Transcranial magnetic stimulation attenuates neuronal firing of trigeminothalamic neurons

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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 pathophysiology[4], receives direct cortico-thalamic inputs that modulate its activity[5], 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].

Fig. 1: Single pulse transcranial magnetic stimulation (sTMS) , using a portable TMS device, can be a promising novel treatment in migraine with aura[1].

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] (Fig. 2; experimental setup B).

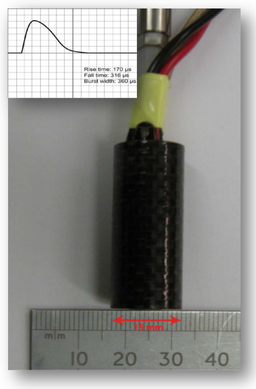


Fig. 2: A bespoke transcranial magnetic stimulator and coil was developed for *in vivo* use in anesthetized male rats.

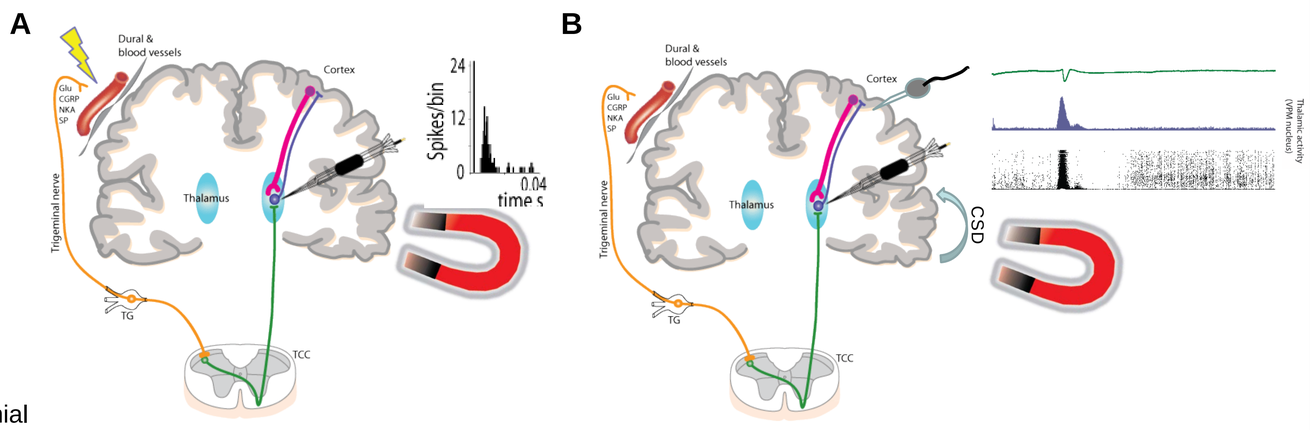


Fig. 3: Experimental set-up.

Results

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

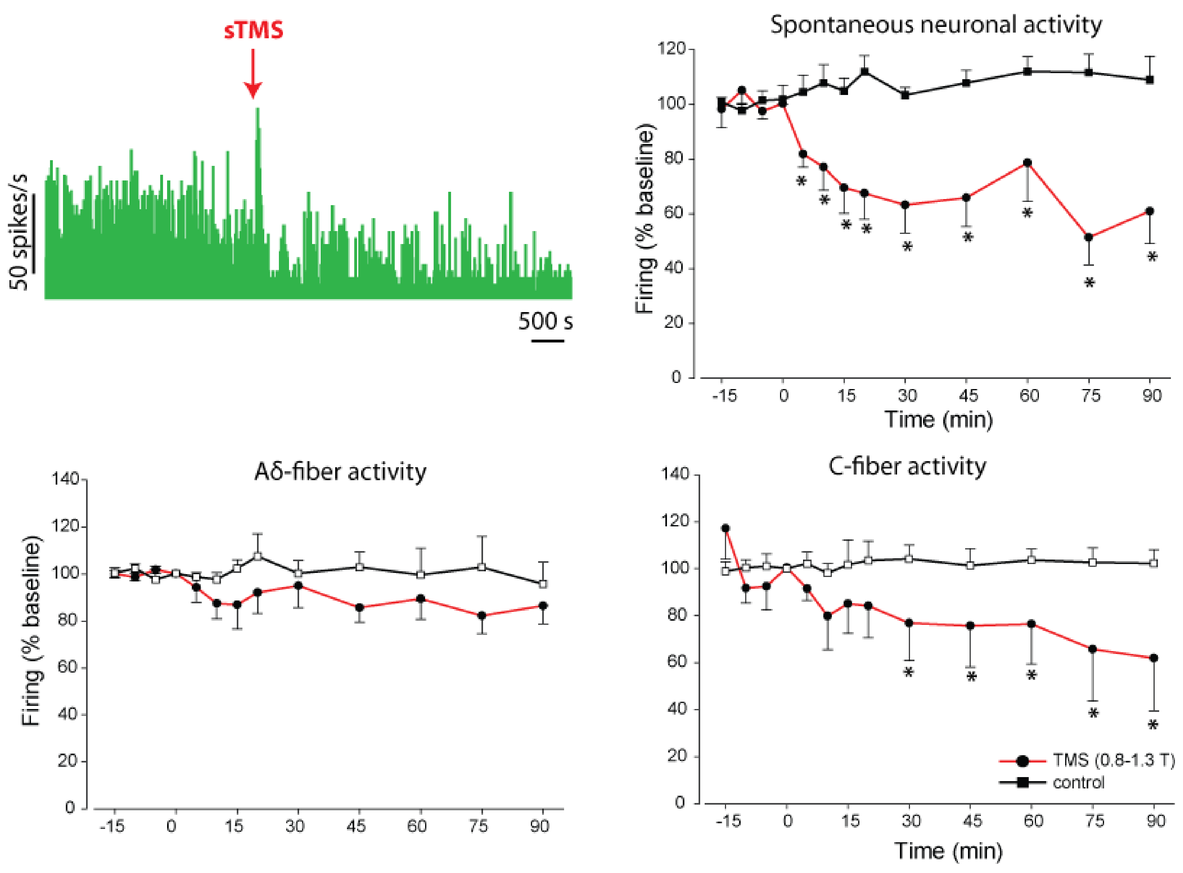
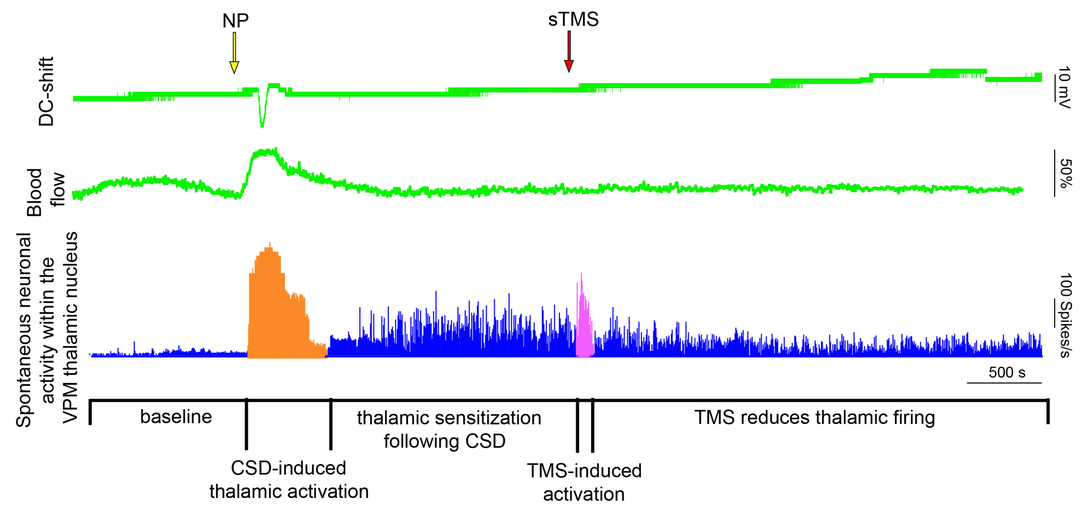


Fig. 4: sTMS (0.8-1.3 Tesla) decreased spontaneous neuronal firing in 8/10 third order neurons tested ($P < 0.05$). In these neuronal population sTMS significantly inhibited C-fiber activity in response to dural vessel stimulation ($n = 5$; $P < 0.05$), but had no effect on Aδ-fiber activity ($n = 8$; $P = 0.29$).

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



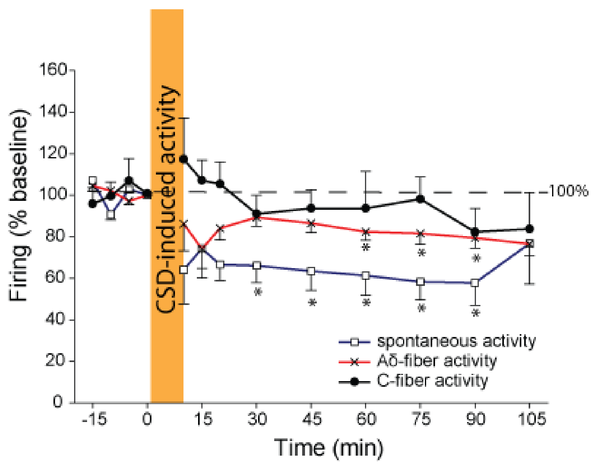


Fig. 5: A single TMS pulse was tested on a cohort of third order thalamic neurons whose activity was significantly amplified following induction of an ipsilateral CSD[6]. Spontaneous neuronal activity ($P = 0.05$) and evoked firing in response to activation of Aδ-fibers ($P < 0.05$) were significantly reduced in 8/13 neurons.

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 ispilateral 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.

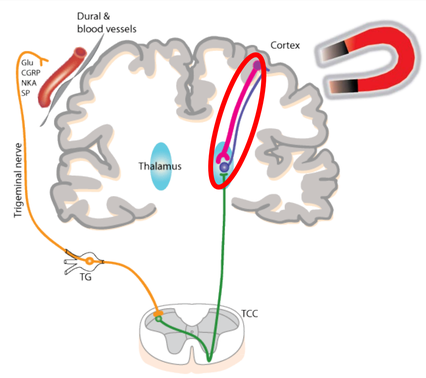


Fig. 6: An important input to the thalamus is the cortical feedback[5]. As sTMS causes neurons in the neocortex under the site of stimulation to depolarize, it is likely to also interact with the cortico-thalamic modulatory system.

References

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Acknowledgments

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