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Case report

Case report: Potential physiological sources of the late response in epidural spinal recordings induced by spinal cord stimulation during intraoperative neuromonitoring

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ABSTRACT

Objective: This study aims to investigate the sources of later response in epidural spinal recordings (ESRs) obtained from implanted leads during spinal cord stimulation, a topic has not been widely studied in previous research.
Methods: Two patients with lower back and lower extremity pain underwent SCS implantation with intraoperative neuromonitoring (IONM). The timing of extracted peaks in ESRs and intramuscular electromyography (EMG) recordings were analyzed and compared to a Monte Carlo simulation for synchronization analysis.
Results: Our data show that, when using two most caudal electrodes for stimulation, late response in ESRs collected from SCS leads was not synchronized with EMG recordings from lower extremity muscles. However, parts of the late responses were synchronized with EMG recordings from abdominal muscle groups.
Conclusions: Late response in ESRs is believed to result from muscle contractions, although the exact sources have not been fully identified. They are likely to originate from muscles near the implanted leads.
Significance: This research indicates that components of the late response may originate beyond the abdominal region, potentially offering additional information for current IONM practice. Additionally, understanding the sources of the late response may be useful for emerging clinical applications in neurorehabilitation.

1. Introduction

Intraoperative neuromonitoring (IONM) with multiple physiological signal measurements is used to assess functional integrity of the nervous system, provide safety monitoring, and confirm proper positioning of electrodes for spinal cord stimulation during asleep procedures (Shils and Arle, 2018). Evoked responses collected during IONM are typically obtained by instrumenting multiple scalp and muscle locations across the body with pairs of percutaneous needle wires and interfacing these with a data acquisition system for real-time viewing during the placement of the spinal cord stimulation (SCS) lead (Macdonald et al., 2013, Park and Hyun, 2015, Falowski et al., 2022). For example, during IONM, percutaneous needle electrodes might be placed through the skin on the scalp and near the cervical plexus to detect the somatosensory evoked responses caused by ulnar/median nerve stimulation, monitoring the perioperative neurologic changes to avoid any potential damage or postural compression to nerves during the surgical procedure (Falowski et al., 2019, Falowski et al., 2022). Additionally, the muscle responses evoked by SCS are recorded using several percutaneous needles placed in various muscle groups throughout the lower body. The change in evoked EMG responses recorded during IONM can be used to map the position of the SCS lead relative to the spinal cord midline, to determine the laterality of lead placement, and to estimate dermatomal coverage of the implanted leads using myotomes as a surrogate (Falowski et al., 2011, Shils and Arle, 2018, Falowski et al., 2019). However, the process of instrumenting muscles and managing the multiple cables, connection points, and complex software interface during the procedure can be time consuming, burdensome and more invasive.

Epidural spinal recordings (ESRs) are recorded directly from the implanted SCS lead which may offer physiological insights that enhance those provided by traditional IONM methods (Falowski et al., 2022). Past studies of ESRs indicate that there are multiple phases of signal

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representing different sources including: 1) the evoked stimulus artifact, 2) the first or early evoked response, 3) the secondary or late evoked response, and 4) a background signal representing cardiac cycles (Falowski et al., 2022, Verma et al., 2023, Verma et al., 2023).

The first or early evoked response is thought to be generated by the compounded neuronal action potentials (Chakravarthy et al., 2020, Sharma et al., 2023). The early evoked response (also referred to as an Evoked Compound Action Potential; ECAP) is well studied and has been shown to originate from synchronized activation of evoked action potentials from *Aβ* fibers in the dorsal column of the spinal cord (Anaya et al., 2020, Parker et al., 2020). The first evoked response (ECAP signal) in an ESR has been used recently to inform paresthesia based-patient programming and dosing adjustments using ECAP based closed-loop control algorithm (Brooker et al., 2021, Vallejo et al., 2021, Brucker-Hahn et al., 2023, Calvert et al., 2023).

The secondary or late evoked response is thought to be generated by EMG signal near the implanted leads. In contrast, the secondary or late evoked response has only been studied in limited contexts. However, the secondary response has already been shown its potential use in some preliminary research as a mean for guiding laterality of lead placement (Falowski et al., 2022), despite a lack of understanding regarding its physiological origins. Thus, the late evoked response may be a potentially useful physiological data source supplementing current IONM practice if its mechanism can be further studied with in-depth investigations.

The aim of this case study is to uncover the physiological origins of the secondary/late evoked responses in ESRs and to provide guidance for future research on this late response component. Specifically, we aim to determine whether there are features in the secondary response that could enhance intramuscular EMG recordings used during IONM or other SCS applications where spinal motor activation is crucial for therapy effectiveness. In this research, we investigated: 1) whether the late response component in ESRs is synchronized with various EMG recordings from intramuscular needles during standard IONM, and 2) which EMG recordings show the highest correspondence with the late response in the ESRs.

2. Methods

2.1. Surgical procedure and data collection

The study was approved by a local Western Copernicus Group Institutional Review Board (WCG IRB) with tracking number 20214221. Two patients with lower back and lower extremity pain with the diagnosis being post laminectomy syndrome and lumbar radiculopathy underwent SCS implantation with IONM. The patients were placed prone on the operating table and underwent general anesthesia with intubation. Total intravenous anesthesia (TIVA) was used with limited inhalants/gas and avoidance of paralytics which could interfere with neuromonitoring signals. Percutaneous Octrode™ leads (Abbott Neuromodulation, Plano TX, USA) were implanted under fluoroscopy guidance utilizing standard epidural access with loss of resistance technique. The individual contacts on the commercial leads used in this study were 3 mm long and 1.4 mm in diameter, with an inter-electrode spacing of 4 mm. During the surgical procedure, the SCS lead with stylet was passed through the needle cephalad under fluoroscopy and advanced carefully to cover T8-T11 levels. Two leads were placed resulting in parallel percutaneous electrodes. The electrodes were offset by 2–3 contacts with the one lead placed more cephalad (Fig. 1). The leads' placement locations were guided by visible and palpable frequency of SCS evoked muscle contraction in the legs and abdominal wall with patient under general anesthesia.

During the experiment, electrode contacts 7 and 8 on the caudal lead were used for stimulation (Fig. 1). Bipolar charge-balanced pulses were delivered with an anodic leading phase. The pulse widths of the stimulation were 200 μs with a stimulation frequency of 2.82 Hz. The stimulation amplitude (intensity) was increased until muscle activation near the back or lower extremity was observed. The stimulation amplitude ranged from 5 mA to 20 mA. At each investigated stimulation amplitude, the stimulation pulses were delivered for about 1 min. Data sets used for the analysis were collected with stimulation amplitude of 12 mA for patient 1 and 16 mA for patient 2, at which stimulating intensities the evoked late responses were clearly observed in ESRs. The ESRs were recorded from contacts that were not being used for delivering stimulation (Fig. 1A). The standard IONM protocol was followed, with intramuscular needle electrodes placed in the abdominal and lower extremity muscle groups to record EMG in a differential configuration (Fig. 2). All recordings were collected using the CADWELL™ system (Kennewick, WA). Recordings from the SCS lead contacts and intramuscular needles were collected using separate recording banks on the CADWELL™ system, with a sampling rate of 12799 Hz.

2.2. Event map generation

To analyze the correlation and synchronization between a given ESR and intramuscular EMG recording, the ESR was divided into two

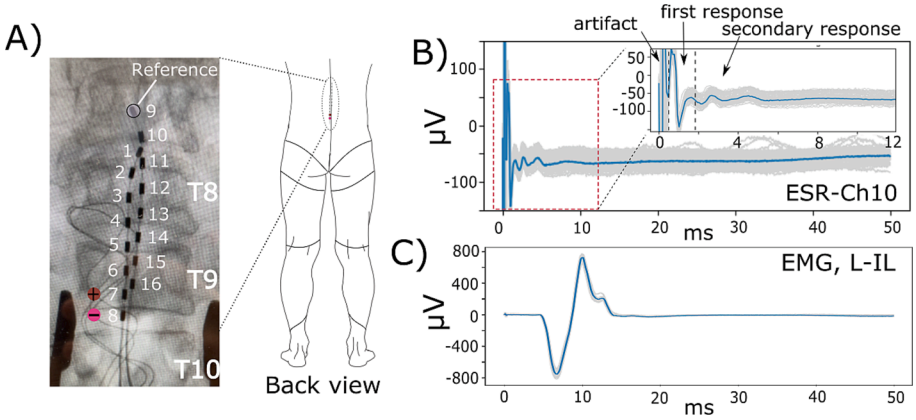

Fig. 1. Implantation of epidural leads during SCS. (A) X-ray image from patient 1 showing two Octrode™ leads implanted to cover spinal levels T8 to T9. **(B)** ESR recording from channel 10 (Ch10) on the lead, displaying the first/early response and secondary/late response. The individual trials (pulses) are shown in grey traces, with the median waveform in dark blue. A total of 93 individual trials were collected. **(C)** Intramuscular EMG recordings from Iliopsoas muscle on the left side of the body. Similarly, 93 individual trials are shown in grey traces, with the median waveform in dark blue. The stimulation amplitude used in both (B) and (C) is 12 mA. Notably, the intramuscular EMG in (C) has a much higher amplitude relative to the stimulus artifact compared to the ESR components shown in (B). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

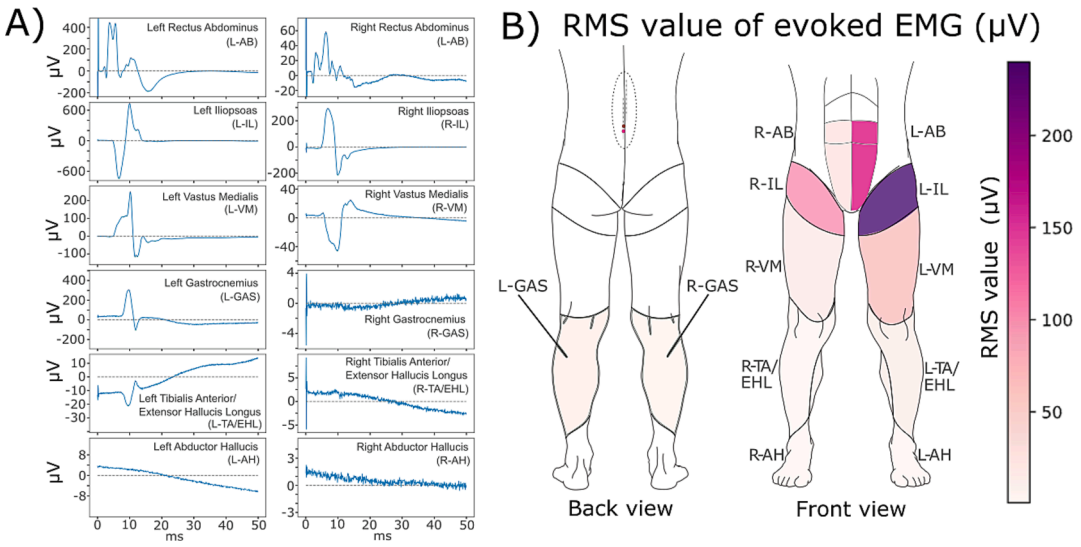

Fig. 2. Intramuscular EMG responses evoked by SCS. (A) Differential EMG recordings collected from the intramuscular needles during IONM. Each EMG recording displays a median waveform from 93 individual trials (pulses). **(B)** Dermatome map of EMG strength for the signals shown in (A). The EMG strength of each muscle was calculated using the Root Mean Square (RMS) of each median recording between the time window from 1.4 msec to 30.0 msec. The stimulation amplitude was 12 mA, and data presented here is from patient 1.

components, with a first or early response occurring from the stimulation artifact to approximately 1.5 msec, and a secondary or late response starting beyond 1.5 msec. These time windows were consistent with data presented in previously published studies (Falowski et al., 2022, Verma et al., 2023). Raw recordings for each channel were processed by first plotting the median waveform from the 1-minute of stimulation (Fig. 3) and then passing the truncated section of recording through a low-pass filter with a cutoff frequency of 2000 Hz. Late responses (the evoked muscle response) in ESRs should be well preserved within this frequency band (Mildren et al., 2017). Then, local extrema of the filtered signal were extracted if their prominence passes both an amplitude and a temporal constraint. The prominence of a peak measures how much a peak or valley stands out from the surrounding concave or convex within a section of its waveform. For the amplitude constraint, the threshold for a peak detection was set to 2 μV for an ESR and 5 μV for an intramuscular EMG recording, as late responses in ESR form smaller concave or convex features around local extrema compared to those from EMG recordings. For the temporal constraint, a constraint window equivalent to 0.5 ms was applied to all local extrema to keep only valid extrema points. Specifically, the temporal constraint was applied by calculating the time delay from the current identified peak to the next neighboring extremum and eliminating the later one if they were too close. This process was continued along the time axis until the amplitude difference of two extrema was below a pre-defined amplitude constraint. The use of the temporal constraint helped to prevent false peak detection for EMG recordings with invalid extrema caused by noise that may have similar amplitude. This time constraint was chosen to apply as the minimum separation between two neighboring peaks since the duration of an ECAP peak is around 1.0 ms. Therefore, the timing from the beginning to the maximum of a peak is half of this duration, or around 0.5 ms (Chakravarthy et al., 2022, Ramadan et al., 2023).

2.3. Analysis of synchronization of two event maps

After identifying the local peaks for both ESR and intramuscular EMG recording, we plotted the event map based on those peaks (Figs. 4 and 5). This event map enables visual assessment of the temporal synchronization between EMG components in the ESR and the

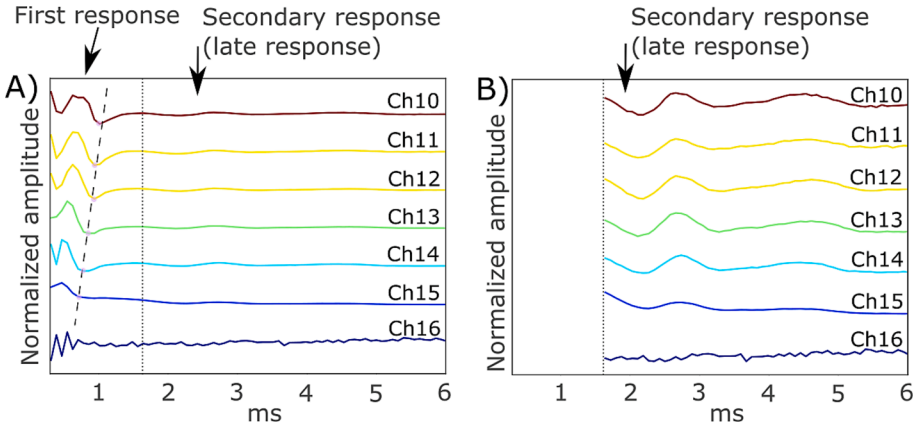

Fig. 3. First and secondary responses captured by ESRs across multiple channels. (A) ESRs collected from channels on the upper lead as shown in Fig. 1. The first response is the ECAP component and clearly visible with increasing latency from more caudal to more rostral channels. The signal in each channel was truncated 0.39 msec after the stimulation artifact. Each trace is the median signal from 93 trials, normalized by subtracting its mean and divided by its standard deviation. **(B)** secondary response shows a different late component in the ESRs across the same channel. The signal was truncated again from time after 1.5 msec (indicated by dashed lines in the two subplots) and renormalized for visualization purposes. The data presented here is from patient 1.

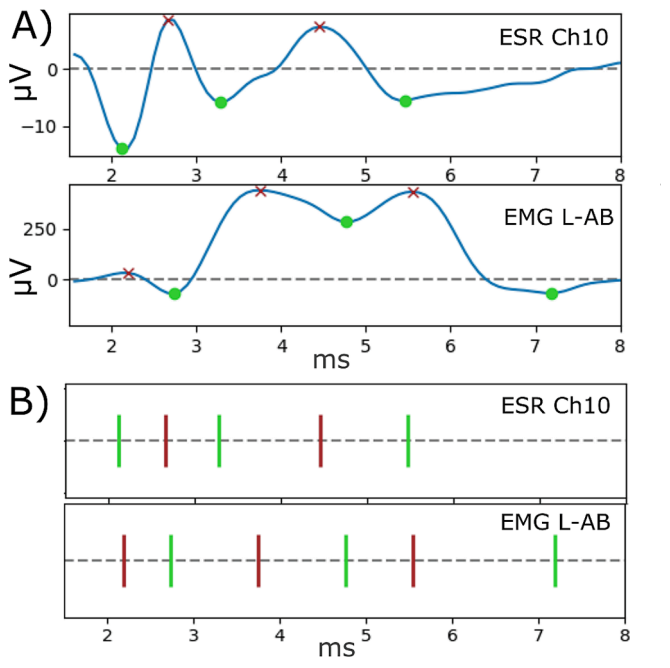

Fig. 4. The events detection and comparison between ESRs and EMG recordings in the secondary response time window. Positive peaks (red) and negative peaks (green) were detected and defined as the events in each signal. The signal was extracted from the secondary response time window shown in Fig. 3, starting around 1.5 msec after the stimulation artifact. **(A)** The events show the footprint of signals across median signal of ESRs from Ch10 (from 93 trials) and median intramuscular EMG recordings from L-AB (from the same 93 trials). **(B)** Direct comparison of the events detected in late response in ESRs and intramuscular EMG recordings from L-AB. The red bars correspond to local positive peaks, and the green bars are local negative peaks. The data presented here is from patient 1. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

intramuscular EMG responses. For each pair of peaks from the ESR and the EMG recording, we defined them as synchronized if the temporal difference was less than 0.5 ms. We then calculated the time difference between each peak-pair, resulting in a series of time difference values for all available peak-pairs. The total number of peak-pairs with time differences smaller than 0.5 ms represents the total number of estimated synchronized peaks for a given pair of ESR and EMG recording.

A Monte Carlo simulation was employed to test whether the number of synchronized peaks in two given recordings was statistically significant. The simulation allowed us to create a probability distribution representing the number of synchronized peaks that could occur by chance. Initially, we broke a 30 ms time axis into smaller 0.5 ms bins, which is the estimated half-size of an ECAP firing. From our data analysis, we found that an average number of 8 peaks can be detected in an ESR. Therefore, in each iteration of the simulation, we randomly generate 8 numbers within these time bins, with timing for each simulation derived from a uniform distribution. Notably, the simulation aimed to study peaks that are in the late response of the ESR. Therefore, we excluded the first 1.5 ms after stimulation artifact in an ESR, as this period is occupied by the ECAP signal (Figs. 1 and 3).

In each iteration of the simulation, 8 different random time bins between 1.5 and 30 ms simulate both ESR and EMG recordings (Fig. 6A). Next, we calculated the number of peak pairs in the ESR and EMG recording simulations that fell within the same time bin, representing the number of synchronized peaks in the random drawing-based simulation process. The same simulation process was conducted for 10,000 different iterations, which allowed us to develop a probability distribution describing the number of synchronized peaks expected to be observed by chance (Fig. 6B). We then established a threshold of $p = 0.05$ to determine the number of synchronous events unlikely to be due to chance.

3. Results

ESRs were collected from contacts that were not used as stimulation channels or a reference electrode. Evoked muscle activity was recorded using standard IONM procedure from the following muscle groups: left and right Rectus Abdominus (L-AB and R-AB), left and right Iliopsoas (L-IL ad R-IL), left and right Vastus Medialis (L-VM and R-VM), left and

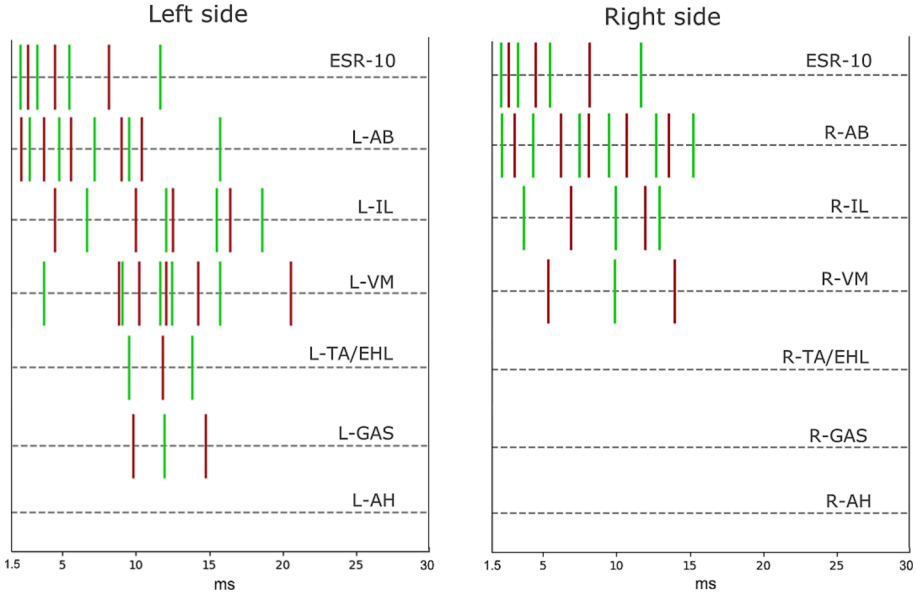

Fig. 5. Event detection between ESRs from channel 10 (ESR-10) and other intramuscular recordings. Following the method shown in Fig. 4, we generated the events map for ESRs from channel 10 and all the intramuscular EMG channels. Local maxima and minima in each recording were marked with red and green, respectively. Event maps for intramuscular recordings from top to bottom in order of proximity to the SCS location. The data presented here is from patient 1. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

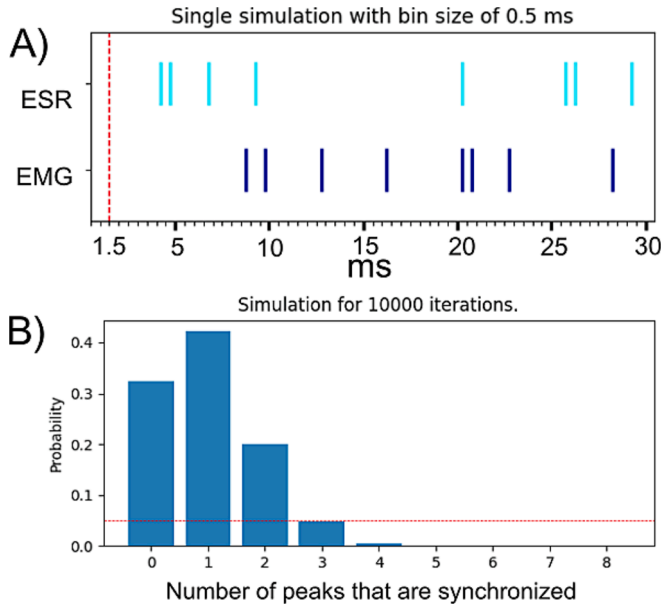

Fig. 6. Monte Carlo simulation of the synchronized peaks between given ESR and EMG events. (A) a single iteration of simulation of 8 peaks randomly located within the time window from 1.5 to 30 ms for an ESR and an intramuscular EMG recording, respectively. **(B)** Probability distribution of the number of synchronized peaks after 10,000 iterations of simulation. The probability is 0.047 when the number of synchronized peaks is 3.

right Gastrocnemius (L-GAS and R-GAS), left and right Tibialis Anterior/Extensor Hallucis Longus (L-TA/EHL and R-TA/EHL), and left and right Abductor Hallucis (L-AH and R-AH). This case report includes data sets from two patients.

3.1. Spinal cord stimulation can trigger early response, late response in ESR and muscle response during IONM procedure

To analyze the evoked late response, the stimulation amplitude needs to be high enough to trigger muscle responses. Among the limited stimulation amplitudes tested during the operation procedure, the stimulation amplitudes of 12 mA for patient 1 and 16 mA for patient 2 were used in this analysis because they reliably triggered evoked intramuscular EMG responses.

In both patients, SCS evoked ESRs showed all expected components including the stimulation artifact, early response (from 0 to 2 msec latency), and late response (from roughly 2 to 6 msec latency; Fig. 1B). Compared to ESRs, intramuscular EMG recordings showed evoked responses with a much larger amplitude and longer latency relative to the stimulation artifact (Fig. 1C). Proximal muscle groups have a large EMG response, while the distal muscle groups have a much smaller or no EMG response upon the delivery of spinal cord stimulation (Fig. 2B). Most intramuscular EMG recordings clearly show activity with latencies falling into the late response window rather than the early response. For example, recordings for L-IL muscle shows activity at 5 msec after the stimulation, while the early response ECAP component typically appears less than 2 msec after the stimulation (Fig. 1). The only two EMG recordings with responses between 0 to 5 ms are those from the left and right Rectus Abdominis (Fig. 2A).

3.2. EMG responses in IONM showed sidedness corresponding to laterality of SCS

The muscle groups from the left side of the body showed a stronger SCS evoked EMG response compared to those on the right side. For example, in patient 1, L-IL had an RMS amplitude of 241.25 ± 10.50 μV, while R-IL has an RMS amplitude of 97.67 ± 14.93 μV from multiple trials (Fig. 2B). This is in line with the spatial bias based on the placement of the stimulation electrodes on the left side of the dorsal column as opposed to the right side (Fig. 1A). In this case, the electrical field coupling would be closer to fibers on the left side and hence produce stronger activation of the rootlets on the left side of the spinal cord as compared to the right.

3.3. ESRs contain both first and secondary responses

In EMG recordings, responses appeared at up to 40 msec after the stimulation (Fig. 2A). In contrast, ESRs consisted of a much more immediate response typically spanning from 0 to 5 msec after the stimulation (Fig. 1B and 3). The ESRs were divided into two time-windows. The first response window is from about 0.39 msec to around 1.5 msec. The small latency changes of the first response across multiple recording channels along the SCS lead within the epidural space clearly indicate that the first response is the ECAP neural component due to the consistent phase shift in the negative peak that corresponds to the conduction velocity of *Aβ* fibers in the dorsal columns (Fig. 3A) (Verma, Romanauski et al. 2023, Lam et al., 2024). Compared to the first response, the secondary response exhibited a lower amplitude, and this phenomenon was observed in both patients. After replotting the figure with only secondary response normalized to itself with an adjusted Y-axis scale, we observed the secondary response has almost no latency shift across recording channels on the SCS lead (Fig. 3B). This indicates that the secondary response is not a propagating neuronal signal, but likely to be evoked muscle responses caused by SCS. We define this signal as the late response or EMG component in an ESR.

In addition, it is important to note that recordings collected from channels 15 and 16 are from locations very close to the stimulation electrodes 7 and 8 (Fig. 1). Although the stimulation artifact itself does not exhibit latency changes across the recording array (Parker et al., 2020, Verma, Romanauski et al., 2023, Deshmukh et al., 2024), the capacitive recovery of the artifact may last longer after the end of the stimulation delivery as the recording contacts get closer to the stimulation site (Verma et al., 2023a, Deshmukh et al., 2024). As a result, ECAP signals in the recording channels near the stimulation site can be severely contaminated by the stimulation artifact recovery, as seen in channel 15. Moreover, recordings collected right next to the stimulation site, such as channel 16, show only artifacts without any signal (Fig. 3A).

3.4. Identifying sources for late response in ESRs and synchronization with EMG activity recorded in IONM

To analyze the synchronization between the EMG component (secondary or late response) in ESRs and intramuscular needle EMG recordings, the signal was truncated to include only the late response in the ESRs (Fig. 3B). The same truncation was applied to intramuscular EMG recordings so to keep the analysis window consistent for both compared signals (Fig. 4A). Represented in Fig. 4 is an example of data zoomed in from a time window of 1.5 to 8 ms in a median waveform of ESRs from electrode 10 and EMG recordings from L-AB. The local detected peaks of both recordings are indicated when there is a physiological event captured in each recording, respectively. This event map indicates that some activity might be synchronized in the early parts of this recording, from 2 to 3 msec, while events later in the map show that activity from both channels is more likely out of phase (Fig. 4). As the intramuscular recordings move distally from the SCS site, the early part of the intramuscular EMG recordings showed little activity before approximately 20 msec, such as left and right IL muscles, and left and right TA/EHL muscles. The very distal muscles, such as AH for both sides, and right-side GAS and TA/EHL muscle groups, recorded no response within the 50 ms recording window (Figs. 2 and 5).

Next, we quantified the number of synchronized late response events in the ESR and the events in intramuscular EMG. Calculations performed

on data from both patients revealed the highest number of synchronized peaks were detected between the ESRs and the intramuscular recordings of rectus abdominus (AB) muscles (Table 1 and 2). In contrast, the intramuscular EMG recordings from very distal muscles in the lower extremity showed few synchronized peaks with ESRs or had no evoked muscle responses.

To determine if the observed number of synchronized peaks exceeded what would occur by chance, we conducted a Monte Carlo simulation to understand the probability distribution of these synchronized peaks. Over 10,000 iterations of simulation, the probability of observing more than 3 synchronized peaks by random chance was lower than 0.05 (Fig. 6). Therefore, the synchronized peaks observed between the AB muscle groups and ESR recordings are likely due to the synchronization of the underlying physiological activity. This measurement was not observed in more distal muscle groups (Table 1 and 2). In summary, the results suggest that AB muscles on both sides of the body likely contribute to the late responses recorded in the ESRs.

4. Discussion

Epidural spinal recordings are signals that are collected from electrodes on implanted SCS leads. In both preclinical and clinical studies, ESRs can be divided into two distinct components: the first/early responses are ECAPs that are a result of compounded neuronal activation from dorsal column fibers and the secondary/late responses have been hypothesized to correspond with nearby evoked muscle activities (Falowski et al., 2022, Lam et al., 2023, Verma et al., 2023). Late responses are usually characterized with larger latency from the stimulation artifact and longer signal duration compared to that of first responses (Falowski et al., 2022, Verma et al., 2023). However, there is a lack of studies identifying the specific physiologic sources of the late response in ESRs. In some rodent preclinical studies, researchers indicated that part of the late responses collected in the spinal recording could be due to the synaptic activity in the dorsal horn of the spinal cord (Sharma et al., 2023). However, a later study in a swine model revealed that the late responses were eliminated by muscle blocker, suggesting that the late response in the ESRs is a result of evoked EMG from muscle contractions (Deshmukh et al., 2023, Deshmukh et al., 2024). Thus, the goal of this case study was to explore the possible correlation between the recorded late responses in the ESRs and the intramuscular needle EMG recordings collected during the intraoperative procedure.

EMG responses recorded from intramuscular needles are commonly used in intraoperative procedures to guide lead placement for SCS therapy (Shils and Arle, 2018, Falowski et al., 2022). The late response in the ESR could potentially be useful for: 1) providing muscular signals without the need to for intramuscular EMG electrodes, or 2) adding additional physiological signals for use in IONM during clinical practice without increasing hardware complexity. A previous study suggested that the late response captured in the ESRs could guide medial–lateral lead placement during SCS surgery by referring to the ratio between first response and secondary response (Falowski et al., 2022). In this case report, our results indicate that when using the two most caudal electrodes for stimulation, the late response in the ESRs is unlikely to correlate with EMG recordings from the distal lower extremity muscles. In contrast, the late response in ESRs is likely correlated with evoked EMG from the abdominal muscle groups. We observed synchronizations of evoked activity events between the recorded late responses in the ESRs and the intramuscular needle recordings from abdominal muscle groups (Figs. 5, 6, Table 1 and 2).

Another finding of this research is that the late response in ESRs is not solely formed from the recorded EMG sources during IONM. Therefore, further studies are needed to understand how the abdominal muscle activation can be separated from the late response in the ESRs, and whether the remaining components of the late response represent other physiologic events. The observation that not all the extracted events of the late response in ESRs synchronize with those in intramuscular EMG recordings from the abdominal muscle groups suggests that abdominal muscles may be just one of several sources for the late response captured in the ESRs (Fig. 5). There may be other muscle groups contracting during SCS near the implanted leads that also contribute to the late responses captured in ESRs. These muscle groups might not be within the coverage of the intramuscular needles, as the standard intraoperative neuromonitoring practice target specific muscle groups (Macdonald et al., 2013, Shils and Arle, 2018, Falowski et al., 2022). Some preclinical studies have shown that paraspinal muscles, such as the intercostal muscle and longissimus muscle groups, can be activated and contract heavily near the implantation site during SCS at higher stimulation amplitudes (Deshmukh et al., 2023, Verma et al., 2023, Deshmukh et al., 2024). In addition, future studies should consider using multiple pairs of electrodes for stimulation to determine if the stimulation location impacts the recorded ESRs.

Although the detailed neurological mechanism behind muscle activity captured in the spinal recording is not fully understood, several hypotheses may explain it. One possibility is that the evoked EMG response in the muscle groups results from orthodromic activity induced by the stimulation placed on the dorsal column of the spinal cord. This stimulation activates sensory afferents, which in turn activates interneuron circuitry in the dorsal horn, ultimately leading to the activation of motor neurons that innervate these muscle groups (Gerasimenko et al., 2006, Deletis et al., 2018, Schlaeppi et al., 2023). In addition, it is possible that stimulation current spreads onto the ventral rootlets which directly activates the motor fibers, given the proximity of dorsal and ventral rootlets on the lateral side of spinal cord (Cuellar et al., 2017, Lam et al., 2024). As a result, the late response recorded from the epidural SCS leads may reflect the muscle activity from nearby abdominal, paraspinal, and other muscle groups. This could be due to their proximity to the implanted SCS leads, or the proximity of neural pathways related to these muscle groups to the implanted SCS leads.

Table 1
Number of synchronized peaks between detected events from each median ESR and intramuscular EMG recording on the right and left sides of the body from patient 1.

ESR channel		AB	IL	VM	TA/EHL	GAS	AH
10	Left	4	2	1	1	1	/
	Right	4	2	1	/	/	/
11	Left	4	1	0	0	0	/
	Right	3	1	1	/	/	/
12	Left	4	1	1	0	0	/
	Right	2	1	1	/	/	/
13	Left	4	1	0	0	0	/
	Right	3	1	1	/	/	/
14	Left	6	3	3	2	2	/
	Right	8	2	1	/	/	/
15	Left	6	2	3	2	1	/
	Right	7	2	1	/	/	/

Table 2
Number of synchronized peaks between detected events from each median ESR and intramuscular EMG recording on the right and left sides of the body from patient 2.

ESR channel		AB	IL	VM	TA/EHL	GAS	AH
10	Left	3	1	0	0	0	/
	Right	3	3	2	/	/	/
11	Left	2	1	0	0	0	/
	Right	3	2	1	/	/	/
12	Left	2	1	0	1	0	/
	Right	6	1	0	/	/	/
13	Left	3	2	0	1	1	/
	Right	4	0	0	/	/	/
14	Left	3	0	1	0	0	/
	Right	5	0	1	/	/	/
15	Left	1	0	1	0	0	/
	Right	3	1	1	/	/	/

With further validation, this information could simplify IONM by eliminating the need for intramuscular EMG electrodes in the abdominal muscles during SCS procedures. All the evidence together indicates that the spinal motor circuitry is activated during SCS, and the late response captured in the ESRs is at least in part an indicator of this motor activation.

Moreover, recent studies on novel applications of spinal cord stimulation have demonstrated potential in restoring some motor functionality during neurorehabilitation for subjects recovering from spinal cord injury and stroke (Darrow et al., 2019, Lorach et al., 2023, Powell et al., 2023, Mukhametova et al., 2024). In these studies, spinal motor circuits associated with distal muscles are thought to be activated during stimulation. Successful targeting of these motor circuitries is critical for effective neurorehabilitation activities (Hofstoetter et al., 2021, Merkulyeva et al., 2021). In this report, we present an initial effort to investigate the origins of late responses collected from the ESRs. These late responses could indicate spinal-motor activation, which may be important for various new applications of spinal cord stimulation in neurorehabilitation.

However, we must recognize the limitations of using industry standard SCS leads to investigate the signal sources of the evoked late response in the ESRs. Previous studies have shown that placement and size of recording electrodes significantly affect the quality of neural recording obtained in the epidural space. Preclinical studies on the swine animal model indicate a more lateral placement of the lead can enhance the recoded late response (Lam et al., 2023, Verma et al., 2023). In another study, researchers employed smaller electrode contacts with a closer inter-contact spacing on a flexible substrate. This design conforms to the spinal cord anatomy and the organization of rootlets entering it, allowing for a detailed investigation of evoked responses in spinal recordings (Russman et al., 2022). The research findings indicated much smaller recording contacts can reveal the detailed spinal signal propagation, with each contact providing much higher spatial and temporal resolution (Russman et al., 2022). In contrast, the individual recording electrodes on a SCS lead used in the study are significantly larger compared to the micro-anatomical structure of dorsal column and rootlets (Cuellar et al., 2017, Chin et al., 2024, Lam et al., 2024). As a result, the recoded signal might have very low spatial resolution. Thus, future studies should consider using smaller recording contacts to further investigate the late responses in the ESRs, while covering a larger medial and lateral anatomical area of the spinal cord. Additionally, understanding the impact of nearby individual spinal dorsal rootlets and stimulation locations on the collected ESRs, along with additional EMG recordings from distal and paraspinal muscles, may provide further insights into the sources of the late responses in the ESRs and their potential clinical applications.

In summary, this case report suggests that the evoked late response captured in the ESRs is unlikely to correlate with contractions of distal muscle groups in the lower extremities but may be synchronized with contraction of nearby abdominal muscle groups. Recordings from more subjects are needed to validate this observation. Although, it is technically feasible to record evoked activity using clinically available SCS leads with their standard electrode size, the ESRs alone cannot yet replace all intraoperative neuromonitoring procedures for lead placement and dermatomal mapping for patient programming. However, with further validation, there is potential value in using the late response in ESRs to simplify IONM practices, such as eliminating the need to instrument abdominal muscles, or to provide new information from other muscle groups that not currently covered by IONM practices, like paraspinal muscles. Furthermore, the late response, as an indicator for spinal-motor activation, may become an important signal for emerging SCS applications in neurorehabilitation for motor control.

5. Conclusion

Standard intraoperative neuromonitoring procedures use evoked intramuscular EMG to indicate dermatomal coverage. Evoked responses recorded directly from the SCS lead are emerging as a new source of information for both intraoperative and postoperative use in SCS. This research shows that when the most caudal contacts on a SCS lead are used for stimulation, the evoked late responses recorded from the other SCS lead contacts are unlikely to originate from lower extremity muscle activation. Instead, this research suggests that late responses in the spinal recordings are likely partially composed from EMG signals from nearby abdominal muscles. Further research is needed to determine if other muscle groups not covered by current intraoperative neuromonitoring procedures, such as intercostal and longissimus muscles in the back, are also represented in the late response. Finally, further validation of these findings may establish the late response in ESRs as a crucial signal for guiding emerging SCS applications in neurorehabilitation.

Author contribution

SF and MZ designed the study. SF performed all the surgeries. SF, AN and MZ collected the data. MT, AD, DP and MZ analyzed the data. SF, AD, AN, DP and MZ contributed to writing the manuscript.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: SF consults for Abbott Neuromodulation and serves as a consultant for Medtronic, Saluda, Vertos, CornerLoc, Mainstay. SF has an equity interest in SurgenTec, SynerFuse, Aurora Spine, Thermaquil, SPR Therapeutics, Saluda, CornerLoc, PainTeq, BackStop Neural, Neural Integrative Solutions, SpineThera, Celeri. Additionally, SF conducts research with Aurora, Mainstay, Medtronic, Abbott, Vertiflex, Saluda, Nalu, CornerLoc, Biotronik. MT, AD, DP, AN and MZ are employee and workers paid by Abbott Neuromodulation.

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