Background

- Transcranial magnetic stimulation (TMS) relies on the conversion of electromagnetic induction to induce weak electric currents that can alter cortical excitability.
- Clinical trials demonstrated that single pulse TMS (sTMS) can be a promising novel treatment in migraine with aura.1

- Initial studies have shown that sTMS could inhibit cortical spreading depression (CSD)2, but had no effect on activity recorded from second order neurons within the trigeminocervical complex, activated by nociceptive trigeminovascular stimulation.3
- The thalamus, a key structure of migraine pathophysiology4, receives direct cortico-thalamic inputs that modulate its activity5, and could be potentially modulated by TMS.

Objectives

- To investigate the potential effects of sTMS on third order thalamic neurons.
- To assess its efficacy in relation to CSD-induced discharges within the sensory thalamus.6

Methods

- Third order thalamic neurons responding to electrical stimulation of the superior sagittal sinus (SSS) were identified in the ventroposteromedial (VPM) thalamic nuclei by means of electrophysiology (Fig. 2; experimental setup A).
- The effects of sTMS (135-170 µs rise time), delivered over the corresponding hemisphere, were studied on spontaneous and trigeminovascular activity of third order thalamic neurons.
- In a separate set of experiments, the efficacy of sTMS was tested on third order thalamic neurons with significantly amplified activity due to induction of an ipsilateral CSD.6 Spontaneous neuronal firing was significantly reduced in 8/10 third order neurons tested ($P<0.05$; Fig. 3).

Results

sTMS Significantly Modulates Neuronal Activity within the Sensory Thalamus (VPM)

![Fig. 4: sTMS (0.8-1.3 Tesla) decreased spontaneous neuronal firing in 8/10 third order neurons tested ($P<0.05$). In these neuronal population sTMS significantly inhibited C-fiber activity in response to dural vessel stimulation ($n=8$; $P=0.02$)](Image 1340x1105 to 2322x1566)

sTMS significantly modulates neuronal activity within the sensory thalamus, induced following CSD

![Fig. 5: A single TMS pulse was tested on a cohort of third order thalamic neurons whose activity was significantly amplified following induction of an ipsilateral CSD. Spontaneous neuronal activity ($P<0.05$) and evoked firing in response to activation of Aβ-fibers ($P<0.05$) were significantly reduced in 8/13 neurons.](Image 1929x2983 to 2458x3352)

Conclusions

- sTMS significantly modulates trigeminovascular activity recorded from third order thalamic neurons and CSD-induced neuronal firing.
- The use of sTMS for the treatment of migraine involves interactions with third order ipsilateral thalamic neurons, possibly through a cortico-thalamic relay.
- The data provide important scientifically based evidence for the use of sTMS in the treatment of migraine with and without aura.

References

1. Lipton RB, Dodick DW, Silberstein SD, Saper JR, Aurora SK, Pearlman SH, Headache Group – Department of Neurology, University of California, San Francisco, San Francisco CA
2. Neuralieve, Inc., dba eNeura Therapeutics, Sunnyvale, CA, USA

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