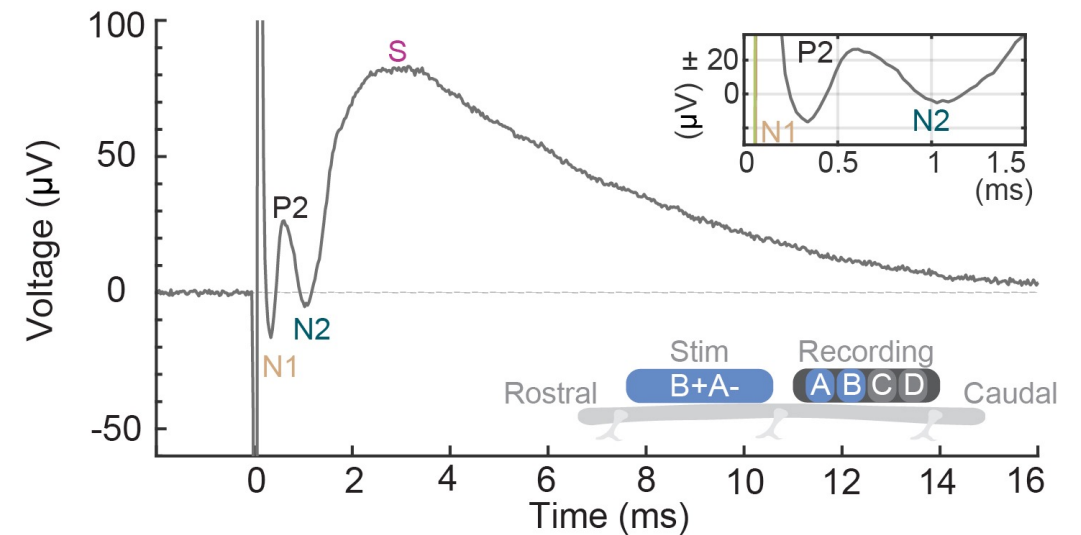


Evoked Synaptic Excitatory Potentials (ESAPs): Origins and implications for Spinal Cord Stimulation

Marom Bikson

The City College of New York, USA

Mahima Sharma, Vividha Bhaskar, Lillian Yang, Nigel Gebodh, Mohamad FallahRad, Tianhe Zhang, Rosana Esteller, John Martin



Disclosure

The City University of New York: Patents on brain stimulation.

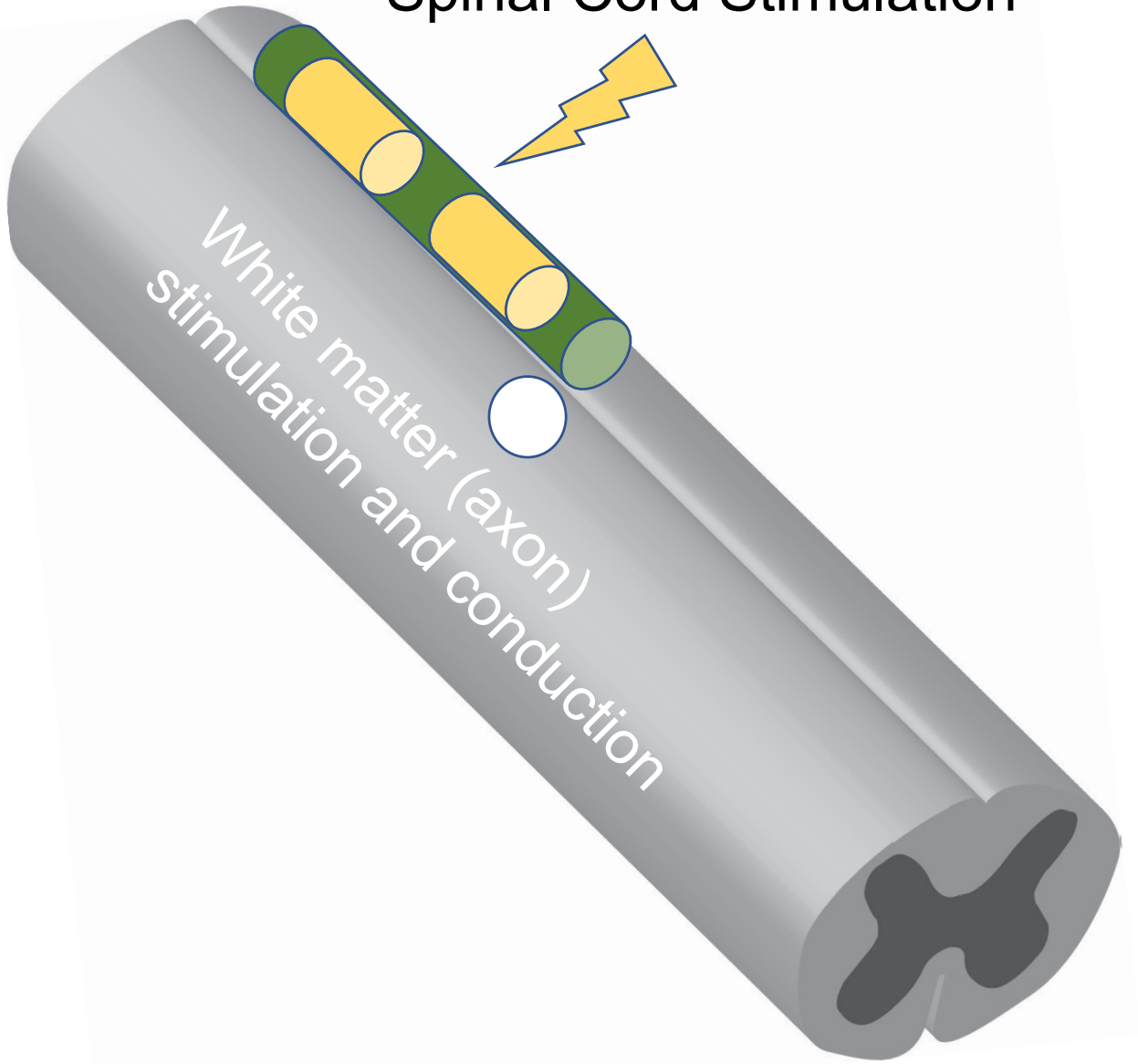
Soterix Medical: Produces tDCS and High-Definition tDCS.

Grants, assigned inventions, and/or serves SAB for SafeToddlers, Boston Scientific, GlaxoSmithKline, Biovisics, Mecta, Lumenis, Halo Neuroscience, Google-X, i-Lumen, Humm, Allergan (Abbvie), Apple

Support

NYS DOH, NIH (NIMH, NINDS) – *BRAIN Initiative*, NSF, Grove Foundation, Harold Shames, CCNY Fund, 21st Century Fund

Spinal Cord Stimulation

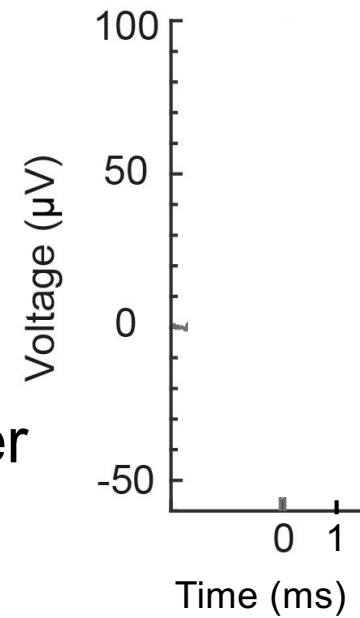
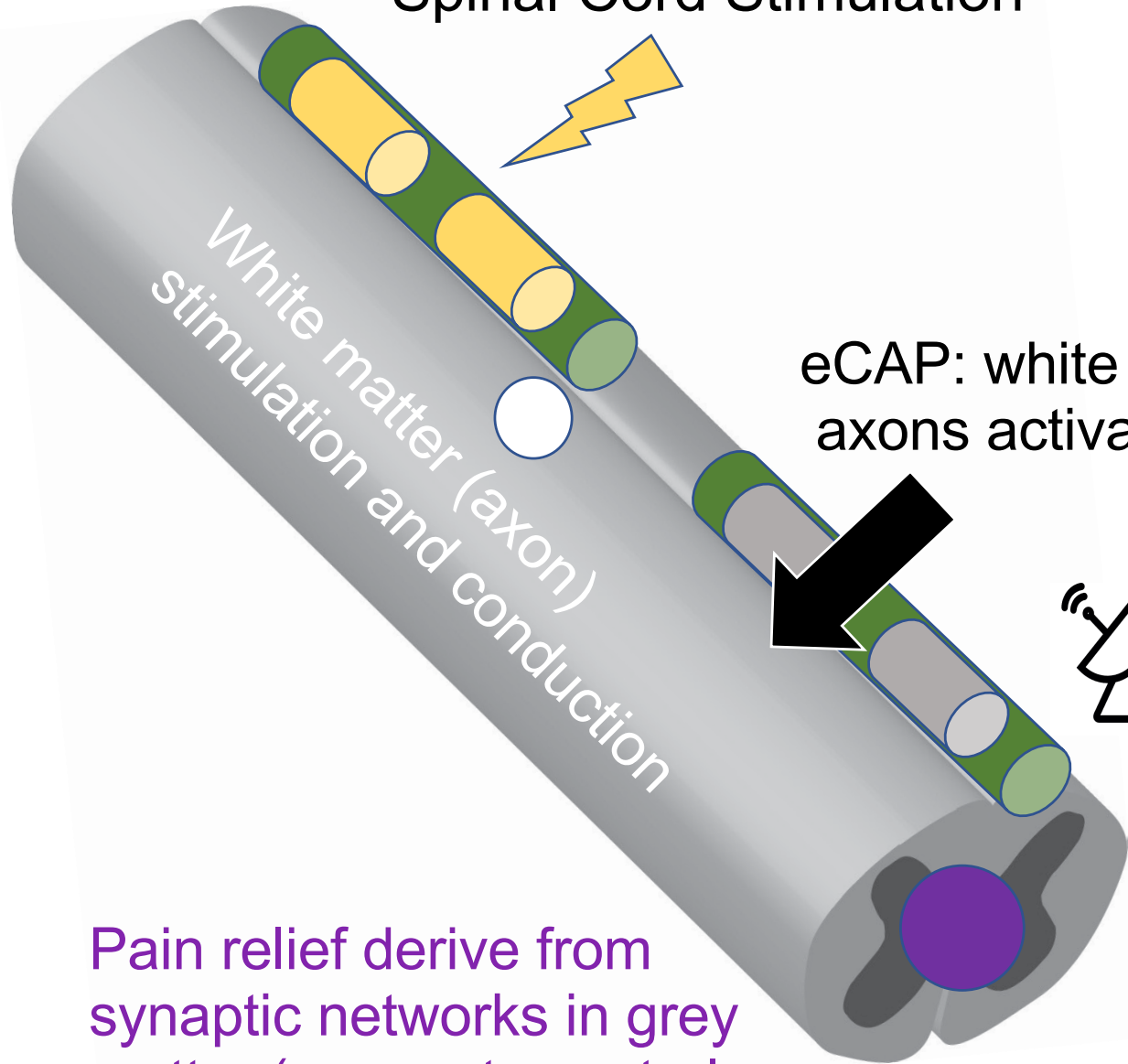


Spinal Cord Stimulation



Pain relief derive from synaptic networks in grey matter (e.g., gate control theory of pain control)

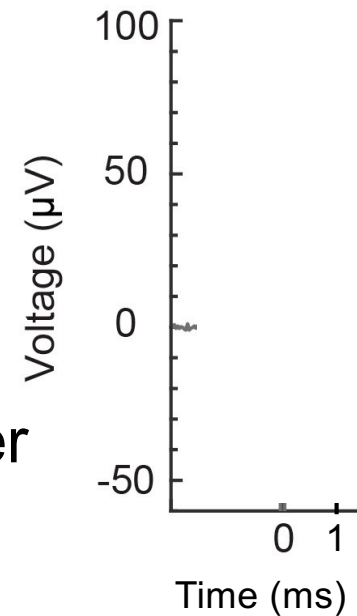
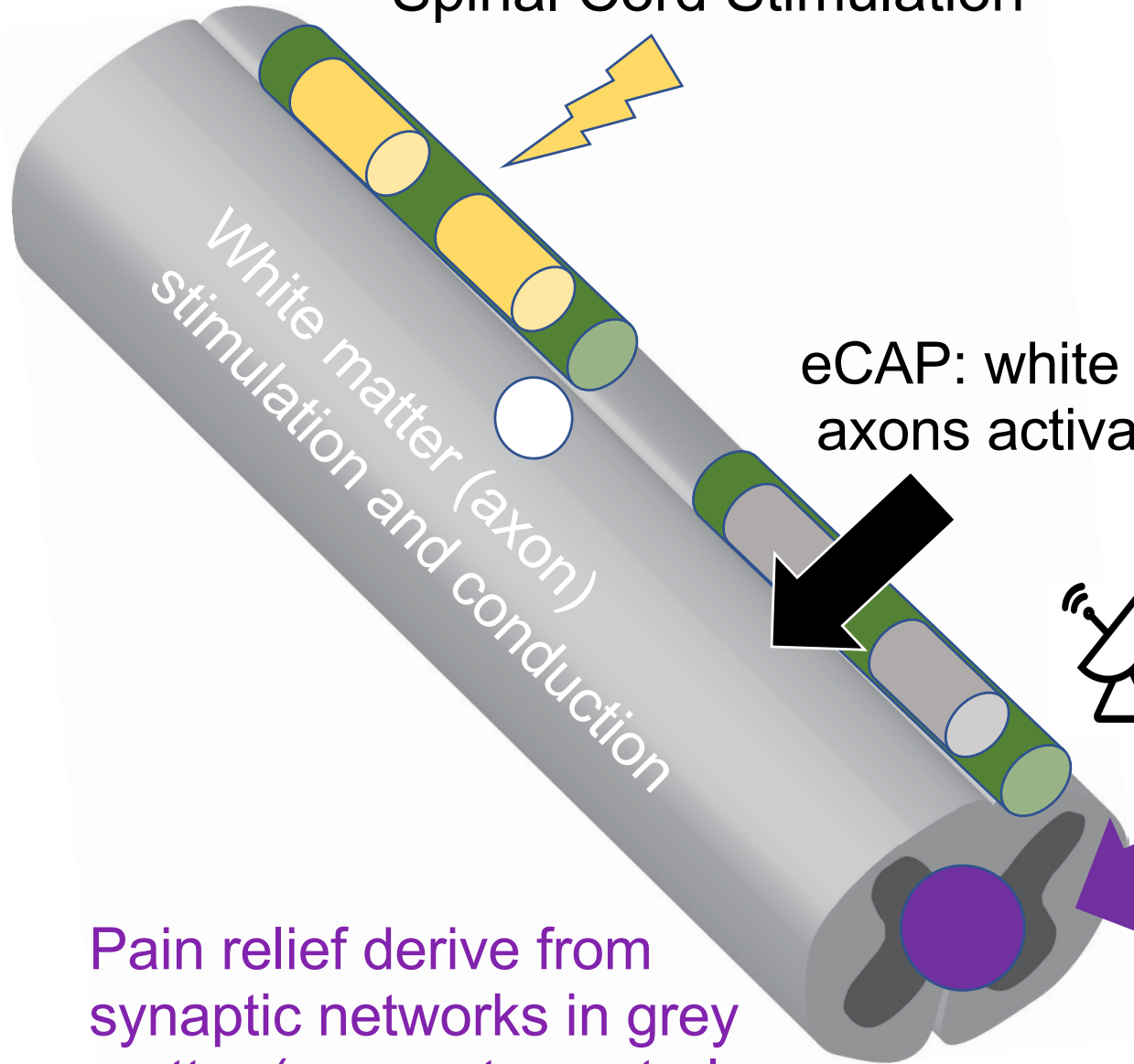
Spinal Cord Stimulation



Epidural recorded evoked electrical response

Pain relief derive from synaptic networks in grey matter (e.g., gate control theory of pain control)

Spinal Cord Stimulation



Epidural recorded evoked electrical response

Can we record epidural evoked potentials that reflect gray matter activity?

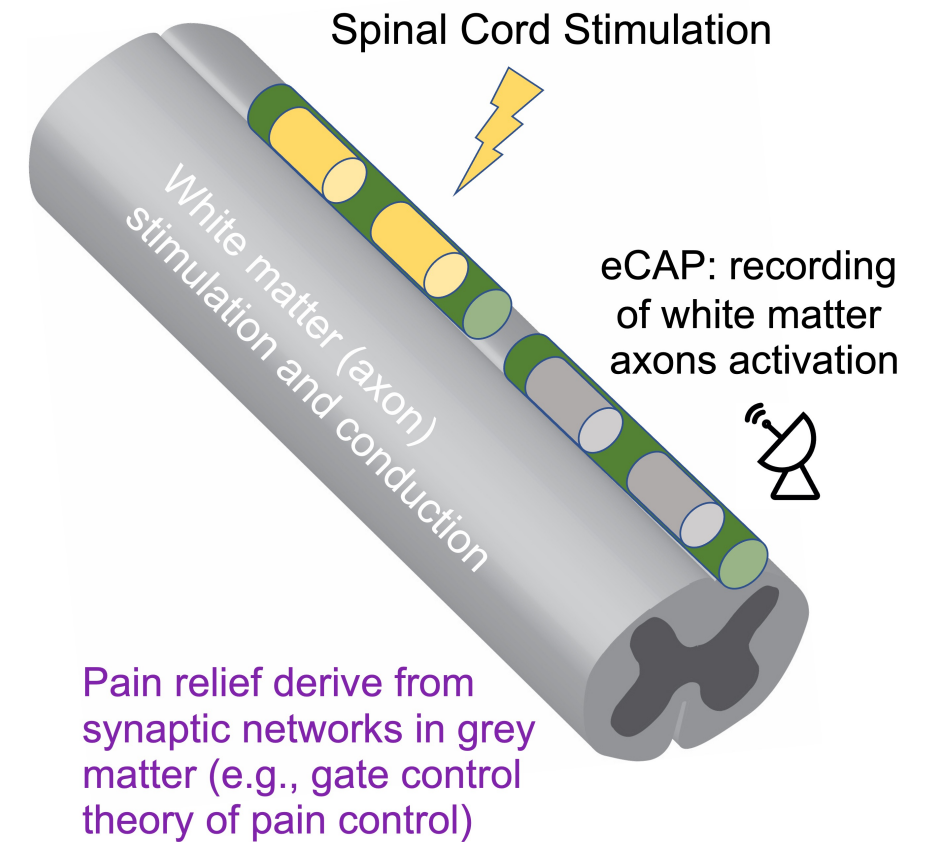
Pain relief derive from synaptic networks in grey matter (e.g., gate control theory of pain control)

Yes. Provided some modifications (e.g., record for longer).

Spinal Cord Stimulation (SCS) for the treatment of neuropathic pain is conventionally hypothesized to:

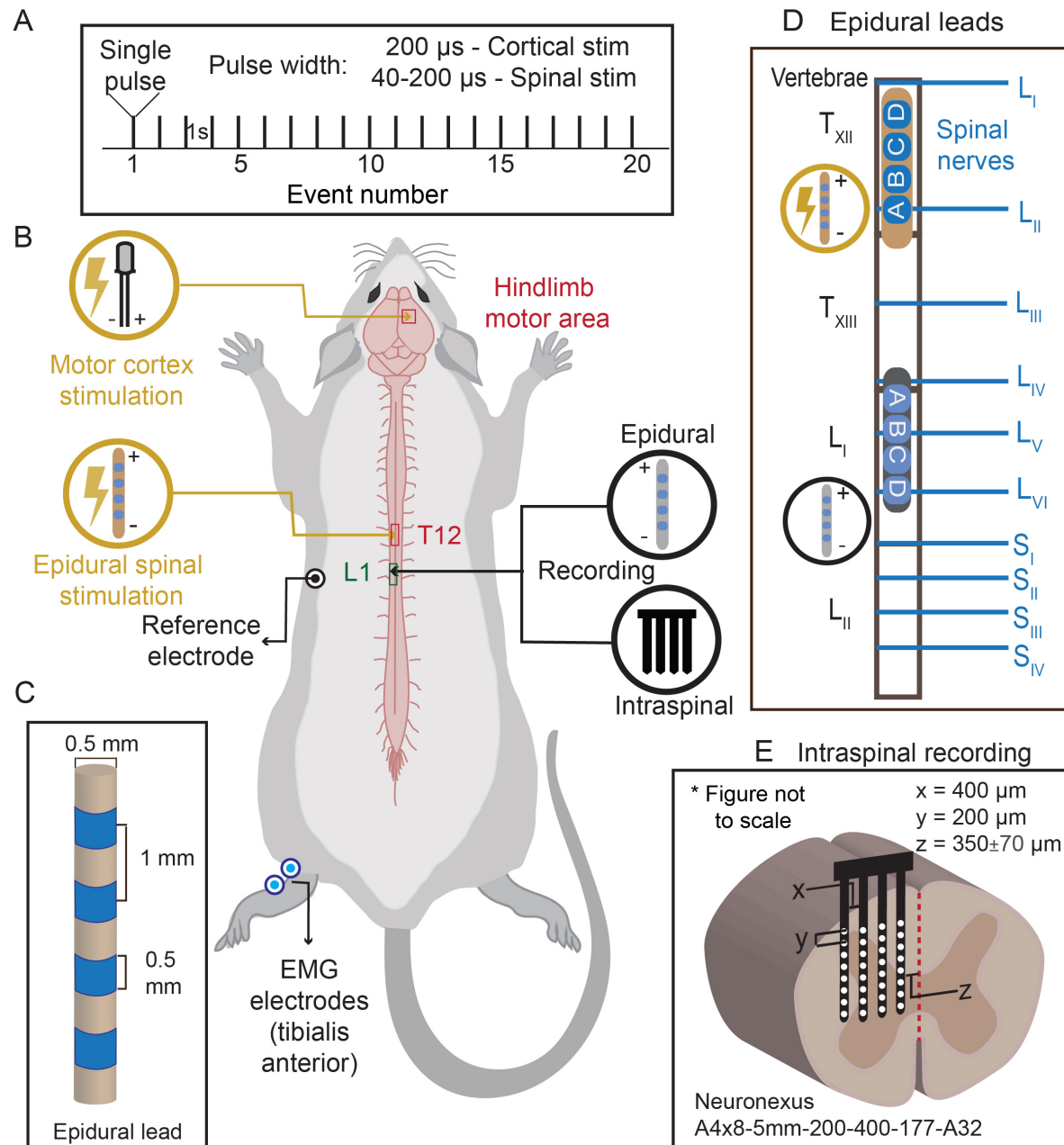
- 1) Stimulate **dorsal column fibers** (white matter)
- 2) Leading to by modification of **dorsal horn intra-spinal circuits** (grey matter)

This follows synaptic Gate-Control theory (Melzack & Wall, 1965)

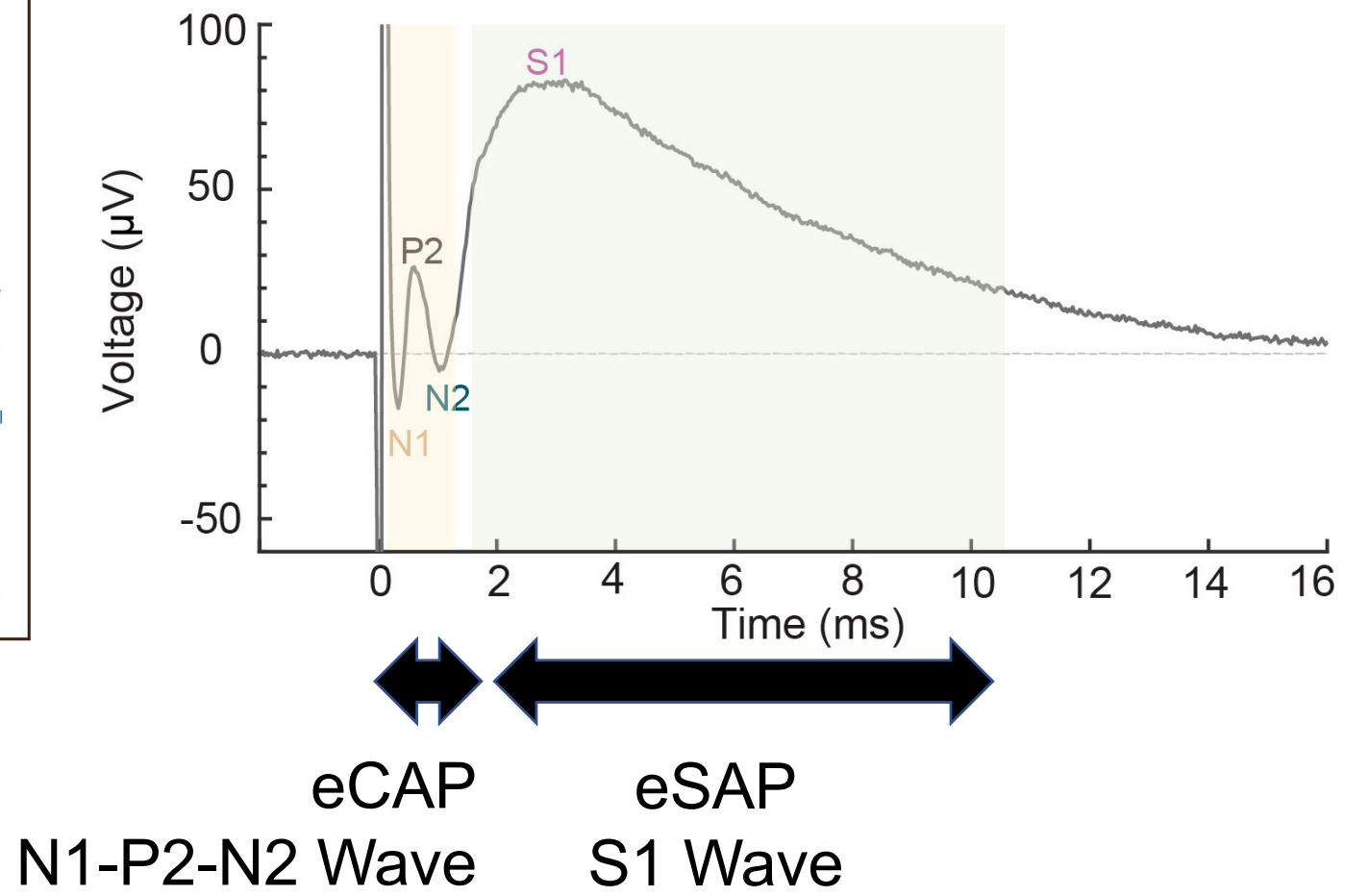
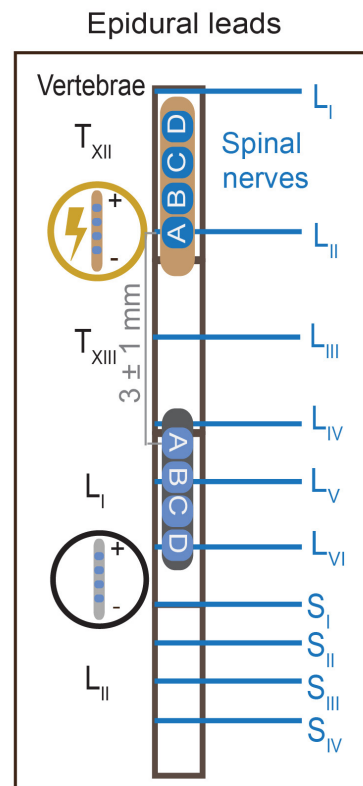
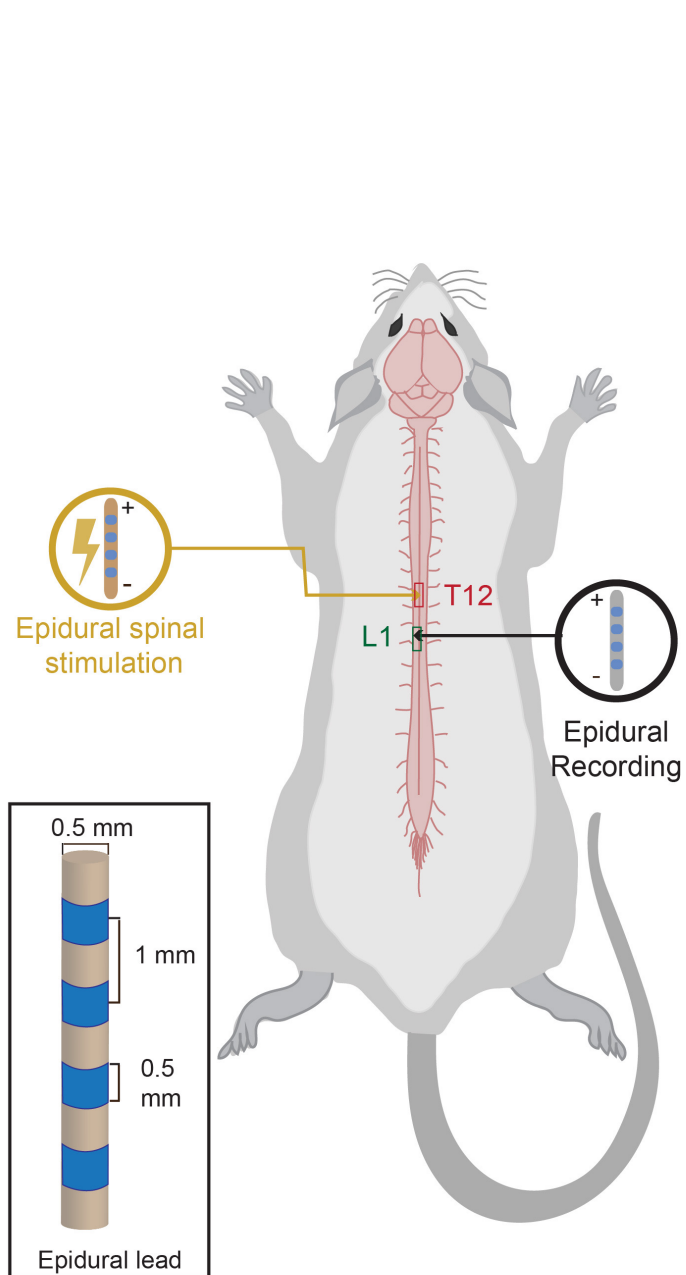


- 1) The **evoked Compound Action Potential (eCAP)** measures dorsal column axon stimulation. This does not directly measure spinal circuit activity (pain control).
- 2) We describe a novel epidural signal, evoked by SCS, that measures synaptically evoked dorsal horn activity: the **evoked Synaptic Activity Potential (ESAP)**. This may measure modulation of pain-regulating spinal circuit (eg. Gate Control).

Rodent model for characterizing the evoked SCS responses



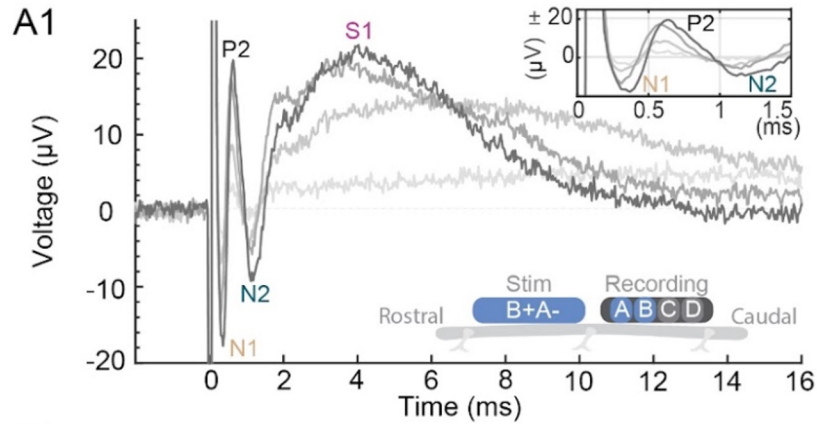
eSAPs are delayed and slower than eCAPs



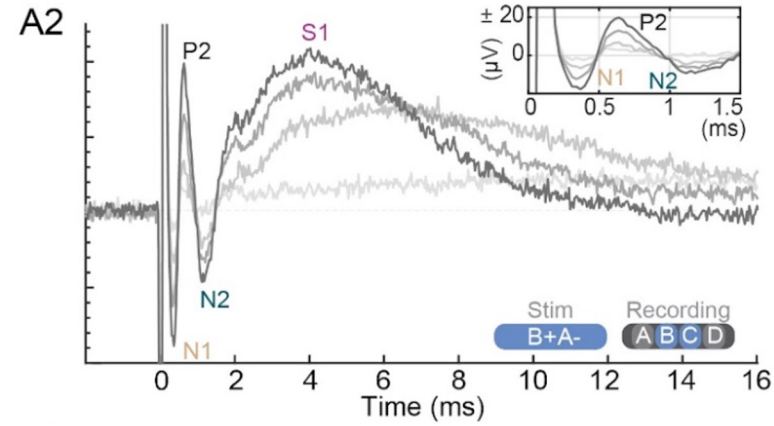
eSAPs waveforms segmentally specific (stimulation and recording electrode locations) unlike eCAPs

Proximal
anodal
stimulation

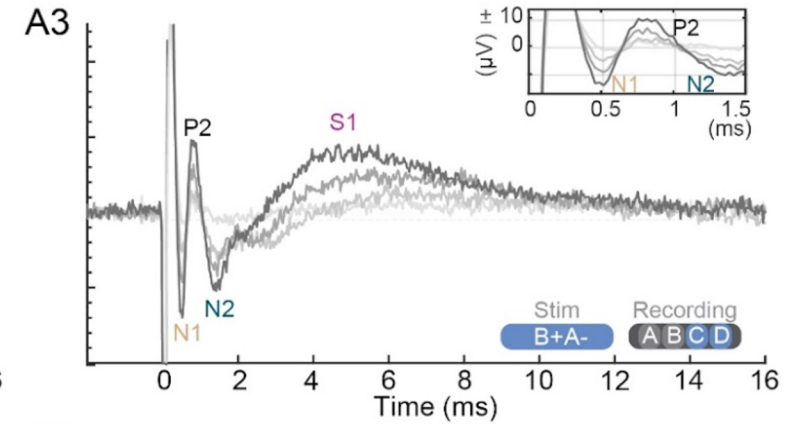
Recording
location AB



Recording
location BC



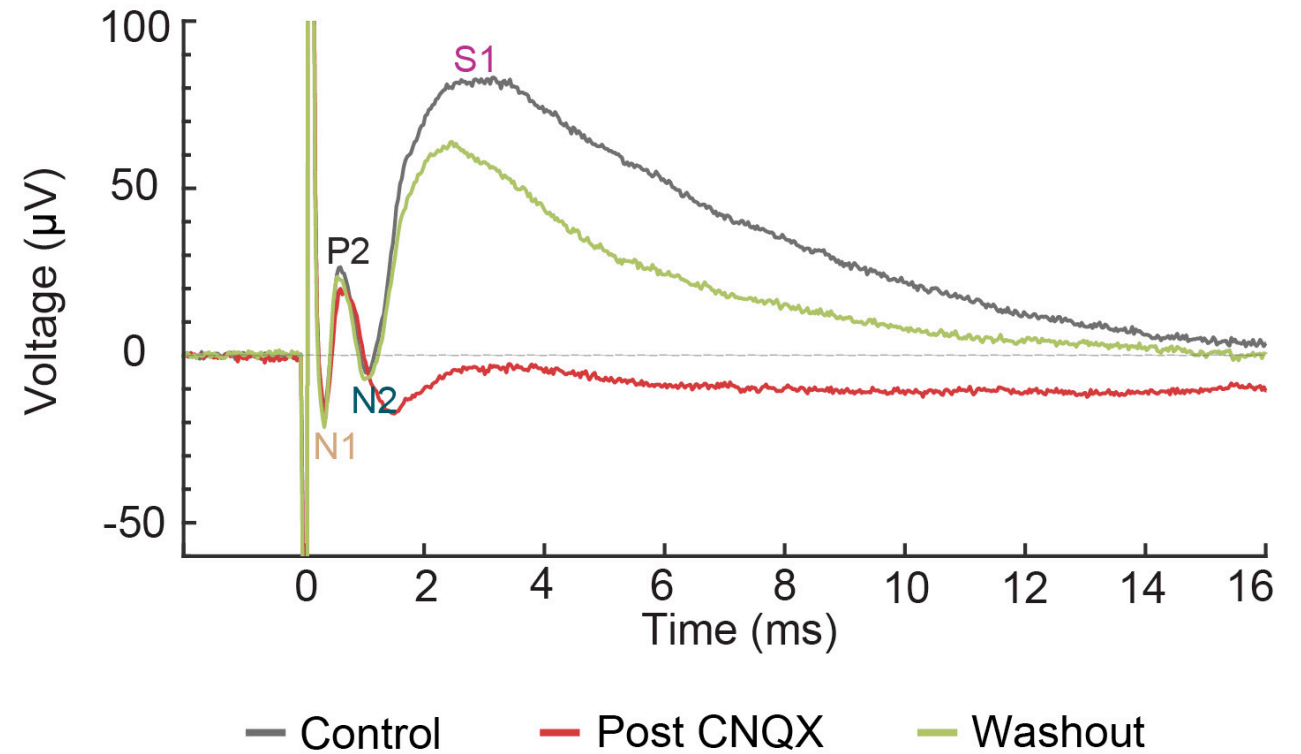
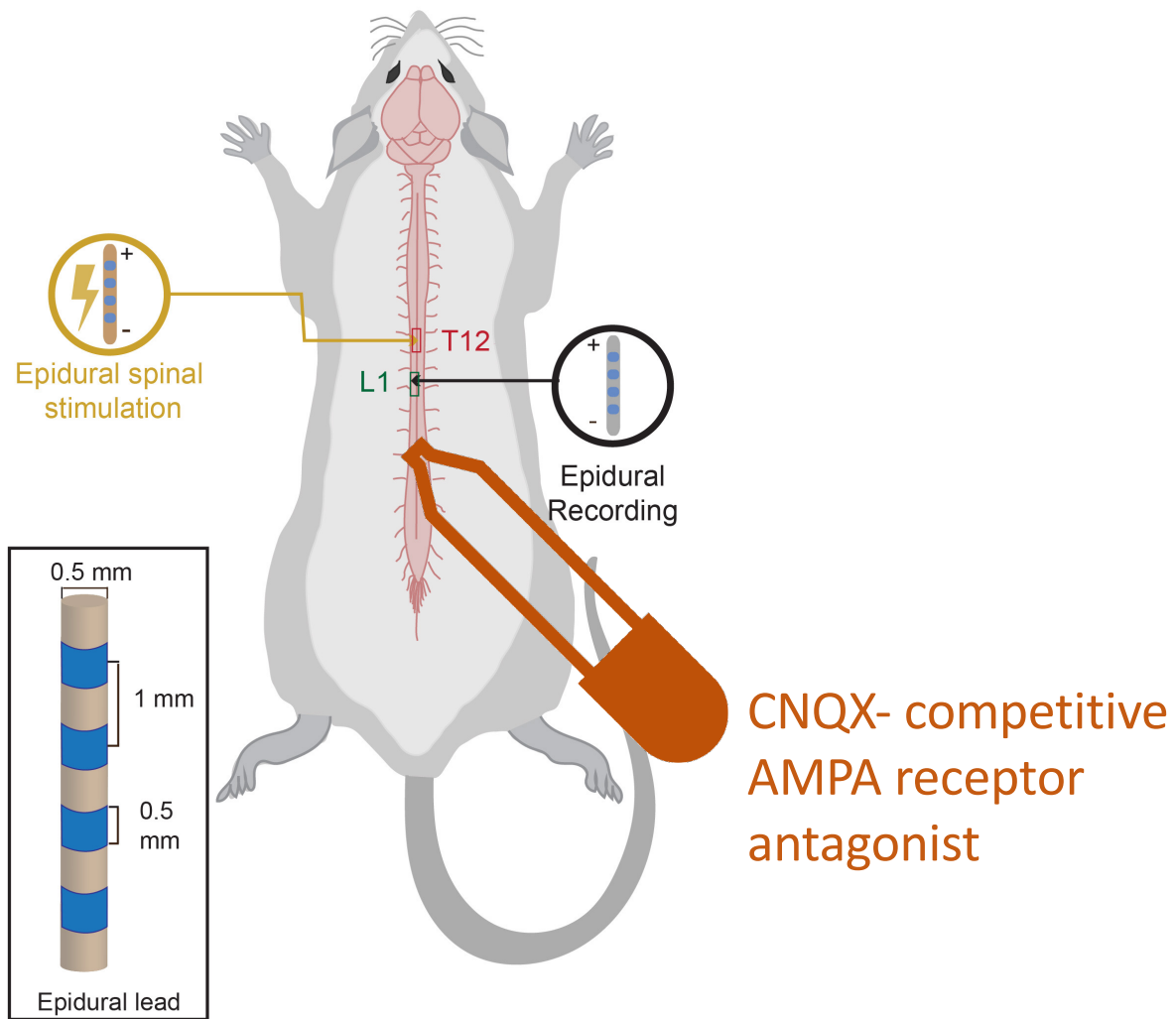
Recording
Location CD



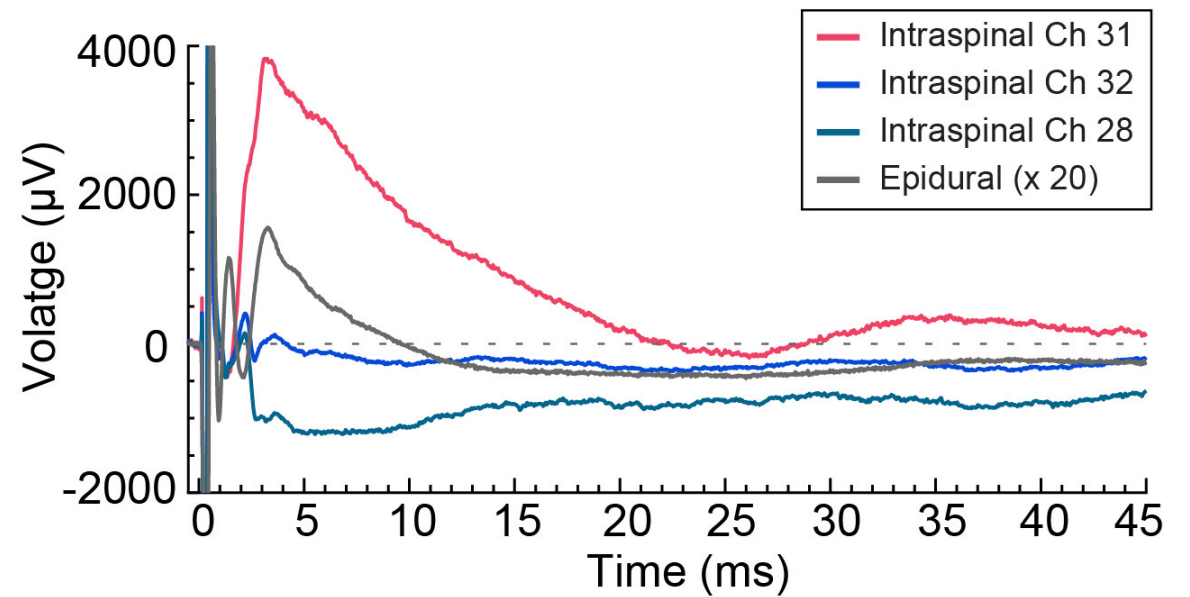
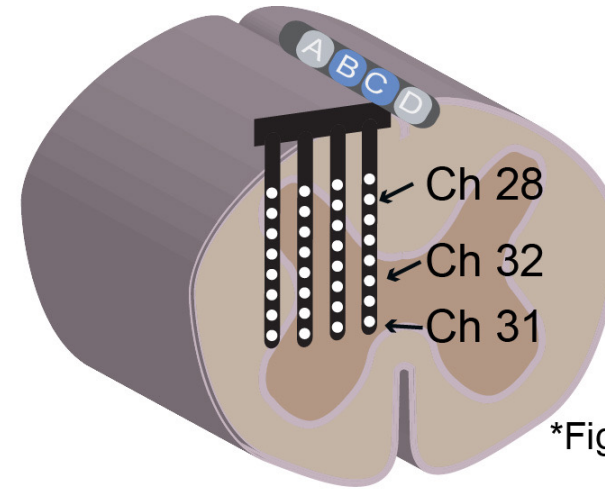
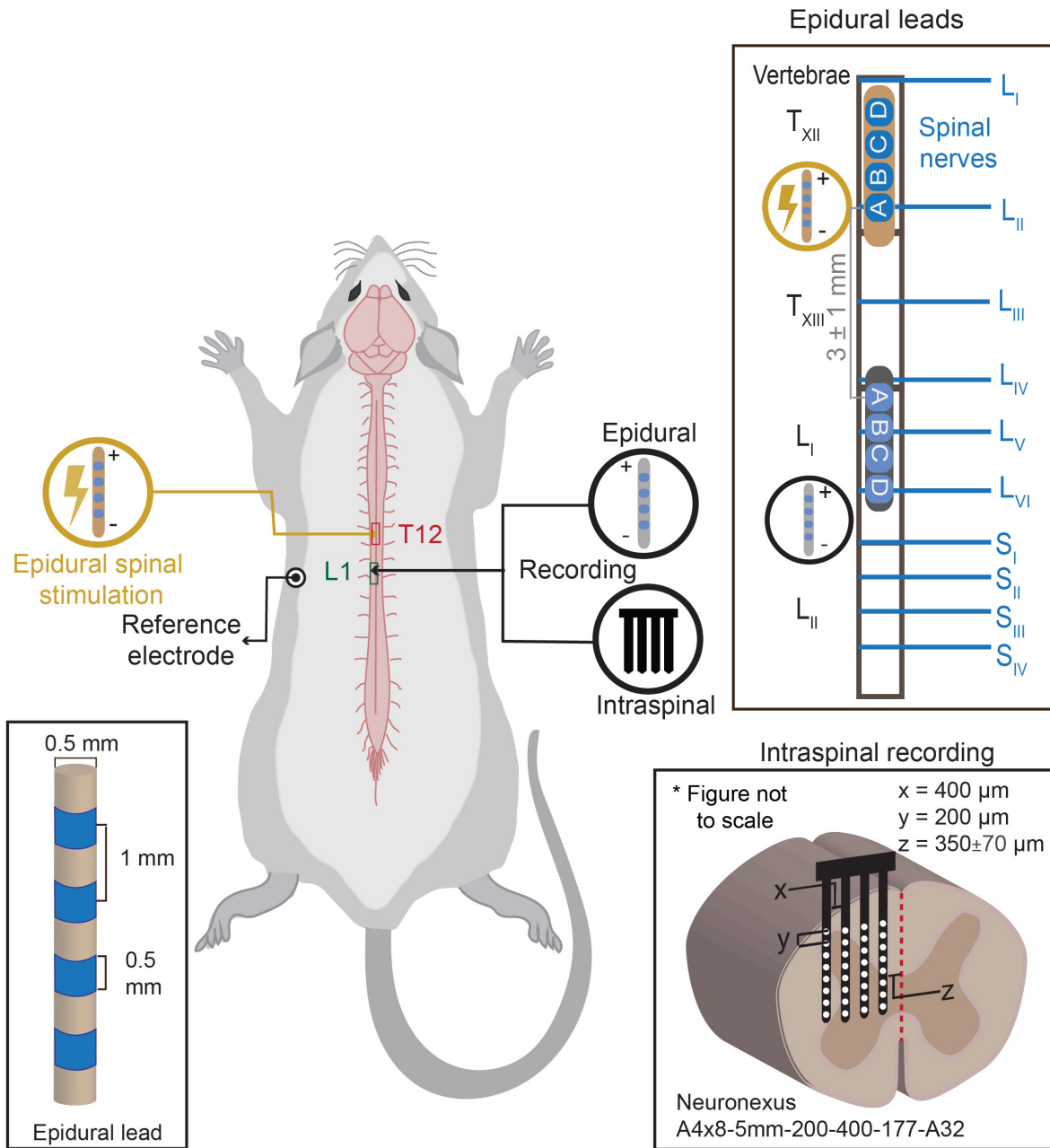
Proximal
cathodal
stimulation

Pulse Amplitude — 350 µA — 400 µA — 450 µA — 500 µA

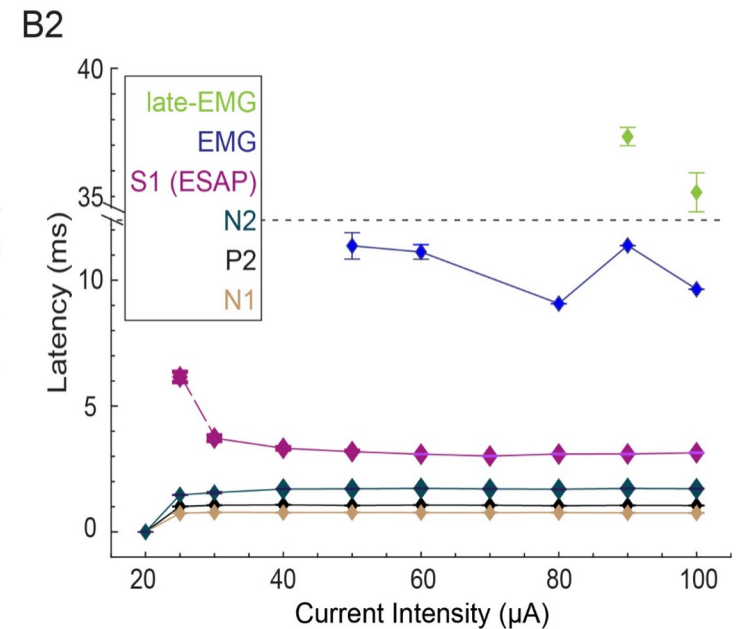
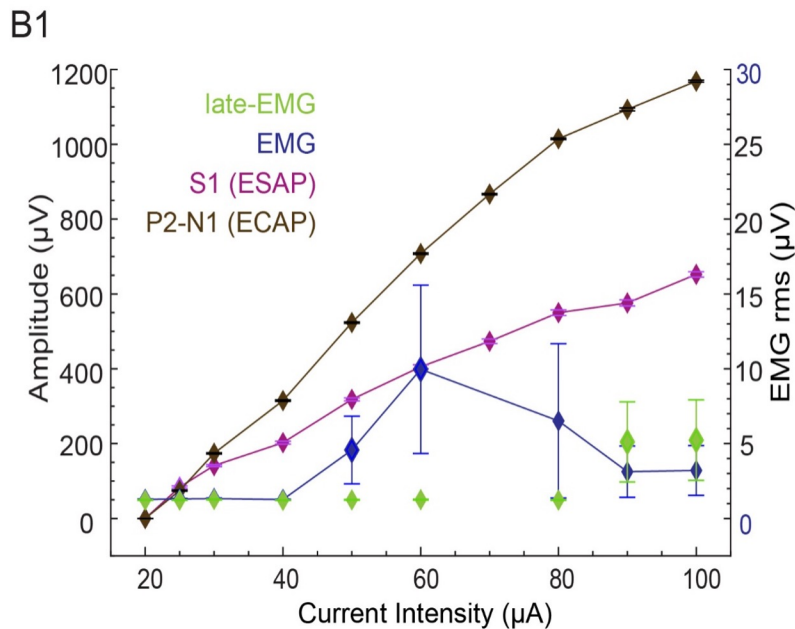
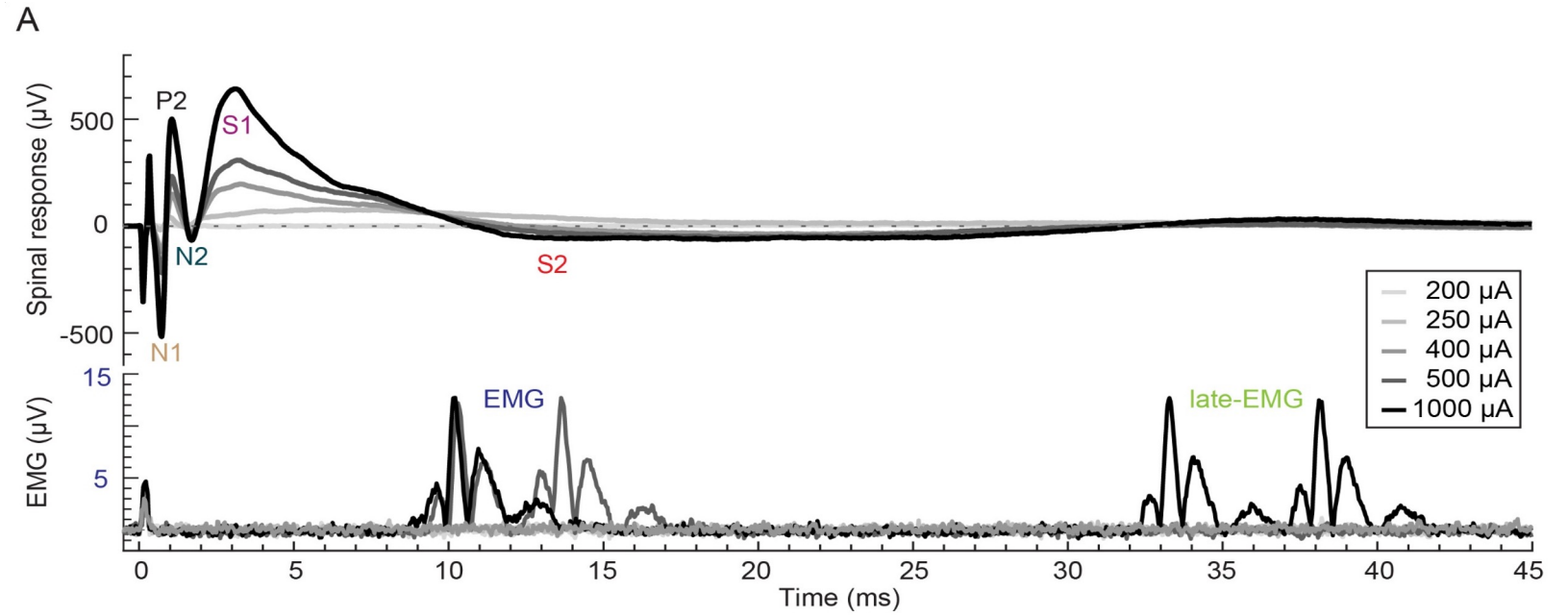
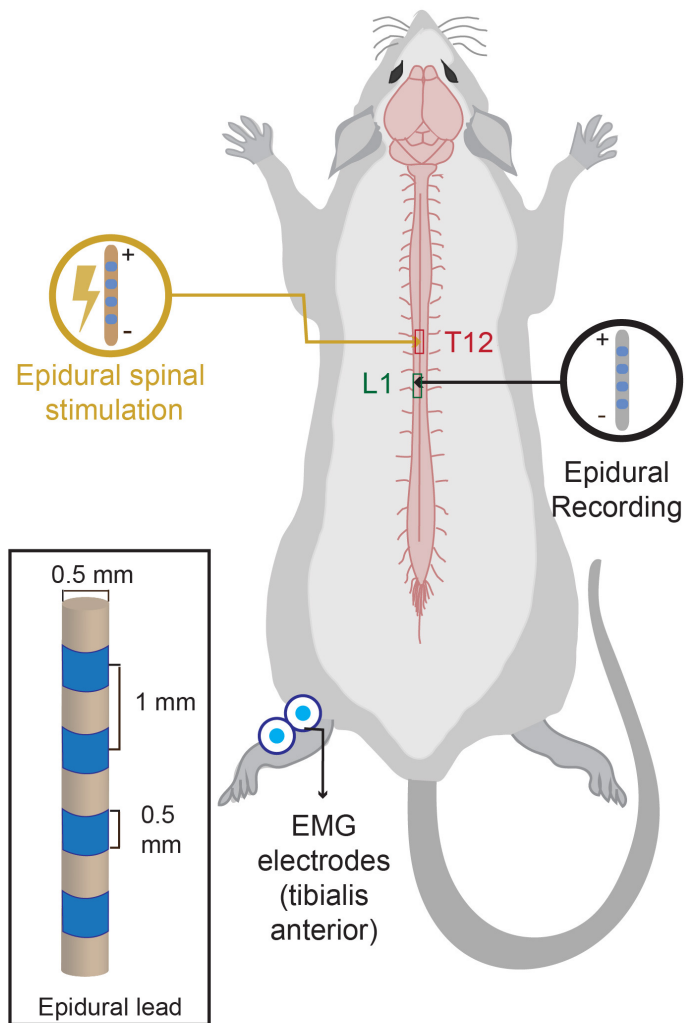
eSAPs (but not eCAPs) suppressed by glutamate synaptic antagonist



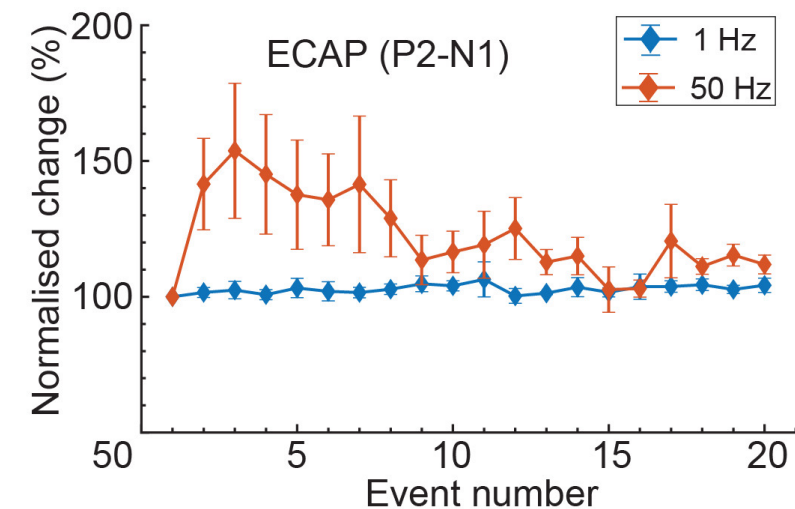
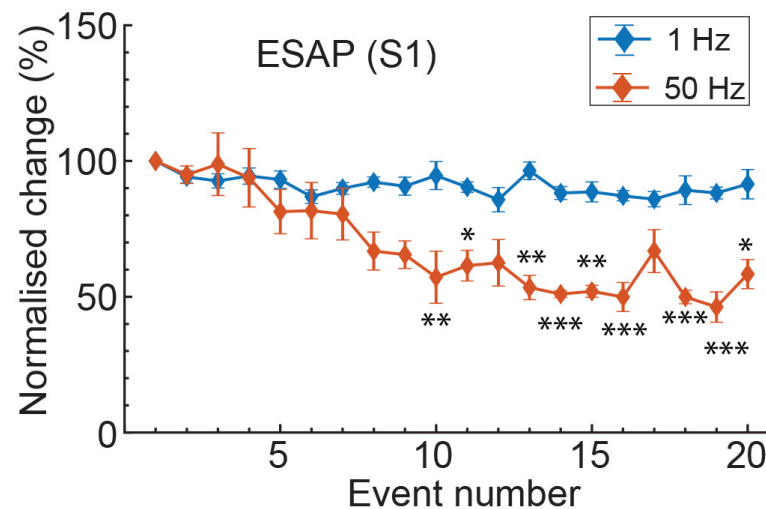
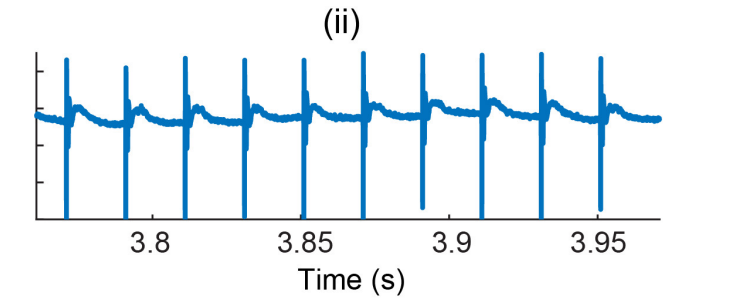
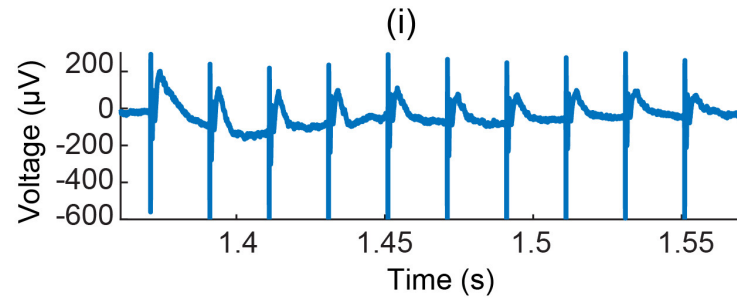
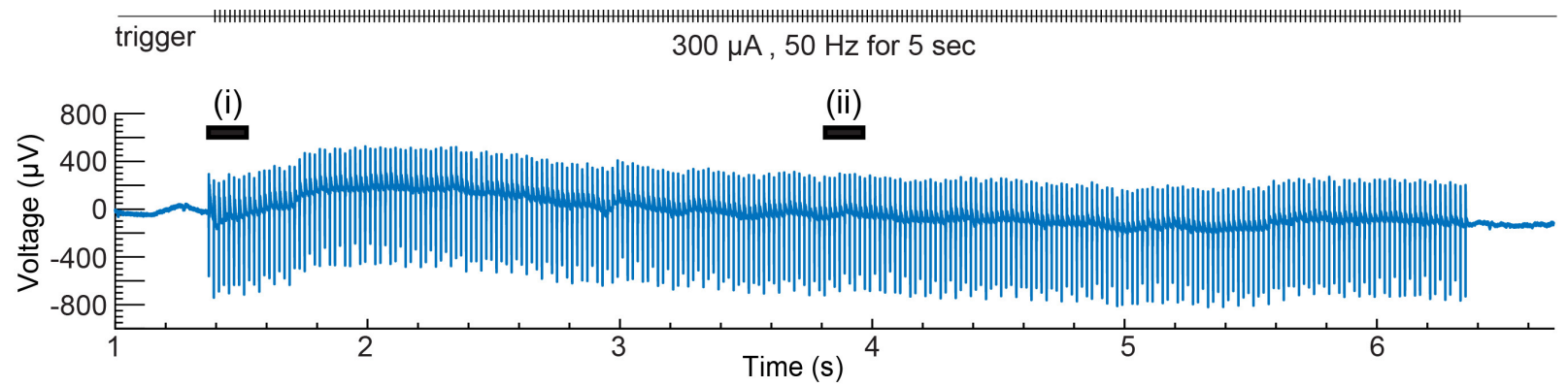
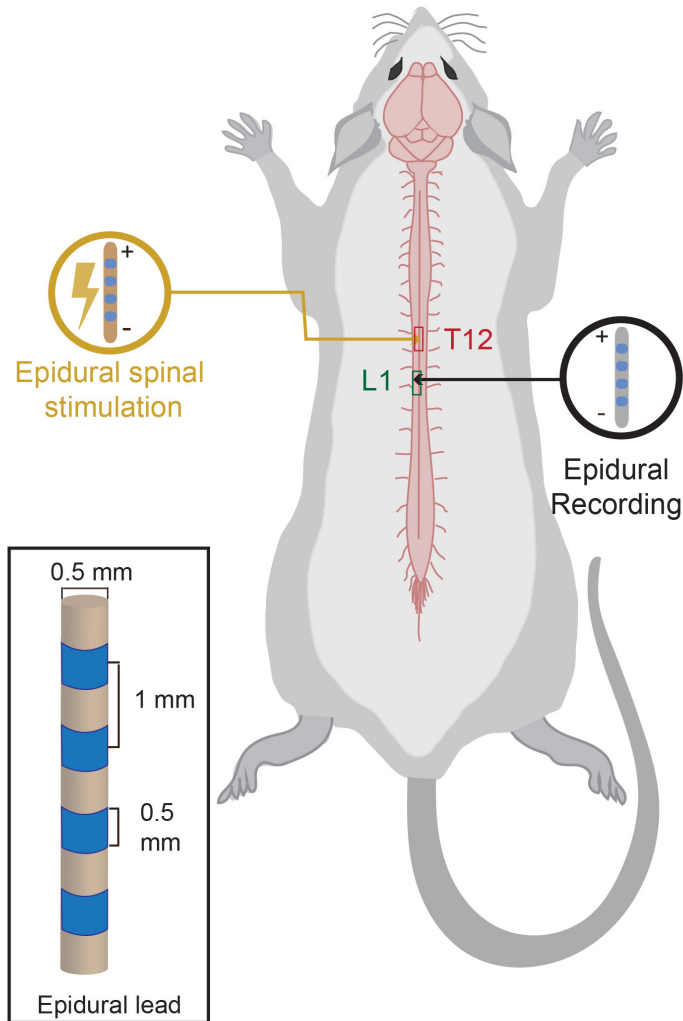
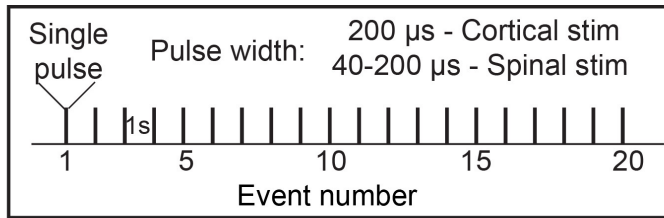
eSAPs have intraspinal correlated consistent with reflecting spinal network activity



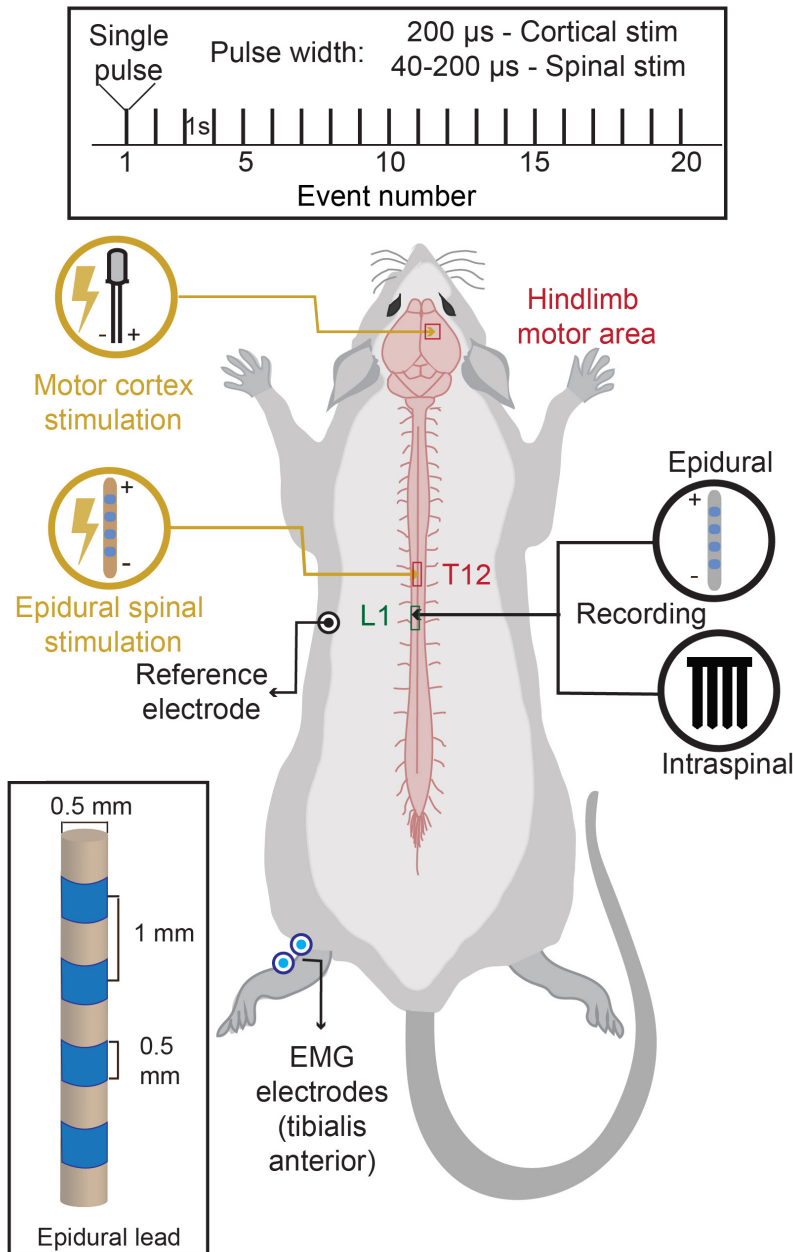
eSAPs are not EMG (having higher threshold, later time, occur independently)



Increasing SCS frequency from 1 Hz to 50 Hz partly diminishes eSAP but not eCAP



eSAP is easy to see (robust) but easy to miss (which means it contains information)



1. Delayed onset and time course: **Synaptic activity (ESAP) follows axon stimulation (ECAP)**
2. Segmental sensitivity (waveform) and dose response distinct from ECAPs: **Providing unique information on segmental mechanism.**
3. Inhibition by glutamatergic-synaptic antagonist, without ECAP block.
4. Intraspinal correlate (suppressed by glutamatergic-synaptic antagonist). Epidural electrodes also measure spinal synaptic responses to cortical stimulation. **Spinal network synaptic state detectable with SCS epidural leads.**
5. Not EMG: Threshold below EMG, peak before EMG initiation & occurring independent of EMG
6. Diminishment (but still detectable) with frequency increases from 1 Hz to 50 Hz, in contrast to relative stability of ECAPs. **ESAPs provide unique information on spinal cord state in response to SCS.**
7. **Translation to humans?** Slow electrical potentials of the human spinal cord have been noted for decades. (Shimizu 1979; Yates et al. 1982, Simohi et al. 1994, Tomita et al 1996...) **Not to be confused with distinct late myogenic responses.**

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