ORIGINAL ARTICLE

Relationship between median nerve somatosensory evoked potentials and spinal cord injury levels in patients with quadriplegia

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Study design: Cross-sectional study.

Objectives: To observe if there is a relationship between the level of injury by the American Spinal Cord Injury Association (ASIA) and cortical somatosensory evoked potential (SSEP) recordings of the median nerve in patients with quadriplegia.

Setting: Rehabilitation Outpatient Clinic at the university hospital in Brazil.

Methods: Fourteen individuals with quadriplegia and 8 healthy individuals were evaluated. Electrophysiological assessment of the median nerve was performed by evoked potential equipment. The injury level was obtained by ASIA. N₉, N₁₃ and N₂₀ were analyzed based on the presence or absence of responses. The parameters used for analyzing these responses were the latency and the amplitude. Data were analyzed using mixed-effect models.

Results: N₉ responses were found in all patients with quadriplegia with a similar latency and amplitude observed in healthy individuals; N₁₃ responses were not found in any patients with quadriplegia. N₂₀ responses were not found in C5 patients with quadriplegia but it was present in C6 and C7 patients. Their latencies were similar to healthy individuals ($P > 0.05$) but the amplitudes were decreased ($P < 0.05$).

Conclusion: This study suggests that the SSEP responses depend on the injury level, considering that the individuals with C6 and C7 injury levels, both complete and incomplete, presented SSEP recordings in the cortical area. It also showed a relationship between the level of spinal cord injury assessed by ASIA and the median nerve SSEP responses, through the latency and amplitude recordings.

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Introduction

The spinal cord conducts nervous impulses between the brain and the peripheral nervous system. People with spinal cord injuries (SCIs) present deficits in motor and sensory functions below the level of injury. This deficit can be assessed by the American Spinal Cord Injury Association (ASIA) impairment scale, a clinical examination of the patient, which establishes the level and type of the lesion.¹ However, evaluation through ASIA is based only on motor and sensory scores.²

Somatosensory evoked potentials (SSEPs), an electrophysiological examination, can be used as a complementary examination to determine the characteristics of the lesion and may be useful in the prognosis of SCI.³

Cerebral responses of SSEPs by electrically stimulating peripheral nerves in humans were first reported by Dawson in 1947. Subsequently, many studies on SSEP techniques have been performed⁴ for specific illness, such as stroke and SCI.

The function of central and peripheral nervous systems has been analyzed by SSEP. Patients with quadriplegia have deficits in the upper and lower limb functions. For upper limbs, the assessment of the median nerve SSEP is used most.⁵

An earlier study on patients with SCI observed cortical SSEP recordings in patients with incomplete lesions, but they were not observed in complete lesions.⁶

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On the other hand, other study showed cortical SSEP recordings both in complete and incomplete lesions. Moreover, it showed that the presence of cortical SSEP recordings does not mean sensory or motor recovery,⁷ but that these allow for a quantitative evaluation of the somatosensory system.⁸

The median nerve SSEP examination is well established to evaluate non-traumatic lesions of the cervical spinal cord. However, in traumatic lesions of the spinal cord, the significance of the median nerve SSEP for both diagnosis and course of lesion is less known.⁹

Earlier studies have reported median nerve SSEP recordings of people with quadriplegia and the data obtained have shown different responses, depending on the level and type of lesion.⁹ However, there are no studies reporting the relationship between injury level obtained by ASIA and SSEP data. Therefore, this study aimed to evaluate the relationship between the level of SCI, assessed by the ASIA protocol, and the median nerve SSEP recording, based on the latency and the amplitude evaluations by electrophysiological examination.

Patients and methods

A total of 22 patients, 14 patients with quadriplegia (C5-C7), without cranio-encephalic trauma association, with lesion for at least 1 year, and 8 healthy patients, all males, participated in this study. All patients with quadriplegia attended the Spinal Cord Injury Rehabilitation Outpatient Clinic at the University Hospital of the State University of Campinas—Campinas—Brazil. This study was approved by the local ethics committee.

Their anthropometric and lesion characteristics are summarized in Table 1.

Neurological examination was performed according to the ASIA protocol. The procedure was performed by the same physician who was familiar with the examination. The electrophysiological examination was carried out using Neuropack Four evoked potential equipment (Nihon Koden, Tokyo, Japan) with four simultaneous recording channels. The SSEPs were elicited by electrical stimuli with square wave of 0.2 ms duration at 5 Hz, applied to the median nerves of both arms sequentially, according to the International Federation of Clinical Neurophysiology standards.¹⁰ The electrode impedance was kept at 10 k Ω . Three sets of 1000 responses each were averaged and superimposed to ensure consistency and to facilitate the analysis, even knowing that two sets of 500 stimuli are enough to reproduce a good graphic response. Also, this procedure was repeated on three different days, for all patients, to calculate the average of the results. The maximum stimulus intensity was 10 mA. The amplifier was set at 5 μ V/division and the time of analysis was set at 50 ms. The stimulus intensity was adjusted to produce a clear muscle contraction or motor threshold level, and the action potential obtained in Erb's point guaranteed the appropriate stimulus. The participants with quadriplegia were evaluated while seated in their wheelchairs at room temperature.

Table 1 Anthropometric and lesion characteristics of patients with spinal cord injury

Patients	Age (years)	Weight (cm)	Time since lesion (years)	Cause of lesion	Level of lesion	ASIA
1	18	185	2	Diving	C ₇	C
2	31	185	9	Diving	C ₆	C
3	27	165	4	Car accident	C ₇	A
4	30	174	3	Car accident	C ₇	A
5	47	175	17	Diving	C ₆	A
6	32	175	10	Diving	C ₅	A
7	41	177	7	Car accident	C ₅	A
8	40	178	7	Car accident	C ₆	A
9	37	170	6	Industrial injuries	C ₆	A
10	37	181	3	Diving	C ₆	A
11	29	170	10	Wound by firearm	C ₅	A
12	35	171	6	Wound by firearm	C ₅	A
13	30	181	11	Diving	C ₅	A
14 ^a	39	167	11	Wound by firearm	C ₅	A

^aThis patient has a very asymmetric lesion; in his left hemi-body, he presents C5 injury level but, in his right hemi-body, he presents C7.

The electrodes (0.7 cm silver-cup electrodes) were attached to the skin and the stimulating electrode was located over the median nerve, near the wrist. The recording electrodes were located on Erb's point referenced to Fz (channel 3), C7 referenced to Fz (channel 2) and the C3' or C4' (based on the international 10/20 system) referenced to Fpz (channel 1). These cephalic references (Fpz and Fz) were chosen to minimize artifacts.¹¹

The electrodes used in recordings performed on the same day were not removed from the patient, but for the recordings performed on different days, the electrodes were removed and then positioned again.

The SSEP recordings were evaluated according to the responses of N₉ (Erb's point response), N₁₃ (cervical spinal cord response) and N₂₀ (cortical response). The parameters used for analyzing these responses were the latency and the amplitude.

The data obtained were analyzed based on the normal or delayed latency, and based on the normal or decreased baseline-peak amplitude (N₉ and N₂₀ peaks), when compared to healthy subjects.

Statistical analysis

Data were analyzed using mixed-effect linear models, considering the latencies and amplitudes of the N₉, N₁₃ and N₂₀ responses. The models were fitted to the data using the individuals as a random factor. Multiple comparisons were performed by contrasts. For each of the linear models, the normality of the residuals was checked using Kolmogorov-Smirnov testing. All statistical analyses were performed using SAS software version 9. The data of the patients (right and left sides) were grouped for analysis.

The results are presented as mean $\pm$ s.d. The differences were considered at $P < 0.05$. Descriptive statistical data were calculated based on the latency (ms) and amplitude (μ V) results.

Figure 1 Latencies of median nerve recordings. (a) Mean values of latency (ms) of the N₉ response of the two groups (control and patients with quadriplegia). The vertical bars represent the standard deviation. (b) Mean values of latency (ms) of the N₂₀ response of the two groups (control and patients with quadriplegia). The vertical bars represent the standard deviation. C, control; P, patients.

Figure 2 Amplitudes of median nerve recordings. (a) Mean values of amplitude (µV) of the N₉ response of the two groups (control and patients with quadriplegia). The vertical bars represent the standard deviation. (b) Mean values of amplitude (µV) of the N₂₀ response of the two groups (control and patients with quadriplegia). The vertical bars represent the standard deviation. C, control; P, patients.

Results

The description of data is illustrated in Figures 1a, b, 2a and b, which show the mean and standard deviation (s.d.) values of the latencies and amplitudes, respectively, of controls and people with quadriplegia for N₉ and N₂₀ responses.

The results show that N₉ response was present in all patients, due to the fact that this represents Erb's point and that SCI is not a peripheral but central nervous system pathology. The latency was 9.6 ± 0.61 ms for healthy people and 9.5 ± 0.54 ms for people with quadriplegia ($P > 0.05$). The amplitude was 2.9 ± 0.32 µV for healthy people and 2.8 ± 0.36 µV for people with quadriplegia, without difference between groups ($P > 0.05$).

The N₁₃ response was present in all normal patients, but not in any patient with quadriplegia. N₂₀ response, on the other hand, was absent in all individuals with C5 injury level. However, in all patients with C6 and C7 injury levels,

the response was present, whether the lesion was complete or incomplete, showing that these results are correlated with the level of lesion. Also, when N₂₀ response was present, the latency was kept as a normal parameter (not delayed), without difference between individuals with SCIs and normal patients. The latency N₂₀ was 19.6 ± 0.45 ms for healthy people and 19.8 ± 0.95 ms for people with quadriplegia ($P > 0.05$). Nevertheless, the amplitude of the N₂₀ responses in C6 and C7 injury levels (1.3 ± 0.24 µV) were significantly reduced when compared with the control group (3.3 ± 0.24 µV) ($P < 0.05$).

Figures 3, 4, 5 and 6 represent the SSEP results obtained from one normal participant, one participant with C5 injury level, one participant with C6 injury level and one with C7 injury level, respectively. The first line indicates the C3', the second line represents the C7 (cervical spinal cord) and the third line represents Erb's point. These graphs show that

Figure 3 Median nerve somatosensory evoked potentials traced from a healthy participant. The first line indicates the C3' showing the N₂₀ response inside the graph; the second line represents C7 showing the N₁₃ response inside the graph and the third line represents Erb's point (located within the angle formed by the posterior border of the clavicular head of the sternomastoid muscle and clavicle, 2–3 cm above clavicle), showing the N₉ response inside the graph.

Figure 4 Median nerve somatosensory evoked potential traced from C5 quadriplegic (no cortical response); The first line indicates the C3' showing that did not possible to observe any response; the second line represents C7 showing that did not possible to observe any response and the third line represents Erb's point (located within the angle formed by the posterior border of the clavicular head of the sternomastoid muscle and clavicle, 2–3 cm above clavicle), showing the N₉ response inside the graph.

individuals with C5 injury level had no cortical response. However, individuals with C6 and C7 injury levels presented cortical response.

Discussion

After SCI, the communication between the sensory and motor fiber tracts and the rest of the nervous system and other systems is limited.

A better understanding of the relation between the lesion level evaluated by ASIA and electrophysiological responses obtained by SSEP is important. Whereas the evoked potential examination is not always possible in clinical practice, ASIA is a simple evaluation, easy to apply and without any cost. Thus, the ASIA evaluation can give an idea about these limits¹ and the expected cortical responses depending on the SCI.¹²

In quadriplegia, the knowledge of SSEP median nerve response can be important for rehabilitation, as the median

Figure 5 Median nerve somatosensory evoked potential traced from C6 quadriplegic (with cortical response). The first line indicates the C3' showing the N₂₀ response inside the graph; the second line represents C7 showing that did not possible to observe any response and the third line represents Erb's point (located within the angle formed by the posterior border of the clavicular head of the sternomastoid muscle and clavicle, 2–3 cm above clavicle), showing the N₉ response inside the graph.

Figure 6 Median nerve somatosensory evoked potential traced from C7 quadriplegic (with cortical response). The first line indicates the C3' showing the N₂₀ response inside the graph; the second line represents C7 showing that did not possible to observe any response and the third line represents Erb's point (located within the angle formed by the posterior border of the clavicular head of the sternomastoid muscle and clavicle, 2–3 cm above clavicle), showing the N₉ latency inside the graph.

nerve is responsible for the sensory and motor control of some parts of the forearm (innervating the deep muscle group of the anterior compartment of the forearm, except for the medial half of flexor digitorum profundus, and supplying sensory innervations to the lateral skin of the hand palm, except for the digits).¹³

The SSEP examination, a non-invasive technique, permits an evaluation of the damage in peripheral and central nervous systems and is less influenced by the patient's

cooperation. Moreover, it can be quantified.¹⁴ The ASIA, on the other hand, needs the patient's cooperation and cannot be quantified.

Some authors defend that the median nerve originates from roots C6–T1.^{15,16} However, there are some authors who defend that C5 roots also belong to the median nerve,^{9,17} or that the median nerve is connected to the musculocutaneous nerve, which originates from roots C5–C7.¹⁷ Despite the aim of this study not to evaluate the upper extremity

anatomy, the results suggest two hypothesis. One of them is that the median nerve really carries the C5 innervation, and the absence of SSEP recording in the cortical area (N₂₀) of patients with SCI who presented C5 injury level probably occurred due to the fact that C5 injury level obstructs the nerve conduction through the median nerve to the brain. On the other hand, the nerve conduction can be partially preserved in lesions below C5, allowing SSEP recording in the cortical area.

The other theory is that only few C6 afferents pass through the compromised spinal territory, not enough to convey any sensation on clinical examination, but enough to evoke a cortical response through central amplification mechanisms. For confirming one of these suggestions, others studies should be carried out with anatomical character.

The statistical results showed that the latencies from N₂₀ responses of the median nerve were very similar between the healthy participants and participants with quadriplegia (C6 and C7 levels) ($P > 0.05$). The normal median nerve latencies were also found in 54% of the patients with chronic SCI observed by Curt and Dietz.⁹ However, the amplitudes results from N₂₀ responses of the median nerve were reduced in C6 and C7 patients when compared with control group ($P < 0.05$). These results are similar with the results found by Iseli *et al.*¹⁸

The SSEP recording for cervical spinal cord (N₁₃) was not observed in any individual with quadriplegia. The explanation can be associated to the presence of gliosis, syrinx or another intramedullary lesion. However, as this was an exploratory study, these results need to be confirmed by other studies with a larger sample, also investigating the reasons for the absence of N₁₃ response.

The SSEP protocol of this study was carried out using the maximum stimulus intensity at 10 mA. This has shown to be enough, as the SSEP recordings in Erb's point in all patients and in the cortical area in normal people and in patients with C6 and C7 injury level were obtained, without the need for higher intensities. Also, to assure the adequate response and to minimize hospital equipment interference, three sets of 1000 stimuli were performed.

The results have shown that the ASIA protocol, considering the injury level, is related with the SSEP responses. These SSEP responses depend on the injury level when considering the individuals with C6 and C7 injury levels, both complete and incomplete, who presented SSEP recordings in the cortical area. However, patients with C5 injury level did not present responses in the cortical area. This study included only individuals with complete C5 injuries, so it was not possible to evaluate the cortical responses in incomplete C5 injuries. Other studies are needed to analyze the electrophysiological results in patients with incomplete C5 injuries, to verify the presence or absence of SSEP recordings in the cortical area.

An intensive program of hand rehabilitation could be performed in future studies to evaluate if the presence of cortical responses in individuals with C6 and C7 injury levels

is related to motor and/or sensory hand recovery. Some authors have suggested that even patients with complete lesion can recover some motor functions below the injury level, when there are areas of partial nerve preservation, detected by SSEP assessment.¹⁹

The limitations of this study were the sample size, types and levels of injury. The latter should be more diversified.

In spite of some limitations, the study fills some gaps in the literature, as preliminary studies^{9,20} have shown that, in higher cervical lesions, it was not possible to record SSEP in the cortex compared to the lower cervical lesions; however, there are no reports specifying which injury level cannot be recorded and the reason why. Also, there are no studies that have compared the SSEP responses to the ASIA protocol. This study showed that there is a relationship between the level of SCI assessed by ASIA and the median nerve SSEP, considering the injury level.

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