CENTRAL SENSITIZATION INVENTORY SCORES IN PATIENTS WITH NEUROPATHIC PAIN COMPARED TO HEALTHY SUBJECTS

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Central sensitization inventory (CSI) was designed as a tool for evaluation of the symptoms that have been found to be related to central sensitization (CS). The aim of this research was to examine differences in CSI scores between subjects with painful lumbosacral radiculopathy (PLSR). This study included 33 subjects with PLSR (mean age 54.12 ± 9.43 years, 6 (18.2%) women) and 30 healthy subjects (mean age 50.87 ± 5.64 years, 12 (40%) women). The Serbian version of the Central Sensitization Inventory (CSI) was used to examine the degree symptoms related to CS. In order to evaluate the emotional status, we used the Serbian version of the Depression, Anxiety, Stress Scale (DASS 21). The obtained results showed a significantly higher value of the CSI score in subjects with neuropathic pain (t = -7.690, p = 0.000). Statistically significantly worse DASS 21 values in subjects with neuropathic pain in all 3 subscales: depression subscale (t = -2.437, p = 0.018), anxiety subscale (t = -3.597, p = 0.001), stress subscale (t = -3.982, p = 0.000). The degree of expression of symptoms related to CS determined, as well as the degree of anxiety, depression and stress is significantly higher in subjects with PLSR compared to the group of healthy subjects. This should be kept in mind when designing a treatment plan for individuals with PLSR. *Acta Medica Medianae 2023;62(3):11-16.*

Key words: neuropathic pain, central sensitization, anxiety, depression, stress

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Introduction

In modern society, chronic pain is a major health problem (1). It frequently leads to impairment and can greatly impair one's capacity for physical activity (2). It is estimated that over 20% of Europeans suffer from chronic pain (3). A subtype of chronic pain is chronic neuropathic pain (4). It occurs as a result of a lesion or disease of the somatosensory nervous system, either peripherally or centrally (5). Radiculopathy is a condition caused by compression and/or irritation of the spinal nerve root, most often in the lumbosacral part of the spinal column (6). It is estimated that lumbosacral radiculopathy is present in 3% − 5% of the population and there is no major difference between the genders (7−9).

One of the important mechanisms in neuropathic pain is central sensitization (CS). According to International Association for the Study of Pain (IASP), central sensitization represents increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input (10). In other words, CS is characterized by increased sensitivity and responses to painful stimuli (11). It is hypothesized that CS represents an important factor in the development and maintenance of chronic neuropathic pain (12).

It is impossible to directly measure CS in humans (13). However, there are certain efforts to indirectly measure this phenomenon. Quantitative sensory testing and self-reported questionnaires are frequently used for this purpose in the literature (13). One of the most frequently used self-reported instrument is Central sensitization inventory (CSI). CSI was designed to evaluate severity of symptoms related to CS (14 − 18).

The phenomenon of central sensitization is associated with a great number of centers in the brain, and the limbic system is particularly important (19, 20). Limbic system has a role in the field of emotional learning and behavior in affective disorders (21). It is also considered to be an important center of the mutual relationship between pain and negative emotions (22, 23). It is well known that pain correlates with the

intensity of psychopathological symptoms - both with depression and with symptoms of anxiety.

Aim

The aim of this study was to examine the difference in symptoms of CS between patients with neuropathic pain due to lumbosacral radiculopathy and healthy subjects. The level of depression, anxiety, stress and length of sleep between the two tested groups was also compared.

Materials and Methods

This study was conducted at the University Clinical Center of Vojvodina in the period from 2019 to 2020. The Ethics Committee of the University Clinical Center of Vojvodina approved the implementation of this study (Decision No. 00-208).

The research included 63 subjects, 30 healthy subjects (HS) without pain and 33 subjects with painful lumbosacral radiculopathy (PLSR).

The criteria for inclusion in the HS group were the absence of any chronic or acute pain in the last month, the age of the subjects >18 years.

The criteria for inclusion in PLSR group were the presence of neuropathic pain from the lumbosacral radiculopathy according to the criteria suggested by Finnerup et al., duration of pain > 3 months, age of the subject > 18 years (24).

The criteria for exclusion from the research for both groups were subjects under 18 years of age, the presence of a malignant disease, patients who had spine surgery in the last 6 months, patients who did not understand the Serbian language, and for the PLSR group, pain that lasted less than 3 months.

The following questionnaires were used:

1. Central Sensitization Inventory (CSI) created for the purpose of assessing the severity of symptoms of CS. It consists of part A and part B. The first part, which was used for this research, consists of 25 items related to symptoms of central sensitivity. The respondent evaluates the frequency of each item on a five-point Likert scale from 0 (never) to 4 (always). The total score ranges from 0 to 100, and higher values indicate a greater degree of central sensitivity symptoms (14, 15).

2. Depression, Anxiety, Stress Scale (DASS 21) consists of 21 questions and has three subscales of 7 items each. It is designed to evaluate emotional states such as depression, anxiety and stress. The respondent evaluates the level of exposure to each condition in the past week on a 4-point Likert scale. A higher score on this scale indicates a higher degree of depression, anxiety and stress (25) .

3. Respondents reported the average length of sleep in the last month in hours.

The SPSS 24 package was used for statistical data processing. Frequency and percentage were used to describe the sample. Descriptive statistics were used to determine measures of central tendency (arithmetic mean), measures of variability (standard deviation). In order to determine differences between groups, Student's t and X^2 tests were used. In the applied tests, $p < 0.05$ was taken as significant.

Results

This study included 63 subjects, of which 30 were healthy subjects without pain, and 33 were subjects with PLSR (see Table 1 for more details). The largest number of subjects were men, although there was no significant difference between the examined groups ($X^2 = 3.665$, $p = 0.093$).

There was no significant difference in the values of body height (t = 1.749, p = 0.085) and body mass (t = -1.173, p = 0.246) between the studied groups.

Table 1. Demographic characteristics of the patient sample

	Healthy subjects	PLSR[1]	t/X^2	p
Age				
N	30	33		
Mean ± SD*	50.87 ± 5.64	54.12 ± 9.43	t = -1.680	p = 0.099
Gender				
Women n (%)	12 (40%)	6 (18.2%)	$X^2 = 3.665$	p = 0.093
Men n (%)	18 (60%)	24 (81.8%)		
Body height (cm)				
N	30	33		
Mean ± SD*	171.9 ± 9.52	168.1 ± 7.9	t = 1.749	p = 0.085
Body weight (kg)				
N	30	33		
Mean ± SD*	75.5 ± 13.3	79.4 ± 13.4	t = -1.173	p = 0.246

1 Painful lumbosacral radiculopathy patients

Table 2. Patient-reported clinical variables

	Healthy subjects (n = 30)	PLSR[3] (n = 33)	t	p
DASS[1] 21 - Depression	4.6 ± 5,8	8.9 ± 8	-2.473	0.018
DASS[1] 21 – Anxiety	3.7 ± 3.6	8.8 ± 7.1	-3.597	0.001
DASS[1] 21 – Stress	8.5 ± 5.5	15.8 ± 8.8	-3.982	0.000
Length of sleep (h)	6.9 ± 0.9	5.9 ± 1.3	-3.532	0.001
CSI[2]	19.4 ± 8.7	40.2 ± 12.3	-7.690	0.000

1 Depression, Anxiety, Stress Scale,
2 Central sensitization inventory
3 Painful lumbosacral radiculopathy patients

As it turned out that there were no significant differences in age, gender, body height and body weight, we continued with the comparison of the remaining variables between the groups.

The following results showed that there was a significant difference in the depression, anxiety and stress subscale of DASS 21 between the studied groups (see Table 2 for more details).

Our data showed that PLSR patients slept one hour less on average than healthy subjects. This difference was statistically significant (t = -3.532, p = 0.001). Finally, we compared the CSI score values between the studied groups. PLSR group had, on average, more than double the CSI scores compared to the control group. This difference was highly statistically significant (t = -7690, p < 0.001).

Discussion

It is believed that 7 – 8% of Europeans suffer from neuropathic pain with lumbosacral radiculopathy as one of the leading causes (26). Central sensitization is one of the mechanisms for maintaining neuropathic pain (15, 16). It is a physiological phenomenon in which neurons of the central nervous system become hyperexcitable (increased excitability), which leads to hypersensitivity to nerve impulses from the periphery (27). Lesions of the somatosensory nervous system could be the pain generator that has potential to push pain processing system into hyperexcited state (28).

The problem with CS is how to measure it. There is no possibility to measure directly CS in humans (13). In the literature, QST and self-reported questionnaire are the most frequently used methods. However, these methods have their flaws. Several specific factors have been found to confound the responses to QST and self-reported questionnaire: anxiety and depression, history of trauma, pre-morbid personality traits, fear of pain and low expectations of recovery, sleep disorder, personal injury claim/compensation, genetic/familial transmission of CS predisposition, behavioural change in response to reactions of others, particularly spouse (13).

Our results showed more than twice the CSI scores in the group of subjects with neuropathic pain due to lumbosacral radiculopathy indicating that central sensitization symptoms are significantly pronounced in subjects with neuropathic pain. Other researchers found similar results (29 – 31).

These finding are important because patients with symptoms of central sensitization require specially adapted physical treatment as well as careful consideration of the drug therapy they will use. It is also important to note that even small changes and lesions seen on imaging can cause severe pain in these patients (32).

Our results indicated that there is a significant difference in the depression subscale between the groups, that is, that patients with neuropathic pain showed a higher degree of depression compared to healthy controls. Such results are expected, especially when the pain is moderate or severe, which is the case with neuropathic pain (33, 34). The reason for this may be a lower quality of life, a reduced work function or a greater need to use health care services (35). Also, it should be emphasized that depression and chronic pain are extremely related when it comes to elderly people. It is estimated that 13% of this population will have symptoms of both depression and chronic pain present at the same time (34). A number of authors suggest that neuroinflammation plays a key role in the pathogenesis of both conditions (36). In addition to depression, the group of patients with neuropathic pain also showed a higher degree of anxiety compared to healthy controls. Pain is essentially related to anxiety in its definition, which is the likely cause of these differences (36), and similar results are found by other authors (37, 38). We noticed that there were also significant differences between the groups of our respondents

in terms of stress. In this case, it was also confirmed that people with PLSR were significantly more susceptible to stress than healthy subjects. The connection between pain and stress is widely known (39). Pain is part of our homeostatic system and tells us that we are in danger (40).

The connection between pain and sleep should not be ignored. Chronic pain negatively affects sleep (41). One of the indicators of sleep quality is its duration (42). In our research, we used the average duration of the length of sleep in the last month. After the comparison, it was concluded that people with PLSR slept an hour less, on average, than the group of healthy subjects, and that there was a statistically significant difference between these groups in terms of this parameter. People with chronic pain are 18 times more likely to suffer from insomnia compared to the healthy population (43, 44). Other researchers also find results similar to ours (45). Also, it has been shown that anxiety and depression often occur together with chronic pain and insomnia (46).

The main limitation of the present study is relatively small sample size and in the future studies larger samples of patients with PLSR should be evaluated. The second limitation is usage of the self-reported questionnaire for evaluation of the CS. However, it is not possible to directly measure CS in humans, and CSI is useful as a screener of the CS presence (14 − 16, 18). In the future studies, we suggest combination of the self-reported instrument such as CSI and QST, as well as other methods (13).

Conclusion

The present study showed that the degree of central sensitization symptoms, depression, anxiety, and stress, as well as sleep problems were significantly more pronounced in the patients with chronic painful lumbosacral radiculopathy compared to healthy controls. These results should be kept in mind when designing a treatment plan for patients with painful lumbosacral radiculopathy.

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SKALA CENTRALNE SENZITIZACIJE KOD ZDRAVIH ISPITANIKA I ISPITANIKA SA NEUROPATSKIM BOLOM

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Skala centralne senzitizacije (engl. *Central Sensitization Inventory* – CSI) osmišljena je kao instrument za evaluaciju simptoma za koje se smatra da su povezani sa centralnom senzitizacijom. Cilj ovog istraživanja bio je da se ispita da li postoje značajne razlike u izraženosti centralne senzitizacije, stepenu anksioznosti, depresivnosti i stresa između zdravih ispitanika i ispitanika sa neuropatskim bolom, usled lumbosakralne radikulopatije (engl. *painful lumbosacral radiculopathy* – PLSR). Ovom studijom obuhvaćeno je 33 ispitanika sa PLSR (prosečne starosti 54,12 godina ± 9,43 godine; 6 (18,2%) žena) i 30 zdravih ispitanika (prosečne starosti 50,87 godina ± 5,64 godine; 12 (40%) žena). Srpska verzija Skale centralne senzitizacije (CSI) korišćena je za ispitivanje stepena simptoma povezanih sa CSI. Za procenu emocionalnog statusa koristili smo srpsku verziju Skale depresije, anksioznosti, stresa (engl. *Depression, Anxiety, Stress Scale* – DASS 21). Dobijeni rezultati pokazali su značajno veću vrednost CSI skora kod ispitanika sa neuropatskim bolom (t = -7,690, p = 0,000). Statistički značajno gore vrednosti DASS 21 dobijene su kod ispitanika sa neuropatskim bolom u trima supskalama: supskala depresije (t = -2,437, p = 0,018), supskala anksioznosti (t = -3,597, p = 0,001), supskala stresa (t = -3,982, p = 0,000). Stepen izraženosti simptoma centralne senzitizacije, kao i stepen anksioznosti, depresije i stresa, značajno je veći kod ispitanika sa neuropatskim bolom (PLSR) nego u grupi zdravih ispitanika. Ovo treba imati na umu prilikom dizajniranja plana lečenja osoba sa bolnom lumbosakralnom radikulopatijom (PLSR). *Acta Medica Medianae 2023;62(3):11-16.*

Ključne reči: *neuropatski bol, centralna senzitizacija, anksioznost, depresija, stress*