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Research report

State-dependent alterations in neural activity induced by the personalized ventrolateral prefrontal cortex stimulation during viewing emotional film clips

Changyue Hou [a,b], Meihua Yan [a,b], Haonan Pei [a,b], Yuting Deng [a,b], Sisi Jiang [a,b,c], Hechun Li [a,b], Huan Huang [a,b], Yufan Zhou [a,b], Roberto Rodríguez-Labrada [d], Cheng Luo [a,b,c,e,*]

[a] The Clinical Hospital of Chengdu Brain Science Institute, MOE Key Lab for Neuroinformation, School of Life Science and Technology, University of Electronic Science and Technology of China, Chengdu 611731, PR China
[b] China-Cuba Belt and Road Joint Laboratory on Neurotechnology and Brain-Apparatus Communication, University of Electronic Science and Technology of China, Chengdu 610054, PR China
[c] Research Unit of NeuroInformation, Chinese Academy of Medical Sciences, 2019RU035, Chengdu, PR China
[d] Cuban Neuroscience Center, La Habana, Cuba
[e] Department of Radiology, The Fourth People's Hospital of Chengdu, Chengdu 610056, PR China

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ABSTRACT

Emotion regulation is crucial for maintaining normal social interactions and individual psychological health. Using transcranial magnetic stimulation (TMS) to modulate emotional regulation may be a powerful method for neurological or psychiatric disorders. However, TMS efficacy varies between protocols and individuals, with the brain's state during treatment being an often-overlooked factor. This study aimed to explore the influence of emotional brain state on TMS effects. Ninety-nine healthy participants were randomly assigned to three groups: one watched neutral film clips and received active TMS (neutral group), while the other two watched sadness film clips and received either active or sham TMS (sad and sham groups, respectively). The amplitude of low-frequency fluctuations (ALFF) and functional connectivity (FC) were investigated using resting-state functional magnetic resonance imaging. Compared with the neutral group, the sad group showed different changes in neural activity (as measured by ALFF) in the right superior occipital gyrus and right middle frontal gyrus after TMS. In the neutral group, the ALFF change in the right superior occipital gyrus was correlated with the baseline FC between this region and the TMS target. Additionally, changes in neural activity in the right superior occipital gyrus and right middle frontal gyrus were related to changes in depression scale scores in the sad group. These findings may suggest that TMS during different emotional states can induce state-dependent alterations in neural activity. By combining emotional induction, TMS, and fMRI, this study offers a unique perspective on state-dependent effects and may improve TMS treatment outcomes.

1. Introduction

Transcranial magnetic stimulation (TMS), a non-invasive neuromodulation technique, can excite neurons in the human brain tissue intact through the skull (Bergmann et al., 2021), and thus can causally manipulate the activity of specific brain regions. There is a growing consensus that TMS is becoming a modulator of synaptic activity, inducing both short-term changes and long-term potentiation-like plasticity (Bergmann et al., 2021; Bradley et al., 2022). TMS, as an FDA-approved treatment tool, has been both clinically and academically used for many neurological or psychiatric disorders such as major depressive disorder, schizophrenia, and posttraumatic stress disorder (Cole et al., 2022, 2020; Diefenbach et al., 2016; Nauczyciel et al., 2014; Wobrock et al., 2015). TMS, combining electrophysiological techniques and neuroimaging such as functional magnetic resonance imaging (fMRI), helps to reveal the relevance between brain activity and cognitive and behavioral performance (Bergmann et al., 2016). Recently, the state-dependent effects of TMS have gradually become the focus of attention, with growing evidence that brain state, in addition to dosage, stimulation intensity, and coil positioning, can influence stimulation

* Correspondence to: No.2006, Xiyuan Ave, West Hi-Tech Zone, Chengdu, Sichuan 611731, PR China.
E-mail address: chengluo@uestc.edu.cn (C. Luo).

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outcomes. The simplest interpretation is motor-evoked potentials (MEPs). When TMS is applied to the primary motor cortex (M1) during hand muscle contraction, it elicits larger MEPs than in a resting state (Bergmann et al., 2016; Rossini et al., 1994). Moreover, several studies have shown that engaging participants in specific tasks—such as voluntary emotion regulation, working memory, or visual attention—to modulate brain state can alter the effects of TMS, producing neural outcomes distinct from those observed in a control state (Grosshagauer et al., 2024a, 2024b; He et al., 2023; Morishima et al., 2009; Taylor et al., 2024; Webler et al., 2022). A better understanding of the state-dependent effects of TMS can systematically control the cognitive and psychological state of patients, thus providing some clinical guidance to lead to better treatment (Carmi et al., 2018; Dinur-Klein et al., 2014; Oathes et al., 2022).

Emotion regulation (ER) is essential for maintaining normal social interactions and individual psychological health, and ER impairments have been widely recognized across numerous neuropsychiatric diseases (Lima et al., 2018; Malhi and Mann, 2018). Braunstein et al. indicated that ER can be implicit or explicit, and explicit-controlled ER involves the ventrolateral prefrontal cortex (VLPFC) (Braunstein et al., 2017; He et al., 2023). The hypoactivity in VLPFC can be recognized as a reliable neural phenotype (McTeague et al., 2020; Sydnor et al., 2022) in many emotional disorders, and the reduction of gray matter volume of VLPFC has been found in depressed individuals (Kohn et al., 2014). Besides, the VLPFC area in conjunction with other areas is essential for generating and appraising emotion and affect (Kohn et al., 2014; Ochsner and Gross, 2005; Phillips et al., 2008). In a word, a therapeutic or intervention method that mobilizes the activity of VLPFC is expected to be a powerful method for patients with neurological or psychiatric disorders to relieve emotional and mental symptoms (Sydnor et al., 2022).

The emotional experience of sadness is common in human social consciousness, can be strongly felt in daily life, and is important for people with mood disorders. When watching sadness videos, depressed people have elevated arousal levels and are unable to suppress sympathetic activity (Ozden et al., 2024). Compared with complex tasks, the naturalistic film-watching paradigm places lower demands on cognitive resource allocation, thereby offering broader applicability, especially for patients with neuropsychiatric disorders who struggle to withstand such high attention and cognition loads. In addition, previous meta-analyses and reviews of emotion induction have demonstrated that film clips appear to be one of the most powerful and effective ways to trigger emotions (Deng et al., 2017; Ge et al., 2019). More importantly, this type of stimulus involves sequential and multi-sensory integration of received information, close to real-life stimulus (Bottenhorn et al., 2018). Furthermore, complex audiovisual stimuli recruit not only sensory networks but also activate the frontoparietal network (Bradley et al., 2022; Nummenmaa et al., 2012; Schlochtermeier et al., 2017).

The current study applied TMS during emotional film viewing over five consecutive days to investigate the interaction between brain state and TMS effects. We hypothesize that five continuous TMS-film sessions would induce state-dependent changes in brain activity across a wide range of networks, including both primary sensory and high-level networks. Furthermore, these changes in brain activity are expected to be associated with behavioral changes following the five-day stimulation protocol.

2. Methods

2.1. Participants

A total of 106 healthy right-handed young adult volunteers were recruited from the University of Electronic Science and Technology of China and randomly assigned into two active TMS groups (sad group and neutral group), differing in the type of films watched during the TMS stimulation process, and one sham TMS group (sham group). All participants had no history of neurological or psychiatric disorders, substance abuse, or any relevant MRI scanning contraindications, and all of them had normal or corrected-to-normal vision. Seven dropouts occurred due to uncomfortable feelings related to TMS or schedule conflicts. All participants were instructed to fill out scales at the beginning and end of the experiment, including the Interpersonal Reactivity Index-C (IRI-C), the Self-Rating Depression Scale (SDS), and the Self-Rating Anxiety Scale (SAS). The IRI-C consists of four dimensions: perspective taking (PT), fantasy (FS), empathetic concern (EC), and personal distress (PD). The MRI data included in this study (N = 99) all meet the criteria of head motion (translation < 2.0 mm, rotation < 2°). There were no significant inter-group differences in age, education level, gender, handedness, and baseline scale scores between the three groups. More detailed information is presented in Table 1.

2.2. Experimental design

The experiment procedures were conducted over six consecutive days for all participants (Fig. 1A), starting with baseline scale assessments, a baseline MRI scan, and resting motor threshold (rMT) determination on the first day. Participants underwent a 40-second continuous theta-burst stimulation (cTBS) session every day for the next five consecutive days. Upon completion of the final day of TMS stimulation, participants received an MRI scan immediately, followed by behavioral assessments using the same scales as the baseline screening.

Of note, before and during each daily TMS session, all participants watched selected film clips, which were either emotionally arousing sad films or neutral films that did not induce sadness or any other intense emotions. Based on this, all participants were randomly divided into three groups. One group watched neutral film clips and received active TMS stimulation (neutral group), while the other two groups watched sadness film clips but received active or sham TMS (sad group and sham group, respectively). The order of film clips was counterbalanced within each experimental cycle. Through the E-prime 3.0 program (Psychology Software Tools Inc., Sharpsburg, USA), the precise synchronization between film watching and TMS stimulation was achieved by applying neuro-navigated TMS at the final 40 s of each film clip. Following the TMS and films, participants were asked to rate their emotional valence level of sadness, pleasure, arousal, and dominance on a scale of 1–9.

Table 1
Demographic characteristics of the three groups[a].

Characteristics	Group[b]			Statistics
	Sad (n = 39)	Neutral (n = 40)	Sham (n = 20)	
Age (years)	23.3 ± 1.3	23.1 ± 1.1	22.9 ± 1.6	0.404[f]
Education(years)	17.3 ± 1.2	17.3 ± 1.0	16.9 ± 1.5	0.303[f]
Male/Female	18/21	20/20	8/12	0.764[g]
Handedness (self-reported)	right	right	right	-
IRI-C[c]	73.3 ± 7.6	72.4 ± 9.2	71.8 ± 6.2	0.765[f]
SDS[d]	31.0 ± 6.6	31.0 ± 7.0	31.5 ± 8.3	0.954[f]
SAS[e]	30.1 ± 6.7	30.0 ± 6.8	30.5 ± 7.4	0.958[f]
Post IRI-C	70.6 ± 6.1	71.9 ± 9.9	71.0 ± 4.5	0.890[f]
Post SDS	31.5 ± 5.8	28.9 ± 7.0	30.2 ± 9.3	0.277[f]
Post SAS	29.8 ± 5.4	28.1 ± 7.1	29.2 ± 6.6	0.489[f]

[a] Data are expressed as mean ± S.D.
[b] The abbreviation of "Sad" group means watching sad films while receiving active cTBS stimulations, "Neutral" means watching neutral control films while receiving active cTBS stimulations, "Sham" means watching the same sad films while receiving sham cTBS.
[c] Interpersonal Reactivity Index-C Scale.
[d] Self-Rating Depression Scale.
[e] Self-Rating Anxiety Scale.
[f] The P-value was obtained using a one-way analysis of variance.
[g] The P-value was obtained using a two-tailed Pearson χ^2 test.

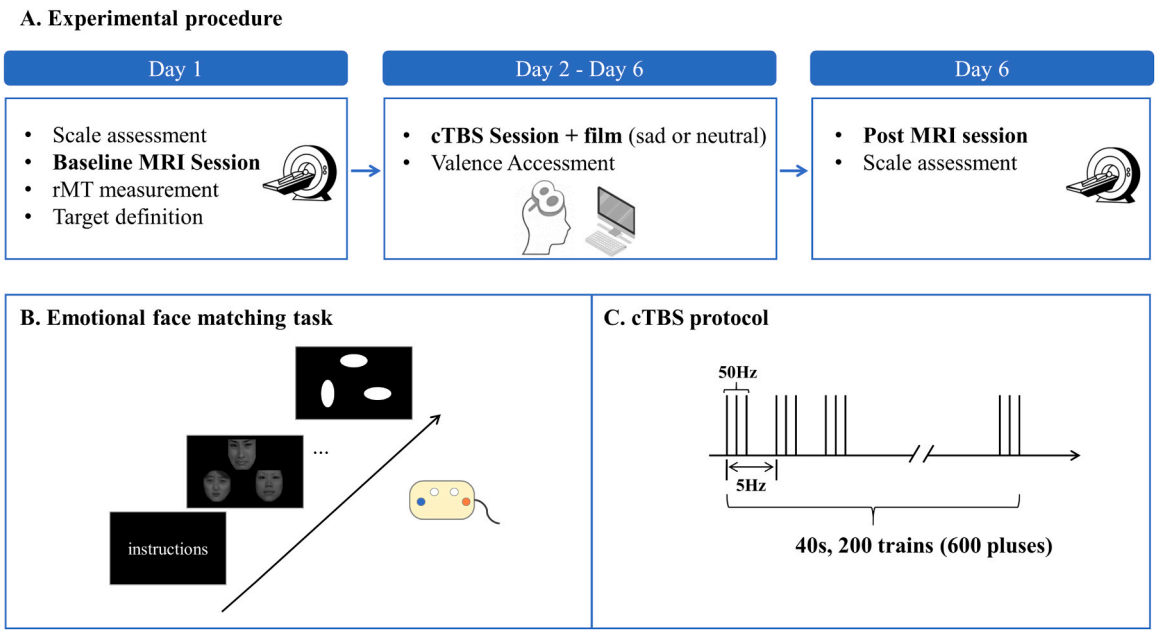

Fig. 1. Experimental schema. A. Experimental procedure. The experiment lasted for six consecutive days. B. TMS site of stimulation localization. The baseline MRI session includes an emotional face matching task used for the analysis of individual targets. C. cTBS protocol. The duration of a cTBS session presented is 40 s, with a total of 200 trains (600 pulses). Each train consisted of a triplet of pulses at 50 Hz repeated every 200 ms.

2.3. TMS site of stimulation localization: emotional face matching task

An emotional face matching task fMRI data was acquired at the baseline to target the right VLPFC region for each subject (Fig. 1B). This task is a standard block-design fMRI paradigm that can effectively engage emotion-related brain regions. There were three pictures displayed on the screen, with the reference image above and two matching images below. These pictures were either the facial expressions of Asians or oval-shaped pictures in two directions. Participants were asked to compare the two pictures below with the one above and then pressed a button to select the picture that matched the emotion of the reference picture above. There were a total of 12 blocks, each consisting of five emotional face picture trials (including positive, negative, and neutral emotions) and two elliptical picture trials. The task lasted for 256 s and collected 128 volumes.

After preprocessing task functional images, the general linear model (GLM) analysis in the statistical parametric mapping (SPM12, http://www.fil.ion.ucl.ac.uk/spm/) (Friston et al., 1994) was conducted. The facial expression and oval conditions as regressors with six realignment motion parameters as the non-interest regressors to modeled as a box-car function and convolved with a hemodynamic response function (HRF). The estimated beta maps from the individual GLM analyses were used for the selection of the targeted region. The peak voxel with maximum activation in the right VLPFC was chosen as the stimulation target.

2.4. TMS protocol

Each active TMS session was administered using the Magstim® super rapid2 stimulator with a 70 mm figure-8 coil (Magstim Company, Whitland, United Kingdom). Sham TMS sessions were implemented using a Magstim sham coil. The T1-weighted structural images of each participant obtained from the baseline MRI scan, along with the individual target coordinates, were imported into the Brainsight software (BrainSight, Rogue Research, Montreal, QC, Canada). During film viewing, the coil was positioned tangentially to the scalp over the target region.

For the definition of resting motor threshold (rMT), with the surface electromyography (EMG) recording the right abductor pollicis brevis (APB) transient muscle contraction, single TMS pulses were delivered to the corresponding left side of the primary motor cortex (M1). The rMT intensity was determined if at least five out of ten single pulses at the lowest intensity could elicit the motor-evoked potentials (MEPs) amplitudes greater than 50 μV. The experiment employed a standard cTBS paradigm in which three pulses were continuously delivered at 50 Hz, repeated every 200 ms, and lasted 40 s (600 pulses) (Fig. 1C). The stimulation intensity was applied at a dose of 80 % of the subjects' rMT, which is within consensus recommendations for safety considerations.

2.5. Image acquisition

The MRI sessions were acquired in a 3.0 T MRI scanner (Discovery MR750, GE, USA) with a 32-channel head coil. The functional MRI images (resting-state fMRI and the emotional face matching task fMRI) were collected with an echo-planar imaging (EPI) sequence (TR = 2000 ms, TE = 30 ms, FOV= 240 × 240 mm^2, slice thickness=3.4 mm, FA = 90°, matrix size= 64 × 64, slices=39). The resting-state fMRI data contains 255 volumes within 510 s of acquisition time. During the resting-state fMRI scan, participants were instructed to keep their eyes closed, avoid falling asleep, and let their thoughts wander.

Sagittal structural images were acquired with T1-weighted magnetization-prepared rapid gradient echo (MPRAGE) sequence (TR = 5.964 ms, TE = 1.972 ms, FOV= 256 × 256 mm^2, slice thickness=1 mm, FA = 9°, matrix size= 256 × 256, and 156 volumes). T1 images were input into BrainSight Software for neuronavigation.

2.6. Image processing and statistical analysis

All preprocessing procedures were conducted using the Data Processing Assistant for Resting-State fMRI (DPARSF) software (http://rfmri.org/DPARSF) (Chao-Gan and Yu-Feng, 2010) based on MATLAB. The first 5 volumes of functional data were discarded to reach signal equilibrium. For the resting-state fMRI data, we performed slice timing, motion-corrected realignment, spatial normalization into the Montreal Neurological Institute (MNI) with a voxel size of 3 × 3 × 3 mm^3, and smoothing using an 8-mm full-width at half

maximum Gaussian kernel. Friston-24 head motion parameters, white matter, cerebrospinal fluid (CSF) signals, and linear drift were regressed. Last, before the functional connectivity (FC) analysis, the time series were band-pass filtered at 0.01–0.08 Hz. The results of an extra global signal regression step can be found in the Supplementary materials. For the face-matching task images, we performed slice timing, realignment, spatial smoothing, and co-registration of structural images and functional images.

The Amplitude of Low-Frequency Fluctuations (ALFF) and FC were calculated through the DPARSF toolkit. ALFF implies the intensity of regional spontaneous neural activity. After the preprocessing of resting-state fMRI data, the time series of each voxel was transformed into the frequency domain after the fast Fourier Transform, and the square root of the power spectrum was further calculated. For each voxel, the average of this square root across 0.01–0.08 Hz (i.e., ALFF) was obtained. ALFF values on voxels were minus by global mean ALFF and divided by the standard deviation to obtain a z-transformed ALFF map for standardization purposes. A one-way analysis of variance (ANOVA) with a 1 × 3 design was conducted to investigate whether there were significant differences in brain activity changes across the three groups. Specifically, this analysis focused on the individual-level △ALFF maps, which were computed by subtracting the ALFF values obtained during the pre-session scan from those obtained during the post-session scan for each subject. These △ALFF maps reflect session-induced changes in spontaneous brain activity. To control for potential confounding effects, sex, age, and years of education were included as covariates in the model. Significances with multiple comparisons were tested with Gaussian random field (GRF, voxel-level $p < 0.005$, cluster-level $p < 0.05$, one-tailed) correction. In the post-hoc test, the mean △ALFF values from significant clusters identified by the ANOVA were extracted for each participant, and pairwise group comparisons were performed using Bonferroni's post-hoc test.

We acquired emotional face matching task fMRI data both before and after the 5-day TMS intervention. Differences in activation changes (post-session activation minus pre-session activation) among the three groups were examined using one-way ANOVA. Statistical significance was set at $p < 0.05$ (voxel-level, uncorrected), with results further assessed for multiple comparisons correction. For post-hoc analysis, the mean activation change values from significant clusters identified by the ANOVA were extracted for each participant, and pairwise group comparisons were performed using Bonferroni's post-hoc test.

For the FC analysis, the mean time series of individual VLPFC targets were extracted using a 6-mm spherical mask that centered on the stimulus target MNI coordinates. For each subject, the Pearson correlation coefficient was calculated in every brain voxel with this extracted time series, and then Fisher's z transformation was performed for the correlation coefficients. FC values of the clusters with significant ALFF differences among the three groups were extracted to assess the potential relationship between △ALFF and FC values.

The two-sample *t*-test was conducted to assess whether participants of two active groups differed in anatomical position (Y and Z coordinates). To evaluate the TMS effect on behavior, we used a one-way ANOVA (1 × 3 design) to examine the differences in changes of scale scores (post-session scores minus pre-session scores) across three groups. In the end, we calculated the partial correlation between scale scores and ALFF values with age, sex, and education years as covariates. The post-measurement scales included non-missing data from only 28 subjects in the sad group and 32 subjects in the neutral group.

3. Results

3.1. Altered neural activity

As predicted, the one-way ANOVA demonstrated significant differences in the effect on the middle frontal gyrus and the right superior occipital gyrus among the three groups (Table 2 and Fig. 2), suggesting the participation of the visual network and prefrontal network. The sad group demonstrated decreased ALFF of the middle frontal gyrus compared with the neutral group. In the right superior occipital gyrus, the sad group showed increased ALFF compared with the neutral group, while the neutral group demonstrated decreased ALFF compared with the sham group. The one-way ANOVA revealed differences in activation changes among the three groups (voxel-wise $p < 0.05$, uncorrected) in several regions primarily involved in the emotion-processing network. However, none of these clusters survived correction for multiple comparisons. These results are presented in Supplementary Fig. S2 and Table S2 for transparency. The two active groups also did not differ in how anteriorly ($t_{77} = -0.627$, $p = 0.532$) or ventrally ($t_{77} = 0.404$, $p = 0.688$) TMS was applied, as determined by stimulation position Y and Z coordinates in standard space.

3.2. Correlation between △ALFF and FC

The individual stimulation target was mainly located in Brodmann areas 44, 45, and 47 (Fig. 3A). In the neutral group, the △ALFF in the right superior occipital gyrus negatively correlated with the baseline FC between the right superior occipital gyrus and the individual VLPFC (r = -0.391, $p = 0.017$), controlling for age, gender, and education years (Fig. 3B). However, there was no similar correlation in the sad group, which may suggest a state-dependent change in cTBS over five days.

3.3. Behavioral results and correlation between △ALFF and changes in behavior variables

Compared with the sad group, the △SDS scores (post-session SDS scores minus pre-session SDS scores) of the neutral group demonstrated a trend of decrease (t_{58} = -1.79, $p = 0.079$) (Fig. 4A). To evaluate the behavior changes, we calculated the correlation between △ALFF and △SDS scores, the results are shown in Fig. 4B. In the sad group, △SDS scores negatively correlated with △ALFF in the right superior occipital gyrus (r = -0.526, $p = 0.007$). There is a trend of positive correlation between the △SDS scores and △ALFF in the right middle frontal gyrus ($r = 0.384$, $p = 0.058$).

4. Discussion

The current study investigated the state-dependency of TMS by applying personalized VLPFC TMS during emotional film clip viewing. We found that the sad group had different △ALFF in the right superior occipital gyrus and right middle frontal gyrus after TMS compared with the neutral group. In the neutral group, the △ALFF in the right superior occipital gyrus was correlated with the baseline FC between the right superior occipital gyrus and the target, whereas there was no similar association in the sad group. Moreover, the △ALFF in the right superior

Table 2
ALFF alteration among the three groups.

Cluster	Region	Cluster size	Peak MNI coordinates			Peak F value	Post-test *p* value		
			x	y	z		Sad vs Neutral	Sad vs Sham	Neutral vs Sham
1	right superior occipital gyrus	800	21	− 87	21	11.06	< 0.001	0.571	0.042
	right calcarine sulcus		24	− 75	9	9.59			
2	right middle frontal gyrus	153	39	21	48	8.59	< 0.001	0.541	0.062

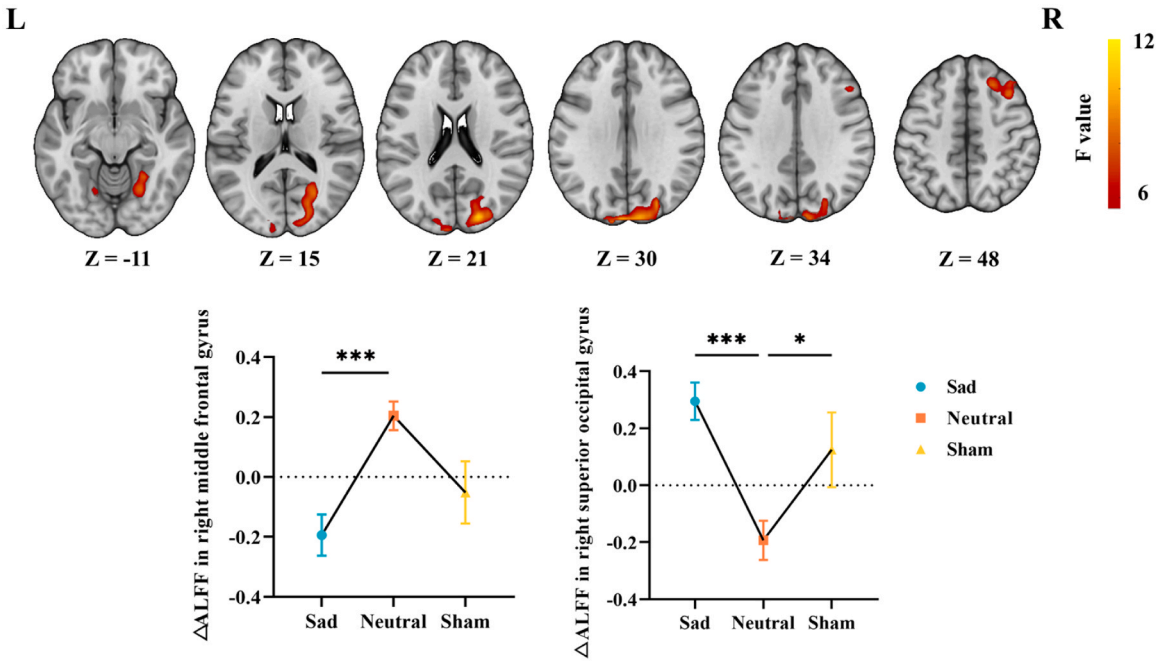

Fig. 2. Group differences in ALFF among the three groups. The axial brain maps above display brain ALFF results (GRF, voxel-level $p < 0.005$, cluster-level $p < 0.05$). Multiple between-group and pairwise comparisons were conducted by Bonferroni's post-hoc test. *$p < 0.05$; **$p < 0.005$; ***$p < 0.001$.

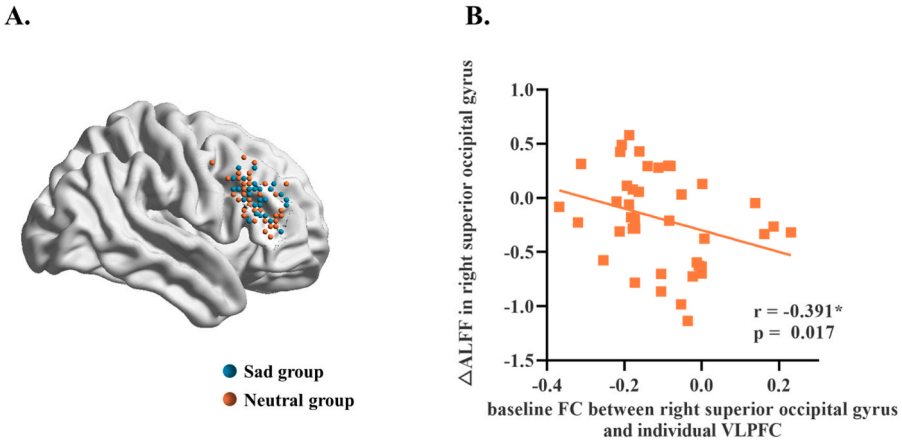

Fig. 3. Individual TMS targets analysis. A. TMS targets. The blue spheres represent the individual targets of the sad group, while the orange spheres represent the individual targets of the neutral group. B. Partial correlation between △ALFF and baseline FC in the neutral group, adjusted for age, sex, and years of education. *$p < 0.05$.

occipital gyrus and right middle frontal gyrus were related to changes in △SDS scores in the sad group. Our findings might suggest that TMS during different emotional film clip viewing could induce state-dependent alterations of neural activity. This study integrates emotional film viewing and TMS with fMRI to offer a novel perspective on state-dependent effects and to inform strategies for enhancing TMS treatment outcomes.

In this study, the sad group demonstrated decreased neural activity of the middle frontal gyrus after TMS compared with the neutral group, whereas the sham group showed no change. This is consistent with previous investigations that TMS can induce local and remote network effects (Sack et al., 2024). VLPFC is closely connected to regions involved in regulation, such as the dorsolateral prefrontal cortex (DLPFC), and in emotional expression, such as the frontal pole (McTeague et al., 2020; Ray and Zald, 2012). The DLPFC plays a key role in both cognitive control and emotional regulation (Marques et al., 2018). Specifically, the DLPFC plays a crucial role in cognitive reappraisal, with increased DLPFC activation being associated with altered amygdala activity during this process (Feeser et al., 2014). Previous studies have shown that enhancing DLPFC activity via transcranial direct current stimulation can facilitate emotion regulation and improve cognitive control (Chen et al., 2023). Moreover, Dolcos et al. and Perlstein et al. demonstrated that there is a reverse pattern of ventral and dorsal PFC regions (Dolcos and McCarthy, 2006; Perlstein et al., 2002). For example, under emotional distractions, the activation of ventrolateral PFC areas increased, while the activation of DLPFC decreased. Therefore, the observed changes in the right middle frontal gyrus may indicate that TMS targeting the VLPFC influences prefrontal circuits underlying both cognitive and affective regulation.

In addition to frontal areas, we also observed that TMS caused different changes in neural activity in the right superior occipital gyrus in the two groups. During reactivity and regulation tasks, the VLPFC has both afferent and efferent connections to sensory systems (Ray and Zald, 2012). Previous studies described emotion regulation as a deployment of

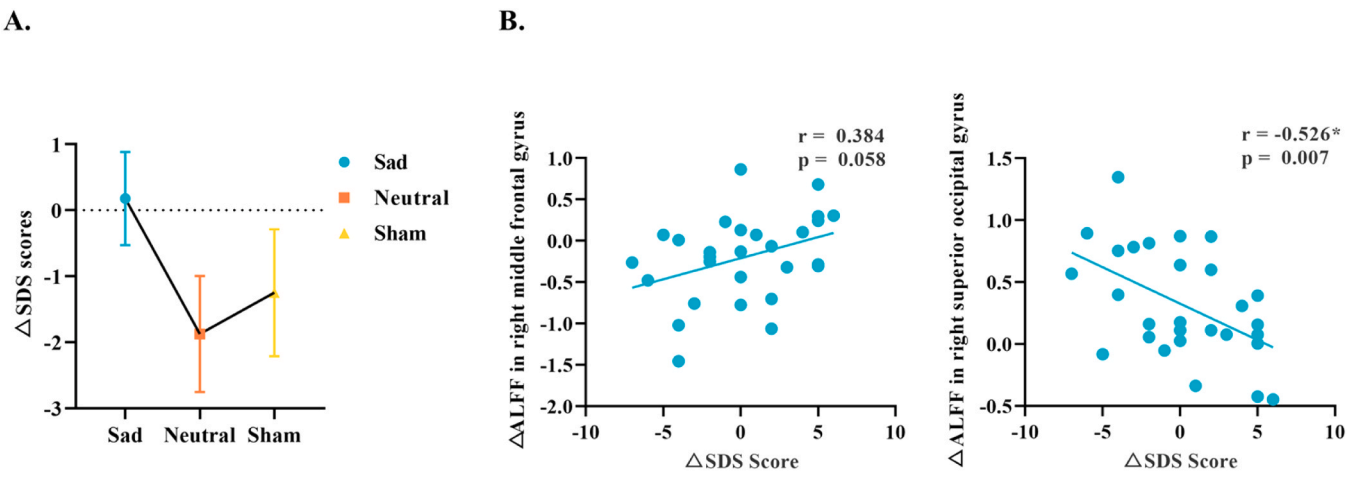

Fig. 4. Behavioral findings. A. Group difference in SDS scores among three groups. B. Changes in neural activity correlated with changes in behavior variables in the sad group. Partial correlation between △ALFF and △SDS scores in the sad group, controlling for age, sex, and years of education. *$p < 0.05$.

PFC top-down cognitive control, allowing for top-down control of the content processed in the information flow (Grossberg, 2007). Moreover, there are loops between the amygdala and the visual cortex that modulate visual processing during the processing of affective visual stimuli (Pessoa and Adolphs, 2010). Previous investigations have shown that the visual area, from striate to various extrastriate areas, is modulated by the emotional content (Carretie et al., 2022). We also found that baseline FC between the TMS target and visual cortices was associated with changes in neural activity in visual cortices in the neutral group, while there was no such relationship in the sad group. In conclusion, these results suggested that VLPFC TMS during different emotional film clips can induce different sensory system effects.

We also found that TMS during different emotional film clips induced opposite alterations of neural activity. In fact, the TMS-induced current interacts with the initial brain state during stimulation. Thus, an individual's cognitive, perceptual, and/or emotional states can significantly affect their network effects, sometimes in opposite directions (Bradley et al., 2022; Grosshagauer et al., 2024a, 2024b). For example, Scangos et al. implanted multi-site intracranial electrodes in a patient with depression and found that emotional responses were context and state-dependent (Scangos et al., 2021). A concurrent TMS-fMRI study showed that the underlying cognitive brain state affects acute TMS effects (Grosshagauer et al., 2024a, 2024b). Li et al. suggested that cognition-modulated pre-rTMS frontal activity could predict and enhance the antidepressant efficacy of rTMS treatment (Li et al., 2016). Isserles and his colleagues found that negative cognitive–emotional reactivation can undermine the antidepressant therapeutic effect of deep TMS (Isserles et al., 2011). Furthermore, we also found that altered neural activity correlated with individual changes in depressive scores in the sad group. This is consistent with previous studies that direct stimulation of VLPFC facilitated the regulation of emotions in healthy individuals (Cao et al., 2021) and depressed patients (Rao et al., 2018). Responses of the prefrontal cortex through VLPFC stimulation may reflect enhanced cognitive reappraisal or executive control over emotional processing. Altered activity in the right superior occipital gyrus may reflect changes in the processing of emotional cues, which are known to be disrupted in depressive states (Li et al., 2013). Together, these findings further suggest that VLPFC stimulation may indirectly modulate a fronto-occipital network involved in mood regulation, and that these effects are modulated by the individual's emotional state. While the correlation results are promising, behavioral changes did not reach strong statistical significance across groups. Therefore, a larger sample size is required to further establish the state-dependent effects of TMS on behavior. Furthermore, although the current study focused on healthy young people, combined with previous findings on clinical populations, the state-dependent effect of TMS is worthy of attention. Therefore, more future work should examine the specific effects of similar TMS-film paradigms on clinical populations, such as patients with depression or post-traumatic stress disorder.

In summary, TMS targeting the VLPFC can modulate local and remote network nodes. Whereas the same TMS protocol can induce different network effects in the brain depending on the emotional brain state at the time of stimulation.

5. Conclusions

In conclusion, this study combined emotional film clips viewing and TMS with the fMRI, demonstrating that TMS applied during different emotional film clips would induce state-dependent changes in neural activity. These findings significantly advance our understanding of state-dependent effects and may contribute to improving clinical outcomes of TMS treatment.

CRediT authorship contribution statement

Hechun Li: Visualization, Methodology. **Sisi Jiang:** Supervision, Methodology, Formal analysis. **Yufan Zhou:** Software, Methodology. **Huan Huang:** Methodology, Data curation. **Cheng Luo:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition, Conceptualization. **Roberto Rodríguez-Labrada:** Supervision. **Meihua Yan:** Visualization, Software, Methodology, Data curation. **Changyue Hou:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Yuting Deng:** Validation, Data curation. **Haonan Pei:** Visualization, Software, Methodology.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.brainresbull.2025.111534.

Data availability

Data will be made available on request.

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