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RESEARCH ARTICLE

Functional specialization in human dorsal pathway for stereoscopic depth processing

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Abstract

Binocular disparity, a primary cue for stereoscopic depth perception, is widely represented in visual cortex. However, functional specialization in the disparity processing network remains unclear. Using magnetic resonance imaging-guic transcranial magnetic stimulation, we studied the causal contributions of V3A and MT+ to stereoscopic depth percepti Subjects viewed random-dot stereograms forming transparent planes with various interplane disparities. Their small detectable disparity and largest detectable disparity were measured in two experiments. We found that the smallest detecta disparity was a ected by V3A, but not MT+ , stimulation. On the other hand, the largest detectable disparity was a ec by both V3A and MT+ stimulation. Our results suggest di erent roles of V3A and MT+ in stereoscopic depth processi

Keywords Depth perception · Binocular disparity · Transcranial magnetic stimulation · Continuous theta burst stimulatio

Introduction

We perceive the three-dimensional world from two-dimensional images projected onto the two retinas. Binocular disparity, the positional di erence between the left and right retinal images, provides a sufficient cue to evoke stereoscopic depth perception (Wheatstone 1838). Rand dot stereograms, which take advantage of binocular dispar information, have been widely used to unravel the corti mechanisms of stereoscopic depth perception with psycl physical, physiological, and computational methods (Q 1997; Cumming and DeAngelis 2001; Parker 2007). Af a point-to-point matching of local dots in the left and ri eyes, the spread of disparity information "fills in" the de for blank space between dots, giving rise to a percepti of surface or figure-ground segmentation based on disp ity (Julesz 1960; Westheimer 1986; Parker and Yang 19 (Fig. 1a).

The response of a substantial proportion of visual neur depends critically on the binocular disparity (Poggio 199 Compared to zero-disparity stimuli, disparity-rich stim evoked greater activation in multiple regions along the d sal and ventral streams (Tsao et al. 2003; Neri et al. 20 Minini et al. 2010). It has been suggested that dorsal ar encode the metric magnitude of disparity, while the vent areas signal disparity in a categorical manner (Preston et 2008; Cottereau et al. 2011).

In the dorsal stream, MT+ and V3A have been mos studied for disparity processing. As a well-known a for visual motion, MT+ has been long discovered to ha disparity-tuned neurons in macaques (Maunsell and v Essen 1983; DeAngelis and Newsome 1999; Roy et 1992). However, MT+ only established moderate dispar

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selectivity in humans (Tsao et al. 2003; Rutschmann and Greenlee 2004). In contrast, V3A received a lot of interest in human disparity research. It has been found V3A showed the strongest e ect of disparity modulation on fMRI BOLD signals (Tsao et al. 2003). Also, the neural code in V3A has a close relationship with functional characteristics of stereoscopic depth perception (Goncalves et al. 2015). Specifically, Backus et al. (2001) compared human psychophysical thresholds with fMRI BOLD responses in two tasks. In a stereoacuity test, subjects were asked to detect the disparity-defined double planes from a zero-disparity plane. They found that V3A had a higher sensitivity than other visual areas including MT+. In the other test, subjects were asked to detect the disparity-defined planes from uncorrelated dots to determine their upper disparity limit. They found that area V3A, together with MT+, demonstrated the highest sensitivity in extrastriate visual cortex.

In spite of the disparity-selective response, a few studies have directly tested the causal contributions of V3A and MT+ in stereoscopic depth processing. Here, we adopted the random-dot stereograms and tasks used by Backus et al. (2001) with off-line continuous theta burst stimulation (cTBS) which transiently attenuates normal cortical function (Huang et al. 2005; van Kemenade et al. 2012). Functional mapping was used to localize V3A and MT+ in individual subjects and to guide cTBS delivery. Disparity thresholds were compared before and after cTBS, and stimuli were presented contralateral or ipsilateral to the stimulation site. The

(> 1 arcmin). As the disparity increased and approached ~ 70 arcmin, the two distinct planes became indistinguishable from dots that were placed uncorrelated in the two eyes' images (Backus et al. 2001). The left and right 2° margins of

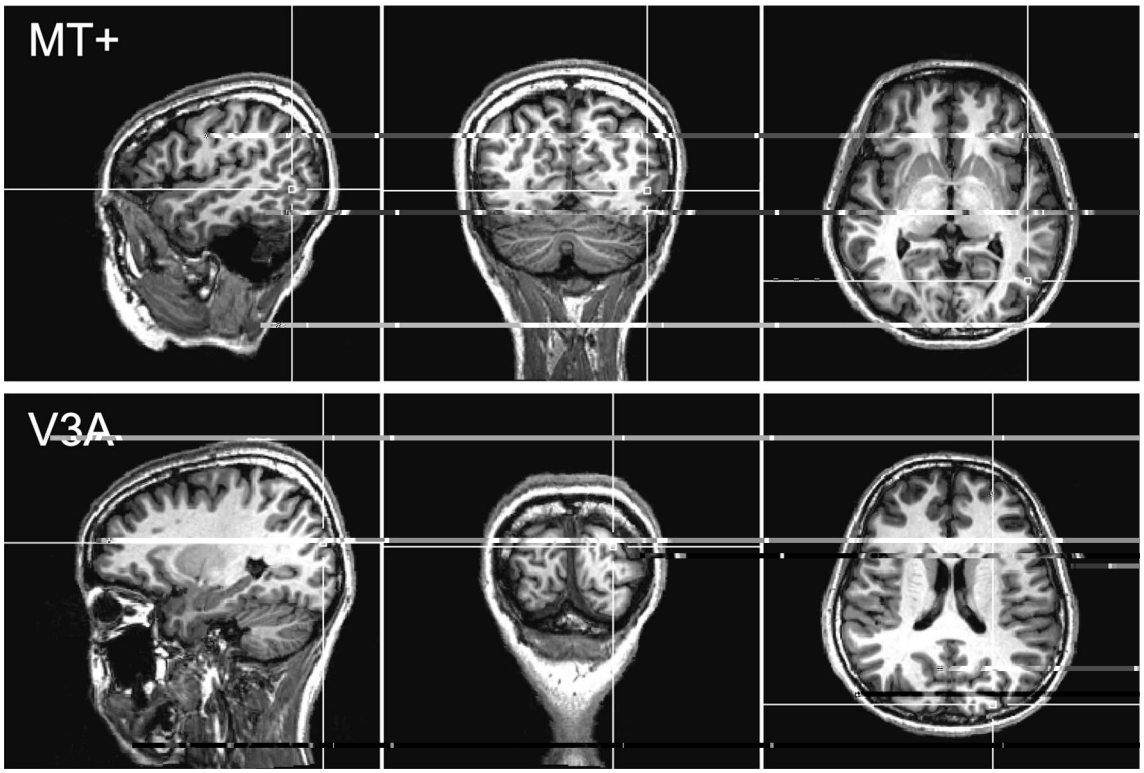


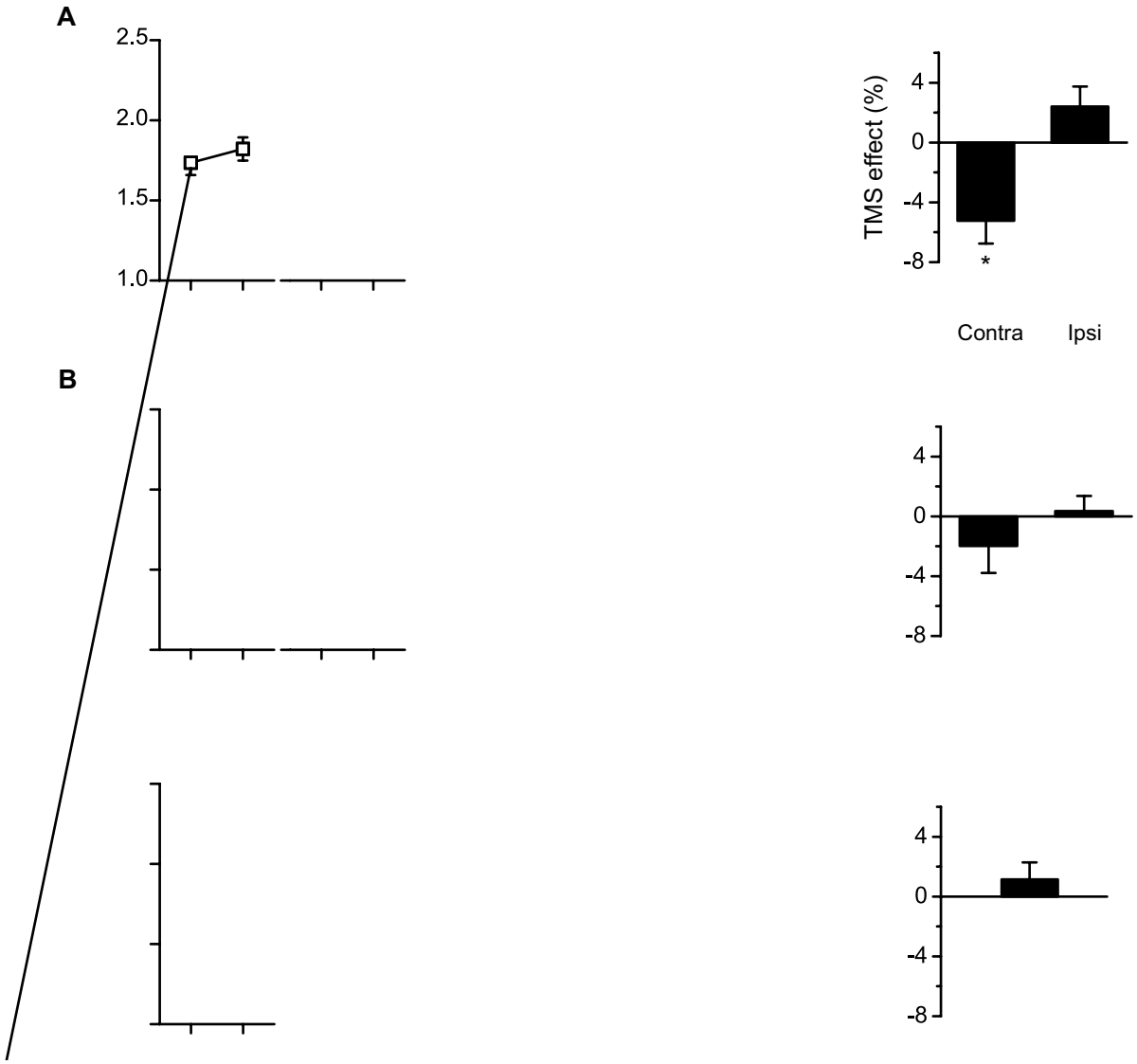
Fig. 2 TMS site at V3A and MT+ of a representative subject. The cross indicates the center of gravity of each ROI

posterior toward the occiput parallel to the subject's spine. The position of the coil was monitored in real time through the course of the 40 s cTBS protocol. The vertex, a site half way between the intertragal notches served as the control site. Each subject received stimulation over unilateral V3A, MT+, and vertex in three sessions. The stimulation hemisphere was randomly determined in each subject, and the stimulation order of the three cortical sites was counterbalanced across subjects. Each session was separated by at least 24 h (Carmel et al. 2010; Cocchi et al. 2015).

Results

Experiment 1 measured subjects' lower disparity limit, i.e., the minimum disparity for perceiving the stereograms as two planes rather than one single plane. An increase in the threshold was associated with a deteriorated performance (Fig. 3). In a daily session, subjects received stimulation over unilateral V3A or MT+. We first compared subjects' stereoscopic thresholds before and after cTBS using a repeated-measures ANOVA with stimulation site (V3A/MT +), visual field (contralateral/ipsilateral), and test (pre-TMS/post-TMS) as independent factors. A significant interaction e ect [$F(1, 9) = 7.80$, $p < 0.05$] was revealed, indicating that the lower disparity limit was modulated by cTBS, stimulation site, and visual field. Next, we performed a two-way repeated-measures ANOVA for each visual area with Bonferroni correction. In the V3A stimulation condition, there was a significant interaction between test and visual field [$F(1, 9) = 38.25$, $p < 0.01$]. The threshold increased in the contralateral [paired t test, $t(9) = 3.19$, $p < 0.05$], but not in the ipsilateral visual field [$t(9) = 1.97$, $p > 0.05$]. This location-specific change indicates a disruptive e ect. In other words, subjects' stereoacuity performance dropped—a larger disparity was needed to di erentiate two planes from one single plane after cTBS. In the MT⇓← stimulation condition, the interaction between test and stimulus position was not significant [$F(1, 9) = 1.03$, $p > 0.05$]. Also, we stimulated the vertex—a location in the middle of the scalp and the visual field could not be categorized as ipsilateral or contralateral. For this control condition, we averaged the thresholds across visual fields. No threshold change was observed before and after TMS [$t(9) = 1.62$, $p > 0.05$].

The TMS e ect was quantified as (pre-TMS threshold − post-TMS threshold)/pre-TMS threshold × 100% (Fig. 3, right panel). A value larger than zero indicates facilitation, and a value smaller than zero indicates disruption. The indices were submitted to a two-way repeated-measures ANOVA with stimulation site (V3A/MT+) and visual field (contralateral/ipsilateral) as two within-subject factors. The location-specific TMS e ect was di erent between the two



stimulation sites as indicated by a significant interaction e ect [$F(1, 9) = 6.92$, $p < 0.05$]. Compared to the ipsilateral visual field, the disruptive e ect in the contralateral visual field was significant in the V3A stimulation condition [$t(9) = 6.18$, $p < 0.01$], but not in the MT+ stimulation condition [$t(9) = 0.93$, $p > 0.05$].

Experiment 2 measured subjects' upper disparity limit, i.e., the maximum disparity for perceiving the stereograms as superimposed planes rather than uncorrelated dots. A decrease in the threshold was associated with a deteriorated performance (Fig. 4). Subjects' stereoscopic thresholds before and after cTBS were submitted to a three-way repeated-measures ANOVA. A significant interaction between test and stimulation site was found [$F(1, 9) = 6.19$, $p < 0.05$]. Next, we performed a two-way repeated-measures ANOVA for each visual area with Bonferroni correction. The interaction between test and visual field was significant in both the V3A [$F(1, 9) = 16.98$, $p < 0.05$] and the MT+ [$F(1, 9) = 12.06$, $p < 0.01$] stimulation conditions. In both conditions, the threshold decreased in the contralateral visual field [both $t(9) > 3.05$, $p < 0.05$], but not in the ipsilateral visual field [both $t(9) < 1.04$, $p > 0.05$]. This location-specific change indicates a disruptive e ect. In other words, after cTBS, subjects were not able to integrate binocular disparity as large as before to perceive

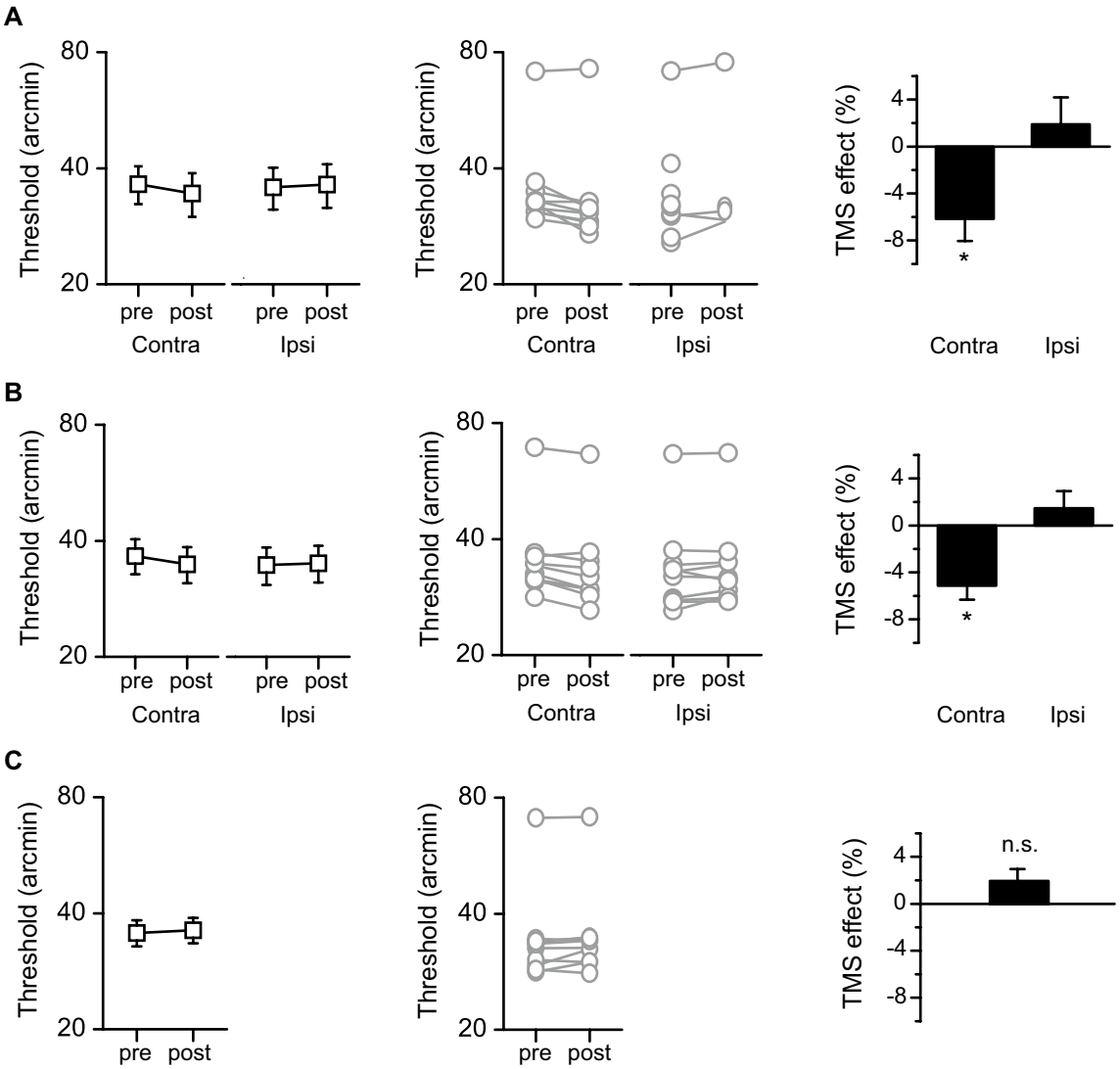


Fig. 4 TMS e ects in the upper limit task. TMS e ects at **a** V3A, **b** MT+, and **c** vertex. Left panel: averaged thresholds before and after stimulation, shown in a logarithmic scale; middle panel: individual thresholds before and after stimulation, shown in a logarithmic scale; right panel: stimulation e ects quantified in percentage change. A value greater than zero indicates facilitation, and a value below zero indicates disruption. *$p < 0.05$ after Bonferroni correction. Error bars denote 1 standard error of mean across subjects

superimposed planes. In the vertex stimulation condition, no threshold change was observed [$t(9) = 1.66$, $p > 0.05$].

The TMS e ect was further quantified as (post-TMS threshold − pre-TMS threshold)/pre-training threshold × 100%. A value larger than zero indicates facilitation, and a value smaller than zero indicates disruption (Fig. 4b). The indices were submitted to repeated-measures ANOVA with TMS site (V3A/MT+) and visual field (contralateral/ipsilateral) as two within-subject factors. A location-specific TMS e ect was indicated by a significant visual field e ect [$F(1, 9) = 7.47$, $p < 0.05$]. Post hoc t test showed a significant disruptive e ect in the contralateral visual field compared to the ipsilateral visual field in both the V3A [$t(9) = 2.75$, $p < 0.05$] and the MT+ [$t(9) = 3.27$, $p < 0.01$] stimulation conditions. However, the interaction e ect was not significant [$F(1, 9) = 0.03$, $p > 0.05$], suggesting that the location-specific e ect did not di er between the V3A and MT+ stimulation conditions.

Discussion

The present study investigated the functional specialization of areas V3A and MT+ in stereoscopic processing. We found that stimulation at V3A, but not MT+, impaired the lower disparity limit, suggesting a unique role of V3A in stereoacuity processing. On the other hand, V3A or MT+ stimulation both impaired the upper disparity limit, suggesting

that both V3A and MT+ contribute in binocular integration for large disparity.

First, our TMS results suggest that V3A has a causal contribution in perceiving both the lower and the upper disparity limits. The previous human fMRI studies have demonstrated that the BOLD signal in V3A was highly sensitive to disparity magnitude, with organized structure correlated with stereoscopic perceptual judgments (Goncalves et al. 2015). Using similar random-dot stereograms forming planes with various interplane disparities, Backus et al. (2001) found that the disparity-related response increased as the interplane disparity increased from undetectable to detectable, and decreased sharply after exceeding the upper depth limit. The covariation between cortical response and perceptual threshold suggests that V3A is an important neural substrate of stereoscopic depth perception.

Second, we found that TMS at MT+ impaired subjects' upper disparity threshold. This is consistent with the long-established link between MT and stereoscopic vision. Macaque studies have demonstrated that MT inactivation a ected extracting a disparity-defined target from noise (DeAngelis et al. 1998; Uka and DeAngelis 2003). Specifically, MT inactivation only impaired the coarse judgment of disparities in noise, but not the fine discrimination of disparities (Uka and DeAngelis 2006; Chowdhury and DeAngelis 2008). Such "fine" versus "coarse" functional specialization between V3A and MT+ has also been found in other visual processes such as local versus global motion (Cai et al. 2014).

The functional specialization revealed in the current study may be explained by a higher sensitivity of V3A in encoding disparity near the lower limit. Early psychophysical studies suggested that the relative disparity provides a crucial cue for stereoscopic depth discrimination (Kumar and Glaser 1992; Westheimer 1979). A steady-state EEG study with fMRI localization examined the population-response dynamics that are evoked by periodically changing disparities in five visual regions of interest (V1, MT+, V4, LOC, and V3A). By comparing responses between the absolute and the relative disparity conditions, Cottereau et al. (2011) found that V3A was the only region exhibiting significant changes both in the response amplitude and the phase lag. These converging evidence from psychophysical, electrophysiological, and brain imaging studies point to a distinct role of V3A for di erentiating fine disparity signals.

It should be noted that the type of stimuli which we used minimized additional cues that may excite neuronal processes for motion or contour identification, allowing us to examine the stereoscopic processing per se. A variety of disparity stimuli have been used to identify the neural correlates of stereoscopic vision. Some had rich edge information (e.g., depth-defined checkerboard and center-surround disparity o sets) which were likely to induce neural processes related to contour-specific mechanisms, while some had slanted or curved surfaces, which contained geometric information for 3D shape processing (Anzai and DeAngelis 2010). When the stereoscopic cues appear in conjunction with other visual cues, di erent neural mechanisms may be engaged. For example, neurons in MT showed a weak selectivity to relative disparity, but only in the context of static visual signals (DeAngelis and Newsome 1999). When motion signals were introduced, transparent moving planes were able to evoke neural responses selective to the relative disparity signal in MT (Krug and Parker 2011). A systematic understanding of the causal roles of cortical areas in the depth-processing network remains to be a topic for future research.

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Availability of data and material The data that support the findings of this study are available upon request.

Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

Ethics approval The experimental procedures and protocols have been approved by the human subject review committee of Peking University.

Consent to participate All subjects gave written, informed consent in accordance with the procedures and protocols approved by the human subject review committee of Peking University.

Consent for publication We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication.

Code availability The codes for stimuli presentation of this study are available upon request.

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