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Central sensitization and adult attention deficit hyperactivity disorder in medical students with chronic back pain: a cross-sectional study

Maha E. Ibrahim*  and Mohamed A. Hefny

Abstract

Background: Chronic back pain is a common health complaint among university students. A subset of chronic back pain patients suffer from increased pain sensitivity, a process termed central sensitization. Chronic pain is also associated with cognitive dysfunction, involving attention, memory, and learning. Those are key features of adult attention deficit hyperactivity disorder. This study aimed to assess the associations between adult attention deficit hyperactivity disorder and central sensitization in students with chronic back pain.

Results: Two hundred twenty-seven students completed the survey, and 90 (39.6%) had back pain for more than 3 months. Students with back pain had significantly higher central sensitization ($P < 0.01$) and higher attention deficit scores ($P = 0.05$). Significant positive correlations were found between scores of the two questionnaires ($r = 0.55$, $P < 0.01$). Regression analysis adjusted for age and gender showed that higher attention deficit scores were associated with back pain (odds ratio: 1.025, $P = 0.05$). The odds ratio was attenuated after adding central sensitization to the model (odds ratio: 0.99, $P = 0.70$).

Conclusions: The findings of this study suggest that attention deficit hyperactivity disorder is associated with elevated central sensitization in patients with chronic back pain. Our results support the hypothesis that central sensitization mediates the effect of attention deficit on back pain.

Keywords: Central sensitization, Back pain, Cognitive dysfunction

Background

Chronic back pain (CBP) has become the first cause of disability worldwide [1]. It has major socioeconomic implications and results in significant personal and societal costs [2, 3]. Back pain affects all age groups and is a prevalent health complaint among university students in general and medical students in particular [4]. In about 85–90% of patients with CBP, no specific mechanical cause can be found [5]. That is why it is now believed that

non-specific back pain results from an interplay between several biological, psychological, and social factors, that contribute to pain occurrence, disability, and progression to chronicity [1, 6, 7]. A subset of people suffering from CBP exhibit features of increased pain sensitivity and altered pain processing, suggesting central sensitization (CS) to pain [8, 9]. The research defines CS as an abnormal augmentation of pain caused by neuronal hyperexcitability to stimuli in the central nervous system [10, 11]. This process is associated with altered sensory processing, dysfunction of the inhibitory pain pathways [10], and an increased activity of pain facilitatory pathways [12].

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Research has identified CS as a key player in chronic pain conditions, including Fibromyalgia [13, 14], osteoarthritis [15, 16], temporomandibular disorders [17], neuropathic pain [18], and most importantly chronic back pain [8, 10, 19], where a recent Lancet series on CBP places CS at the core of the biopsychosocial model utilized to understand and address CBP [1, 20]. Despite recent research, the mechanisms behind CS are, to date, not fully understood. Evidence shows that it is mediated by several psychosocial factors, such as pain catastrophizing, fear-avoidance beliefs, depression, and anxiety [21, 22].

In addition to psychological determinants, studies show that chronic pain conditions are associated with a disruption in cognitive functioning [23]. Examples of such functions include psychomotor speed [24], attention [25], memory, and learning [26]. A recent study showed that over two thirds of patients with chronic back pain had an impairment in one or more cognitive functions [26].

Another condition associated with cognitive dysfunction in adults is attention deficit hyperactivity disorder (ADHD). Originally thought to be a disorder of childhood, studies show that in 30–70% of cases, the disorder persists into adulthood and can cause various physical and psychological comorbidities [27]. ADHD manifests as either inattentiveness or hyperactivity and impulsiveness, or a mixture of both presentations [28]. Recent studies show that patients with ADHD are at an increased risk of experiencing chronic pain [29, 30] and that chronic pain patients exhibit several features of ADHD [31, 32].

Interestingly, central sensitization and ADHD may share some neurobiological mechanisms [33, 34], and ADHD is thought to induce altered pain sensitization in animal models [33]. This link between ADHD and CS was not tested in pain populations. Thus, the objective of this study was to assess the relation between CS and features of ADHD, and the possible mediation effect in a cohort of medical students suffering from CBP.

Methods

Study design and participants

Data for this cross-sectional study were derived from an online database collecting health-related data from health sciences students at the university. The database comprises data about various physical and psychological health complaints, including questions assessing musculoskeletal conditions and psychological functioning. Data for this study were collected from students during the academic year 2019–2020 using an online survey. The survey was shared with students attending the faculties of medicine, dentistry, and pharmacy via social media

platforms. Inclusion criteria were male and female students from freshman to senior years, excluding interns and house officers. Students with chronic illnesses, psychiatric disorders, back pain lasting less than 3 months, and back pain caused by specific conditions (radiculopathy, ankylosing spondylitis, and spinal canal stenosis) were excluded from the analysis. An incentive for participation was offered to students in the form of a 5 EGP donation made to Aboelrish Children Hospital for every completed form. The study was approved by the university's ethics committee, and all participants were provided an online consent form to participate in the study.

Measures

Chronic back pain

After providing their demographic data, students were asked to fill a section on self-reported musculoskeletal pain. The section inquired about pain lasting more than 3 months in 19 body areas including pain in the spine. Students were asked to indicate the site of pain (neck–upper back–lower back) and duration of pain, and whether they were given a specific diagnosis by their healthcare provider.

Central sensitization inventory (CSI)

The CSI is a validated tool that measures central sensitization [35], and it consists of 25 symptom-related questions that students score on a 5-point Likert scale. A cut-off point of $\geq 40/100$ indicates the presence of CS (sensitivity: 81%, specificity: 75%). This tool demonstrated good psychometric properties in back pain patients [36].

Adult attention deficit hyperactivity disorder self-report scale (ASRS-v 1.1)

The ASRS-v1.1 is a self-reported symptom checklist developed by the World Health Organization to screen for ADHD [37]. Its eighteen questions cover the eighteen Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision (DSM-IV-TR) criteria for ADHD. The questionnaire consists of two parts, part A and part B. A score of 24 or more on either part A or part B signifies the presence of ADHD. The questionnaire has 9 questions assessing inattentiveness, and 9 questions assessing hyperactivity, distributed between the two parts. The first 6 items out of the eighteen questions were found to be the most predictive of symptoms consistent with ADHD and are used as a screener. The ASRS v1.1 is an effective tool for detecting ADHD, with a sensitivity of 68.7% and a specificity of 99.5% [38].

Statistical analysis

Data for this study were analyzed using IBM SPSS Statistics Version 25 (SPSS Inc., Chicago, Illinois). For descriptive statistics, means and standard deviations were used to describe continuous variables, and frequencies and percentages were used for categorical variables. Differences in ADHD and CS between students with and without back pain were analyzed using the independent *t* test for continuous variables and the chi-square test for categorical variables. The correlation between CSI and ADHD scores was assessed using Pearson's correlation. To test the mediation effect of CS between ADHD and back pain, two logistic regression models were developed. The first was used to estimate the association between ADHD and back pain in the absence of CS, and in a second model, CS was added to the model. *P*-values < 0.05 were considered significant. The sample size calculation was performed using OpenEpi [39]. Based on a prevalence of back pain among university students of 21.2% [4], and an alpha error of 0.05, the minimum required sample size was 236 students.

Results

Two hundred twenty-seven students fulfilling the inclusion criteria completed the survey, and 90 (39.6%) had back pain for more than 3 months. The sample was predominantly female students (75.8%), and the mean age was 21.86 ± 2.29 (Table 1). When comparing mean scores using an independent sample *t* test, students with CBP had significantly higher CS than students without back pain ($P < 0.01$) (Fig. 1, Table 2). Similarly, the CBP group had higher ADHD according to ASRS-v 1.1 scores ($P = 0.05$). When decomposing the analysis to the section assessing hyperactivity and that assessing attention deficit, differences between the two groups were more significant in the attention deficit section ($P = 0.02$) (Table 2).

A categorical analysis using chi-square was done to identify percentages of students with and without CBP who exhibit features of ADHD and CS. In the CBP group, 68 (75.6%) fulfilled ADHD criteria, as opposed to 47 (34.3%) in the no back pain group (Table 3). For CS, 88 students (97.8%) fulfilled CS criteria according to the CSI, compared to 108 (78.8%) in the group with no back pain. Pearson's correlation results showed a strong positive association between CS and total ADHD scores, as well as attention deficit scores and hyperactivity scores (Table 4).

Two logistic regression models were designed to identify the mediation effect of CS on ADHD while controlling for age and gender. In the first model, the binary back pain variable was used as the outcome variable, and associations with ADHD alone were measured. There was a

Table 1 Sociodemographic characteristics of the study sample ($N = 227$)

Characteristics	Number	Percentage
Age (mean \pm SD)	21.86 \pm 2.29	
Gender		
Male	55	24.2
Female	175	75.8
BMI (mean \pm SD)	23.95 \pm 3.10	
Obesity		
Yes	57	25.1
No	170	74.9
Faculty		
Medicine	197	86.8
Dentistry	16	7.0
Pharmacy	14	6.2
Presence of back pain		
Yes	90	39.6
No	137	60.4
Site of pain (multiple answers were possible)		
Neck	48	53.3
Upper back	23	25.5
Lower back	55	61.1

SD standard deviation, BMI body mass index

marginally statistically significant association between ADHD symptoms and back pain (OR 1.025, 95%CI 0.99–1.05, $P = 0.05$). Students with higher ADHD had higher odds of experiencing back pain compared to those with lower ADHD scores (Table 4). In the second model, CS was included in the analysis, ADHD no longer showed a significant association, and the OR was diminished (OR 0.89, 95%CI 0.86–0.99, $P = 0.70$). Conversely, CS scores showed a strongly significant association with the outcome variable (i.e., back pain) (OR 1.03, 95%CI 1.01–1.05, $P < 0.01$) (Tables 5 and 6).

Discussion

The current study aims to uncover part of the interplay between CS to pain and cognitive dysfunction in students with chronic back pain. Chronic back pain is a major health problem, affecting the general population. In young adults, including university students, CBP is related to poor quality of life and low social functioning [40]. The current study found that 39.6% of the studied sample of university students had CBP. Other studies have shown similar results. A study in India found a prevalence of CBP among university students at 42.4% [41]. In Saudi Arabia, a prevalence of 48.8% among health sciences students was found [4]. These figures place young adults and university students in a high-risk group for developing CBP. It is important it identifies the risk

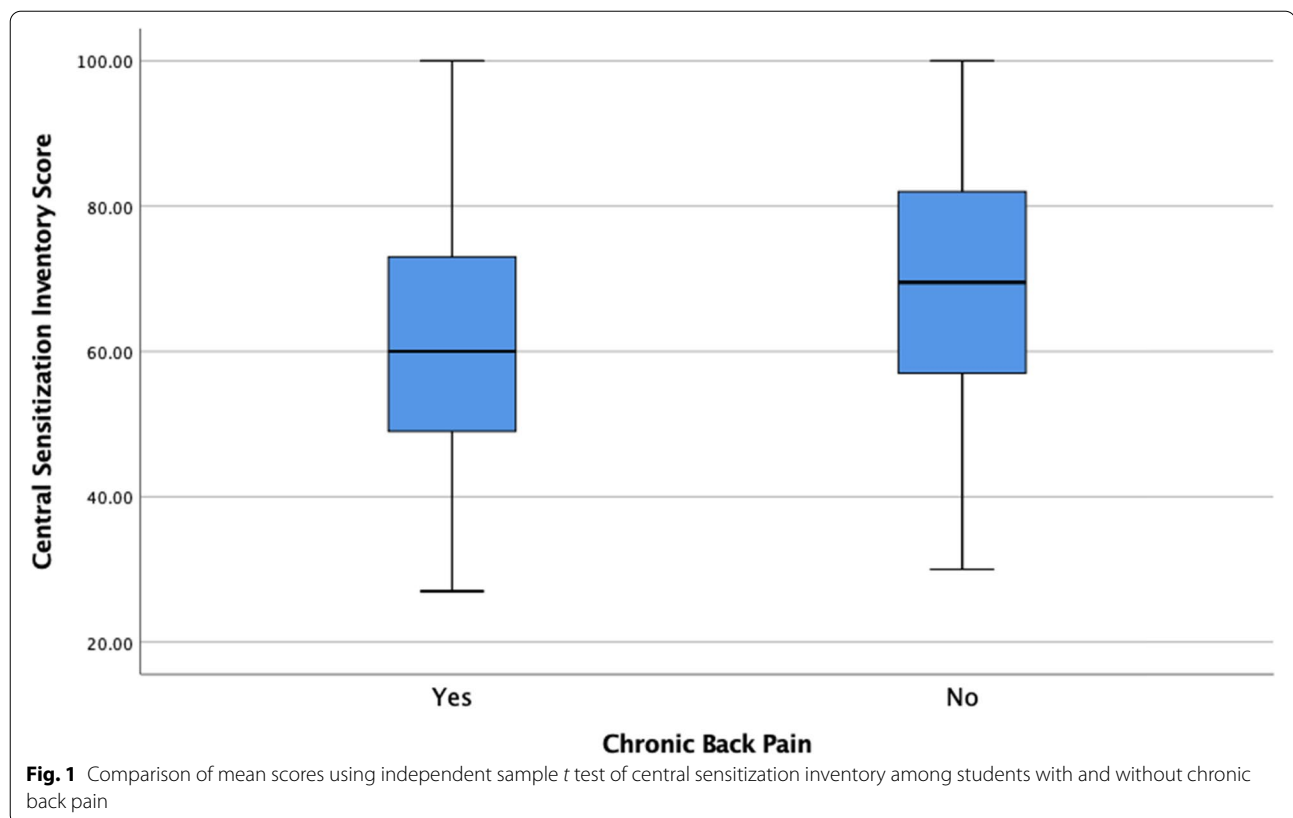


Table 2 Mean scores of attention deficit hyperactivity disorder (ADHD) and central sensitization (CS) among students with and without chronic back pain

	Back pain group (n=90)	No back pain group (n=137)	P value
Mean total score of ADHD scale	52.76±10.49	50.11±9.97	=0.05*
Mean score for attention deficit section	27.06±5.79	25.25±5.41	=0.02*
Mean score for hyperactivity section	25.70±6.17	24.87±6.23	=0.32
Mean score of CSI	69.31±17.43	60.75±17.0	<0.01**

ADHD attention deficit hyperactivity disorder, CSI central sensitization inventory

*Significant P value if P-value ≤0.05, **P-value ≤0.01

P-values were calculated using independent sample t test

factors at an early age, to prevent progression to chronicity and the resulting reduction in productivity [41].

Results of the current study indicate that 97.8% of the students with CBP had features of CS. Previous studies have shown a wide variation in the prevalence of CS in chronic back pain, ranging from 37 to 98% [19, 42]. A recent study found that in patients with chronic pain, those in the age group 18–34 have the highest percentage of CS [43]. This could explain the high percentage of CS we found in our sample. Research suggests that CBP patients with high CS show higher degrees of pain, worse

pain behaviors, and more disability [22]. In the current study, results point to an additional element related to CS, namely, poor cognitive functioning. Students with CBP were found to have significantly higher ADHD symptoms than those without back pain, and strong positive correlations were found between the CS and ADHD. To our knowledge, this is the first study to report such a correlation in a cohort of CBP patients. This finding should alarm clinicians to search for these determinants, since CS combined with other cognitive and psychological factors is known to lead to poor functional outcomes [44].

Table 3 Percentage of students fulfilling criteria for attention deficit hyperactivity disorder and central sensitization with and without back pain

	Back pain (n=90)	No back pain (n=137)	P-value
ADHD score \geq 24 points	68 (75.6)	47 (34.3)	=0.07
ADHD score <24 points	22 (24.4)	90 (65.7)	
CSI score \geq 40 points	88 (97.8)	108 (78.8)	<0.01**
CSI score <40 points	2 (2.2)	29 (21.2)	

ADHD attention deficit hyperactivity disorder, CSI central sensitization inventory

*Significant P-value if P-value \leq 0.05, **P-value \leq 0.01

P-values were calculated using chi-square test

In the current study, patients with CBP showed higher ADHD scores. In concordance, a recent study found that a high percentage of CBP patients show features of ADHD [45]. Indeed, several previous studies have reported the presence of attention and memory deficits in chronic low back pain [46]. These deficits, in addition to reducing the quality of life of those patients, they also pose challenges to rehabilitation [47].

Adults with ADHD report impaired pain processing [48], which has also been demonstrated in animal models [33]. Symptoms of inattentiveness and hyperactivity are thought to be due to reduced dopaminergic activity [49]. Interestingly, the same dysfunction of the dopaminergic system is strongly implicated in the hypersensitivity to pain observed in chronic pain conditions such as fibromyalgia [50].

The current study supports the presence of a strong association between ADHD and CS. Additionally, current results support a specific direction for this relationship, namely that CS mediates the effect of ADHD symptoms on CBP. Our results add evidence to the hypothesis that ADHD is one of the precursors of CS in CBP. This was evident through the attenuation of the effect of ADHD in the regression model when CS was added.

The main strength of the current study is that it is the first study to report associations between central

Table 5 Logistic regression model to test the effect of attention deficit hyperactivity disorder on back pain in the absence of central sensitization

Independent variables	OR (95% CI)	P-value
ADHD score	1.025 (0.99–1.05)	0.05*
Age	0.94 (0.83–1.06)	0.33
Gender†	0.80 (0.42–1.51)	0.48

ADHD attention deficit hyperactivity disorder, CS central sensitization

† Reference is male

Table 6 Logistic regression model to test the effect of attention deficit hyperactivity disorder on back pain in the presence of central sensitization

Independent variables	OR (95% CI)	P-value
ADHD score	0.89 (0.86–0.99)	0.70
CSI score	1.03 (1.01–1.05)	<0.01**
Age	0.93 (0.82–1.05)	0.25
Gender ^a	0.89 (0.46–1.75)	0.74

ADHD attention deficit hyperactivity disorder, CSI central sensitization inventory

^a Reference is male

sensitization and adult ADHD in CBP patients. This adds evidence to the link between the biological and cognitive domain of the biopsychosocial model used to conceptualize and treat CBP. It also serves to direct clinicians to the possible value of screening for ADHD in patients with CBP.

Limitations

The main weakness is that the study relied on self-reported measures for key variables, instead of a formal clinical assessment. However, the tools utilized in the study design have high sensitivity and specificity in detecting the key determinants. Also, the study's cross-sectional design reduced the possibility of identifying causal relationships between the variables. Further research on a larger clinical sample is warranted to ascertain these relationships.

Table 4 Correlation between central sensitization inventory and total attention deficit hyperactivity disorder scores in the studied sample (n=227)

	Total ADHD score		Attention deficit score		Hyperactivity score	
	r	P-value	r	P-value	r	P-value
Central sensitization score	0.55**	<0.01	0.49**	<0.01	0.59**	<0.01

*Correlation is significant at <0.05 level

**Correlation is significant at <0.01 level

P-values were calculated using Pearson correlation

Conclusions

This study shows that students with CBP exhibit high levels of CS and high levels of ADHD. It provides evidence that a relationship exists between CS and ADHD and suggests that CS mediates the effect of ADHD on patients suffering from CBP. Further research is needed to confirm the direction of the relationship and to confirm the value of screening patients with CBP for ADHD.

Abbreviations

ADHD: Attention deficit hyperactivity disorder; ASRS v1.1: Adult attention deficit hyperactivity disorder self-report scale version 1.1; CBP: Chronic back pain; CS: Central sensitization; CSI: Central sensitization inventory; DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision; OR: Odds ratio.

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Authors' contributions

MEI and MAH designed the study, MAH designed the analysis, MEI analyzed the data, and MEI and MAH drafted the manuscript. The authors critically appraised and approved the final version of the manuscript.

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Availability of data and materials

The dataset used in the current study is available from the corresponding author on reasonable request.

Declarations

Consent for publications

Not applicable.

Ethics approval and consent to participate

All procedures performed in the study were in accordance with the ethical standards of the research ethics committee of the Faculty of Medicine, Suez Canal University (reference number 4237), and with the 1964 Helsinki Declaration and its later amendments. Informed consent were obtained from all participants included in the study.

Competing interests

The authors declare that they have no competing interests.

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