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Can excitatory neuromodulation change distorted perception of one's appearance?

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Body dysmorphic disorder (BDD) is marked by preoccupation with misperceived appearance flaws. Previous functional magnetic resonance imaging (fMRI) studies have found reduced neural activity and connectivity of visual areas specialized for global/holistic visual processing in BDD [1–3], suggesting that aberrant dorsal visual system functioning might contribute to distorted perception. In this proof-of-concept study we tested if intermittent theta-burst stimulation (iTBS), a form of excitatory repetitive transcranial magnetic stimulation (rTMS), would enhance dorsal visual system utilization as quantified through dynamic effective connectivity (DEC) modeling [4]. This is a single-session study with the application of iTBS and an fMRI scan immediately afterwards (within 15 min after the stimulation). We hypothesized that those undergoing active iTBS would show enhanced connectivity in dorsal visual areas responsible for global/holistic visual processing compared with sham.

Fourteen unmedicated adults with BDD, all with face concerns, were randomly assigned to receive active (n = 7) or sham (n = 7) offline iTBS (Supplementary Material S1). Stimulation targets were in the left and right lateral parietal cortical regions corresponding to CP3 and CP4 from the EEG 10-10 system. Stimulation was applied at 100 % active motor threshold (MT) for the active group and 10 % active MT for sham (Supplementary Material S2). The Yale-Brown Obsessive-Compulsive Scale Modified for BDD (BDD-YBOCS) and the Brown Assessment of Beliefs Scale (BABS) were administered before the experiment to assess BDD symptoms and insight, respectively. The Body Image States Scale (BISS) was administered before and after the experiment to explore iTBS effects on evaluative/affective experiences of appearance (Supplementary Material S3). FMRI data were then immediately acquired after stimulation while participants viewed their face naturalistically (Fig. S1a and Supplementary Material S4–S5).

For analyses, fMRI data preprocessing was first done using fMRIPrep 1.4.0 [5] (Supplementary Material S6–S7). Regions-of-interest (ROIs) were identified through Neurosynth functional meta-analysis (neurosynth.org). The ROIs included two in primary visual cortex (V1), six in dorsal visual stream (DVS), and six in ventral visual stream (VVS) (for exploratory analyses) (Fig. S1b). DEC, a time-varying measure of directional connectivity among pairs of ROIs, was computed at each timepoint using time-varying Granger causality [4]. There were six intra-hemispheric connections, divided into four categories: DVS_{Lower}, DVS_{Higher}, VVS_{Lower}, and VVS_{Higher}. From these connections, the timepoints associated with those trials of face viewing were extracted for statistical analysis (Fig. S1c and Supplementary Material S8).

Linear mixed models tested whether DEC was significantly influenced by treatment group and connectivity categories. Spearman correlation was used in exploratory follow-up analyses to determine associations between DEC and clinical measures. As an additional comparison, given the possibility of sham stimulation effects, these analyses were also done for data collected separately from 37 BDD participants and 30 healthy controls during an identical task of viewing their face naturalistically, but without iTBS beforehand. Nonparametric tests were used to analyze the BISS scores among the four groups (Supplementary Material S9–S10).

From tests of fixed effects, there was a significant two-way interaction between group and connectivity category, $F(3,17290) = 146.48$, $p < 0.001$. From univariate tests, the simple group effects were significant for DVS_{Higher}, $F(1,16.40) = 40.37$, $p < 0.001$ (active > sham), and for DVS_{Lower}, $F(1,20.34) = 16.06$, $p = 0.001$ (active < sham), during face viewing (Fig. 1b). In the non-iTBS comparison sample, there were no significant differences between BDD and healthy controls for any of the connectivity categories (Fig. 1c). Comparing all four groups (active iTBS, sham iTBS, BDD without iTBS, and controls without iTBS), there was a significant two-way interaction between group and connectivity category, $F(9,40734) = 8.66$, $p < 0.001$, from tests of fixed effects. The simple group effect was significant for DVS_{Higher}, $F(3,108.8) = 3.19$, $p = 0.027$. BDD participants with active iTBS exhibited greater DEC for DVS_{Higher} during face viewing compared to: those with sham iTBS ($p = 0.031$, Bonferroni-corrected), healthy controls without iTBS ($p = 0.043$, Bonferroni-corrected), and BDD participants without iTBS ($p = 0.077$, Bonferroni-corrected) (Fig. S2). Post-hoc, we examined associations between DEC for DVS_{Higher} and clinical measures. BDD-YBOCS scores significantly

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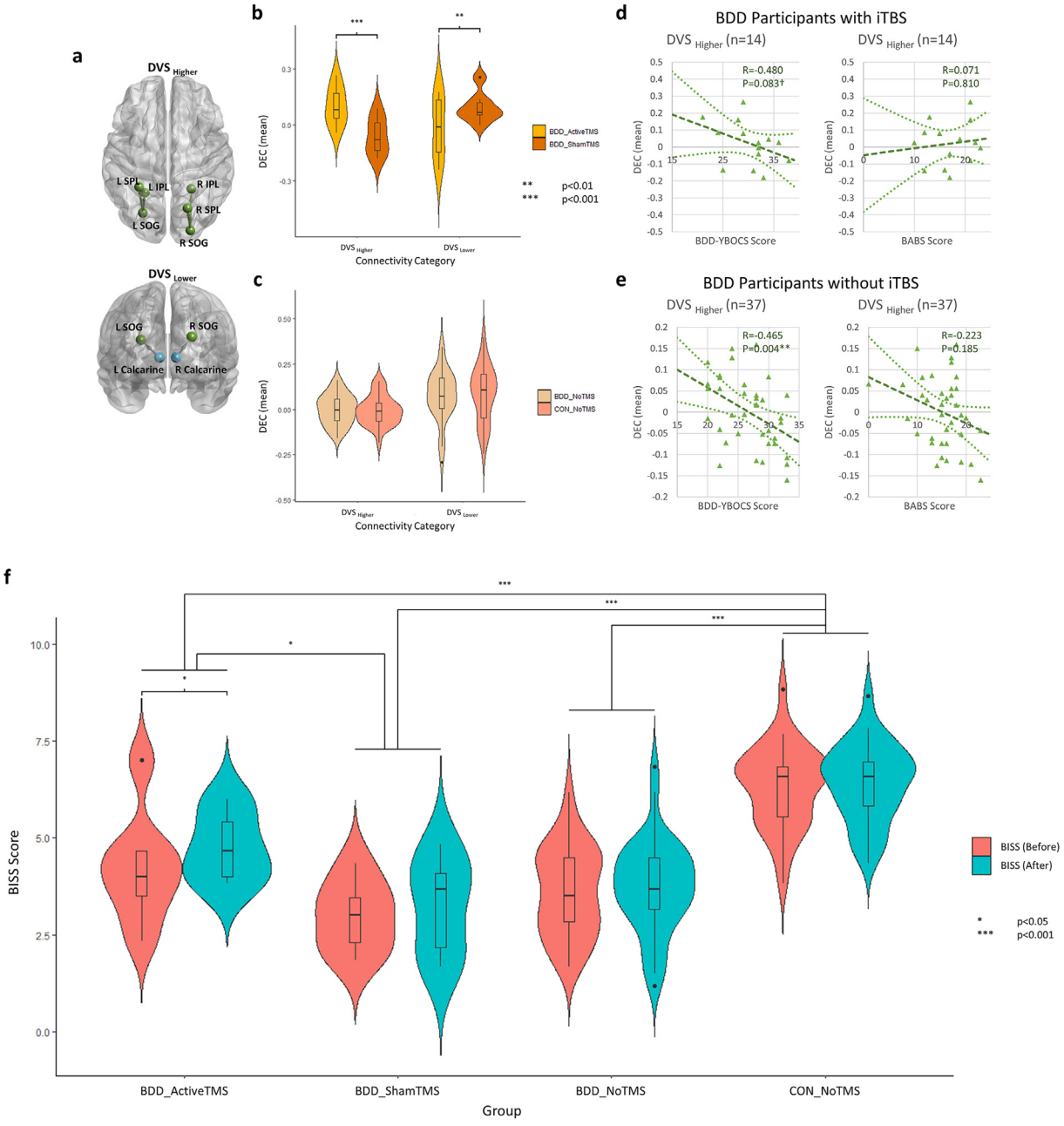

Fig. 1. Effects of iTBS on DEC patterns and appearance self-evaluations. (a) ROIs and directional connections for DVS_{Higher} and DVS_{Lower}. Comparison of DEC patterns for DVS_{Higher} and DVS_{Lower} (b) between BDD participants with active and sham iTBS, and (c) between BDD participants and healthy controls without iTBS. Associations between mean DEC and clinical scores (d) across BDD participants with iTBS, and (e) across BDD participants without iTBS, during face viewing. (f) Body Image States Scale (BISS) scores were obtained before and after the experiment from BDD participants who received active iTBS (BDD_ActiveTMS) and sham iTBS (BDD_ShamTMS), and BDD participants (BDD_NoTMS) and healthy controls (CON_NoTMS) who did not receive iTBS. Higher BISS scores indicate better body image perception.

negatively correlated with DEC for DVS_{Higher} in BDD without iTBS (rho = −0.465, p = 0.004, uncorrected) (Fig. 1e). The same pattern was evident in BDD with iTBS; BDD-YBOCS scores were similarly correlated negatively with DEC for DVS_{Higher} (rho = −0.480, p = 0.083, uncorrected) (Fig. 1d). There was also a significant improvement in BISS in BDD from before to after active iTBS (p = 0.0497, Bonferroni-corrected). There were no significant changes in BISS in BDD receiving sham iTBS, or among BDD or healthy controls who did not receive iTBS (Fig. 1f).

In this proof-of-concept study, we tested if iTBS alters DVS connectivity in individuals with BDD, as quantified through DEC modeling, and explored the effects on evaluative/affective experiences of their physical appearance. Excitatory neuromodulation induced by iTBS enhanced dynamic connectivity for DVS_{Higher}. This was accompanied by significant improvement in body image (BISS scores) in active iTBS but not sham iTBS cases. Moreover, the non-iTBS BDD and control groups showed no significant changes in BISS scores before and after the experiment.

Disturbances of visual information processing in BDD are important neurobiological contributors to the psychopathological feature of perceptual appearance distortions [6]. From our previous neuroimaging studies [1–3], abnormally reduced DVS activity was found in BDD when viewing filtered images that conveyed configural/holistic information. This, in addition to neuropsychological and psychophysical evidence [7–9], contributes to a model of imbalances in global vs. local processing such that hyper-scrutiny of miniscule appearance details could be mechanistically related to failing to "see" the appearance feature as an integrated whole. The current results provide early evidence that active iTBS over parietal areas may enhance information transfer within later ("higher") connections of the DVS which, in turn, may favor global/holistic visual processing. Although DEC for DVS_{Lower} decreased in active iTBS compared with sham, the four-group analysis (active iTBS, sham iTBS, and BDD and healthy controls not receiving iTBS) revealed that only DVS_{Higher} showed significant group effect. Further, DVS_{Higher} may have a stronger link to clinical symptoms, as DEC for DVS_{Higher} but not DVS_{Lower} during face viewing was negatively correlated with BDD symptom severity.

These findings provide evidence of altered dynamic connectivity in DVS regions responsible for global/configural visual processing when viewing faces naturalistically after excitatory neuromodulation over parietal areas. The potential clinical relevance is suggested by the significant improvement in evaluative/affective body experiences specifically observed in those with BDD receiving active iTBS. These results demonstrate that excitatory neuromodulation may engage DVS connectivity, a potentially important target that is mechanistically involved in holistic perception. Given the potential of iTBS to enhance neuroplasticity [10], these results (with the caveats of a small sample size of those receiving iTBS and some methodological considerations in Supplementary Material S11) provide early promise that such interventions could help remediate perceptual distortions for appearance in those with BDD, and maybe in other disorders with perceptual disturbances. Future studies measuring global/local visual processing will be useful to determine if associations between changes in DVS connectivity and subjective experience are linked by changes in perception.

Declaration of competing interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2021.07.010.

Author contributions

WW, MSL, and JPD were responsible for data analysis and paper writing. RD, RT, and AL contributed to the study design. JDF was responsible for clinical assessment, experimental design, and paper writing. All authors read and approved the submitted manuscript.

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