

Comparison between Somatosensory-Evoked Potential Parameters in Patients with Nonspecific versus Specific Chronic Low Back Pain

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Abstract

Background: Modern pain neuroscience has revolutionized our understanding about pain, including the role of central sensitization in amplifying pain experiences with increased neuronal response to central nervous system stimuli. During external upper and lower limb perturbation, it has been shown that Chronic low back pain (CLBP) was associated with longer reflex response latencies of trunk muscles. One theoretic but rarely examined possibility for longer reflex latencies is related to modulated somatosensory information processing. **Objectives:** The objective of the study was to compare the somatosensory-evoked potential (SSEP) parameters of the right median and left tibial nerves between patients with nonspecific and specific CLBP. **Materials and Methods:** The study includes 102 CLBP patients, clinically and radiologically confirmed and divided into two groups: 48 patients with nonspecific pathology and 54 patients with specific pathology. During this SSEP study the right median and left tibial nerves of all patients were examined. Recorded parameters include the latency and amplitudes. **Results:** The means of the latencies of all the SSEP waves of the right median and left tibial nerves were only significant in the peripheral SSEP waves in the upper and lower limbs (N9 and N10, respectively) and highly significant in cortical right median N20 SSEP wave. Regarding the central sensory conduction time values, both in the median and tibial SSEP study, The significant differences was noted only in the median nerve SSEP study. Regarding the means of the amplitudes of differently studied SSEP components of the right median and left tibial nerves, it was only significant in the peripheral SSEP (N9) wave of the right median nerve and in the subcortical and cortical (P37 and N45) waves in the tibial nerve SSEP study. **Conclusions:** Results showed a significantly higher SSEP amplitude and latency in nonspecific CLBP patients as compared to their counterpart CLBP patients. This could reflect a higher excitability of sensory cortex and sensory pathways in patients with nonspecific CLBP as compared to their counterpart patients.

Keywords: Central sensitization, chronic low back pain, compound muscle action potential, somatosensory-evoked potential

INTRODUCTION

Low back pain is the most frequent complaint of humanity after the common cold.^[1,2] It is described as pain and discomfort, situated under the costal margin and above the inferior gluteal folds, with or without referred leg pain. Chronic low back pain (CLBP) is identified as low back pain persisting for at least 12 weeks. This includes all cases that may be considered as subacute back pain, cases that have continued for very long periods of time, and cases of recurrent pain in which the current episode has lasted for approximately 12 weeks. It also includes the type of patients being considered range from those who continue to function well in spite of pain to those who are severely disabled by continued back pain.^[3] Nociceptive pain means pain arising from the stimulation of nociceptors of

nonneural tissue in response to noxious chemical, mechanical, or thermal stimuli (e.g., the activation of the nociceptors in lumbar ligaments, thoracolumbar fascia, or zygapophyseal joints).^[4]

The neuropathic pain is described as a pain secondary to a disease or a lesion of the somatosensory nervous system^[4] (e.g., lower back pain [LBP] correlated with lumbar radiculopathy),

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which is a common type of lumbar neuropathic pain, whereas myofascial tissue (i.e., thoracolumbar fascia)^[5] and some lumbar ligaments^[6] have nociceptors able of creating nociceptive pain. Both Nociceptive and neuropathic pain can be classified as “specific LBP” when there is a clear pathoanatomical diagnosis. However, in about 85% of LBP patients, a defined pathoanatomical diagnosis cannot be given resultant in the label “nonspecific low back pain;” i.e., low back pain that is not attributable to a detectable, known specific pathology (e.g., infection, tumor, osteoporosis, fracture, structural deformity, inflammatory disorder [e.g., ankylosing spondylitis], and radicular syndrome or cauda equina syndrome).^[3] “Central sensitization” (CS) is explained as “an amplification of neural signaling within the CNS that provokes pain hypersensitivity.”^[7] “CS” implies that innocuous inputs from the periphery might be felt as painful if the “pain pathway” is facilitated either at the spinal or cerebral level. By extension, the hyperalgesia is documented in the subgroups of people with CLBP,^[8] in addition to the alteration of brain connectivity and morphology (e.g., dorsolateral prefrontal cortex and periaqueductal gray matter). CS is likely to show the variation of pain modulation by descending pathways that might prefer the pain persistence.^[9]

The aim of the present work is to study somatosensory-evoked potential (SSEP) values of the right median and left tibial nerves in patients with nonspecific CLBP and compare findings with those of patients with specific CLBP, mainly lumbosacral radiculopathy.

MATERIALS AND METHODS

This case-control study was conducted in the Neurophysiology Unit at Al-Imamain Al-Kadhymain Medical City, Baghdad, Iraq, for a period extended from May 2017 to January 2018. All the selected participants were enlightened about the electrophysiological examination, and informed consent for participation in the study was obtained. The examination procedure was carried out in a room with a temperature of 25°C–27°C, and a skin temperature was measured by a thermometer at the axilla, and it ranged between 36°C and 37°C. The study was approved by the Institute Review Board of the College of Medicine, Al-Nahrain University.

The study included 102 clinically and radiologically confirmed CLBP patients. These patients were referred from neurosurgery, orthopedic surgery, or rheumatology clinics by specialists, and are divided into two groups: Group 1 (48 patients) with nonspecific structural pathology and Group 2 (54 patients) with specific structural pathology. CLBP patients should meet the following inclusion criteria (minimum of 3 months history of low back pain, previous disk-related operation, clinical, radiological, and/or electrophysiological evaluations that reveal the signs of lumbosacral radiculopathy, plexopathy, spinal tumors, posttraumatic stenosis, or spondylolisthesis). The exclusion criteria include metabolic diseases, such as thyroid disease, diabetes, and uremia, and organic diseases,

such as multiple myeloma, renal disease, and collagen disease as well as psychiatric disorders. The recruited 54 patients with specific pathology were all having lumbosacral spinal stenosis. All patients were subjected to SSEP study of the right median and left tibial nerves. Conventional sensory nerve conduction, motor nerve conduction, and electromyography study were done prior to the commencement of the study to exclude peripheral neuropathy. In this routine SSEP study, Nihon Kohden subdermal monopolar needle electrodes (Ref. no. NE-115 B, manufactured by Technomed Europe Amerikalaan 17, 6199 AE) of 1.5 m length and 13 mm × 0.40 mm diameter (27G) were used. The electrode has a bared tip of 0.3 mm² surface area and 1.2 cm length.^[10]

Median nerve somatosensory-evoked potential waveforms

The median nerve was stimulated by bipolar-stimulating electrode placed over the median nerve at the wrist with the cathode proximal to the anode. The electrical stimuli were square wave pulses given at a rate of 2–3/s at high-pass filter 4 Hz, low-pass filter 500 Hz with time base 50 ms duration, and gain 5 µV/div. Stimulus intensity was adjusted to produce a visible twitch in the Abductor Pollicis Brevis (APB) muscle without causing any discomfort. The number of trials averaged for adequate waveform identification is 300. To confirm the reproducibility of the SSEP study, each measurement was carried out twice.

The recording disposable subdermal monopolar needle electrode was placed at the following locations: Erb’s point on each side (EPi) and (EPc), over the fifth cervical spine process (C5s), scalp over the contralateral parietal cortex (CPc), and cephalic Fz electrode (as a reference). Erb’s point is 2–3 cm above the clavicle, just lateral to the attachment of the sternocleidomastoid muscle. The fifth spinous process is identified by counting up from the seventh spinous process, notably by its prominence at the base of the neck. CPcs are scalp electrodes halfway between C3 and P3, where CPc is contralateral to the stimulus. These electrodes are placed over the motor sensory cortex. EPi is Erb’s point ipsilateral to the stimulus; EPc is Erb’s point contralateral to the stimulus. The recommended montage is: Channel 1: Epi-EPc showing the (N9) evoked potential (EP); brachial plexus activity (near-field action potential), Channel 2: C5s-Fz showing the (N13) EP; near-field cervical potential is likely to be generated by the dorsal horn neurons and from ascending afferents in the cuneate tract (dorsal columns). Activities in the nerve root entry zone and dorsal columns in the Cervical Spinal Cord are represented as follows: Channel 3 –CPc-Fz showing the (N20) EP; parietal cortex activity, a near-field potential recorded over the CPc. It is likely to be generated from thalamocortical radiations projecting from the ventral posterior lateral thalamus.^[11] Figure 2 showed the wave form generated. The parameters studied in the SSEP study of median nerve include the latency, amplitude, and central sensory conduction time (CSCT).

Tibial nerve somatosensory-evoked potential waveforms

Left tibial nerve was stimulated just behind the medial malleolus, with an intensity to create a slight twitch in the

toes. Stimulation was done using the stimulating electrode, fixed over the nerve with an elastic strap, with the cathode placed at midpoint between medial malleolus and Achilles tendon and the anode about 3 cm distal to the cathode.^[11] The responses were recorded at 2 μ V/division gain, 100 ms time base, and 14 Hz–2.5 kHz filtration range. The average of 250–300 cortical responses was taken. To confirm the reproducibility of the Somato Sensory Evoked Potential (SSEP), each measurement was carried out at least twice. Recordings were made using the recording electrodes that were put in the following positions: scalp over the Cz', over the twelve spine process (T12), popliteal fossa (PF) on the left side, and cephalic Fz electrode (reference). A common montage for left tibial nerve SSEPs using these electrodes is: Channel 1 showing the (N45) EP: active electrode was placed at Cz' (2 cm posterior to Cz) and referred to Fz according to the international 10–20 system, detects near-field potentials over cortex, Channel 2 showing the (N21) EP: active electrode was placed at 12th thoracic spinous process (T12s) and referred 4 cm rostrally. Near-field potentials from the lumbar cord are detected. T12S is the first blade-like spinous process. Felt by tracing upwards and inwards on the floating 12th rib to find it, Channel 3 showing the (N9) EP: active electrode was placed at the PF (4–6 cm above popliteal crease) and referred to medial knee. This lumbar potential is likely to be generated by activity in the dorsal roots, dorsal root entry zone, and by postsynaptic activity in the lumbar cord enlargement.

This site is between the tendons of the semitendinosus and semimembranosus muscles. From these channels, negative waves (i.e., pointing upward from isoelectric line) of SSEP were recorded. For each EP waveform, both latency and amplitude were recorded in addition to the CSCT which represent the interpeak latency between N45 and N21. Results were statistically evaluated. Most of the data were continuous and expressed in terms of mean $\pm$ standard deviation (SD); comparison of these data was done using unpaired Student's *t*-test. Only sex was expressed in terms of frequency and percentage; comparison of these data was done using Fisher's exact test. $P < 0.5$ was considered statistically significant. Microsoft excel 2016 and Statistical Package For the social Sciences version 23 (SPSS, IBM Company, Chicago, USA) were used for the statistical analysis.

Ethical consideration

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with the patient's verbal and analytical approval before the sample was taken.

RESULTS

One hundred and two participants were enrolled in this study: 48 nonspecific CLBP patients and 54 specific CLBP patients mainly lumbosacral stenosis. The mean age $\pm$ SD of those with nonspecific CLBP patients was 39.83 ± 10.24 years, comprising 17 males and 31 females,

compared to specific CLBP patients (45.7 ± 10.06 years), comprising 20 males and 34 females. The mean ages of the nonspecific CLBP patients were significantly lower than that of their specific CLBP counterpart patients ($P = 0.003$). No significant difference was noticed regarding the gender and height between the two studied patient groups ($P = 1.0$ and 0.388 , respectively) [Table 1].

Somatosensory-evoked potentials

Right median nerve

The latency, amplitude, and CSCT of different SSEP components of the right median nerve SSEP study are presented in Table 2. The means of the latencies of the N9, N13, and N20 SSEP waves were all shorter in the nonspecific CLBP patients as compared to that of the specific CLBP group, and the difference was statistically significant in the peripheral N9 SSEP wave and highly significant in cortical N20 SSEP wave ($P = 0.012$, 0.105 , and <0.001 , respectively) [Table 2]. The means of the amplitudes of differently studied SSEP components of the right median nerve (N9, N13, and N20) were all higher in the nonspecific CLBP patients as compared to that of the specific CLBP group (3.5 ± 2.1 mV vs. 2.5 ± 1.15 mV, 1.81 ± 0.79 mV

Table 1: Demographic characteristics of the studied patients with specific chronic low back pain and nonspecific chronic low back pain regarding the sex, age, and height

Parameters	Specific CLBP patients (n=54)	Nonspecific CLBP patients (n=48)	P
Sex			
Male	20	17	1
Female	34	31	
Age (year)			
Mean $\pm$ SD	45.7 $\pm$ 10.06	39.83 $\pm$ 10.24	0.003
Range	22-70	22-58	
Height (cm) ²	167.65 $\pm$ 10.6	165.05 $\pm$ 18.93	0.388

CLBP: Chronic low back pain, SD: Standard deviation

Table 2: The somatosensory-evoked potential components recorded from right median nerve study of the nonspecific versus specific chronic low back pain patients

Parameter	Mean $\pm$ SD		P
	Specific CLBP patients (n=54)	Nonspecific CLBP patients (n=48)	
N9 L (ms)	10.04 $\pm$ 0.89	9.64 $\pm$ 0.67	0.012
N9 Amp (μ V)	2.5 $\pm$ 1.15	3.5 $\pm$ 2.1	0.005
N13 L (ms)	13.27 $\pm$ 0.84	12.98 $\pm$ 0.96	0.105
N13 Amp (μ V)	1.58 $\pm$ 0.75	1.81 $\pm$ 0.79	0.123
N20 L (ms)	19.87 $\pm$ 1.15	18.95 $\pm$ 0.96	<0.001
N20 Amp (μ V)	1.17 $\pm$ 0.51	1.36 $\pm$ 0.89	0.186
CSCT N20-N13 (ms)	6.6 $\pm$ 1.1	5.97 $\pm$ 1.12	0.005

The data presented as mean $\pm$ SD. CSCT: Central sensory conduction time, CLBP: Chronic low back pain, SD: Standard deviation

vs. 1.58 ± 0.75 mv, and 1.36 ± 0.89 mv vs. 1.17 ± 0.51 mv, respectively); however, the difference was only significant in N9 SSEP wave potential ($P = 0.005$) [Table 2]. The mean CSCT measured from subtracting the N13 latency from the cortical N20 latency in the right median SSEP study shows a lower mean conduction time in the nonspecific CLBP patients as compared to the specific CLBP patients (5.97 ± 1.12 ms vs. 6.6 ± 1.1 ms), and the difference was statistically significant ($P = 0.005$) [Table 2].

Left tibial nerve

The latency, amplitude, and CSCT of different SSEP components in the left tibial nerve SSEP study are presented in Table 3. The means of the latencies of the left tibial SSEP study (N10, N22, P37, and N45) were all shorter in the nonspecific CLBP patients as compared to that of the specific CLBP group, but the difference was only significant in the peripheral N10 SSEP wave ($P = 0.025$) [Table 3]. The means of the amplitudes of differently studied SSEP components of the left tibial nerve (N10, N22, P37, and N45) were all higher in the nonspecific CLBP patients as compared to that of the specific CLBP group; however, they were only significant in the P37 and N45 SSEP waves (1.6 ± 0.9 mv vs. 1.19 ± 0.95 mv, $P = 0.03$, and 1.91 ± 1.11 mv vs. 1.41 ± 1.02 mv, $P = 0.021$, respectively) [Table 3]. The mean CSCT measured from subtracting the N22 latency from the cortical N45 latency in the left tibial SSEP study shows a shorter mean conduction time in the nonspecific CLBP patients as compared to that of the specific CLBP patients (22.61 ± 3.91 ms vs. 22.97 ± 5.82 ms), but the difference was statistically nonsignificant, ($P = 0.718$), [Table 3].

DISCUSSION

The important drawback of LBP on health-care systems can be explained by an extremely high annual prevalence worldwide, i.e., up to 36% of the population. The pathophysiological mechanisms of CLBP must, therefore, be better understood in order to identify which therapy is most efficient per individual

so as to overcome the refractoriness to treatment. Especially, the plasticity of the central nervous system (CNS) in response to pain (CNS adaptation to pain) represents one of the most important phenomena that could highlight why people with CLBP are poorly responsive to conventional therapies.^[12]

The goal of this study is to explore the characteristics of sensory cortical excitability in chronic-nonspecific low back pain against a group of chronic-specific low back pain (CLBP) by SSEP. In the current study, no significant difference was noticed regarding the gender and height between the two studied groups. However, the findings that the mean ages of the nonspecific CLBP patients were significantly lower than that of their specific CLBP counterparts can be explained in such a way that most of the specific CLBP patients in this study had lumbosacral radiculopathy, which is manifested more with advancing age.^[13] Therefore, patients of older ages have participated in the current study as the specific CLBP group compared to the younger ages of those with nonspecific CLBP.

The means of the latencies of all the SSEP waves of the right median and left tibial nerves were all shorter in the nonspecific CLBP patients as compared to that of the latencies of the counterpart waves in the specific CLBP group, but the differences were only significant in the peripheral SSEP waves in the upper and lower limbs (N9 and N10, respectively) and highly significant in cortical right median N20 SSEP wave. On the other hand, the CSCT values in the median and tibial SSEP study were shorter in patients with nonspecific CLBP than in the specific CLBP patients, with a significant difference in the median nerve study.

Comparison with SSEP values of 41 healthy controls stimulating the right median nerve and 40 healthy participants stimulating the left tibial nerve in previous studies shows a highly significantly shorter SSEP cortical (N20) latency and CSCT in the patients with nonspecific CLBP compared to controls (18.95 ± 0.96 vs. 20.59 ± 1.23 and 5.97 ± 1.12 vs. 7.53 ± 1.43 , $P < 0.001$, respectively). No other significant differences were found between patients with nonspecific CLBP and healthy controls concerning the latencies of the SSEP waves, whether in the right median or left tibial nerves, despite a significantly higher latency of the peripheral N9 wave in these patients compared to controls (9.64 ± 0.67 vs. 9.27 ± 0.23 , $P = 0.001$).^[14,15]

These findings point to a possible increment in the sensory conduction velocity in patients with nonspecific CLBP as compared to those with specific CLBP and to control healthy controls, which is more evident in the upper segments of the somatosensory pathway and in the peripheral part of the sensory nervous system. The specific features of the somatosensory system and the presence of different order neurons with different impulse conduction characteristics could stand for the limited appearance of the clear differences in SSEP wave latencies between patients with nonspecific versus specific CLBP, but, in close proximity to the stimulation sites. Results of studies examining the responsiveness to

Table 3: The somatosensory-evoked potential components recorded from left tibial nerve study of the nonspecific versus specific chronic low back pain patients

Parameter	Specific CLBP patients (n=54)	Nonspecific CLBP patients (n=48)	P
N10 L (ms)	10.12±2.26	9.21±1.75	0.025
N10 Amp (µv)	0.89±0.74	1.29±1.78	0.132
N22 L (ms)	22.88±4.95	22.79±3.46	0.916
N22 Amp (µv)	0.22±0.17	0.71±2.63	0.176
P37 L (ms)	39±5.98	37.21±5.94	0.133
P37 Amp (µv)	1.19±0.95	1.6±0.9	0.030
N45 L (ms)	45.85±6.91	45.4±3.23	0.680
N45 Amp (µv)	1.41±1.02	1.91±1.11	0.021
CSCT N45N22 (ms)	22.97±5.82	22.61±3.91	0.718

CSCT: Central sensory conduction time, CLBP: Chronic low back pain

various stimuli in patients with CLBP are conflicting. Several studies reported hyperalgesia to pressure to sites unrelated to the lumbopelvic region in patients with CLBP, indicating generalized or widespread hyperalgesia at least in a subgroup of patients with CLBP.^[16,17]

Contradicting results are also reported in the literature, suggesting that patients with CLBP do not experience sensitization. Studies have reported no differences in pain perception threshold and pain tolerance threshold between patients with CLBP and healthy controls when the noxious stimulation occurred at the finger,^[18] the arm,^[19] or other remote sites.^[20] One study even observed significant higher pain thresholds in patients with CLBP when compared with healthy controls.^[21] Some studies showed the changes at the peripheral level in chronic nonspecific and pseudoradicular back pain;^[22,23] “pinprick allodynia” was found to punctate low-intensity stimuli,^[24] and somatosensory abnormalities for painful and innocuous stimuli in female nonspecific CLBP patients;^[23] which were detected both at the affected site (dorsum of the lower back) and at a site distinct from the region of pain, the dominant hand.^[23,24]

Somatosensory-evoked potential amplitudes

The means of the amplitudes of different studied SSEP components of the right median and left tibial nerves were all higher in the nonspecific CLBP patients as compared to that of the specific CLBP group; however, the difference was only significant in the peripheral SSEP (N9) wave of the right median nerve and in the subcortical and cortical (P37 and N45) waves in the tibial nerve SSEP study [Table 3]. However, comparison with SSEP values in healthy participants from previous studies of 41 healthy controls stimulating the right median nerve and 40 healthy participants stimulating the left tibial nerve, shows significantly lower SSEP amplitudes in all the studied SSEP components in the median nerve study (N9, N13, and N20) (3.5 ± 2.1 vs. 4.70 ± 1.43 , $P = 0.003$; 1.81 ± 0.79 vs. 4.04 ± 1.23 , $P < 0.001$; and 1.36 ± 0.89 vs. 4.74 ± 1.67 , $P < 0.001$, respectively) and only in the peripheral N10 component of the tibial nerve study (1.29 ± 1.78 vs. 3.03 ± 1.0 , $P < 0.001$).

The equivocal results of the somatosensory wave amplitude, which point in the direction of axonal degeneration in nonspecific CLBP in some parameters and deny the presence of axonal affection in others, while refer to sensory nerve potentiation when compared to patients with specific CLBP, uncertainty their value in the study of CNS modifications in SSEP studies. It was stated that the equivocal results of the tibial nerve SSEP amplitudes can be explained by the complex relationship between neuronal pathways in the CNS, with the presence of different-order neurons (first, second, and third) and lots of convergence and divergence along the pathway, which probably lower the validity of the SSEP amplitude measurements in the diagnosis of lumbosacral stenosis compared to latencies.^[15]

In summary, despite the fact that several studies point in the direction of CS and suggest altered central pain mechanisms

in patients with CLBP, the results are equivocal.^[16,25] Whereas reduced pain thresholds suggestive of widespread or extrasegmental hyperalgesia are observed in some studies,^[16] other studies observe only a segmental hyperalgesia^[26] or report no hyperalgesia at all.^[19] The difference in the results between studies may be ascribed to some methodological concerns, such as small sample size, differences in experimental protocols or definition of outcome parameters, study design, and medication used.^[25]

CONCLUSIONS

From this study, we conclude that SSEP latency points to the direction of a possible somatosensory enhancement, at least in the upper segment of this pathway in patients with nonspecific CLBP as compared to patients with specific back pain or to healthy controls. The insignificant results in the lower limb study could be explained by the complex somatosensory neuronal pathways, with the possible dilution effect of the prolonged distance on the somatosensory plastic adjustments; precipitating insignificant results. On the other hand, the conflicting SSEP amplitude study questions their validity in the study of CNS plastic modifications in nonspecific CLBP.

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Conflicts of interest

There are no conflicts of interest.

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