOC, AG) stream to test their functional contribution to visually-guided real-time reaching in egocentric (placeholders absent) and allocentric (placeholders present) conditions.

4.1. Reaching in the allocentric (placeholder) condition

For reaching in the displays with placeholders (the allocentric condition), we found that cTBS delivered over LOC (ventral stream) slowed down MT to all target locations; in addition, it abolished the last-target advantage. These findings strongly link the ventral stream to allocentric information processing during online reaching. Lee and Van Donkelaar [29] also reported that TMS over LOC disrupted pointing movements to a (large) target circle surrounded by (small) distracter circles (the Ebbinghaus illusion). Together, these findings reveal the influence of allocentric coding by the ventral system on *immediate, direct* reaching movements.

It is relevant to note that other studies also have reported the influence of ventral stream processing on reaching movements, but these studies used paradigms that required delayed hand movements to memorized targets (e.g., [19]), novel, unpracticed movements (e.g., [21]), or hand movements in an allocentric (not target-directed) task [45]. As argued by Milner and Goodale [35] these types of movement may benefit from the more persistent (i.e., longer duration) allocentric visual information provided by the perceptual networks in the ventral stream. Hence, the present finding is important because it suggests that the ventral system also modulates fast, immediate reaching movements executed in real time.

cTBS delivered over AG (dorsal stream) abolished the last-target advantage. To our knowledge, this is the first demonstration that the dorsal stream processes (salient) allocentric information when reaching to a target. It is unclear, however, whether the dorsal stream processes allocentric information directly and independently from the ventral stream, or that it receives this information from the ventral stream. The latter possibility would be consistent with evidence for interactive connections between the two streams (e.g., [38]), and by the present finding that cTBS over LOC (ventral stream) also slowed down reaching.

cTBS over SPOC (dorsal stream) did not affect reaching performance relative to the control condition. This finding was unexpected as SPOC has been related to processing the spatial reach goal (e.g., [51]), but as we will discuss later this discrep-

ancy might depend on task factors (i.e., free versus imposed gaze fixation).

In sum, the present findings regarding LOC and AG in the placeholder condition provide the first causal evidence for allocentric coding in ventral and dorsal routes during real time reaching. This supports the updated perception-action model, which postulates a role of ventral and dorsal visual streams in processing spatial context information for goal-directed action [35].¹

4.2. Reaching in the egocentric (no-placeholder) condition

In the egocentric (no-placeholder) condition, we did not find any significant effect of cTBS on MT. The lack of a ventral stream (LOC) effect in the egocentric condition is not surprising as it is well established that egocentric coding is a dorsal stream function. If so, then why did we not observe a cTBS-disruption effect for the dorsal regions AG and SPOC in the no-placeholder condition? A possible explanation is provided by the notion of functional specificity in the dorsal stream (e.g., [50,15]). In particular, two recent TMS studies showed a disruptive effect of TMS over AG, but only when the hand was invisible during the reach, not when the hand was visible [51,52]. Vesia et al. concluded that visual feedback of the hand corrected errors induced by TMS over AG, and that AG calculated the reach movement based on somatosensory information [51,52]. Furthermore, TMS over the dorsal site SPOC disrupts reaches to targets in the peripheral visual field on condition that the eyes remain fixated on a central fixation cross [51]. The present study, however, used a free-gaze and not an imposed-gaze fixation paradigm, and thus explicitly allowed eye movements to the target location. In a previous study, we recorded eye movement behavior in a similar paradigm and confirmed that participants, after fixating the start location, invariably moved their eyes to the target when it appeared in the peripheral visual field [1].

The importance of distinguishing between reaching toward targets in foveal vision versus extrafoveal vision is corroborated by the fact that *optic ataxia*—a disruption of visually guided hand movements by lesions in the posterior parietal cortex—mainly occurs in peripheral vision and disappears when patients are allowed to orient their eyes and head toward the target (e.g., [25]). This clinical observation suggests the existence of two distinct neural systems that underlie reaching in central and peripheral vision, a hypothesis that has been confirmed in an event-related fMRI study with healthy subjects [39]. In particular, these studies suggested that reaching in central vision involves the medial intraparietal sulcus (a region not targeted for cTBS in the present study), whereas reaching in peripheral vision involves the parieto-occipital junction [12]. Hence, in this perspective, SPOC may play a strong role in reaching to *peripheral* targets but not in reaching to *foveated* targets.

4.3. Movement accuracy

In general, the reaching movements in the present study were executed with great end point accuracy, showing a small mean AE of 2.30 mm from the center of the target box. Furthermore, there was a gradient of improved accuracy (AE) for more distant targets. This outcome accords with the notion that more distant targets are generally associated with longer-duration movements, which allow

more time to implement time-consuming movement corrections based on feedback (e.g., [32]).

The signed end point deviation (CE) revealed the typical range-effect, that is, stronger overshoots for near than distant targets (e.g., [3]). However, the presence of placeholders attenuated this effect, especially for the first and last target position. This phenomenon has been observed before [2] and can be explained by the so-called repulsion effect [17]. In this view, placeholders may act as distracters, causing movement endpoints to be biased away from their location. In case of the nearest (first) placeholder, the strong overshoot is counteracted by the repulsion effect, which reduces the overshoot. The opposite happens for movements to the last placeholder, where the repulsion effect increases the (weak) overshoot.

In the no-placeholder condition, cTBS over AG produced a significantly smaller CE for all target positions, suggesting a tendency to produce shorter movements. This is consistent with evidence that AG calculates the movement vector based on somatosensory information of initial hand position [50] and suggests that vision of the hand might not be sufficient to fully compensate for the loss of this type of sensory information. Note that the slightly shorter movement amplitudes with cTBS over AG were accompanied by slightly shorter (but not statistically significant different) movement durations (see Fig. 2A).

4.4. Visual saliency

The finding that cTBS affected movement times as a function of target position in the placeholder condition but not in the no-placeholder condition highlights the importance of visual saliency, that is, the relative distinctiveness of objects in the visual field. The notion of a salience map has proven powerful in explaining why salient objects are prioritized (e.g., [30]). Interestingly, using TMS, Zenon et al. [53] demonstrated a specific role of AG in goal-directed salience representations in humans, consistent with earlier demonstrations in monkeys (e.g., [14]). Until recently, the notion of saliency has largely been overlooked in the study of goal-directed motor behavior (for a recent exception, see Ref. [26]). This is unfortunate as it is becoming increasingly clear that the classic boundaries between perception and action are no longer valid (e.g., [22,11]), and that reaching to targets in single and multiple-items visual displays are mediated by different visuomotor mechanisms (this study; [27,9]). To reiterate, a single target in an empty display provides a single focus of salience—it “pops out”—whereas multi-item displays provide parallel inputs that compete for attention and action. Models of selective motor action, therefore, should be sensitive to the concept of visual saliency, and, in addition, need to specify a selection regime that solves the competition among parallel potential action plans in the brain triggered by multiple visual inputs (e.g., [50,11,31]).

4.5. Conclusion

In conclusion, using imaging-guided multi-site cTBS, this study causally demonstrates the processing of allocentric information in both ventral and dorsal streams during immediate reaching to targets presented in a structured visual display, thereby providing direct empirical evidence in support of the updated perception-action model [35].

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¹ Rizzolatti and Matelli [42] have proposed that the dorsal stream as defined by Milner and Goodale [33] exists of two distinct functional subsystems: the ventro-dorsal stream and the dorso-dorsal stream. While the dorso-dorsal stream (which includes SPOC) is specialized in online action control, the ventro-dorsal stream (which includes AG) is assumed to play a key role in action organization, action understanding, and space perception. The present finding of differential cTBS effects for SPOC and AG is consistent with this functional subdivision of the dorsal stream.

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