

in patients diagnosed with diagnosis of Parkinson's disease⁹ and depression.¹⁰

Because of increasing evidence supporting the notion that prefrontal HF-rTMS apparently increases heightens dopaminergic neurotransmission in the striatum, one can predict that this HF-rTMS-based increase may alter cognitive functions-function in a degree-dependent on striatal dopaminergic neurotransmission manner.

The striatum and dopaminergic neurotransmission have been implicated in probabilistic reward learning that, which involves gradual acquisition of stimulus-reward association overwith repetition and feedback.¹¹ Optimal behavior in a given environment is dependent on the ability to learn contingencies between antecedent events and their positive or negative outcomes. Because of the probabilistic nature of the contingencies in a dynamic environment, individuals have to integrate reward history over time in order to behave advantageously. This integration is

knownbelieved to be dependent onmediated by non-declarative learning processprocessing, which occurs just outside of the medial temporal lobes.¹¹ Tasks assessing probabilistic reward learning typically include selections have a participant select among two or more alternative stimuli that are differentially associated with reward.¹²⁻¹⁴ During the tasks, healthy participants typically develop preferencesa preference for a stimulus associated with better reward outcomes. For example, in a probabilistic reward task developed by Pizzagalli and colleagues,¹³ colleagues¹³ participants were presented with two alternative stimuli, and correct responses to the two stimulusone were associated with different frequenciesa higher frequency of reward outcome. Participants than the other. Over time, participants developed a response bias toward the more frequently rewarded stimulus over time. Administering. For this task, administering drugs facilitatingthat facilitate or disruptingdisrupt dopaminergic neurotransmission was associated with either has resulted in enhanced or impaired performance in this probabilistic reward learning task, respectively.¹²⁻¹⁴ When treated with a substance disruptingthat disrupted dopaminergic neurotransmission, participants showedhad a reduced a response bias compared to with those treated with placebo.¹³ On the other hand, participants receiving a substance increasing dopaminergic neurotransmission increased their enhancing it had a higher response bias compared to those receiving than the placebo recipients.¹⁴

Based on these lines of evidence, we hypothesized that HF-rTMS would enhance reward responsiveness to a reward. To test this hypothesis, we used a probabilistic reward task with two alternative alternating stimuli rewarded with

註解 [Editor1]:

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註解 [Editor2]:

CHECK: "Outside of the medial temporal lobes" indicates that the region is not in the medial temporal lobes: i.e., it does not indicate the real location. This could be more specific, naming its real location ("which occur in the parietal lobe / the superior colliculus", etc.) or more clearly designating its approximate area ("just outside / medial to / superior to", etc.)

different probabilities. ~~rates.~~ We assessed ~~the~~ response shift toward ~~athe~~ more frequently rewarded stimulus as a measure of reward responsiveness.^{13,14} Healthy volunteers participated in this study ~~with~~~~in~~ a randomized, within-subject crossover design. Each participant ~~was tested twice in~~ ~~had~~ two separate ~~testing~~ sessions separated by an interval of one week: ~~once~~ after active rTMS over the left dorsolateral prefrontal cortex, ~~and once~~ and after sham stimulation over the same site.

Methods

Repetitive transcranial magnetic stimulation (rTMS)

High-frequency rTMS was administered using ~~a~~ Magstim 200 magnetic stimulator (Whitland, UK) connected to a figure-of-eight-shaped coil. The stimulation site was the left dorsolateral prefrontal cortex and defined as the region ~~6 cm~~ ~~6 cm~~ anterior ~~and~~ ~~1 cm~~ ~~lateral~~ in ~~the~~ parasagittal plane ~~and~~ ~~1 cm~~ ~~lateral~~ from the primary motor hand area (M1_{HAND}). The precise location of ~~the~~ ~~M1_{HAND}~~ ~~M1_{HAND}~~ was ~~determined~~ ~~assigned~~ as the optimal position for stimulation of the right abductor pollicis brevis (APB) muscles by focal TMS.¹⁷ The stimulation threshold was determined ~~individual by~~ ~~individual~~, by measuring the minimum stimulus intensity necessary for a motor evoked potential to occur on the right APB muscle.¹⁸ Stimulation was applied at 90% of ~~individual~~ ~~the~~ motor threshold and ~~the~~ frequency of stimulation was ~~set at~~ 10 Hz. The location ~~information~~ ~~of~~ ~~the~~ ~~M1_{HAND}~~ ~~M1_{HAND}~~ and ~~the~~ motor threshold were determined one day prior to the first rTMS session. Stimulation was performed ~~based on~~ ~~with~~ these parameters for both active and sham stimulation sessions.

During active stimulation, participants received three consecutive blocks of stimulation; each block consisted of 15 trains of ~~2 s~~ ~~2 s~~, repeated every ~~12 s~~ ~~12 s~~ (900 pulses ~~total~~). The interval between stimulation blocks was 10 minutes, during which participants were asked to rest with their eyes closed ~~in order~~ to avoid ~~distraction~~ ~~distractions~~. This particular paradigm was adopted from previous studies.^{4,7}

Sham stimulation was applied in the same manner except that the coil was placed at a 90° angle to the skull and only one edge of it rested on the scalp. All other parameters ~~of the stimulation~~ were applied in the same manner as ~~for~~ ~~in~~ active stimulation. The study was conducted ~~as~~ ~~with~~ a randomized within-subject crossover design, where each participant ~~was~~ ~~is~~ tested after ~~receiving the~~ active rTMS and sham stimulation on two ~~different~~ ~~separate~~ days, ~~which were~~ separated by a one-week interval. The order of stimulation was counterbalanced across participants.

註解 [Editor3]:

CHECK: Please double-check that this is lateral and not medial.

註解 [Editor4]:

CHECK: Consider defining the muscle function here: i.e., “...right abductor pollicis brevis (APB) muscles, which abduct the thumb, by focal TMS.”

註解 [Editor5]:

CHECK: Please check that this conveys your meaning. “90% of individual motor control” in the next sentence is less clear than denoting here that the stimulation threshold varies.