Theta burst stimulation of extrastriate body area for body perception in anorexia nervosa: A Randomized Controlled Trial

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Abstract

Anorexia nervosa is a severe and potentially life-threatening psychiatric disorder characterized by self-starvation, intense fear of weight gain, and a distorted body perception. Treatment remains challenging, and effective interventions for adults are limited. The extrastriate body area (EBA), a cortical region involved in body representation, may contribute to the body-image disturbances central to the disorder. In this double-blind, placebo-controlled, randomized trial, we investigated the therapeutic potential of targeted theta burst transcranial magnetic stimulation (TMS) of the EBA in patients with anorexia nervosa (n = 40). Participants received four weeks of active or sham TMS combined with body perception training, while a treatment-as-usual group and a healthy control group served as comparators. Active TMS produced significant improvement on the primary outcome measure, the Body Shape Questionnaire, relative to both control groups. Moreover, active stimulation normalized EBA responses to self- versus non-self touch, aligning neural activity patterns more closely with those of healthy individuals.

These findings demonstrate that individualized neuromodulation targeting a disorder-relevant neural substrate can effectively recalibrate disturbed body perception. By integrating brain stimulation with behavioral retraining, this study exemplifies a precision psychiatry approach that links neurobiological mechanisms to personalized therapeutic interventions in anorexia nervosa.

Introduction

Anorexia nervosa (AN) is a severe, potentially lethal disorder, typically affecting adolescent girls and young women. AN is characterized by self-starvation accompanied by fear of gaining weight and distorted body perception. This body-image disturbance, a central diagnostic criteria for AN (1), seems to be a consequence of patients' failure to integrate the subjective experience of their own body with actual visual and sensorimotor percepts (2). It has been suggested that AN patients are stuck in an allocentric perception of their body which is not being updated in spite of contradicting sensory feedback (3). Targeting body image disturbances is difficult and altered body perception often persists even in remission (4, 5). From a precision psychiatry perspective, such enduring distortions highlight the need for individualized interventions grounded in neurobiological mechanisms. Understanding how specific neural systems contribute to maladaptive body representations can inform the development of targeted, mechanism-based treatments rather than one-size-fits-all approaches.

The internal representation or model of one's body is developed and maintained based on a variety of factors, including sense of agency, sensory side sensations from within the own body (interoception), information about the position of limbs (proprioception), and exteroceptive information (e.g. vision and audition). Differences in motoric (6) and interoceptive tasks (7, 8) are reported in AN. As something in between intero- and exteroception, the sense of touch plays an especially important role in forming the sense of the bodily self (9). The skin forms the clearest border of the body, and touch is important for learning the difference between self vs. other, starting prenatally. AN patients experience touch from

others as less pleasant (10), evaluate vicarious touch as less pleasant (11), and show lower neural involvement of reward structures during social touch (12). We previously found heightened neural activity to both touch from others as well as self-touch in somatosensory and social processing areas (13). We interpreted this as potentially increased prediction errors. If the body is represented or modeled incorrectly (i.e. larger than it actually is), any conflicting evidence that arises during touch to the body's actual boundaries would cause prediction errors.

Regarding exteroceptive representation, the visual perception of the own body is studied extensively in AN. Two regions emerge as potentially affected in AN: the extrastriate body area (EBA) and the fusiform body area (FBA) (14). They are located in lateral-occipital cortex and activate to images of bodies and body parts (15, 16). The EBA activates more in response to one's own body images than to those of others (17–19), and plays a role in aesthetic judgement (20, 21). Interestingly, TMS to the EBA in healthy individuals altered how they thought others perceived their body (22, 23), supporting the idea that EBA is involved in the allocentric representation of one's own body (24). Furthermore, AN patients display reduced EBA gray matter density (25), altered EBA activation (26–29) and connectivity (30). After a three-month body exposure treatment for AN, activation of the EBA in response to own-body images increases compared to pre-treatment (31), indicating that EBA might be involved in the veridical perception of one's own body.

Identifying such disorder-relevant neural targets provides an opportunity to develop personalized neuromodulatory strategies that directly address the biological mechanisms underpinning psychiatric symptoms. We here hypothesized that targeting the individually localized right EBA with transcranial magnetic theta burst stimulation (TMS) followed by body-image-perception training could improve body perception disturbances in AN, contributing to better treatment outcomes. Intermittent theta burst TMS produces a period of cortical excitation and can be used to temporarily activate a brain region (33). Following TMS, cortical excitability and plasticity potentials are increased (34). We aimed to therapeutically engage the patients during this window of opportunity with a focused body perception training.

Our preregistered hypotheses (https://osf.io/z9jv3) included an improvement in our primary outcome measure, the body shape questionnaire (35), for the group receiving a body perception training (BPT) compared to the group receiving treatment as usual (TAU). Within BPT, we expected to find a larger improvement for those receiving active vs. sham TMS. Furthermore, we expected an increase in neural activity in the EBA, which would be more pronounced in the active TMS group. Finally, we expected to find a similar change in our secondary outcome measures (additional questionnaires) and a relationship between EBA neural activity and treatment efficacy.

Methods

Participants

The study was performed at Linköping University Hospital. The patient sample (n = 40, female) was recruited via the eating-disorder subunit of the Child and Adolescent Psychiatric clinic and the Psychiatric clinic in Linköping, Region Östergötland. Inclusion criteria were: DSM-5 diagnosis of anorexia nervosa, includingatypical and unspecified (restrictive type) with body perception disturbances, 18–35 years of age, BMI ≤ 20 kg/m^2, and MRI-compatibility (see supplement for more details, Table 1 for patient characteristics, and figure S1 for recruitment/attrition).

Table 1
Demographic data on clinical AN sample (n = 40) presented by treatment allocation: TMS (n = 10), sham TMS (n = 10) and TAU (n = 20)

	TMS *n* **(%)**	**Sham TMS** *n* **(%)**	**TAU** *n* **(%)**
Gender			
Female	10 (100)	10 (100)	20 (100)
Age (*m*, *sd*)	21.10 (3.31)	21.50 (3.87)	21.55 (3.33)
Country of origin			
Born in Sweden	7 (70.0)	10 (100)	20 (100)
Born in other European country	3 (30.0)	0 (0)	0 (0)
Living situation			
With partner	2 (20.0)	1 (10.0)	6 (30.0)
Separated	3 (30.0)	1 (10.0)	3 (15.0)
Single household	0 (0)	1 (10.0)	1 (5.0)
With parents	3 (30.0)	7 (70.0)	8 (40.0)
Other	2 (20.0)	0 (0)	2 (10.0)
Education			
Comprehensive school	1 (10.0)	2 (20.0)	4 (20.0)
Theoretical high-school	7 (70.0)	4 (40.0)	12 (60.0)
Vocational training	2 (20.0)	3 (30.0)	3 (15.0)
University	0 (0)	1 (10.0)	1 (5.0)
Occupation			
Working	4 (40.0)	3 (30.0)	2 (10.0)
Sick-leave	1 (10.0)	0 (0)	2 (10.0)
Studying	2 (20.0)	4 (40.0)	11 (55.0)
Unemployed	1 (10.0)	0 (0)	0 (0)
Not known	2 (20.0)	3 (30.0)	5 (25.0)
Body Mass Index (*m*, *sd*)	18.63 (1.20)	18.58 (1.47)	19.21 (1.27)
NEO-FFI-3 (*m*, *sd*)			

	TMS	Sham TMS	TAU
	n (%)	*n* (%)	*n* (%)
Neuroticism	34.20 (9.57)	31.20 (5.33)	32.60 (6.30)
Extraversion	21.70 (12.10)	26.10 (7.39)	26.25 (9.49)
Openness	25.20 (5.33)	26.50 (7.31)	25.85 (8.13)
Agreeableness	38.50 (5.74)	38.60 (6.29)	36.95 (6.71)
Conscientiousness	27.40 (9.77)	33.20 (8.36)	30.90 (6.57)
AQ (*m*, *sd*)	23.70 (12.17)	16.40 (6.48)	19.40 (9.68)
EQ (*m*, *sd*)	48.60 (14.03)	53.22 (13.95)	49.60 (14.03)
MADRS-S (*m*, *sd*)	25.20 (10.84)	22.40 (3.87)	19.60 (8.49)
SCSS (*m*, *sd*)	31.90 (9.54)	37.30 (6.62)	32.50 (7.72)

Note. TMS = transcranial magnetic stimulation, TAU = treatment as usual, AN = anorexia nervosa, NEO-FFI-3 = Neo five-factor inventory personality, AQ = Autism spectrum Quotient, EQ = Empathy Quotient, MADRS-S = Montgomery Åsberg Depression Rating Scale, Self-Report; SCSS = Self-Concept Clarity Scale

As a comparison group, healthy control subjects (n = 40 female) were recruited via flyers, social media, and email advertisement. They were matched to the patients with respect to age. During the first phone contact, volunteers were interviewed to exclude any history of psychiatric illness or substance dependence. Further exclusion criteria were MRI contraindications and any serious health concerns.

Procedure

This study followed a double-blind, randomized, controlled design. Patients were randomized to treatment as usual (TAU, n = 20), body perception training with sham TMS (BPT, n = 10) or with active TMS (TMS-BPT, n = 10). Participating staff involved in interaction with the patients and with data analysis were blinded to the TMS-condition, except for the researcher applying the TMS (authors AW, MT) and the study nurses.

Data was collected from September 18th 2019 to April 2nd 2024. We pre-registered our hypotheses and planned analyses before any formal data analyses (https://osf.io/z9jv3). Blinding was broken after group-statistics had been performed.

In a first experimental visit, all participants answered questionnaires and underwent functional magnetic resonance imaging (fMRI). Patients in the TAU group continued their treatment at the eating disorder unit and then came back for a second experimental visit with questionnaires and fMRI after four weeks.

Patients in the two intervention groups participated in the BPT over a period of four weeks. They received TMS/sham-TMS for 6 minutes before participating in the 20–30 min therapist-led intervention (see details below), five days per week, resulting in 20 sessions. Within a week after successfully participating in the treatment (min. 17 out of 20 sessions), patients took part in a second experimental visit with questionnaires and fMRI. Two patients did not want to participate in the second fMRI scan but filled in the questionnaires (TMS-BPT = 1, TAU = 1). Analysis was based on intention to treat.

At a follow-up after 6 months, patients filled in the clinical questionnaires for a third time.

The study and procedures were approved by the Regional Ethical Board of Linköping (2017/443 – 31, 2018/444 – 32) and the Swedish Ethical Review Authority (2019–02821). The participants received oral and written information about the study. Written consent was obtained before the initiation of any study procedures.

Self-report measures

The primary outcome measure to evaluate success of TMS and body perception training was the Body Shape Questionnaire (BSQ; (35)).

In addition, the following clinical measures were collected at experimental visits one and two and at the 6-month follow-up: Eating Disorder Examination Questionnaire (EDE-Q; (36)), Body Attitude Test (BAT; (37)), Figure Rating Scale (FRS; (38)).

To further characterize the sample, the following measures were collected: Montgomery Åsberg Depression Rating Scale (MADRS-S; (39)), Empathy Quotient (EQ; (40)), Autism spectrum Quotient (AQ; (41)), Neo five-factor inventory personality scale (NEO-FFI-3;(42, 43)), and the Self-Concept Clarity Scale (SCCS) (44).

Brain Imaging

See supplement for details on data acquisition during MRI. The total time in the scanner was maximally 1 hour. There were four different tasks: Resting state, a body-image paradigm (to be reported elsewhere), an EBA-localizer task, and a self-other-touch task (45).

Resting state (12 min)

Participants were asked to relax and visually fixate on a cross presented through scanner-compatible goggles.

EBA-localizer task (8 min)

Patients were presented with 8 blocks of body images and 8 blocks of landscape images (10 per block, each 2 s, pseudorandomized order). Between blocks, a fixation cross was displayed for 10 s.

Self-other-touch task (13 min): The previously established self-other-touch task (45) contained three conditions (3 s cue, 12 s touch, 10 repetitions each, in random order): self-touch (touching the own arm), other-touch (touch on the arm by the experimenter), and object-touch (touching a pillow by the participant, movement control condition). All touch occurred on the left forearm. Participants were instructed to use slow, soft stroking typically perceived as being pleasant and effective in evoking C-tactile fiber activity (46).

TMS

TMS was performed on the individually localized right EBA with a figure-eight coil driven by a Super Rapid Transcranial Magnetic Stimulator (MagVenture MagPro X100 incl. MagOption, MagVenture, Farum, Denkmark). During the first session, the patients´ structural MRI was co-registered to their head position, which was tracked in real time using a Nexstim ITMS Navigation system (Nexstim Ltd., Helsinki, Finland) allowing us to navigate coil position relative to the target (i.e. the EBA). The location was marked on a neoprene cap, which was then used to target the location during the following sessions of this participant. Right EBA was identified based on the individual patients' fMRI data. For this purpose, statistical fMRI analysis (see below) was performed on the non-normalized images. Maps were thresholded at $p < 0.05$ or higher if the peak activation was clearly visible. The activation map was overlayed over the individual T1 and the local maximum within the approximate location of the EBA in right lateral occipital lobe was identified.

The subject's resting-motor threshold was determined by the minimum intensity of pulses over the motor cortex that elicited visible thumb twitches. Then, intermittent theta burst stimulation was administered consisting of bursts containing 3 pulses at 50 Hz and an intensity of 90% of the resting-motor threshold repeated at 200 ms intervals (i.e., at 5 Hz) and 10 s between burst interval (i.e. 2 s stimulation followed by 8 s rest) for a total of 190 s (600 pulses).

In the sham condition, the stimulator was tilted transversely so that the electromagnetic pulses did not stimulate the brain. The participants had no previous TMS experience and therefore no reference for the typical sensations that TMS produces.

Body perception training

Within thirty minutes after the TMS treatment, the patients participated in one of five different body perception trainings focusing on their body perception (psychoeducation, drawing of estimated and actual body size, estimating the size of different body parts using a piece of string, or different sized hula hoop rings, and adjusting the size of a computerized morph of their body; see supplement for detailed description). The five sessions were repeated in random order during each week. Together with a

therapist, the patients explored and estimated their body size and discussed the accuracy when confronted with their actual size. The therapist also discussed cognitive, emotional, and perceptual aspects of the exercises with the patient.

Analysis

Task fMRI

Data was analyzed using statistical parametric mapping (SPM12; Wellcome Department of Imaging Neuroscience) in Matlab R2015b (MathWorks). See supplement for pre-processing details.

For statistical analyses of the blood oxygen level dependent (BOLD) response, the general linear model approach was used. We used the FAST-option (48) due to the short repetition time, which improves autocorrelation modeling performance (49). Realignment parameters were added as regressors-of-no-interest. The first temporal derivative of motion parameters in x,y,z-directions and a regressor censoring volumes with more than 1 mm volume-to-volume movement (50) were added in addition to improve movement correction.

For the EBA task, the regressors of interest were the body- and landscape-blocks. The body condition was contrasted with the landscape condition at the subject level. For the touch task, the regressors of interest were the self-, other-, and object-touch conditions, and regressors of no interest were: the cue phase (3 s) and the motion after the active conditions (1 s after self-touch and object touch conditions when the participants moved their hand back to the resting position). Self-touch was contrasted with object-touch to account for arm movement effects. Subsequently, other-touch was contrasted with the movement-corrected self-touch contrast at the subject level.

For both tasks, the main contrasts of interest (body vs. landscape for the EBA, other- vs. self-touch for the touch-task) were entered into three different group-level models. First, a two-sample t-test comparing patients (all treatment groups) and controls, pre-treatment. Second, a flexible factorial ANOVA with main effects of subject, group (BPT vs. TAU), and time (pre- and post-treatment), as well as the interaction between group and time. Third, within the BPT group, a flexible factorial ANOVA with main effects of subject, group (TMS vs. sham), and time, as well as the interaction between group and time.

At the whole brain-level, statistical significance was assessed at a family-wise-error (FWE) corrected level of $p < .05$ (peak-level). Small-volume-corrected analyses were performed for the bilateral EBA and right FBA. Masks for these regions were created by drawing 18mm spheres around the peak voxels from the meta-analytic NeuroSynth tool (neurosynth.org), keyword ‘body’ (see supplement, Fig. 1 for a visualization of these masks). These spheres were masked with a standard brain mask (FMRIB Software Library (51)) to exclude out-of-brain voxels. For the touch-task, small-volume-corrected effects were also assessed in the right anterior cingulate cortex, right superior temporal gyrus, and right insula, in line with previous work (45, 52).

For each participant, additional individual masks were created within the bilateral EBA and right FBA masks. An 8-mm sphere was drawn around the peak voxel coordinates for the body vs. landscape contrast at the individual level. These masks were used as seed regions in the resting state fMRI analyses described below.

Questionnaires

Questionnaires were analyzed using JASP (JASP Team (2024) Version 0.19.1). For each questionnaire, three repeated measure ANOVAs were run, with time as within-subject factor in each case and the following grouping factors: (1) BPT (both TMS groups combined) vs. TAU, (2) TMS-BPT vs. sham-BPT, and (3) all three groups (TMS-BPT vs. sham-BPT vs. TAU). Significant main and interaction effects were followed up by post-hoc comparison corrected by the Holm method.

Results

Effect of body perception training and TMS

Body shape Questionnaire (primary outcome)

BSQ scores improved significantly over time (main effect of Time $F(2, 70) = 12.02$, $p < .001$). The general effect of the body perception training (i.e. combining sham and active TMS groups) compared to TAU was non-significant (pre-post-6month: Time*Group $F(2, 72) = 2.90$, $p = .062$), but the full BPT group showed a tendency towards faster improvement (pre-post: Time*Group $F(1, 38) = 3.92$, $p = .055$).

When comparing all three groups (TMS-BPT, sham-BPT, TAU), improvements differed between groups and time points (interaction Time*Group $F(4, 70) = 3.62$, $p = .010$, Fig. 1A). Post-hoc tests suggested that this was driven by a faster and longer lasting improvement in the TMS-BPT group (Holm-corrected, Pre vs. post: $p = .018$; Pre vs. follow-up: $p = .019$), while there were no significant differences between time points in the sham-BPT group and only a significant improvement for Pre vs. follow-up in the TAU group ($p = .037$). All other pairwise comparisons rendered a p-value > .05.

This was further supported when comparing the two BPT groups directly: The active TMS group showed a longer-lasting decrease in BSQ scores than the sham-group (interaction Time*TMS-Group $F(2, 34) = 4.80$, $p = .015$).

Other clinical measures

Comparing the BPT (combined TMS- and sham) and TAU groups revealed a significantly larger improvement for BPT regarding BAT scores and FRS cognitive sub-scores after 4 weeks (pre-post: BAT: $F(1, 38) = 13.57$, $p < .001$; FRS: $F(1, 37) = 5.06$, $p = .031$, Fig. 1B & C), and an interaction effect (Time*Group, BAT: $F(1, 38) = 12.43$, $p = .001$; FRS-think $F(1, 37) = 6.01$, $p = .019$, Fig. 1B & C), indicating a stronger decrease for the BPT group.

When comparing all three groups (TMS-BPT, sham-BPT, TAU, Fig. 2B), BAT decreased over time ($F(2, 70) = 12.47$, $p < .001$) and showed an interaction effect (Time*Group $F(4, 70) = 4.12$, $p = .005$). Holm-corrected post-hoc tests revealed that this was driven by Pre-Post differences in the TMS-BPT group ($p = .001$). FRS and EDE-Q showed a similar directionality but were non-significant (see supplement).

There were no adverse events related to TMS or BPT.

Task-based fMRI

The localizer task activated the EBA, however, the peak was found in the FBA (see supplemental Fig. 1). There was no difference in activation between patients and controls. There was no group*time interaction for the activity of the EBA or the FBA. There was no significant relationship between EBA activity and BSQ at baseline, or between EBA activity and BSQ change over time.

For the self-other-touch task, AN patients showed stronger activation for self-touch compared to other-touch in the right fusiform gyrus (FG)/EBA at baseline. This pattern was opposite in the healthy controls (see Fig. 2A). Compared to controls, patients showed a smaller difference in activation between other-touch and self-touch in the right STG and right ACC (see Fig. 2A), two regions important for self-other differentiation of touch in healthy participants (45), as well as in the right FBA.

At the post-treatment timepoint, the two BPT subgroups showed changes of EBA activity in opposite directions (exploratory analysis; Time*Group interaction [38–80 10], $T = 4.84$, $p(SVC) = 0.045$, note that this a different cluster than the one showing a difference at baseline, see supplemental figure S4 for illustration). The difference in EBA activity between self-touch and other-touch became smaller in the BPT-TMS group, while the BPT-sham group displayed the opposite: an increase in difference between the two conditions (Fig. 2B). This effect was especially driven by the self-touch condition: activation in the EBA during self-touch decreased in the TMS-BPT group (thereby becoming more similar to controls) while it increased in the sham-BPT group (see supplemental Fig. 3).

Discussion

TMS of the EBA in combination with body perception training over the course of four weeks improved body perception concerns in all AN patients. This effect was accompanied by specific changes in EBA activation in a touch paradigm evaluating self-other-distinction. Additional measures of symptom improvement showed a comparable directionality.

The additional benefit of TMS became apparent when comparing the main outcome measure (BSQ) between the groups receiving active vs. sham TMS: the improvement in the group receiving active TMS lasted until the follow-up at 6 months. Previous studies using TMS for depression also find sustained effects for 3–12 months (55–57). The longer-lasting improvement in the active TMS group might be related to TMS-induced neural changes in the EBA.

While the neural activity in the group that received active TMS became more similar to that of control participants, the neural activity in the group that received sham TMS showed results in the opposite direction. We hypothesized that TMS EBA would allow for a more accurate perception of own body shape. It is possible that TMS-induced changes in the EBA made the patient more susceptible to the body perception training. The initial improvement in several of the patients in the sham-TMS group likely reflects a placebo response. Another explanation could be that the sham-TMS group used different mental strategies to engage in the training, leading to an initial improvement, but without a longer lasting effect.

Contrary to our hypothesis, there was no difference in activation in the EBA localizer task between controls and patients. Our task evoked peak activation in the FBA, not the EBA, potentially because it employed pictures of full bodies, not body parts (58) suggesting that it was not sensitive enough to evoke the expected response. In addition, it only showed the bodies of *other* people, which might not engage processes specifically related to *own* body perception. EBA connectivity during rest, however, was different for AN patients and controls.

We found differential effects between treatment groups in the EBA during the self-other-touch task. The EBA integrates multimodal signals and is involved in processing tactile body-related sensations, e.g. in the embodiment of a rubber hand (59, 60) and in the enhancement of touch when viewing it (61). Already in infants, seeing touch activates the EBA (62). Our participants did not see the touch, as they were viewing a screen through googles. However, visual input might not be necessary, since EBA activates when haptically exploring body parts (63) and in blind people, suggesting a supra-modal role not fully dependent on visual input (64).

Both self- and other-touch involve processes relating to representations of the own body as both types of touch contribute to the development and maintenance of the bodily self (9, 65). Here, we found that EBA activation during self-touch (compared to other-touch) became more similar to the controls, in the group that received active TMS and showed longer lasting treatment effects.

Controls showed no or minimal activation of this EBA-cluster during self-touch, in line with previous work (45). AN patients showed EBA activation during self-touch and deactivation during other-touch at baseline. EBA activation during self-touch could indicate prediction error signals, when the sensation does not match the predicted or expected representation of the own body. This could have to do with dysfunctional integration or reduced updating of visual representations of the own body based on tactile signals, and could explain aversiveness of touch in AN observed previously (66). After active TMS, this difference was reduced: responses during self- and other-touch became more similar to controls.

The group that received sham-TMS showed the opposite trajectory of EBA activity during touch, indicating a different underlying mechanism. The effect was driven by the self-touch condition: EBA activity during self-touch increased in this group (i.e. became more different from controls). It is possible that this group used a different strategy to integrate the experiences during the training. The body perception training led to a faster improvement of symptoms (after 4 weeks) than treatment as usual

(indicated by the additional outcome measures (BAT, FRS). However, it seems that in the sham-TMS group the training altered EBA functionality in the “wrong” direction, i.e. further away from the controls. This did not lead to long-term improvements in body shape perception, as this group’s values returned to baseline levels after 6 months.

This study is one of the few that have used TMS as a treatment or treatment add-on for AN. Most previous studies target dorsolateral prefrontal cortex, insula, or the inferior parietal lobe (67). A recent meta-analyses indicates efficacy of these previous studies on BMI and disordered eating behavior (67). It can be assumed that different underlying mechanisms are at play since prefrontal cortex is involved in higher cognitive functions, not body perception *per se*. However, the insula is involved in own body perception and the inferior parietal lobe is involved in self-other-distinction. Therefore these regions are most comparable to our target, the EBA.

We here tried to employ potentially increased plasticity by training body perception *after* the TMS session (68). A previous study targeting insula used cue provocation, where the targeted brain region is engaged *before* the TMS through presentation of cues (images of high caloric food) (69). That study found improvements in depression, anxiety, and AN compulsions. However, there was no placebo group. Another study targeting the inferior parietal lobe also evaluated BSQ and found no effect (70). This could be due to a different neural target than in our study.

We were trying to employ a potential window of opportunity where increased plasticity might contribute to improved learning or higher updating potential (71, 72). Since we found more robust improvements in the TMS group compared to the sham group, there is support for this theory. It might be important which activities and thoughts a patient engages in during this sensible time window.

Limitations

The relatively small sample sizes of the active and sham TMS groups (n = 10 each) limit the generalizability and statistical power of the present findings. Future studies with larger and more diverse samples are needed to confirm the robustness of these effects and to assess individual variability in treatment response – a key consideration for precision psychiatry approaches. While we pre-registered an expected effect on EBA activity, this was specified for the EBA localizer task rather than the touch-task used here. Thus, the current neural findings only partially align with our preregistered hypotheses but nevertheless support the role of the EBA in body perception processing.

Conclusion

This study provides preliminary evidence that targeted theta burst stimulation of the extrastriate body area, combined with focused body perception training, can beneficially modulate body image perception in patients with anorexia nervosa. The differential neural and behavioral responses observed between active and sham TMS groups suggest that individualized neuromodulation may engage distinct mechanisms contributing to sustained therapeutic effects. These findings advance the development of

biologically informed, personalized interventions in psychiatry by demonstrating how specific neural targets can be leveraged to recalibrate maladaptive perceptual processes. Future work integrating neuroimaging, computational modeling, and patient-specific neural profiling could further refine such precision-based treatment strategies for anorexia nervosa and related disorders.

Declarations

Contributions

Rebecca Boehme: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Supervision, Writing – original draft, Writing – review and editing

Reinoud Kaldewaij: Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review and editing

Morgan Frost-Karlsson: Data curation, Formal analysis, Investigation, Project administration, Writing – review and editing

Andrew Wold: Conceptualization, Data curation, Investigation, Methodology, Writing – review and editing

Adam Enmalm: Data curation, Investigation, Writing – review and editing

Isabel Khoure: Investigation, Therapy, Writing – review and editing

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Sara Barsjö: Investigation, Therapy, Writing – review and editing

Magnus Thordstein: Conceptualization, Investigation, Methodology, Resources, Software, Supervision, Writing – review and editing

Per A Gustafsson: Conceptualization, Supervision

Håkan Olausson: Conceptualization, Supervision, Writing – review and editing

Maria Zetterqvist: Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – review and editing

Conflict of interest

The authors have no conflict of interest.

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Figures

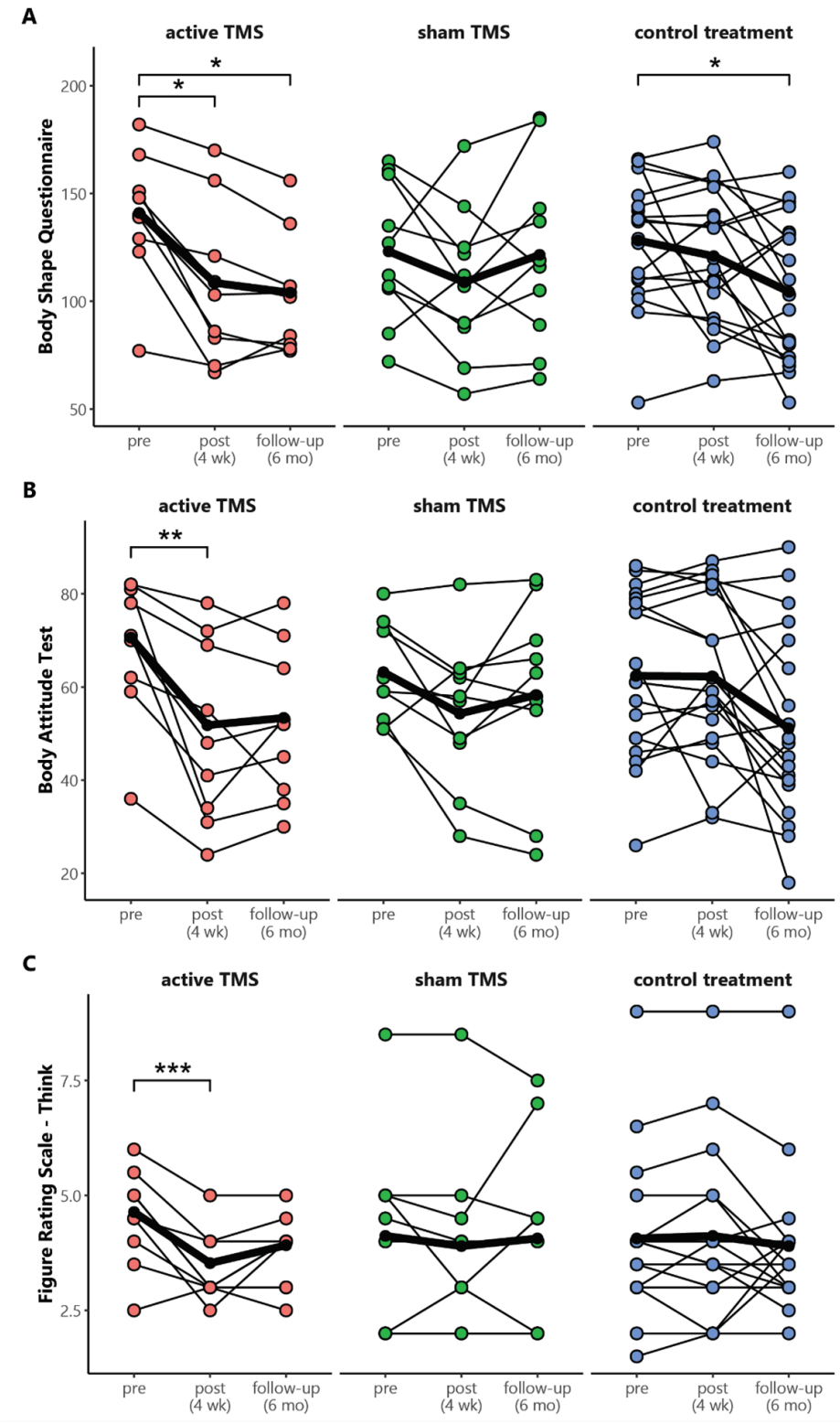

Figure 1

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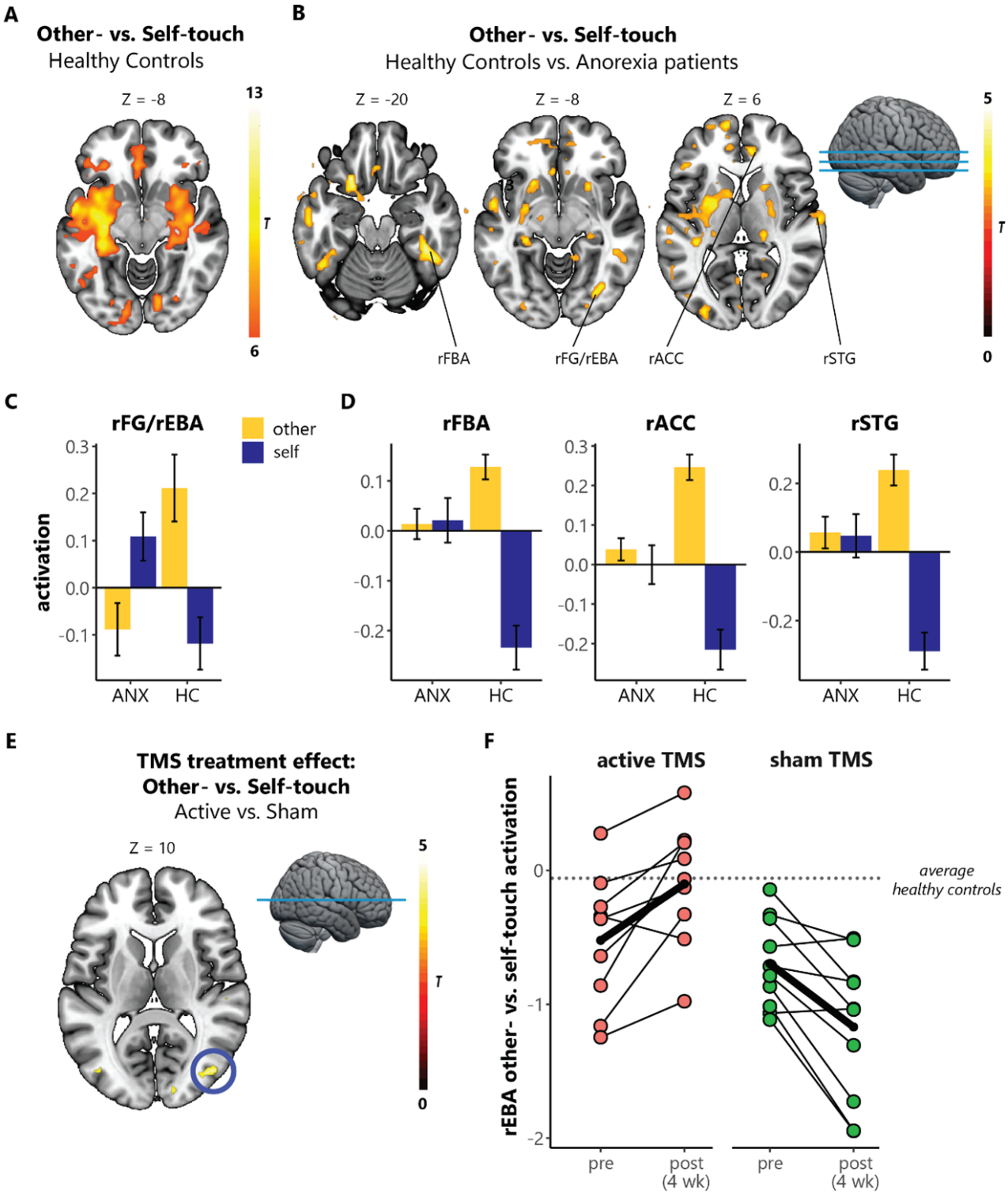

Figure 2

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