

Similar morphology, different timing: Cortico-spinal response delays following median and ulnar nerve stimulation

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ABSTRACT: Understanding the temporal propagation of sensory signals from peripheral nerves to the central nervous system remains challenging due to limited access to spinal cord activity. In this study, we investigate the capability of electrospinography (ESG) to resolve conduction delays following transcutaneous stimulation of the ulnar (UNS) and median (MNS) nerves. ESG and electroencephalography (EEG) recordings were obtained, preprocessed, and analyzed using latency estimation and cross-correlation methods. Spinal responses exhibited condition-specific latency differences, with UNS stimulation consistently preceding MNS stimulation by approximately 2–3 ms, in agreement with delays predicted from peripheral nerve anatomy and conduction velocity. Comparable delay patterns were observed in cortical EEG responses after averaging across participants, and waveform morphology remained similar between conditions. These findings suggest that ESG provides temporally precise information on ascending sensory signal propagation that may not be detectable at the cortical level alone. The results highlight the potential of ESG as a complementary tool for studying spatiotemporal dynamics within the human sensorimotor system.

INTRODUCTION

Understanding the temporal dynamics of neural signal propagation along somatosensory pathways is essential for characterizing the functional organization of the human nervous system and for developing neurophysiological biomarkers of neurological disorders. Peripheral nerve stimulation provides a controlled and reproducible means of probing these pathways, eliciting afferent responses that ascend from the peripheral nerve through the spinal cord to cortical processing stages within a few milliseconds.

Electroencephalography (EEG) has long been used to non-invasively record cortical somatosensory evoked potentials with high temporal resolution, enabling detailed investigation of sensory processing at the level of the brain. However, a comprehensive understanding of signal transmission along the entire somatosensory pathway requires access to neural activity at earlier stages of processing. In this context, electrospinography (ESG) has re-

cently reemerged as a promising non-invasive technique for capturing spinal cord responses using surface electrodes placed over the spine [1, 2]. The simultaneous acquisition of cortical and spinal signals therefore offers a unique opportunity to investigate conduction timing across hierarchical levels of the somatosensory system. While latency characteristics of responses following median nerve stimulation have been already studied [1–3], comparatively little is known about the temporal properties of responses evoked by stimulation of other upper-limb nerves, such as the ulnar nerve, particularly at the spinal level.

Anatomical and Neurophysiological Considerations: Somatosensory signals from the upper limb are conveyed by large myelinated first-order afferent fibers entering the spinal cord through the dorsal roots and ascending within the dorsal column pathways. These fibers synapse in the dorsal column nuclei of the brainstem, after which second-order neurons project to the thalamus. Subsequent thalamocortical projections transmit the signal to the primary somatosensory cortex. During this ascending transmission from the peripheral nerve to the brain, afferent volleys also engage segmental spinal circuits. These spinal circuits give rise to early spinal somatosensory evoked potentials that can be recorded non-invasively. Following median nerve stimulation, these responses typically manifest as a sequence of characteristic components, including an initial positive deflection (P1) at approximately 9 ms, a prominent negative peak (N1) around 13 ms, and a later positive component (P2) between 20 and 25 ms [1, 3]. This tri-phasic spinal cord potential (SCP) has been consistently described for median nerve stimulation at standard stimulation sites like the wrist [1, 2, 4]. Variations in stimulation location or afferent pathway length are expected to result in corresponding shifts in component latencies while preserving the overall waveform morphology. Detailed physiological interpretations of the individual components have been discussed elsewhere [5, 6] and are beyond the scope of the present study.

Aim and hypothesis: Whether comparable temporal response patterns are present following ulnar nerve stimulation relative to median nerve stimulation, and how dif-

ferences in conduction distance and pathway characteristics influence the timing of spinal and cortical responses, remains largely unexplored. Addressing this question is particularly relevant for understanding pathway-specific timing mechanisms and the morphological consistency of evoked responses. It also contributes to extending non-invasive multilevel electrophysiological approaches beyond well-established stimulation paradigms.

In the present study, we therefore combine high-density EEG and ESG recordings to quantify pathway-specific conduction timing following median and ulnar nerve stimulation. We hypothesize that stimulation of these anatomically distinct but functionally similar peripheral nerves evokes responses with comparable waveform morphology that are shifted in time due to differences in stimulation location and conduction distance. To test this hypothesis, we employ cross-correlation-based latency analysis of participant-specific evoked responses to assess both waveform similarity and relative temporal delay between stimulation conditions.

MATERIALS AND METHODS

Preliminary results of this ongoing study are based on data acquired from six healthy participants (3 male, 3 female; age 24 ± 2.3 years). All participants provided written informed consent prior to participation and were free to withdraw from the study at any time without providing a reason. The study protocol was approved by the Ethics Committee of Graz University of Technology.

Paradigm: Participants were positioned in a forward-inclined seated massage chair with dedicated chest and head supports, allowing relaxation of the neck and back muscles while reducing motion-related artifacts. They were instructed to remain still and to keep their eyes open throughout the recordings in order to reduce contamination of the data by increased alpha-band activity associated with eye closure.

Electrical stimulation was applied to the median nerve at the wrist and to the ulnar nerve at the elbow. The stimulation current amplitude was individually adjusted for each participant. The current was gradually increased until visible muscle contractions associated with activation of the stimulated nerve were observed and subsequently reduced to a level below motor threshold to avoid movements. This procedure ensured mixed-nerve stimulation with predominant activation of sensory afferents. Across participants, the stimulation intensity was 10 ± 2.7 mA for median nerve stimulation (MNS) and 9 ± 3.7 mA for ulnar nerve stimulation (UNS).

For each nerve, 3600 stimuli were delivered in 12 runs of 300 stimuli each, using random inter-stimulus intervals between 700 and 900 ms. In addition to the stimulation runs, three resting-state recordings of five minutes duration were acquired to obtain a comparable number of rest and stimulation epochs.

Between runs, participants were allowed to stand up or adjust their seating position to prevent muscle fatigue and

tension, as electromyographic (EMG) activity represents a major source of artifacts in ESG recordings.

Stimulation and measurement setup: Electrical stimulation was delivered using a DS7R constant-current stimulator (Digitimer Ltd., Letchworth Garden City, UK) in combination with 32-mm Flextrode Plus surface electrodes (Krauth+Timmermann GmbH, Hamburg, Germany). Stimulation electrodes were positioned at the wrist for median nerve stimulation and at the elbow for ulnar nerve stimulation.

EEG and ESG signals were recorded using a BrainAmp Standard amplifier system (Brain Products GmbH, Gilching, Germany) with active electrodes. A total of 64 electrodes were arranged according to a standard EEG montage, while 54 additional electrodes were positioned over the neck and upper back to capture electrospinographic activity (see Fig. 1) For a more detailed description of the ESG electrode montage and layout see [Golser *et al.*, 2026 - accepted manuscript].

The reference electrode was placed on the tip of the nose and the ground electrode on the forehead. Two mastoid electrodes were used for virtual re-referencing, and one electrode placed below the left thorax was used for electrocardiogram (ECG) recording. Furthermore, two electrodes were positioned close to the stimulation sites to enable precise extraction of stimulation onset timing - these electrodes are hereafter referred to as stimulation signal channels. All signals were recorded with respect to a reference electrode located at the tip of the nose and were sampled at 5000 Hz.

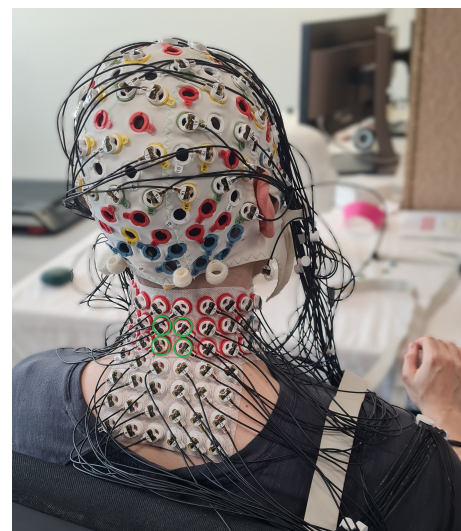


Figure 1: Electrode setup for recording brain and spinal cord activity during median and ulnar nerve stimulation. ESG electrodes marked with green rings are used as ROIs.

Data processing: All data processing was performed in Python using custom scripts in combination with the MNE-Python toolbox [7]. For both EEG and ESG recordings, signals were initially re-referenced to the mastoid electrodes prior to further preprocessing. Although stimulation triggers were logged via Lab Stream-

ing Layer (LSL) [8], hardware-induced delays and temporal jitter limited the reliability of these markers for latency analyses. To ensure accurate onset extraction, anomalous signal segments were automatically identified in the stimulation channels using robust thresholding of sample amplitude and sliding-window variance (median-absolute-deviation based z-scores). Detected samples were merged into bad intervals, and stimulation events within these intervals were excluded from further analysis to ensure reliable temporal alignment for EEG and ESG epoching.

EEG signal processing: First, line noise was removed using a notch filter at 50 Hz and its harmonics, and a band-pass filter between 1 and 1000 Hz was applied. Both filters were implemented as fourth-order Butterworth infinite impulse response (IIR) filters.

Bad channels were identified by visual inspection of the raw data and were interpolated using spline interpolation. Artifact correction was then performed using independent component analysis (ICA). Components were automatically classified by the MNE algorithm, and those associated with eye blinks, muscle activity, or channel noise were removed when the predicted artifact probability exceeded 90%. Finally, the data were re-referenced using a common average reference (CAR).

Cleaned signals were epoched relative to stimulation onset, including a pre-stimulus interval of 100 ms and a post-stimulus interval of 300 ms. For resting-state recordings, fixed-length epochs of identical duration were generated.

ESG signal processing: To attenuate power line interference, a notch filter at 50 Hz was applied. In addition, a high-pass filter at 1 Hz was used to remove slow signal drifts. Both filters were implemented as fourth-order Butterworth infinite impulse response (IIR) filters applied in a forward-backward (zero-phase) manner. Bad channels were identified by visual inspection and interpolated using local spatial averaging of adjacent electrodes. Due to the anatomical proximity of cervical recording sites to the heart, ESG signals were strongly contaminated by electrocardiographic (ECG) activity. To suppress this interference, signal space projection (SSP) was performed using the simultaneously recorded ECG channel [9]. Projection vectors were computed using the MNE-Python function `mne.preprocessing.compute_proj_ecg()`. In all participants, the first projection component accounted for more than 90% of the ECG-related variance and was therefore removed from the data.

Following artifact correction, the data were epoched relative to stimulation onset, including a pre-stimulus interval of 100 ms and a post-stimulus interval of 300 ms. Resting-state recordings were segmented into fixed-length, partially overlapping epochs (40 ms overlap) to increase the number of available rest trials. Epoch rejection was performed using joint probability and kurtosis criteria with an absolute z-score threshold of 3 (corresponding to ± 3 standard deviations). On average, approximately 10% of epochs were excluded from further

analysis.

Region-of-interest definition: For the analysis of evoked responses, regions of interest (ROIs) were defined based on the expected spatial distribution of somatosensory evoked potentials. For EEG, the cortical ROI comprises electrodes over the left motor cortex, namely C3, CP5, CP3, CP1 and P3. In contrast to cortical somatosensory evoked potentials, the spatial distribution of electrospinographic responses is less well established. Therefore, ESG regions of interest were defined using a data-driven approach. After preprocessing and averaging, ESG waveforms were visually inspected to identify electrodes exhibiting the strongest and most consistent deflections after around 13 ms post stimulus, corresponding to the expected arrival time of afferent activity following median nerve stimulation.

Based on this criterion, four centrally located cervical electrodes showing robust early responses were selected as the ESG region of interest. The selected electrodes are indicated by green rings in Fig. 1.

Similarity and latency analysis: For each participant and stimulation condition, preprocessed epochs were averaged to obtain subject-specific evoked responses. Subsequently, signals were averaged across channels within the predefined EEG and ESG regions of interest to derive representative ROI waveforms. All similarity and latency analyses were performed at the participant level to avoid bias related to unequal numbers of trials across participants. To assess whether responses evoked by median and ulnar nerve stimulation exhibited comparable signal patterns with a relative temporal shift, z-normalized cross-correlation analysis was performed. This puts the emphasis on the waveform shape rather than absolute amplitude differences. The normalized cross-correlation between stimulation conditions was computed as

$$R_{xy}(\tau) = \frac{1}{N} \sum_{t=1}^N \tilde{x}^{\text{MNS}}(t) \cdot \tilde{x}^{\text{UNS}}(t + \tau) \quad (1)$$

where τ denotes the temporal lag and N is the number of samples within a predefined post-stimulus analysis window. To focus on early somatosensory responses while avoiding contamination by stimulation artifacts, the correlation analysis was restricted to a time interval from 5 ms to 40 ms after stimulus onset. The lag corresponding to the maximum correlation coefficient

$$\tau^* = \arg \max_{\tau} R_{xy}(\tau), \quad (2)$$

was interpreted as the relative temporal delay between responses evoked by median and ulnar nerve stimulation. The corresponding peak correlation value was used as a measure of waveform similarity.

To ensure physiologically plausible delay estimates, the search range for τ was restricted to ± 10 ms. For visualization, grand-average ROI waveforms were computed by averaging participant-specific responses. Estimated temporal shifts were subsequently used to align ulnar nerve responses to median nerve responses.

RESULTS

After preprocessing, epoching, and averaging ESG and EEG signals across their respective ROI channels, condition-specific evoked response waveforms were obtained for the MNS, UNS, and REST conditions (Fig. 2). A pronounced negative deflection at approximately 13 ms post-stimulus (N1) is observed in the MNS condition of the ESG recording, indicating the arrival of the stimulus-evoked afferent volley at the recording site (Fig. 2 (b)). This component is followed by a subsequent positive deflection. A qualitatively similar response pattern is present in the UNS condition. However, the response exhibits reduced amplitude and a temporal shift relative to MNS. In the MNS EEG recordings, a negative peak at approximately 18 ms post-stimulus suggests the arrival of the afferent signal at the cortical level. Again, a similar signal morphology shows for the MNS and UNS condition in the EEG.

Similarity and delay analysis: Cross-correlation analysis of ESG responses between MNS and UNS conditions across participants indicates a consistent temporal ordering, with the UNS response preceding the MNS response. The mean ESG lag across participants was 3.57 ± 2.23 ms (mean $\pm$ SD), with a corresponding maximum correlation coefficient of 0.50 ± 0.20 . Individual participant values are reported in Table 1. When signals were averaged across participants prior to cross-correlation, the estimated lag between MNS and UNS responses was 2.60 ms (see Fig. 3). For EEG recordings, the mean lag between MNS and UNS responses was 2.43 ± 1.10 ms (mean $\pm$ SD), with maximum correlation coefficients of 0.73 ± 0.15 . After averaging EEG signals across participants, the temporal lag between MNS and UNS response was 3.12 ms.

Spatial distribution of ESG signal: Topographic maps in Figs. 4 and 5 illustrate the spatial distribution of ESG potentials across the electrode array at selected latencies for MNS and UNS, respectively. Prior to stimulation (Fig. 4 (a)), only low-amplitude background activity is visible. At approximately 9 ms post-stimulus (Fig. 4(b)), a focal negative potential emerges on the right side of the electrode array. The N1 component (13 ms) and the subsequent positive P2 component (22 ms) are clearly identifiable in the topographic distributions shown in Fig. 4(c) and (d), respectively.

The topoplots in Fig. 5 show the same time points from the MNS condition minus the calculated delay of 2.60 ms. While the pattern is similar to the MNS condition, it is less pronounced.

DISCUSSION

The ESG and EEG responses observed in this study are broadly consistent with previously reported somatosensory evoked potentials in terms of waveform morphology and latency. In particular, the characteristic negative ESG deflection around 13 ms post-stimulus aligns with

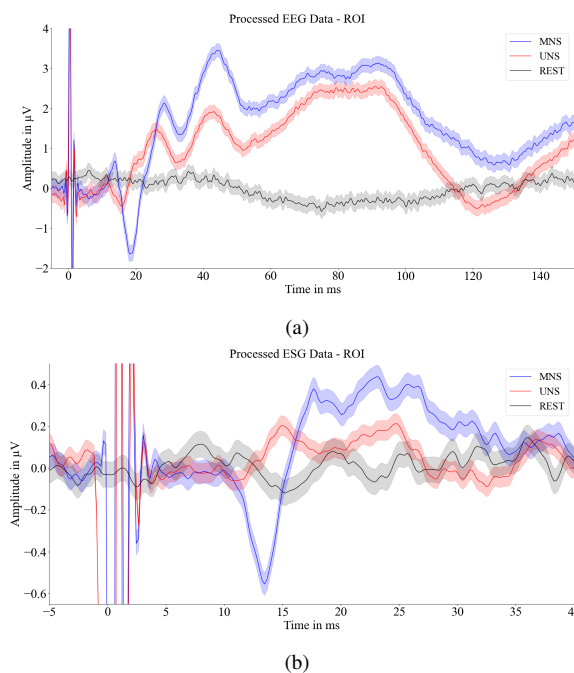


Figure 2: Signal in time-domain for the (a) EEG and (b) ESG recordings averaged over their respective ROI channels. Solid curves represent the mean over all epochs and the shaded surrounding area is the standard error.

Table 1: Participant-specific latency differences between median nerve stimulation (MNS) and ulnar nerve stimulation (UNS) derived from normalized cross-correlation analysis of evoked responses. Positive lag values indicate that responses following UNS occurred earlier than MNS. The maximum correlation coefficient reflects the degree of waveform similarity between stimulation conditions after temporal alignment.

#	ESG		EEG	
	Lag (ms)	max. Corr.	Lag (ms)	max. Corr.
1	7.8	0.41	2.8	0.49
2	4.6	0.53	2.0	0.78
3	0.6	0.86	0.6	0.64
4	3.2	0.26	3.1	0.89
5	2.6	0.46	3.8	0.74
6	2.6	0.47	2.3	0.84

reported spinal components following peripheral nerve stimulation, while the cortical response observed at approximately 18 ms in EEG corresponds to early cortical processing stages. A central finding of this work is the systematic temporal difference between UNS and MNS stimulation at the spinal level. Cross-correlation analysis revealed that ESG responses following UNS stimulation precede MNS responses by 3.57 ± 2.23 ms across participants, with a lag of 2.60 ms when signals were averaged prior to analysis. This temporal shift is physiologically plausible. Assuming an average forearm length of approximately 22 cm and a large-fiber conduction velocity of approx. 70 m/s [10], the expected conduction time difference between proximal (UNS) and distal (MNS) stimulation sites would be approximately 3.10 ms. The experimentally observed delay therefore

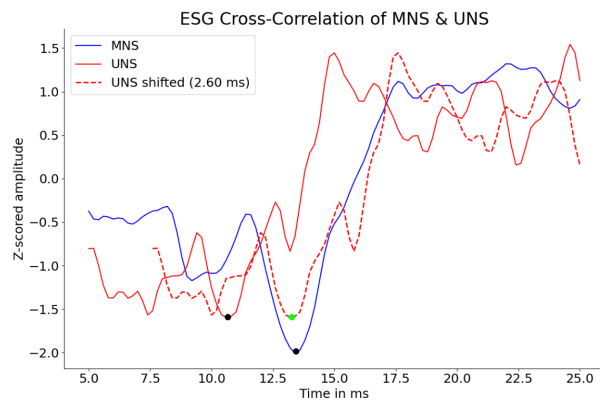


Figure 3: The lag between MNS and UNS signal after z-normalization in the ESG and a shifted UNS to show the overlay to MNS. The timepoints of the MNS and UNS signal that indicate arrival at the spinal cord are marked with a black circle, the green circle indicates the shifted point of arrival of UNS.

closely matches the delay predicted by peripheral nerve anatomy and conduction physiology, suggesting that the ESG recordings reliably capture propagation of the afferent volley along the peripheral nerve towards the spinal cord. Consistent with the latency difference observed at the spinal level, comparable delays were also identified in cortical EEG responses after participant-level averaging. This finding suggests that peripheral conduction differences between stimulation sites are preserved along the ascending sensory pathways and can be detected not only at the spinal level but also at the cortical level. Thus, both ESG and EEG appear sensitive to conduction-related timing differences, indicating consistent temporal propagation of afferent signals from the peripheral nerve to the cortex following MNS and UNS stimulation. After z-normalization, UNS and MNS responses exhibited highly similar waveform morphology in both ESG and EEG recordings, further supported by moderate cross-correlation values. The comparable waveform morphology suggests that both stimulation paradigms evoke similar spinal response dynamics of afferent fibers and engage functionally analogous ascending sensory pathways. The observed latency differences therefore most likely reflect variations in conduction distance between stimulation sites rather than fundamentally different neural processing mechanisms. Across all recordings, the amplitude of UNS responses was consistently lower than that of MNS responses in both ESG and EEG. The underlying cause of this amplitude difference remains unclear. Possible explanations include differences in effective recruitment of sensory fibers due to electrode placement and tissue impedance. Additionally, differences in anatomical depth and orientation of the nerve relative to the stimulation electrodes may influence the resulting signal strength.

Limitations: A limitation of these preliminary findings is related to the stimulation paradigm. Although stimulation intensity was selected to remain below the visible motor threshold in order to preferentially activate sensory

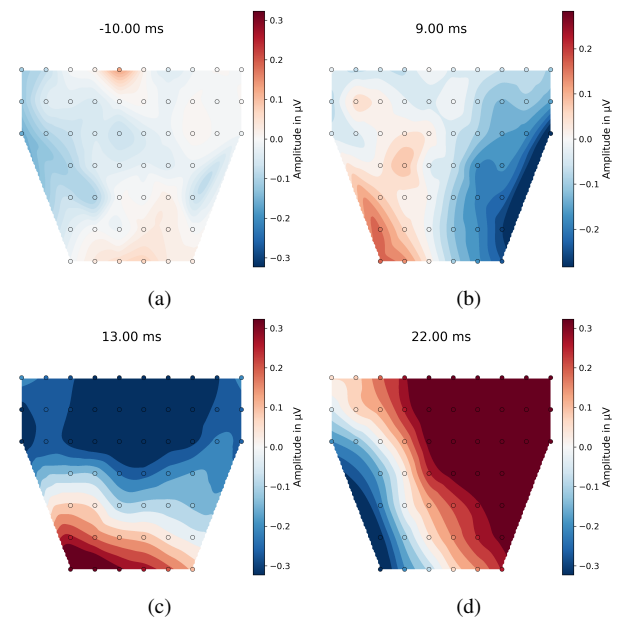


Figure 4: Topoplot of averaged ESG recording during MNS stimulation at (a) 10 ms pre stimulus, (b) 9 ms post stimulus, (c) 13 ms post stimulus and (d) 22 ms post stimulus.

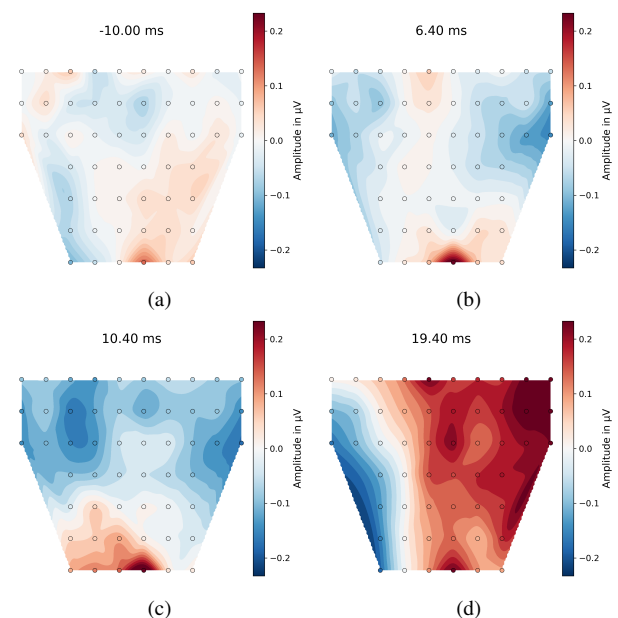


Figure 5: Topoplot of averaged ESG recording during UNS stimulation at (a) 10 ms pre stimulus, (b) 9-2.6 ms post stimulus, (c) 13-2.6 ms post stimulus and (d) 22-2.6 ms post stimulus.

fibers, purely sensory stimulation cannot be guaranteed when stimulating transcutaneously at anatomically complex sites such as the wrist or elbow. Consequently, contributions from motor fibers or muscle artifacts cannot be fully excluded. Furthermore, the current sample size limits statistical inference. Future studies with a larger cohort are required to determine whether observed components, such as the ESG deflection at approximately 13 ms post-stimulus, differ significantly from the REST condition and whether similar condition-specific effects can be robustly demonstrated for UNS stimulation.

Future work: Beyond increasing the number of participants, an important next step is to investigate functional connectivity between spinal and cortical activity [11]. Such analyses could provide insights into bidirectional communication within the sensorimotor system and help identify network-level interactions between brain and spinal cord during sensory processing. Another promising direction is the application of source localization techniques to both EEG [12] and ESG recordings [13]. While EEG source localization is well established, the extension of inverse modeling approaches to spinal recordings remains largely unexplored. Combining cortical and spinal source estimates could enable a more comprehensive spatiotemporal characterization of sensory signal propagation within the central nervous system.

CONCLUSION

The present results demonstrate that spinal evoked potentials recorded with ESG can resolve physiologically meaningful conduction delays associated with different peripheral stimulation sites. UNS stimulation elicited earlier spinal responses than MNS stimulation, with measured delays closely matching values predicted from peripheral nerve anatomy and conduction velocity. Similar latency differences were also observed in EEG recordings after participant-level averaging, and both stimulation paradigms exhibited comparable waveform morphology, suggesting activation of related spinal dynamics. These findings highlight the potential of ESG as a temporally sensitive method for investigating sensory signal propagation in the human nervous system and motivate future studies with larger cohorts and advanced connectivity and source localization analyses.

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