



Clinical and functional connectivity outcomes of 5-Hz repeated transcranial magnetic stimulation as an add-on treatment in cocaine use disorder: a double-blind randomized controlled trial.

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Introduction

Cocaine use disorder (CUD) is a global condition lacking effective treatment. Repeated magnetic transcranial stimulation (rTMS) is a technique that has shown promise by reducing craving and frequency of cocaine use, but little is known about its efficacy and physiological brain effects.

Methods

Using a double-blind placebo-controlled randomized clinical trial (RCT) [NCT02986438], we sought to elucidate short- and long-term clinical benefits of 5-Hz rTMS as an add-on to standard treatment in CUD patients and discern underlying functional connectivity effects using magnetic resonance imaging. Forty-four randomly assigned CUD patients completed the 2-week double-blind acute phase [Sham (n=20, 2 female) and Active (n=24, 4 female)], in which they received 2 daily sessions of rTMS (5,000 pulses) on the left dorsolateral prefrontal cortex (IDLDFC). Subsequently, n=20 CUD patients continued to open-label maintenance (2 weekly sessions for up to 6 months). Measures were acquired at baseline, 2 weeks, 3 months and 6 months.

Figure 1. Design

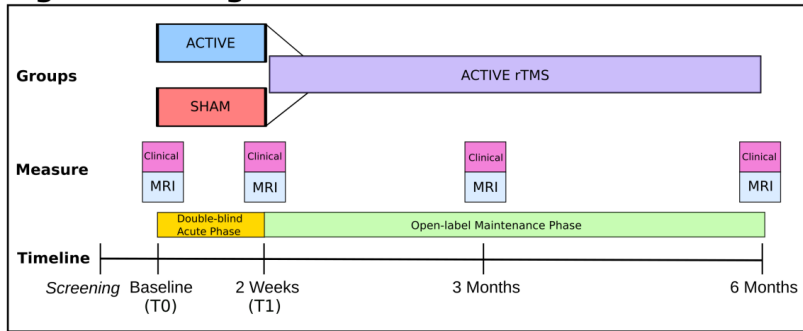
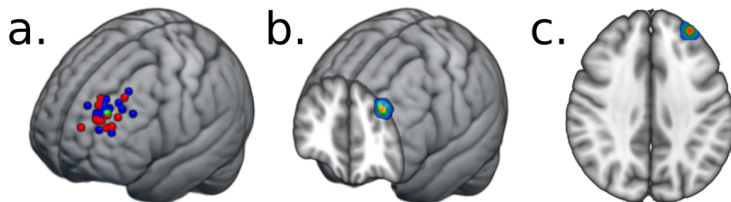


Figure 2. TMS location and average seed.



Results

Overall, 5-Hz rTMS plus standard treatment for 2 weeks significantly reduced craving (Sham group: baseline (T0), 2.6 +- 2.8; 2 weeks (T1), 2.3 +- 2.5 | Active group: T0, 3.9+-3.6; T1, 1.5+- 2.4, p = 0.013, d=0.77) and impulsivity (Sham: T0, 60.8 +- 17; T1, 59.8 +- 21.4 | Active: T0, 64.8 +- 16.8; 53.1 +- 17.4, p = 0.011, d=0.79) in the Active group; decreased impulsivity correlated with improvements in functional connectivity in IDLPFC-ventromedial PFC (vmPFC) (r=-0.35, p=0.02) and vmPFC-right angular gyrus (r=-0.34, p=0.03).

Figure 3. Acute phase clinical results

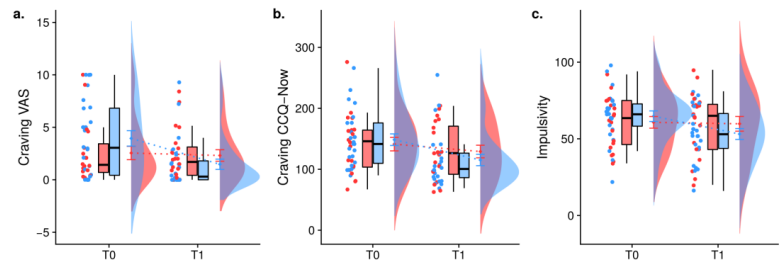
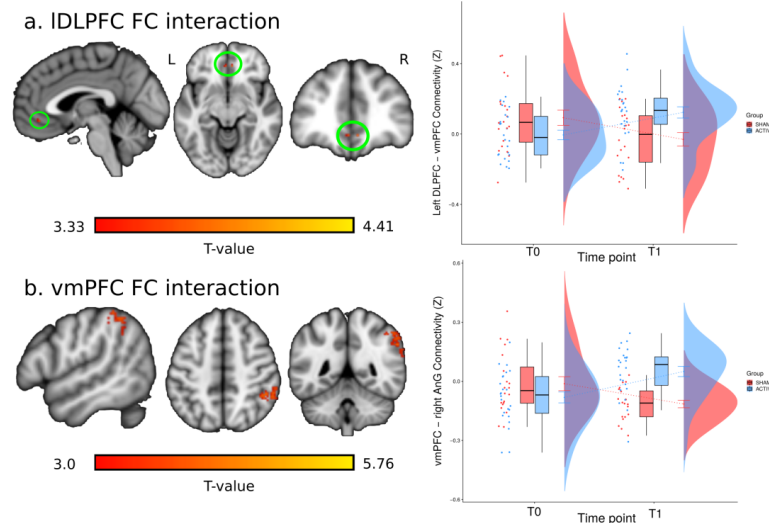


Figure 4. Connectivity results



Conclusions

Clinical and functional connectivity effects were maintained for 3 months but dissipated by 6 months of maintenance rTMS. We did not observe reduction of positive cocaine urine tests, however, self-reported frequency and grams consumed for 6 months were reduced.