Automatic clustering of spinal reflexes evoked by epidural electrical stimulation of the cervical spinal cord in non-human primates

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***Abstract*— Epidural electrical stimulation of the spinal cord elicits motor responses by recruiting large sensory afferents in the posterior roots. Divergence of excitatory inputs provided by these fibers generates a variety of shapes, latencies and amplitudes in the electrical responses recorded from skeletal muscles. Interpretation of these signals is pivotal to the tuning and optimization of stimulation parameters. Here we present an automatic approach to identify and sort different arm muscle responses elicited by epidural stimulation of the cervical spinal cord in monkeys. We tested the efficiency of our algorithm both at rest and during behavior.**

I. Introduction

Epidural Electrical Stimulation (EES) of the spinal cord could facilitate movements both animal models and humans with spinal cord injury. EES trans-synaptically recruits motor responses by activating large sensory fibers [1]. The complex and non-univocal connectivity of spinal circuits causes a divergence of excitatory input that results in motor responses featuring multiple shapes, latencies and amplitudes. Efficacy and specificity of EES depends on the targeted circuits whose responses are modulated during movement and in responses to different stimulation frequencies [1]. Therefore, a mapping of the reflex responses to different stimulation configurations and parameters is pivotal for an accurate selection of the stimulation pattern. Here we present an automatic approach that allows to identify and analyze differences in shapes of evoked muscle responses thus allowing an interpretation of the targeted spinal networks.

II. Methods

The experimental protocol was approved by the cantonal (Fribourg) and federal (Swiss) veterinary authorities (authorization No. 2014_42E_FR). We implanted a macaque monkey with a tailored soft spinal implant with eight stimulation contacts targeting C6 to T1 dorsal roots. We delivered single pulse stimulation at different current amplitudes and inter-pulse intervals, from each contact of the spinal implant in two experimental conditions: 1) while the animal was kept in deep anesthesia (0.1–0.4 mg/kg/min); 2) while the animal was performing a three-dimensional reach and grasp task. In both conditions, we recorded intramuscular EMG activity from n=8 muscles. We segregated each muscle response by looking at an interval of 20 ms after each stimulation pulse and performed a Principal Component Analysis on the waveforms. This analysis allowed us to highlight clusters of evoked muscle responses. After optimizing the number of clusters, we applied k-means clustering. As a result, motor responses with different shapes and peaks amplitudes were sorted in clusters.

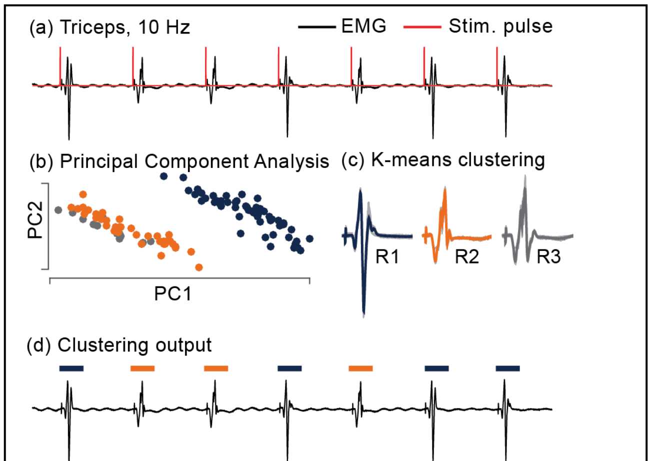

Figure1 : (a) Triceps muscle responses to stimulation pulses delivered at 10 Hz; (b) Clustering of the different responses in principal components space; (c) Muscle responses clustered in three different classes. The colored trace shows the average response. (d) Results of the clustering output on the electromyographic trace shown in (a).

III. Results and Conclusions

We analyzed the temporal sequence of spinal reflexes for each clusters to investigate the dynamic effects of repetitive stimulation on the shape of muscle evoked-potentials. Our method was able to efficiently segregate complex muscle responses, highlighting specific differences in peaks latencies and amplitudes. Figure 1 shows an example of muscle responses evoked by a series EES pulses delivered at 10 Hz. The PCA analysis highlighted the presence of two distinct evoked potentials that strongly differentiated in terms of amplitude and latency of peaks. In conclusion, our algorithm could sort different muscle responses, therefore allowing the analysis of the effects of stimulation parameters on spinal reflex networks both at rest and during behavior.

References

[1] Hofstoetter, U. S., et al, Periodic modulation of repetitively elicited monosynaptic reflexes of the human lumbosacral spinal cord. *J Neurophysiol* **114**, 400-410, doi:10.1152/jn.00136.2015 (2015)

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