Proc. Annual Meeting of the Austrian Society for Biomedical Engineering 2021

DOI: 10.3217/978-3-85125-826-4-11

POLYSYNAPTIC RESPONSE ACTIVITY IS PREFERABLY ENGAGED BY SPINAL CORD STIMULATION WITH REPETITIVE PATTERNS

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Abstract— *In the last couple of decades, Spinal Cord Stimulation (SCS), either epidural or transcutaneous, has become a strong research branch in neuromodulation. In an initial effort to understand the mechanisms behind SCS, the monosynaptic reflex loops have been well studied; however, very few studies focus on the polysynaptic responses, which appear after 50ms. Here we study how low repetition continuous stimulation promotes the appearance of such responses as well as basic characteristics of their behaviour. Although limited to a single case, it shows that the versatility of the polysynaptic responses might be a pivotal element to understand how polysynaptic circuitry can be engaged to help the restorative neurological process.*

Keywords— *SCS, monosynaptic reflex, polysynaptic reflex*

Introduction

Spinal Cord Stimulation (SCS) to treat paralysis, either with an epidural or transcutaneous approach, has become a strong research branch in neuromodulation in the last couple of decades. In an initial effort to understand the mechanisms behind SCS, the monosynaptic reflex loops have been well studied; however, very few studies focus on the polysynaptic responses, which appear after 50ms. On the other hand, the application of SCS already as a possible treatment had led to some promising results [1]–[3]. However, these reports remained a limited series of clinical cases, and the generalized application remains limited by the lack of information on how to identify responders from non-responders.

SCS relies on the selective activation of the posterior afferent branches of the spinal roots. After an electrical stimulus, axons in the posterior roots are activated, triggering the reflex circuits in the lumbosacral spinal cord. Multiple reports have helped characterize the output of such a circuit, but most of them have focused on the mono- and oligosynaptic phase only or in evoked EMG-like activity.

This report analyses the posterior root reflex activity at latencies between 50 and 400ms and how they evolve with increasing intensity and repetitive stimulation.

Methods

Low-frequency SCS stimulation was applied in a person with a motor discomplete Spinal Cord Injury (SCI).

SCS was applied non-invasively using a transcutaneous bipolar setup [4]. Briefly, the cathode was placed at the vertebral level T11-T12 and the anode 10cm below. The stimulation pulses consisted of biphasic current-controlled rectangular pulses of 1ms per phase. Stimulation was delivered by a STMISOLA stimulator (Biopac Systems Inc., USA). A custom programmed Labview (National Instruments Inc., USA) interface was used to control the stimulator via a D/A converter module (USB-6221 OEM, National Instruments Inc., USA).

SCS was applied in single pulses and continuous mode. For single pulses, 8s delay was allowed between pulses. Recruitment curves were acquired by a stepwise increase of amplitude, starting from 60mA until 100mA per pulse phase in increments of 5mA. For continuous mode, a rate of 2 pulses per second (pps) was used. In the present case, the maximum intensity applied was 95mA, the individual threshold for perceiving discomfort.

The response of the central nervous system was indirectly monitored via surface electromyography on the lower limb muscle groups. Specifically for this report, left Quadriceps (LQ), Hamstrings (LH) were chosen.

The monosynaptic responses were quantified as the peak-to-peak value (mVpp) of the short-latency re-

Published by Verlag der TU Graz
Graz University of Technology

 DOI: 10.3217/978-3-85125-826-4-11

sponse, which appears between 5-50ms post-stimulus.

The polysynaptic responses were identified as bursts of activity higher than the noise level (15µV) that last for at least 3ms. If at least 5ms separated above-threshold activity, then they were considered part of different polysynaptic discharges.

Results

Consistent with other reports, the results show that SCS can elicit monosynaptic responses in all muscles (Fig. 1). These responses have an intensity-dependent amplitude, aligning with the concept that higher intensities synchronously recruit a higher number of afferent nerve fibres. Even at the low stimulation rate used in continuous mode, post-activation depression is already visible in the monosynaptic responses (Fig. 2).

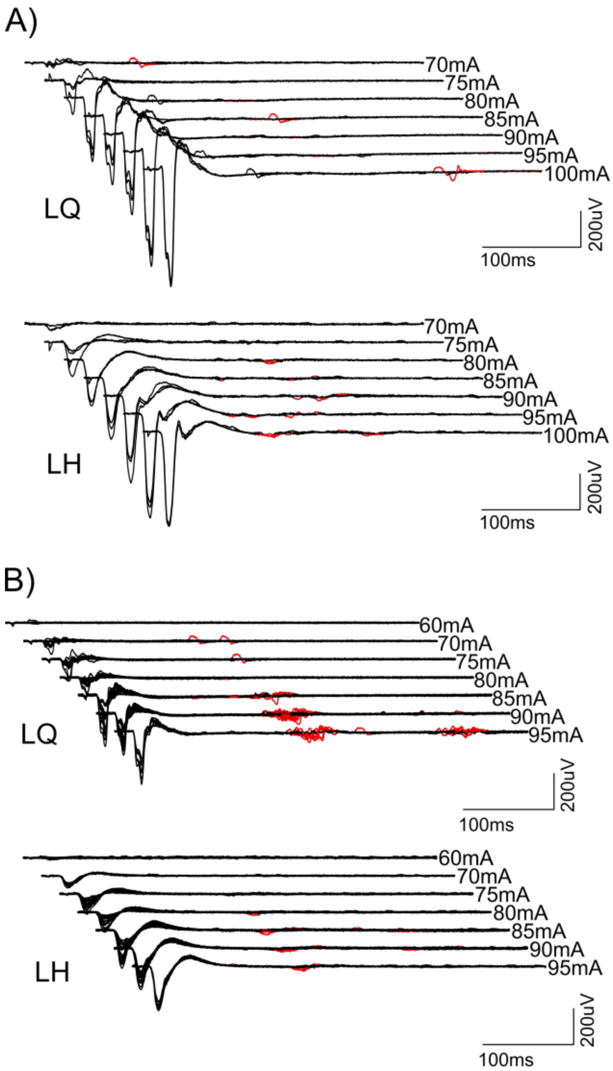

Figure 1: Responses elicited by A) single and B) 2pps repetitive stimulation. Red marks correspond to polysynaptic activity,

Polysynaptic responses are characterized by asynchronous motor unit discharges distributed in tens to hundreds of milliseconds.

Polysynaptic responses were observed mainly at 2pps stimulation and only at LQ and LH. Polysynapic responses had a higher stimulation threshold with 85mA and 80mA for LQ and LH, respectively, in contrast to their monosynaptic threshold of 75mA and 70mA.

On each muscle, the aspect and behaviour of the polysynaptic responses looked different in shape, latency, and duration. On the other hand, within the same muscle, the responses were consistent, at least regarding the latency.

Interestingly, in LQ, a second group of polysynaptic activity started to appear at 90mA and was fully established at 95mA.

Discussion

While intensity has a significant effect on the occurrence of polysynaptic responses, higher stimulation intensity does not necessarily lead to higher response amplitudes; but instead, other complex changes could be observed, like the grouping of spread discharges or triggering spasms-like activity [5].

Here is shown how, on the same subject, single and still low repetitive stimulation with 2pps produced an input to the central nervous system that resulted in entirely different behaviour. Since the electrode configuration and setup remain the same, the only explanation is the role of temporal variables evoked with continuous though slow repetition of stimulation. In this case, we report observations with 2pps only, since it allows us to observe the responses directly. However, it is expected that with higher stimulation rates, where the period between stimuli is shorter than the latency of the polysynaptic responses, the effects would be observed not as direct discharges but as modulation. Thus, while the post-activation depression is well studied and explains observed habituation of the monosynaptic reflexes, the control strategies for polysynaptic responses are still to be studied and understood in more detail.

This case report shows how the rhythmical activation of the same motor pool can facilitate the consistent activation of the polysynaptic circuitry. It also shows how the polysynaptic response amplitude is dependent on the intensity, but not in a linear way. Specifically, it appears that increasing the intensity facilitates the synchronization of all elicited responses. Moreover, the triggering of a completely new group of polysynaptic responses suggests complex interneuron processing, namely since in the presented example,

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it appeared only in one of the four main lower extremity muscle groups.

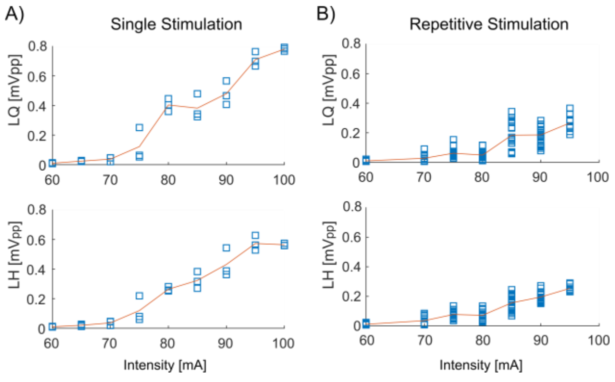

Figure 2: Recruitment curves of the monosynaptic reflexes evoked by A) single and B) 2pps repetitive stimulation. Squares represent the single points and continuous line the average.

Mono- and oligosynaptic reflex loops are essential to characterize the lumbosacral circuits. However, they remain just an artificial response to an unphysiological grouped sensory input, which does not exist in the same form in natural conditions and, therefore per se, are not enough to understand the engagement of deeper polysynaptic circuits involved in the volitional movement.

Further studies on the behaviour of these polysynaptic responses will be necessary to characterize individual functional profiles of spinal cord injury and understand how to gain reliably control over these reflex mechanisms, as well as to understand their role in coordinated interaction between multiple bilateral muscle groups and how to neuromodulate the motor behaviour as a whole, rather than just in limited reflex loops.

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