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A novel reflex analysis of healthy and spinal cord-injured individuals

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Abstract: Spinal cord injury (SCI) has a drastic effect on the quality of life of those affected. There is thus a great need for new knowledge that may increase their quality of life. The goal of this research was to develop and set up a measurement system for exact measurements of times between events in a patellar reflex test and a transcutaneous spinal cord stimulation (tSCS) and compare the two in healthy and spinal cord-injured individuals. 21 individuals with a healthy nervous system and 2 spinal cord-injured individuals were subjected to the patellar reflex test and tSCS. The patellar reflex of one individual with a complete SCI at vertebras C6-C7 after an accident was delayed by 24% compared with the healthy subjects, while the reflex time of the other SCI individual, who had cancer in vertebra T3, was shortened by 23%. There was also a difference in the reflex between the patellar reflex test and the tSCS due to action potential conduction distance. In this study, a processing method was created for comparing muscle signals generated by patellar strikes or electrical stimulation to the posterior nerve roots. Data from the subjects with central nervous system lesions showed characteristic differences from reference data.

Keywords: Electromyography (EMG), Posterior root-muscle (PRM) reflex, Patellar reflex test, Spinal cord injury (SCI).

1 Introduction

In Iceland, population 360,000, around 7.8 individuals are diagnosed with SCI annually [1] and 250-500 thousand people suffer from it worldwide [2]. Spasticity is a known common side effect of SCI. Lance published this commonly cited definition in 1980: "Spasticity is a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper excitability of the stretch reflex, as one component of the upper motor neuron syndrome" [3]. In the past, human spinal motor control has been considerably researched in connection with SCI. But there is a huge potential for progress through research on SCI neurophysiology, for a better understanding of the mechanism behind the patients' symptoms, and for the development of new therapies [4].

Stretch reflex plays an important part in maintaining muscle tone and posture. A classic example of a stretch reflex is the patellar reflex, which is used routinely in neurological examinations. The patellar reflex is elicited by tapping the patella tendon. The stretch stimulates the muscle spindles, which leads to impulses being sent to the spinal cord via sensory afferents. The sensory fibers branch as they reach the spinal cord and make monosynaptic contact with the lower motor neurons, which stimulates the muscles to contract. The muscle shortens when it contracts, the muscle spindles stretch, and their afferent activity decreases. Furthermore, sensory neurons act indirectly with interneurons to inhibit flexor motor neurons that would otherwise contract the opposite muscle, the hamstring. As a result of this, the leg extends at the knee joint as the quadriceps muscle contracts suddenly and the hamstring relaxes [5, 6].

Transcutaneous spinal cord stimulation (tSCS) is a non-invasive method by which electrodes are placed on the skin above the spine and generate stimulation waveforms that appear to travel via the dorsal roots and activate the spinal circuitry [8]. The H-reflex, which is analogous to the stretch reflex, is triggered when the sensory fibers are electrically stimulated. The H-reflex differs from the patellar reflex in that it is caused by electric stimulation [7]. Posterior root-muscle (PRM) reflexes are spinal reflexes elicited by electrical stimulation of the posterior roots of the lumbar and upper sacral area. PRM reflexes have several physiological properties in common with the H-reflex, however, they can be elicited bilaterally in all major lower limb muscle groups by a single stimulus pulse [8]. This study examined the difference between signals from tSCS and patellar tendon stretching to see whether it provided information on changes to the neural system after damage.

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2 Materials and methods

Units from *KISO KineLive* containing a wireless surface electromyography (EMG) biofeedback system (Kiso ehf., Reykjavík, Iceland) were used to record EMG data. Their sampling frequency was 1600Hz and the signal bandwidth was 16-500Hz, with 20dB/dec filtering. A 64-channel electroencephalography (EEG) cap from *antNeuro* was used to record EEG along with the eegomylab amplifier. The sampling rate of the EEG was 2048Hz and the bandwidth was 0-532.48Hz (0-0.26*sampling rate). A reflex hammer, custom-built by our group, was used to elicit the patellar reflex. It was designed to work with the Kine EMG device and included an accelerometer to accurately measure the force on the subject's tendon and its timing.

2.1 Physiological measurements

The physical characteristics of the measured individuals are presented in table 1.

Tab. 1 – Physical characteristics of the participants.

Healthy	N	Age (years)	Height (cm)	Weight (kg)
Male	11	23.83±2.37	187.17±7.72	83.58±11.84
Female	10	23.4±1.5	169.2±7.4	69.2±7.4
SCI	**Age (years)**	**Height (cm)**	**Weight (kg)**	**SCI level**
S01	60	185	63	C6-C7 (complete)
S02	31	185	78	T3 (incomplete)

The first SCI subject (S01) had a spastic right arm and suffered from neuropathic pain. On the day of measurement, he had recently taken the medication Gabapentin which can influence both the creation of electrical impulses in nerve cells and the function of neurotransmitters. The second SCI subject (S02) had a spastic and hypersensitive right leg. He was able to walk without the help of devices. He occasionally underwent Botox treatments for the spasticity. These SCI subjects were older than the members of the reference group, however, measurements of all age groups are planned for a later time.
During the physiological measurements, EEG and EMG were recorded, taking special care of synchronization. The protocol is illustrated in figure 1.

Transcutaneous spinal cord stimulation

The electrode placement was determined by locating vertebrae L4, which is in line with the top of the iliac crest, and counting upwards to T11 and T12. A single (hydrogel) surface electrode with a 5 cm diameter was then placed between vertebras T11 and T12 and a 5 cm wide surface reference node was placed below vertebra L2, as there is little active tissue in

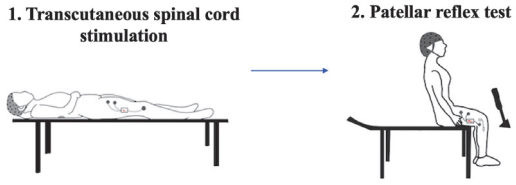

Fig. 1 – Protocol for the physiological measurements. Transcutaneous spinal cord stimulation was first established and then the patellar reflex test.

that area. The KineLive EMG units were used to capture EMG data from the quadriceps muscle during tSCS. The EMG anode was placed one-third of the length from the subject´s hip joint to the upper edge of the patellar bone. The EMG cathode was positioned 6 cm lower. Before the EMG electrodes were applied on each leg, the skin was exfoliated with alcohol, and conductive gel was added to the electrodes to increase conductivity. The subject then lied down in a supine posture with a pillow under his or her neck to ensure that the EEG cap did not rub against the bench and produce noise. A charge-balanced, symmetrical, biphasic rectangular pulse of 1 ms width per phase was delivered by a current-controlled stimulator (type r2X from Schuhfried). For eliciting PRM reflex, the current was varied from 30 to 55 mA. The pulse pause was set to 2 seconds as it was found to suffice for effective contraction and for data analysis. The recording lasted 3 minutes.

Patellar reflex test

The patellar reflex test was triggered by the hammer impacting the patellar tendon. The EMG electrodes were placed on the quadriceps of both legs in the same positions as for the tSCS, and a goniometer was positioned beside the right knee. The subject was seated on a bench with his or her legs hanging freely. The patellar tendon was struck with the reflex hammer for 5 minutes (each leg) while EMG and EEG were recorded. The patellar reflex test then continued while the subject performed the Jendrassik maneuver (locking fingers together and pulling the hands apart with as much power as possible while keeping them locked) for 15 seconds, resulting in approximately 7 strikes.

2.2 Data analysis

This study followed existing research into evoked potentials and brain connectivity in relation to EEG. However, this study only focused on the EMG data. The pipeline to analyse the data was implemented in *Matlab R2020a*. A flowchart of the pipeline is illustrated in figure 2. The recorded data was imported into Matlab and each hammer/impulse peak was collected so that the EMG from the muscle could be synced with the impact/impulse. By detecting and synchronizing these

peaks, the EMG data could be divided into epochs each of which comprised a response to the hammer/stimulus. The response (epoch) was then plotted for visualization. The code was designed so that the interface asked the user whether the reflex was acceptable, i.e. free from digital noise resulting from low amplitude (<0.05 mV) and able to detect the critical time points, e.g. the latency. Unacceptable responses were dropped. Acceptable responses were stored in a new vector and subjected to a frequency domain analysis. If it indicated that 50 Hz noise was disrupting the signal, the signal was filtered with a 50 Hz notch digital filter. The signal was then ready for further analysis. The timepoints of each wave were captured, i.e the latency, peak, and end of the wave. Also, mean values and standard deviations were calculated for each subject.

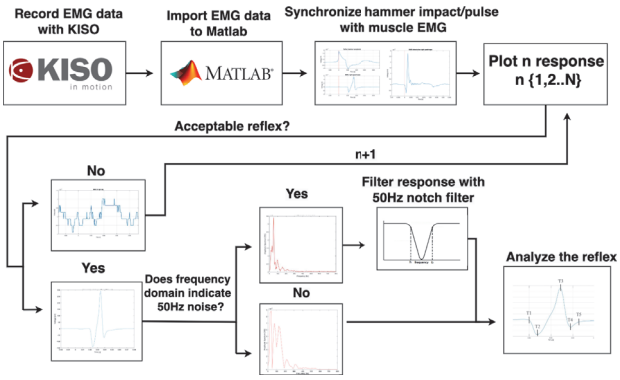

Fig. 2 – Pipeline for data analysis.

3 Results

A result from the study was a tested methodology for time measurements between events in reflex tests as well as a developed pipeline for their further analysis. For young healthy individuals a reference database has been established. This database enables a statistical evaluation from this group. The mean values and standard deviations from tSCS and the patellar test are illustrated in table 2. From the healthy subjects, the results indicated that the PRM reflex latency, peak, and endpoint started 6.91±2.67 ms, 17.03±6 ms, and 28.75±7.36 sooner than the patellar reflex. The measured patellar reflex from S01 started 24.3% later and ended 29% later than the healthy group. From S02, the patellar reflex began 22.57% sooner in the right leg while it started 9.46% sooner in the left leg compared to healthy. Additionally, the reflex ended 15.9% sooner in the right leg and 4.9% sooner in the left leg compared to healthy. This demonstrates a difference between legs. The PRM reflex could not be elicited from S01 with tSCS, possibly due to bad scoliosis, not optimal electrode position or medication intake. The PRM reflex latency difference between the healthy subjects and S02 was 1.95±1.74 ms in the right leg and 1.99±1.71 ms in the left leg, whereas the endpoint was 6.97±3.07 ms in the right leg and 6.98±4.87 ms in the left leg, resulting in a quite high standard deviation.

Tab. 2 – Average EMG time values between stimulus and start (latency), peak, and endpoint of muscle reaction. Note: The standard deviation for healthy is calculated from the average of all subjects, whereas the standard deviation for S01 and S02 is calculated from all responses. R indicates the right leg and L the left leg.

Patellar test

Subject	Latency [ms]	Peak [ms]	Endpoint [ms]
Healthy (n=19)	16.7±2.12	35.23±3.72	58.44±6.78
SCI S01 (R)	20.76±0.77	43.72±0.91	75.42±2.04
SCI S02 (R)	12.93±0.53	31.22±0.85	49.12±1.30
SCI S02 (L)	15.2±1.17	33.67±1.12	55.57±1.17

tSCS

Subject	Latency [ms]	Peak [ms]	Endpoint [ms]
Healthy (n=14)	9.79±1.63	18.2±4.7	29.69±2.87
SCI S02 (R)	11.74±0.63	22.88±1.47	36.66±1.11
SCI S02 (L)	11.78±0.54	25.18±1.3	36.53±1.46

For tSCS, simple linear regression showed a correlation between the endpoint and height (p-val=.06) and between the endpoint and weight (p-val=.023). For the patellar reflex, a correlation was found between latency and height (p-val=.016) and between latency and weight (p-val=.0036). For other timepoints there was no correlation. A comparison between the patellar reflex performed with and without the Jendrassik maneuver is illustrated in figure 3. The patellar test performed with the Jendrassik maneuver resulted in a higher amplitude and a shorter latency than when performed without Jendrassik maneuver in the healthy subjects. In contrast the patellar test performed with Jendrassik maneuver by S02, resulted in a lower amplitude than without.

4 Discussion

The difference in the latency from the patellar reflex and the PRM reflex can be explained by the increased distance between the muscle and the spinal cord. However, an explanation for why the patellar reflex endpoint is longer than the PRM reflex endpoint can be due to better synchronization of the neurons depolarization in the latter case. When the patellar is struck, the activation of the muscle spindles is more likely to be asynchronous than when the sensory neurons are directly

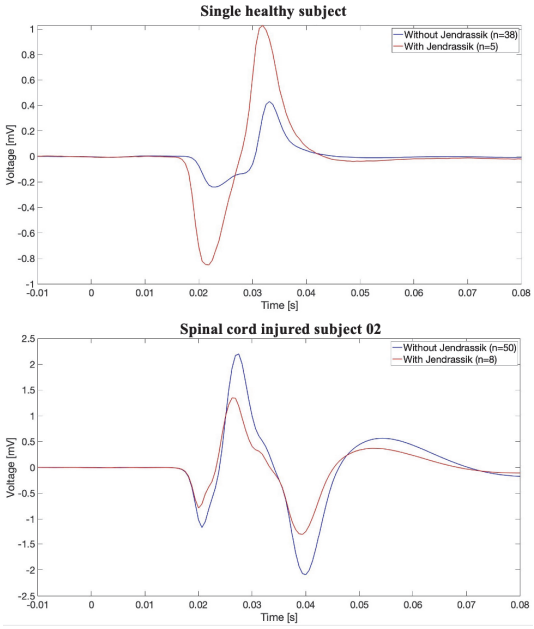

Fig. 3 – Mean patellar reflex values with and without the Jendrassik maneuver. In this example, the results are from one healthy and one spinal cord injured subject where there is no difference in the latency between the subjects. The red line represents measurements with the Jendrassik manevuer performed and the blue one without it.

stimulated. The patellar reflex latency in S02 was shorter compared to the healthy and there was a greater difference between the EMG answer in the legs in S02. This can be explained by spasticity and hypersensitivity in the right leg. The Jendrassik maneuver had additionally an inhibiting effect on S02's reflex, indicating that it reduces the sensitivity of the patellar reflex in this special case. The patellar reflex in S01, who is unable to walk, was delayed in comparison to the average value from the healthy group. The damage in the cervical spinal cord might trigger plastic changes in the spinal neural network controlling muscle contraction. The medicine Gabapentin, on the other hand, might also be influencing the reflex. As the lower limit of the deviation from the healthy average in PRM reflex reaches the mean value for S02, it is not reasonable to conclude that there is a difference in PRM reflex between healthy and S02. However, the difference is diminished when comparing the reflex between legs in S02, opposite to the results from the patellar test. This could indicate that the gamma system is affected by the injury.

Future perspective

Further research on people with and without SCI of all ages needs to be done in order to statistically significantly reveal the changes caused by damage to the central nervous system. Nevertheless, the results of the reflex tests of the healthy and SCI subjects described herein add to existing knowledge about the properties of the neuro-muscular interaction which may possibly be further transferred into the clinic.

5 Conclusion

A measurement methodology and a pipeline for data analysis was developed and tested, giving a powerful tool for further research. A reference database with recordings from young individuals with a healthy nervous system was established. A reference database for other age groups has to be established. The variability within the healthy has to be mapped. Our results indicate a significant difference between the muscle response to patellar tendon impact compared to tSCS as well as a difference in the latency and duration of the muscle answer between healthy and these two SCI subjects at stake. In this one case, we detect a lower amplitude but earlier response in the spastic leg of S02, indicating a difference that characterizes the spasticity. Further research with a higher number of SCI subjects is needed before these variables can be classified and characterized.

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