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• LETTER •
Special Focus on Brain Imaging and Addiction

Potential neural mechanism of single session transcranial magnetic stimulation on smoking craving

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Dear editor,

Roles of left dorsolateral prefrontal cortex (DLPFC) in smoking craving and relapse have been highlighted [1–3]. Converging evidence has also showed the therapy of the repetitive transcranial magnetic stimulation (rTMS) on the left DLPFC for interventions of substance use disorders (SUD) [4,5]. In present study, we aim to test the rTMS treatment efficacy of smoking craving in smokers. In addition, the potential neural mechanisms of the possible effects would be investigated systemically from regional and circuits level. We hypothesize that the DLPFC-striatum pathways would be implicated with the therapy efficacy. It is hoped that our primary results could verify the roles of the DLPFC in SUD and help to promote the applications of brain stimulations in SUD individuals.

The ethics committee of medical research at the First Affiliated Hospital of Baotou Medical College approves our research. All subjects give written informed consent after they are told the study procedure, which are carried out according to the guidelines of human medical research (Declaration of Helsinki).

At baseline, smoking cue-reactivity task is collected for the 23 smokers in a 3T Philips scanner. Two weeks later, a single session 10-Hz rTMS on the left DLPFC is performed in 12 smokers (real rTMS), 11 smokers (sham rTMS) randomly. The second smoking cue-reactivity task is recorded immediately in the same scanner. The smoking-cue induced craving scores is acquired and compared between baseline and rTMS conditions. Similarly, the regional activations are extracted and psychophysiological interaction (PPI) analysis by choosing left DLPFC is carried out. Paired t-test is employed to reveal the therapy effect of rTMS on smoking craving and brain function changes.

After the resting motor threshold (rMT) is determined, high-frequency rTMS (10 Hz) with an "8"-shaped coil over the left DLPFC is applied with a CCY-I TMS instrument (Yiruide Co., Wuhan, China) (100% rMT, 5-sec on, 10-sec off for 10 min; 2000 pulses) (Figure 1(a)). Sham TMS is also carried out as the coil is turned away from the skull at 90° [4]. No side effects are reported during or after brain stimulation.

Sham rTMS results reveal no significant changes in craving (pre-rTMS: 41.2±4.1; post-rTMS: 40±4.3; $t = 0.88$, $p = 0.4$). Among 12 real rTMS subjects, 7 smokers show reduced smoking cue-induced craving (pre-rTMS: 45.3±6.2; post-rTMS: 28.8±4.7; $t = 2.76$, $p = 0.03$) (Figure 1(b)). Neuroimaging findings of 7 rTMS responders demonstrate that the posterior cingulate cortex (PCC) shows decreased cue-induced activation after rTMS ($p < 0.005$ uncorrected) (Figure 1(c)). Moreover, the functional coupling of the

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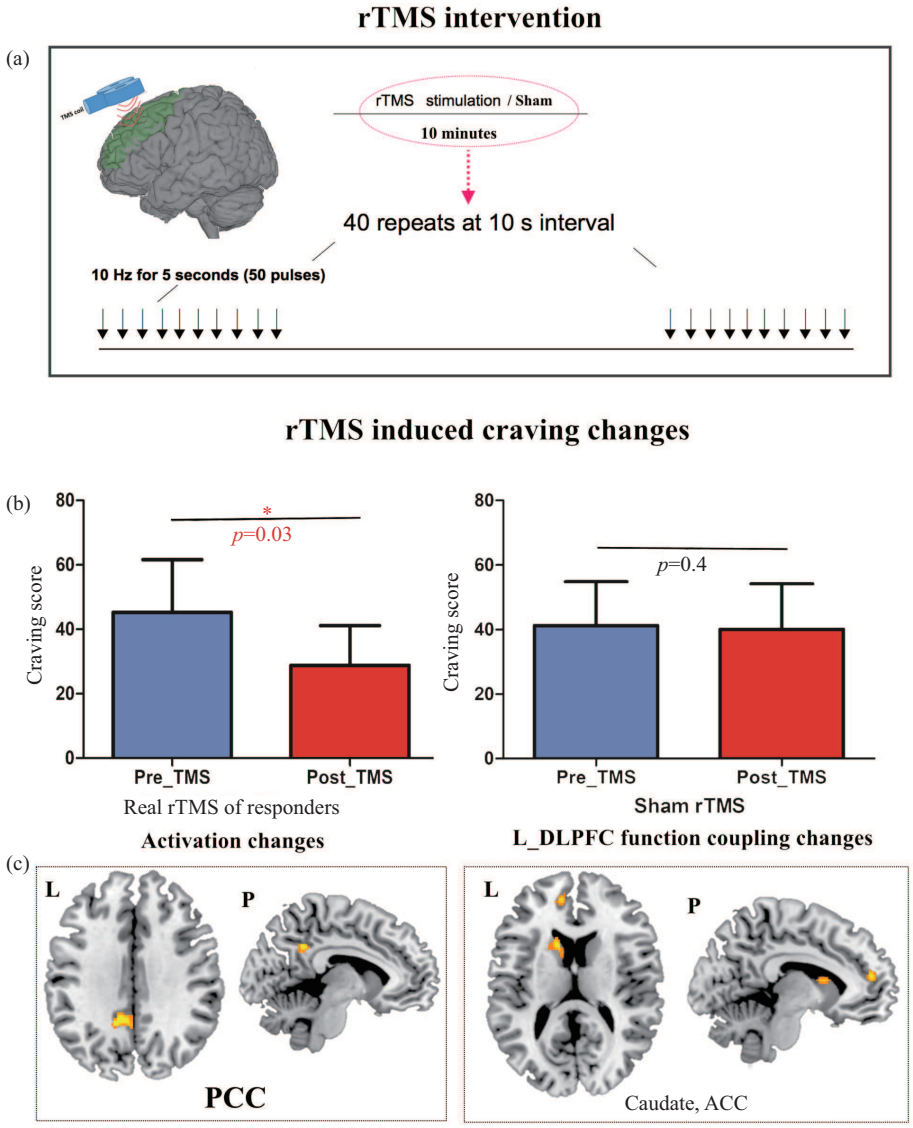

Figure 1 (Color online) rTMS intervention over the left DLPFC induced craving reduction and decreased function coupling of the left DLPFC-caudate in smokers. (a) rTMS intervention paradigm; (b) single-session rTMS induced smoking craving changes; (c) single-session rTMS induced brain function changes.

left DLPFC-caudate and left DLPFC-ACC pathway is reduced after rTMS intervention ($p < 0.005$ uncorrected) (Figure 1(c)), although the significance level does not survive the multiple comparisons.

By targeting DLPFC using rTMS and transcranial direct current stimulation, previous researchers had demonstrated the possibility to reduce craving and cigarette consumption in smokers [5]. However, few studies revealed the crucial roles of the DLPFC in rTMS interventions. The present double-blind and sham-controlled design study fills this gap by exploring the therapy effects and corresponding neural mechanisms of rTMS for smoking craving. Consistent with previous findings, we demonstrate that 7 of 12 volunteers show reduced craving scores after a single rTMS treatment (Figure 1(b)). The behavioral effects are accompanied by the decreased coupling of the left DLPFC-caudate pathway (Figure 1(c)). DLPFC plays crucial roles in smoking craving by integrating motivational, affective (e.g., current desires in the initiation of drug-seeking behavior) and cognitive information (e.g., the exertion of inhibitory control over behavior) [6]. Cognitive strategy by recruiting left DLPFC to modulate striatum activation has been used to successfully suppress smoking craving [7]. Consistently, the neuroimag-

ing biomarker of the left DLPFC-caudate pathway as smoking craving has also been observed in our previous study [1], which is likely to serve as the common mechanism in rTMS management of craving. Together with previous findings, this study provides the potential mechanisms underlying the intervention of rTMS over the left DLPFC for reduced smoking craving.

It is worthy to note that single session rTMS treatment effect on smoking craving might be not enough for the whole group (41.7% failed to respond). This encourages us to consider long-term rTMS intervention for treating smoking. Evidently, a larger sample of subjects and a more comprehensive experimental design are necessary to reveal the accurate mechanism of rTMS efficiency for smoking treatment.

This study reports potential mechanisms underlying the intervention of rTMS over the left DLPFC on reduced smoking craving, which is probably owing to the modulation of the left DLPFC-caudate pathway.

Compliance and ethics The authors report no biomedical financial interests or potential conflicts of interest.

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References

1 Yuan K, Yu D H, Bi Y Z, et al. The left dorsolateral prefrontal cortex and caudate pathway: new evidence for cue-induced craving of smokers. Hum Brain Mapp, 2017, 38: 4644–4656
2 Yuan K, Yu D H, Zhao M, et al. Abnormal frontostriatal tracts in young male tobacco smokers. Neuroimage, 2018, 183: 346–355
3 Yuan K, Zhao M, Yu D H, et al. Striato-cortical tracts predict 12-h abstinence-induced lapse in smokers. Neuropsychopharmacol, 2018, 43: 2452–2458
4 Shen Y, Cao X Y, Shan C L, et al. Heroin addiction impairs human cortical plasticity. Biol Psychiatry, 2017, 81: 49–50
5 Salling M C, Martinez D. Brain stimulation in addiction. Neuropsychopharmacol, 2016, 41: 2798–2809
6 Goldstein R Z, Volkow N D. Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. Nat Rev Neurosci, 2011, 12: 652–669
7 Kober H, Mende-Siedlecki P, Kross E F, et al. Prefrontal-striatal pathway underlies cognitive regulation of craving. Proc Natl Acad Sci USA, 2010, 107: 14811–14816