Non-invasive Spine Stimulation using Temporal Interference (TI) with Applications in Neuromuscular Disorders

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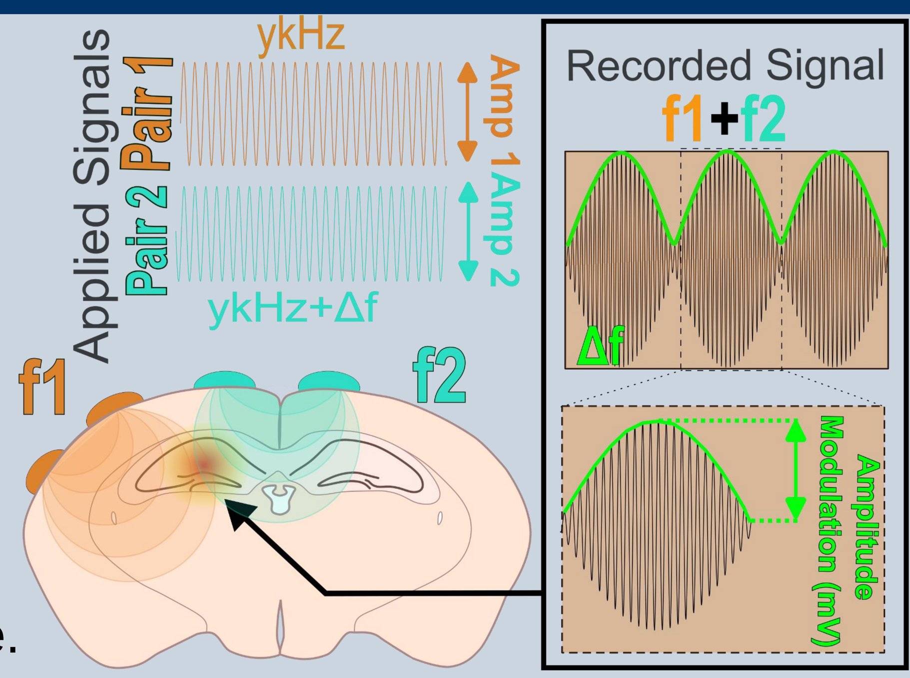
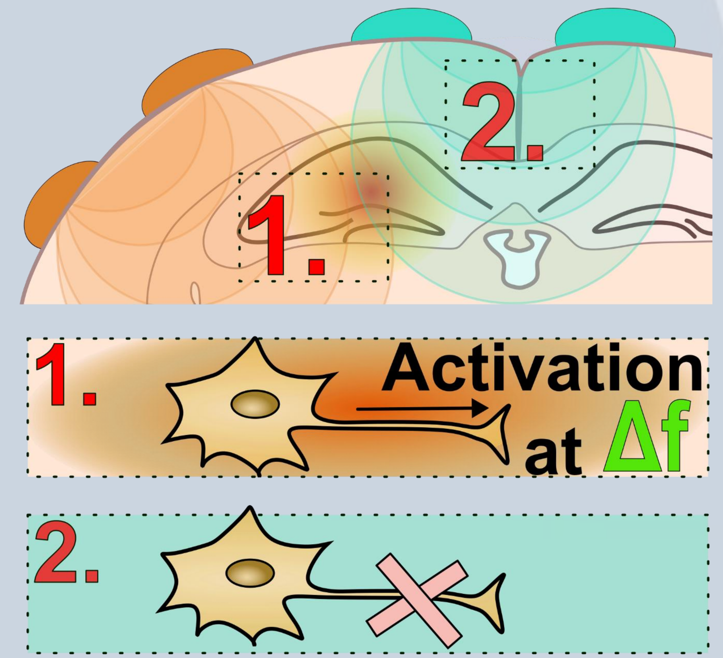
Rationale

- **Temporal Interference (TI)** allows a focal **noninvasive deep brain stimulation** with tunable parameters[1].
- The addition of the two high frequency signals (f1 & f2 >1kHz) creates an amplitude modulation which will become the stimulating signal **(at Δf).**
- TI has been applied in the context of epilepsy, to both reduce epileptic biomarkers[2] and evoke seizures[3] by targeting the hippocampus in mice.



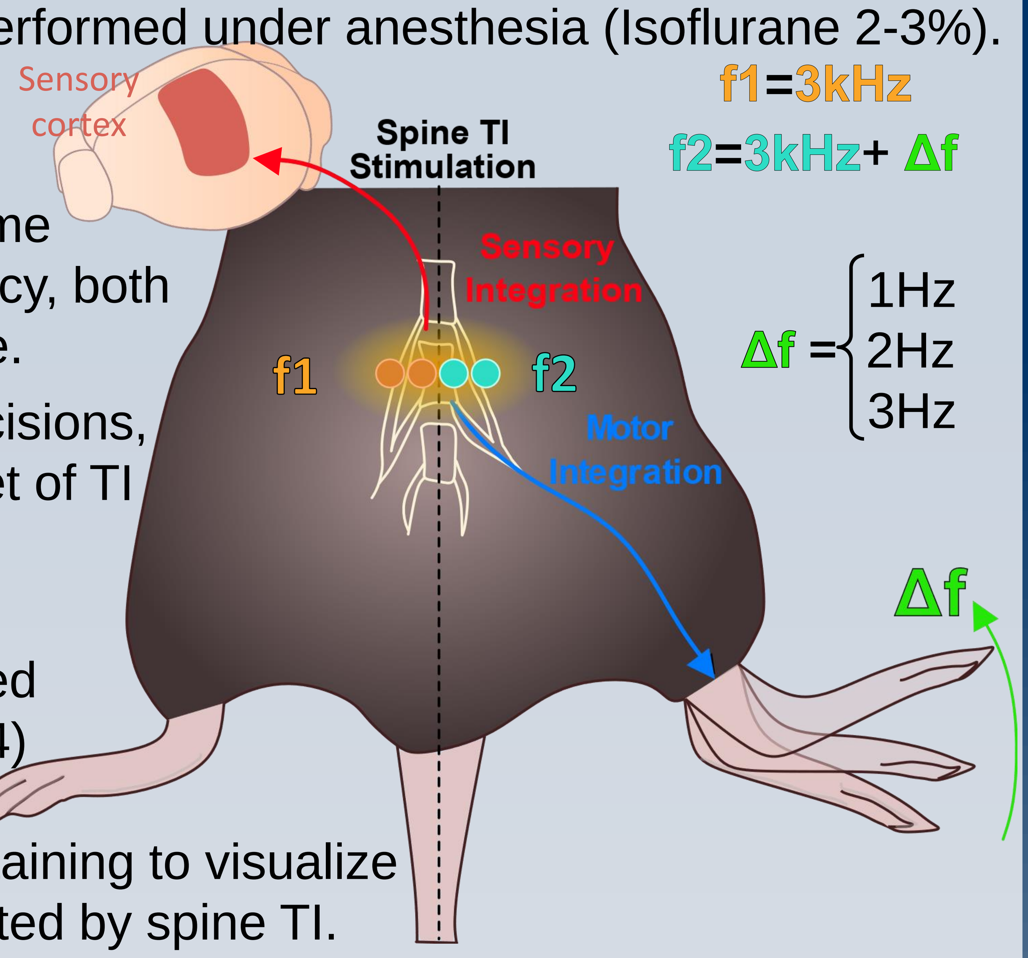
- Activation of cortical neurons at the Δf frequency as been shown using by 2 photon imaging[4] and wild field imaging[5] in mice.
- TI has been extensively investigated in the Central Nervous System (CNS) due to the challenges and unknown mechanisms underlying its functioning[5], but it has been less studied in the Peripheral Nervous System (PNS).



- However, TI in the PNS has been shown to be highly effective in evoking movement at the Δf frequency[6], likely due to the stimulation of multiple bound axons, resulting in a straightforward output.
- **Here we investigate the impact of TI stimulation on the spinal cord—a highly organized component of the CNS—in wild-type mice, examining both motor and sensory pathways.**

Methods

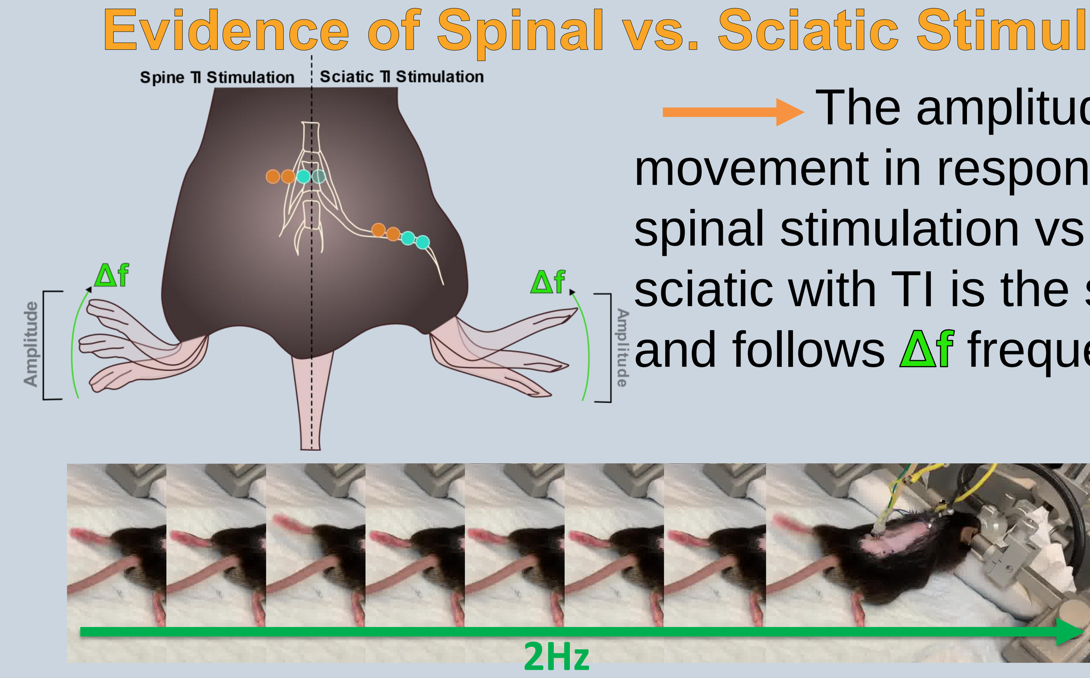
- 8 adult wild type mice (C57bl/6) underwent spine TI stimulation.
- TI stimulation was performed using current sources (DS5s, Digitimer, UK) driven by a function generator (Keysight, USA).
- Parameters were 3kHz and 3kHz+Δf. The Δf frequency ranged from 1 to 4 Hz, enabling the movement to synchronize with the changing frequency.
- All stimulation were performed under anesthesia (Isoflurane 2-3%).
- To investigate motor integration, we stimulated with the same amplitude and frequency, both spine and sciatic nerve.
- We then performed incisions, to investigate the target of TI stimulation. (n=3)
- To investigate sensory integration, we collected the brains of mice (n=4) stimulated for 20 min, and performed c-fos staining to visualize the brain region impacted by spine TI.



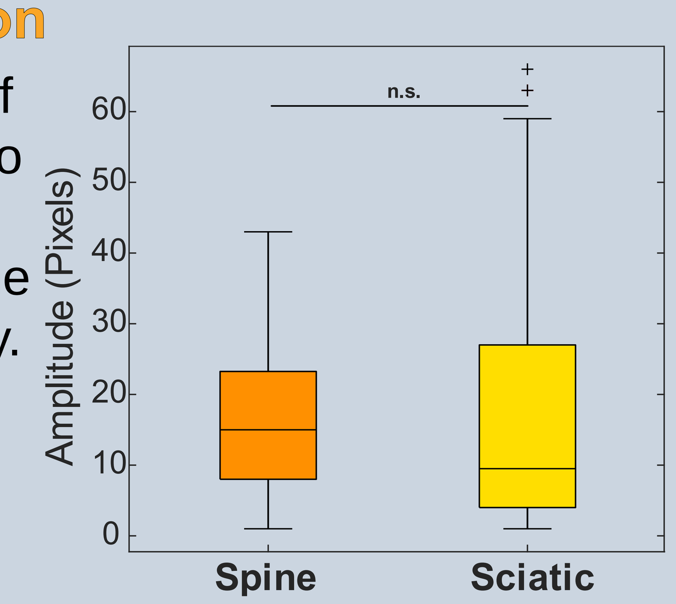
Results

Effect on the motor tracts

Evidence of Spinal vs. Sciatic Stimulation



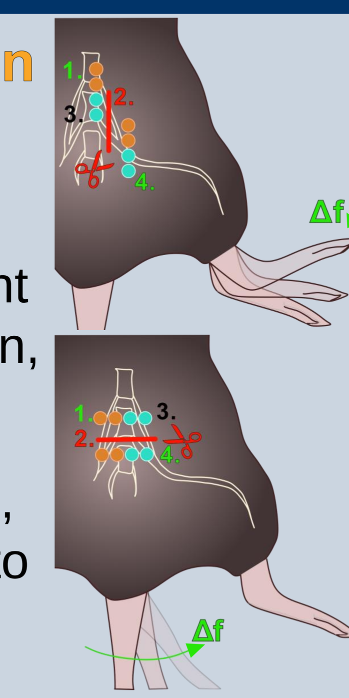
→ The amplitude of movement in response to spinal stimulation vs sciatic with TI is the same and follows Δf frequency.



Evidence of Effective Spinal Stimulation

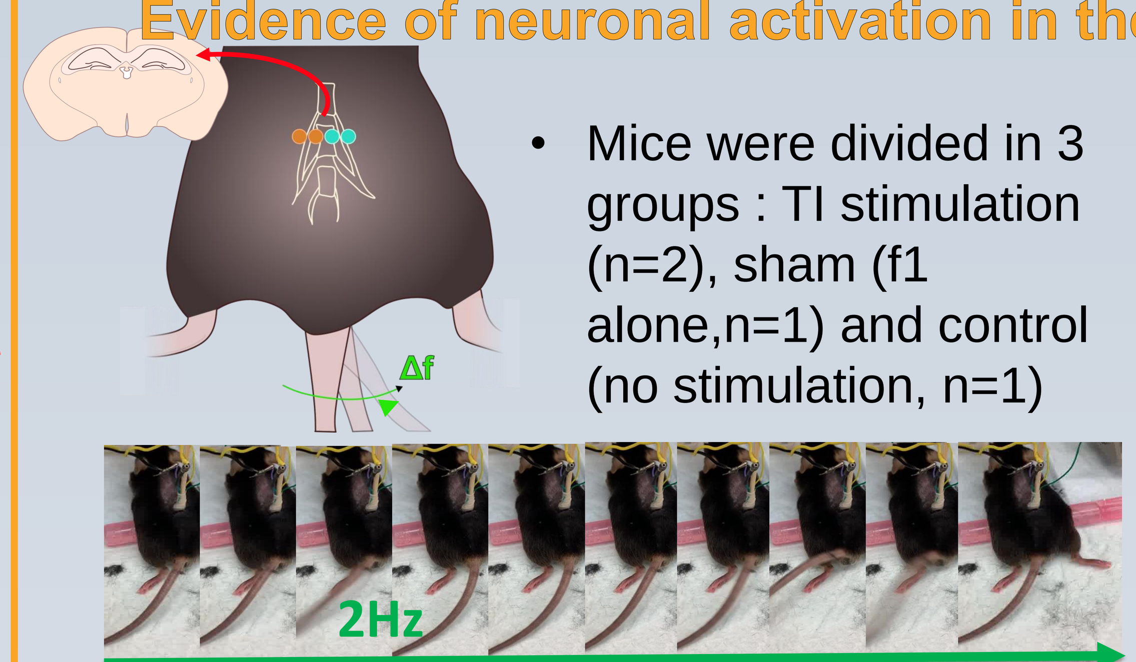
1. TI spine stimulation evoked movement
2. Partial or complete root/ spine sectioning
3. TI stimulation no longer produced movement
4. After repositioning the electrodes post-lesion, movement was restored

→ Results emphasize TI spinal stimulation, showing that evoked movements were due to spinal targeting rather than root stimulation

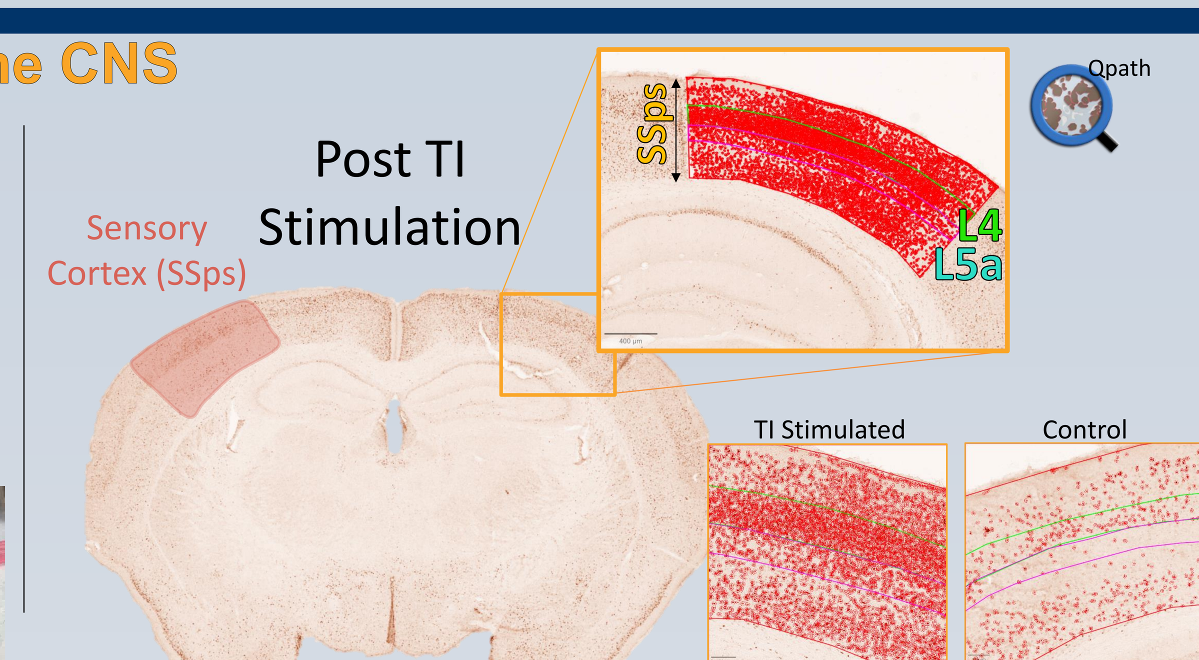


Effect on the sensory tracts

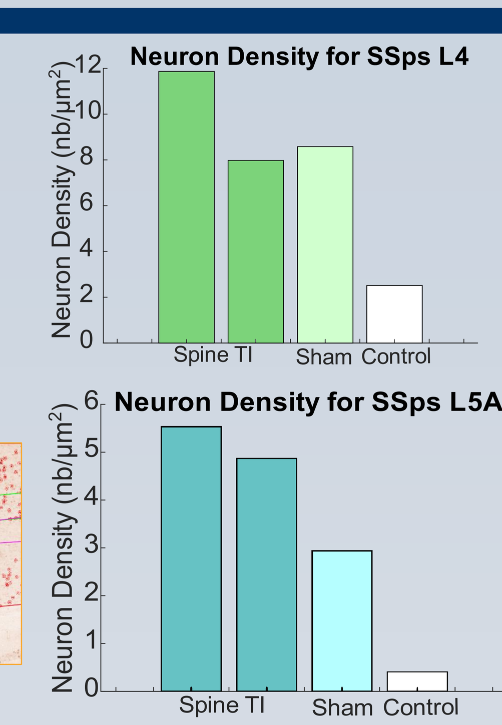
Evidence of neuronal activation in the CNS



- Mice were divided in 3 groups : TI stimulation (n=2), sham (f1 alone,n=1) and control (no stimulation, n=1)



C-fos ICC → Neuronal Activation



→ Results emphasize that TI & Sham stimulation can activate neurons in the sensory cortex

Conclusion & Discussion

- Preliminary results indicate that spinal TI can activate the spinal cord, leading to leg and tail movement.
- Spinal TI can also activate the sensory pathways, resulting in cortex activation.
- We collected spinal cord samples and will investigate c-fos activation in these mice.
- We need to further explore whether the activation is specifically due to spinal cord stimulation rather than root stimulation, which is a limitation of our study.
- We should experiment with different electrode arrangements to target the ventral area of the spinal cord more effectively.
- This research could be innovative for axon regeneration in the context of traumatic injuries and neuromuscular disorders.

Fundings & Additional Data

- This work was supported by the National Institutes of Health (NIH) (C-A.G. 1R01NS138733-01) and by the American Epilepsy Society (E.A.)
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