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Research report

Online feedback enhances early consolidation of motor sequence learning and reverses recall deficit from transcranial stimulation of motor cortex

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ABSTRACT

Feedback and monetary reward can enhance motor skill learning, suggesting reward system involvement. Continuous theta burst (cTBS) transcranial magnetic stimulation (TMS) of the primary motor area (M1) disrupts processing, reduces excitability and impairs motor learning. To see whether feedback and reward can overcome the learning impairment associated with M1 cTBS, we delivered real or sham stimulation to two groups of participants before they performed a motor sequence learning task with and without feedback. Participants were trained on two intermixed sequences, one occurring 85% of the time (the "probable" sequence) and the other 15% of the time (the "improbable" sequence). We measured sequence learning as the difference in reaction time (RT) and error rate between probable and improbable trials (RT and error difference scores). Participants were also tested for sequence recall with the same indices of learning 60 min after cTBS. Real stimulation impaired initial sequence learning and sequence knowledge recall as measured by error difference scores and impaired sequence knowledge recall as measured by RT difference score. Relative to non-feedback learning, the introduction of feedback

Abbreviations: AMT, active motor threshold; cTBS, continuous theta burst stimulation; DA, dopamine; EMG, electromyogram; FB, feedback; FDI, first dorsal interosseous muscle; HD, Huntington's disease; M1, primary motor area; MEP, motor evoked potential; MRI, magnetic resonance imaging; NART, National Adult Reading Test; non-FB, non-feedback; PD, Parkinson's disease; PDP, process dissociation procedure; PET, positron emission tomography; PMc, premotor cortex; pSRTT, probabilistic serial reaction time task; RT, reaction time; RMT, resting motor threshold; SOC, second order conditional; SMA, supplementary motor area; SRTT, serial reaction time task; TBI, traumatic brain injury; TMS, transcranial magnetic stimulation; VTA, ventral tegmental area.

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during sequence learning improved subsequent sequence knowledge recall indexed by RT difference score, in both real and sham stimulation groups and feedback reversed the RT difference score based sequence knowledge recall impairment from real cTBS that we observed in the non-feedback learning condition. Only the real cTBS group in the non-feedback condition showed no evidence of explicit sequence knowledge when tested at the end of the study. Feedback improves recall of implicit and explicit motor sequence knowledge and can protect sequence knowledge against the effect of M1 inhibition. Adding feedback and monetary reward/punishment to motor skill learning may help overcome retention impairments or accelerate training in clinical and other settings.

1. Introduction

Procedural learning, the process by which skills are acquired by practice, is a fundamental and critical function of the brain. It is a key component of higher skills, such as math, where the rules can be understood explicitly, but facility comes only with repeated problem solving (Fayol & Thevenot, 2012). The benefit of repeated practice is evident in rehabilitation strategies for brain damaged patients where outcome is improved by extensive practice of specific movements (Nadeau, 2002). It also allows acquisition of intuitive skills that help humans and animals function in uncertain environments.

One popular procedural learning paradigm is the serial reaction time task (SRTT, Nissen & Bullemer, 1987), where participants respond rapidly to a stream of cues by pressing buttons with the fingers of one hand. If a long, repeating sequence is embedded in the stream, speed improves before the participant is aware that a sequence is present. That is, the knowledge that a particular cue is likely to follow another is acquired as an unconscious motor skill through practice. This predictive knowledge, built from associations between events, could be acquired through reinforcement learning and promoted by the dopamine (DA) reward system (Schultz, 2002). An implication of this theory is that boosting the activity of the reward system could make procedural learning more efficient and aid skill acquisition. Acquisition of motor sequence learning on the SRTT is not always exclusively an implicit process, and depending on the learning environment, implicit and explicit/conscious sequence learning can occur in parallel (Willingham & Goedert-Eschmann, 1999; Willingham, Salidis, & Gabrieli, 2002). While this fact makes the task unsuitable for studying implicit knowledge in isolation, it is consistent with much learning in the real world.

The reward system is considered one of the networks involved in procedural motor sequence learning. For example, learning on the SRTT is impaired in patients with Parkinson (PD) and Huntington (HD) diseases (Doyon et al., 1997; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995; Knopman & Nissen, 1991; Muslimovic, Post, Speelman, & Schmand, 2007; Wilkinson & Jahanshahi, 2007; Wilkinson, Khan, & Jahanshahi, 2009), focal lesions of the basal ganglia (Obeso et al., 2009), and traumatic brain injury (TBI) (De Beaumont, Tremblay, Poirier, Lassonde, & Theoret, 2012; Mutter, Howard, & Howard, 1994; Vakil, 2005) as well as in an animal models of DA depletion (Matsumoto, Hanakawa, Maki, Graybiel, & Kimura, 1999).

There is also evidence from studies in healthy humans that incentive and feedback can improve motor skill learning. For instance, adding monetary reward to a force-tracking task which incorporated a repeating pattern improved retention as demonstrated by offline gains (Abe et al., 2011). Adding similar feedback and incentive to the SRTT improved learning (Wachter, Lungu, Liu, Willingham, & Ashe, 2009). These findings imply that monetary reward might augment rehabilitation after injury or accelerate learning in healthy people.

Human learning deficits can also be produced in the laboratory. When delivered to the primary motor cortex (M1), inhibitory transcranial magnetic stimulation (TMS), in particular continuous theta burst stimulation (cTBS), reduces local cortical excitability (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005) and temporarily impairs motor sequence learning (Rosenthal, Roche-Kelly, Husain, & Kennard, 2009; Wilkinson, Teo, Obeso, Rothwell, & Jahanshahi, 2010). The magnitude of these deficits in healthy volunteers is similar to those in patients (De Beaumont et al., 2012; Doyon et al., 1997; Jackson et al., 1995; Knopman & Nissen, 1991; Muslimovic et al., 2007; Mutter et al., 1994; Obeso et al., 2009; Vakil, 2005; Wilkinson & Jahanshahi, 2007; Wilkinson et al., 2009). However, the addition of feedback, including monetary reward, does not improve non-motor procedural learning in PD and HD (Holl, Wilkinson, Tabrizi, Painold, & Jahanshahi, 2012; Shohamy et al., 2004; Wilkinson, Lagnado, Quallo, & Jahanshahi, 2008).

Adding feedback and incentive to procedural tasks in clinical and training settings to boost learning has great appeal. Unlike interventional strategies currently under investigation, including the several forms of noninvasive brain stimulation (Reis et al., 2008; Sandrini & Cohen, 2013), there is no need for devices requiring large clinical trials and regulatory approval. There are no ethical problems posed by its use in healthy populations. However, its viability and comparative value depend on the magnitude of its effects and the ability to produce them in impaired or otherwise refractory subjects. Therefore, we decided to investigate whether adding feedback and monetary incentives to the SRTT can overcome the healthy volunteers' temporary impairment produced by inhibitory TMS and whether the size of its statistical effects is of clinical interest. We delivered sham and real cTBS to M1 just before administering a probabilistic version of the SRT, which is less likely than the conventional task to produce