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ORIGINAL ARTICLE

Dysfunctional pain inhibition in patients with chronic whiplash-associated disorders: an experimental study

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Abstract Inefficient endogenous pain inhibition, in particular impaired conditioned pain modulation (CPM), may disturb central pain processing in patients with chronic whiplash-associated disorders (WAD). Previous studies revealed that abnormal central pain processing is responsible for a wide range of symptoms in patients with chronic WAD. Hence, the present study aimed at examining the functioning of descending pain inhibitory pathways, and in particular CPM, in patients with chronic WAD. Thirty-five patients with chronic WAD and 31 healthy controls were subjected to an experiment evaluating CPM. CPM was induced by an inflated occlusion cuff and evaluated by comparing temporal summation (TS) of pressure pain prior to and during cuff inflation. Temporal summation was provoked by means of 10 consecutive pressure pulses at upper and lower limb location. Pain intensity of first, fifth, and 10th pressure pulse was rated. During heterotopic noxious conditioning stimulation, TS of pressure pain was significantly depleted among healthy controls. In contrast, TS was quite similar prior to and during cuff inflation in chronic WAD, providing evidence for dysfunctional CPM in patients with chronic WAD. The present study demonstrates a lack of endogenous pain inhibitory pathways, and in particularly CPM, in patients with chronic WAD, and hence provides additional evidence for the presence of central sensitization in chronic WAD.

Keywords Chronic whiplash-associated disorders · Chronic pain · Pain modulation · Pain inhibition · Central sensitization

Introduction

About half of the persons involved in a whiplash trauma recover within 3 months [1]. However, 10–50 % develop chronic pain and disability [2–5]. Chronic whiplash-associated disorders (WAD) are characterized by persistent neck pain, headache, dizziness, concentration disturbances, sleep difficulties, and fatigue which interfere with activities of daily living.

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The recovery rate after whiplash trauma varies greatly between various countries. Whiplash-associated disorders seem to be non-existent or have a good prognosis in some countries (e.g., Greece, Lithuania, Germany, and Denmark) [6–9] while in others (e.g., Sweden, Canada, and Great Britain) a high prevalence of chronic WAD has been observed [10–12]. Social factors based on different cultural attitudes and insurance and legal systems may affect the expectations of chronic disability due to whiplash trauma and hence, contribute to the huge differences from one country and society to another. Canadians had the poorest expectations for recovery [13–15]. Recent studies showed that only 24 % of a Canadian sample and 27 % of a Swedish sample reported having good expectations for recovery [16, 17]. The authors hypothesized that the low expectation of chronic symptoms after whiplash trauma in persons from countries such as German, Greece, and Lithuania may account for the lower prevalence of chronic WAD there; although social and cultural beliefs alone may not explain the development of persistent symptoms after whiplash trauma.

Recent scientific research provided new insights concerning underlying mechanisms of chronic WAD. Radiological findings and/or cervical dysfunctions do not account for the development of chronic WAD [18, 19]. In addition, treatment of cervical dysfunctions in patients with chronic WAD rarely results in pain relief or improved quality of life [20]. Instead, a growing body of research suggests that chronic WAD results from altered central pain processing or central sensitization [21–24].

Central sensitization refers to the augmented responsiveness of the central neurons to input from low-threshold mechanoreceptors [25]. This means that central pain processing pathways localized in the spinal cord and the brain sensitize, resulting in an increased sensitivity to a variety of stimuli including mechanical pressure, chemical substances, light, cold, heat, and electrical stimuli [26–28]. Widespread hypersensitivity to mechanical, electrical, and thermal stimuli has been observed in patients with chronic WAD [21, 29–32]. Changes in descending pain modulatory pathways, which can be inhibitory as well as excitatory, are proposed to take part in the central sensitization process [33–35]. There is evidence of decreased pressure pain thresholds due to exercise in patients with chronic WAD [36], suggesting deficient endogenous pain inhibition since exercise normally results in pain inhibition [37, 38].

Another part of the endogenous pain inhibitory process is attributed to diffuse noxious inhibitory controls, which include descending pain inhibitory pathways arising from periacqueductal gray matter and subnucleus reticularis dorsalis in the caudal medulla, and which are activated by nociceptive input and then modulate the nociceptive input by inhibition of the dorsal horn wide dynamic range neurons [39]. Diffuse noxious inhibitory controls refer to the powerful nociceptive inhibition in one part of the body when painful stimulation is applied in another part of the body. Recently, the term conditioned pain modulation (CPM) was recommended to describe the psychophysical paradigm of diffuse noxious inhibitory controls in humans [40]. CPM will be further used in this article to design the psychophysical paradigm of diffuse noxious inhibitory controls in humans.

Inefficient CPM was reported in some patients groups such as fibromyalgia, chronic tension-type headache, and chronic fatigue syndrome, among others [41–43] while it appears to function normally in patients with chronic low back pain [44]. Data addressing CPM in chronic WAD are currently unavailable. In spite of its key role in central sensitization, CPM has not been studied in depth in chronic WAD. Moreover, the effect of CPM on temporal summation (TS) of second pain [43, 45] is yet to be investigated in chronic WAD. Hence, the present study aimed at examining the effect of CPM on TS of pressure pain in patients with chronic WAD. We anticipate dysfunctional CPM in patients with chronic WAD in comparison to controls.

Methods

Subjects

Participants were recruited from the medical database of the local Red Cross medical care unit. Criteria for inclusion were experiencing chronic symptoms resulting from a whiplash trauma and fulfilling diagnostic criteria of WAD I to III as defined by the Quebec Task Force classification [5]. Subjects with WAD grade I, II, as well as III were included in order to achieve a broadest group of patients suffering from persistent symptoms after whiplash trauma. Patients were not allowed to participate if an obvious injury (e.g., lesion to nerve, disk, and brain structures) was diagnosed at time of injury or at time of clinical assessment by a specialist/physician. Subjects were excluded if they were classified as WAD IV (fracture or dislocation) [5]. Chronic was defined as complaints persisting for at least 3 months.

Healthy pain-free control subjects were recruited among university college staff and family and acquaintances of the researchers. Control subjects were not allowed to participate if they ever had experienced a whiplash trauma, suffered from pain or neck–shoulder–arm pain, or if they had sought medical help for neck–shoulder–arm pain in the past 6 months. The control group was recruited, age- and gender-matched to the chronic WAD group.

Only Dutch-speaking participants aged between 18 and 65 qualified for the study. Patients were asked to discontinue analgesic and anti-inflammatory drugs 48 h before testing

and all participants were instructed to avoid physical exertion and to refrain from consuming nicotine, alcohol, and caffeine 24 h before testing. Subjects were excluded if they were pregnant, or when they suffered from any cardiovascular or neurological disease.

An a priori power analysis determined that at least 30 participants per group were required to examine the effect of CPM on TS of pressure pain, with a Power of 0.80 and $\alpha \leq 0.050$. A control group was recruited, age- and gender-matched to the chronic WAD group.

Procedure

Before study participation, subjects were asked to carefully read an information leaflet and to sign the informed consent; written informed consent was obtained from all participants before study participation in accordance with the Declaration of Helsinki. The study was approved by the Human Research Ethics Committee of the Antwerp University Hospital. A standardized questionnaire was used to collect personal and accident- and health-related information. A battery of questionnaires, Neck Disability Index, Beck Depression Inventory, Pain Catastrophizing Scale, Pain Vigilance Awareness Questionnaire, and Impact of Event Scale, was filled out. Next, participants were subjected to an experiment to evaluate CPM. The paradigm of heterotopic noxious conditioning stimulation was used [46, 47]. The effect of tonic painful and ischemic stimulation at one part of the body, i.e., painful occlusion cuff inflation at the left upper arm, on the sensation provoked by a phasic stimulus at another part, i.e., mechanical pressure pain at the shoulder and the thigh, was investigated.

Measurements

Questionnaires

Self-reported measurements were used to assess pain, disability, psychosocial factors, pain cognition, and post-traumatic stress. The scoring method and clinimetric properties of the Neck Disability Index [48], Beck Depression Inventory [49], Pain Catastrophizing Scale [50], Pain Vigilance and Awareness Questionnaire [51], and Impact of Event Scale [52] have been described in detail elsewhere.

Conditioned pain modulation

All experimental pain assessments were carried out by the same researcher. The details and data supporting the test–retest reliability and validity of the protocol for examining CPM are described elsewhere [43, 53]. First, pressure pain thresholds were measured at right trapezius belly (middle between processus spinosus T1 and lateral part acromion) and at right quadriceps belly (middle between groin and proximal part patella) with an analogue Fisher algometer (Force Dial model FDK 40 Push Pull Force Gage, Wagner Instruments, P.O.B. 1217, Greenwich CT 06836). In order to determine pressure pain thresholds, pressure was gradually increased at a rate of 1 kg/s until first onset of pain. The pressure pain threshold was taken as the mean of two consecutive (30 interstimulus interval) measurements. The pressure pain threshold technique was found to be reliable [54].

Second, TS was provoked by means of 10 consecutive pulses at previously determined pressure pain threshold at each location. TS started 2 min after pressure pain threshold measurement. For each pulse, pressure was gradually increased at a rate of 2 kg/s to the determined pressure pain threshold and maintained for 1 s before being released (1 s interstimulus interval). Pain intensity of first, fifth, and 10th pulse was rated on a numerical rating scale (0 = no to 10 = worst possible pain). Afterwards, a rest period of 5 min was allowed.

Third, CPM was induced by inflating an occlusion cuff at the subject's left arm to a painful intensity. The occlusion cuff was inflated at a rate of 20 mmHg/s until 'the first sensation of pain' and maintained for 30 s. Afterwards, pain intensity, as a result of cuff inflation, was rated on a numerical rating scale (0 = no to 10 = worst possible pain). Next, cuff inflation was increased or decreased until pain intensity at left arm was rated as 3/10. TS assessment was then repeated during maintenance of the cuff inflation.

Statistical analysis

Statistical analyses were conducted using SPSS 12.0 for Windows (SPSS inc. Headquarters, Chicago, Illinois, USA) and SAS 9.2 (SAS Institute Inc., Cary, NC) software.

Normality of variables was tested with the Kolmogorov–Smirnov test. Comparability of groups for gender distribution and age was verified with Pearson's χ^2 test and Independent-sample *t* test, respectively. A multi-level mixed effects model was used to assess for CPM effect on TS of pressure pain within the control and the experimental group and to identify differences in CPM between both groups. Since multiple pain measurements of the same individual tend to be correlated, independence may not be assumed. A mixed effects model, consisting of a random and a fixed component, was used to account for this correlation [55, 56]. The random part of the model in which individual repeated observations were nested within experimental stage within patient, accounts for the hierarchical structure of the data. In the fixed part of the model an interaction between pulse (first, fifth, and 10th pulse), experimental stage (prior/during cuff inflation) and experimental group (control versus chronic WAD) was used to assess TS prior to and during cuff inflation and CPM on TS of pressure pain within the

control and the experimental group and to identify differences in TS prior to and during cuff inflation and CPM on TS of pressure pain between both groups. For TS of pressure pain (pain increase from first to 10th pressure pulse), the pain intensity scores after the first, fifth, and 10th pressure pulse, were used. To measure CPM effect, TS of pressure pain prior to and during cuff inflation were compared. In order to check the effect of psychosocial factors on the outcome parameters, the statistical model was extended with these factors. The scores of the Beck Depression Inventory, Pain Catastrophizing Scale, Pain Vigilance Awareness Questionnaire, and Impact of Event Scale were put in the mixed effects model as covariates.

Results

Group characteristics

Thirty-five patients with chronic WAD (26 women and nine men) and 31 healthy controls (24 women and seven men) volunteered for the study. Mean age was respectively 43.8 (±9.58) and 43.19 (±16.11)years. Both groups were comparable for age and gender distribution. Mean scores for neck pain and disability, depression, pain catastrophizing, pain vigilance, and awareness and post-traumatic stress are presented in Table 1. Mean pain scores of the Beck Depression Inventory, Pain Catastrophizing Scale, Pain Vigilance Awareness Questionnaire, and Impact of Event Scale were significantly different between both groups ($p<.05$, data not shown). In the chronic WAD group, one participant reported mild pain and disability (10–28 Neck Disability Index), and 34 participants were classified as having moderate/severe pain and disability (>30 Neck Disability Index).

Conditioned pain modulation in chronic WAD

Results of TS of pressure pain in patients with chronic WAD and healthy controls prior to and during cuff inflation at shoulder and thigh are presented in Table 2. Repeated mechanical noxious stimuli resulted in TS of pressure pain in both groups, as shown by significant increases in experienced pain intensity from the first to 10th pulse prior to cuff inflation (both at shoulder and thigh; $p<.01$). No significant differences in TS prior to cuff inflation were observed between both groups ($p>.05$).

The lower rows of Table 2 present TS of pressure pain during cuff inflation. For the chronic whiplash group, significant increases in pain intensity from the first to 10th pressure pulse were found at both locations ($p<.01$). Hence, pain intensity increased significantly from the first to fifth and from the fifth to 10th pulse ($p<.01$). In the control group, a significant increase in pain intensity from the first to 10th pulse was found at shoulder and thigh ($p<.001$). In contrast, healthy controls displayed no significant pain increase from the fifth to 10th pressure pulse at either location ($p>.05$). Temporal summation of pressure pain during cuff inflation was significantly higher in patients with chronic WAD in comparison with healthy controls at both locations ($p<.0001$). In addition, increase in pain intensity from the first to fifth pulse and from the fifth to 10th pulse was significantly different between both groups at both locations ($p<.05$).

Figures 1 and 2 demonstrate CPM in both groups at both locations illustrating depleted TS of pressure pain during cuff inflation (compared with no cuff inflation) in healthy controls at both locations ($p<.001$). In contrast, the increase in pain intensity from the first to 10th pulse was quite similar prior to and during cuff inflation in the chronic WAD group at both locations ($p>0.5$). This points towards less efficient CPM in patients with chronic WAD. For both locations, CPM was significantly less efficient in the chronic WAD group compared to the healthy control group ($p<.001$).

The role of cognitive and emotional factors on the outcome

Neither Beck Depression Inventory, Pain Catastrophizing Scale, Pain Vigilance Awareness Questionnaire, nor Impact of Event Scale score had a significant effect on TS of pressure pain or CPM on TS of pressure pain ($p>.05$).

Table 1 Mean scores self-reported measurements per group

	NDI	BDI	PCS	PVAQ	IES
Chronic WAD (n=35)					
Mean (SD)	44.36 (12.64)	16.00 (8.75)	17.52 (11.57)	35.21 (12.27)	18.97 (16.84)
Median (IQR)	40 (14)	14 (17)	18 (20)	35 (16)	16 (29)
Control (n=31)					
Mean (SD)		2.73 (2.65)	8.43 (8.92)	23.63 (12.19)	
Median (IQR)		2 (4)	5 (9)	23 (20)	

NDI Neck Disability Index, *BDI* Beck Depression Inventory, *PCS* Pain Catastrophizing Scale, *PVAQ* Pain Vigilance and Awareness Questionnaire, *IES* Impact of Event Scale, *SD* standard deviation, *IQR* interquartile range

Table 2 Mean increase in pain intensity scores during temporal summation in patients with chronic WAD (n=35) and healthy controls (n=31)

	Shoulder			Thigh		
	cWAD	Control	p	cWAD	Control	p
Prior to cuff inflation						
Pain increase 1–5	1.37**	1.19**	.507	1.31**	1.47**	.592
Pain increase 5–10	1.17**	0.90**	.317	0.91**	0.60**	.270
Pain increase 1–10	2.54**	2.10**	.098	2.22**	2.07**	.569
During cuff inflation						
Pain increase 1–5	1.31**	0.58**	.007	1.03**	0.40*	.029
Pain increase 5–10	1.17**	0.12	.0002	1.20**	0.33	.003
Pain increase 1–10	2.49**	0.70**	<.0001	2.23**	0.73**	<.0001

cWAD chronic whiplash-associated disorders, *Pain increase 1–5* mean increase in pain intensity score from the first to fifth pulse (mean pain intensity score at the fifth pulse minus mean pain intensity score at the first pulse), *Pain increase 5–10* mean increase in pain intensity score from the fifth to 10th pulse (mean pain intensity score at the 10th pulse minus mean pain intensity score at the fifth pulse), *Pain increase 1–10* mean increase in pain intensity score from the first to 10th pulse (mean pain intensity score at the 10th pulse minus mean pain intensity score at the first pulse)

*p<.05; **p<.01

Hence, outcome measurements were not influenced by psychological factors such as depressive thoughts, catastrophic thinking, and hypervigilance to pain or stress.

Discussion

The primary objective of this study was to examine the efficiency of pain inhibition, and in particular CPM, in patients with chronic WAD. Patients with chronic WAD are characterized by significantly less efficient descending pain inhibition, compared to healthy controls.

Chronic pain might be the result of unresolved peripheral damage or persisting plastic changes in central nervous system despite tissue healing. It has been assumed that peripheral nociceptive input contributes to central hypersensitivity [57]. However, peripheral lesions are rarely identified after a whiplash trauma [58–60]. Involvement of supraspinal mechanisms (i.e., inefficient descending inhibitory pathways and overactive facilitatory pathways) may explain spinal cord hyperexcitability and hence the chronic pain experience in patients with WAD.

Impaired descending pain inhibitory pathways, and in particular dysfunctional CPM, have been observed in patients with fibromyalgia and chronic fatigue syndrome [41, 42, 61]. In the present study, intense and tonic stimulation of nociceptive fibers by occlusion cuff inflation lead to an attenuation of TS of pressure pain in healthy controls, indicating appropriate CPM functioning. In contrast, pain increase from the first to the 10th pressure pulse was identical prior to and during cuff inflation in the chronic WAD group at both locations, indicating dysfunctional CPM. In

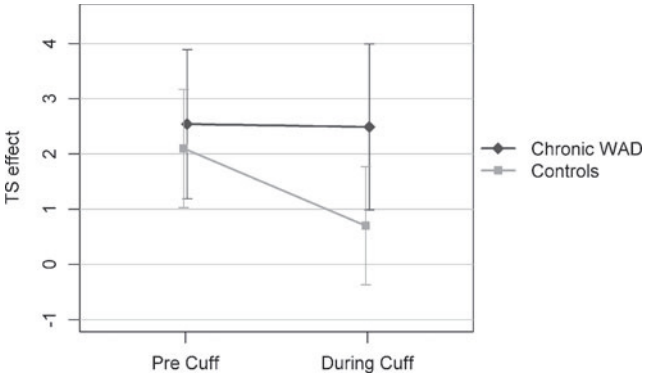

Fig. 1 Conditioned pain modulation in patients with chronic WAD (n=35) and healthy controls (n=31) at the shoulder; TS effect = increase in pain intensity score from the first to 10th pulse

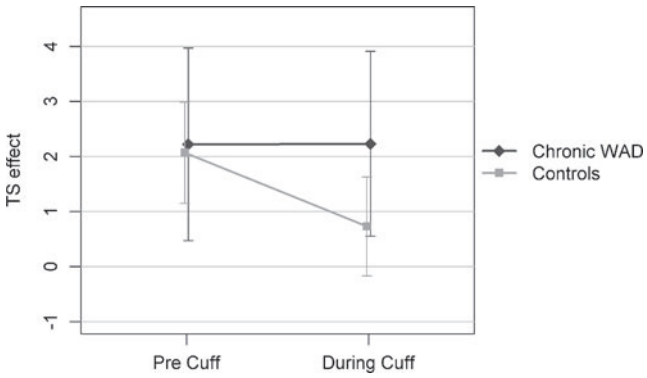

Fig. 2 Conditioned pain modulation in patients with chronic WAD (n=35) and healthy controls (n=31) at the thigh; TS effect = increase in pain intensity score from the first to 10th pulse

concordance with our findings, Staud et al. [41] and Cathcart et al. [62] demonstrated inefficient CPM on TS of second pain in patients with fibromyalgia and chronic tension-type headache, respectively. Inefficient CPM on TS of second pain may contribute to the development of central sensitization in patients with chronic WAD. Further study is needed to examine the role of dysfunctional CPM on the transition from acute to chronic WAD. A prospective longitudinal study design is warranted in order to evaluate and follow-up functioning of descending pain modulation mechanisms at different time intervals following injury, i.e., within the acute (<1 month) and chronic stages (e.g., 3, 6, and 12 month) post-whiplash. This allows to investigate whether CPM differ between patients with persistent symptoms and those who recovered after whiplash trauma.

The extent of pain inhibition during heterotopic noxious conditioning stimulation increased with pressure pulse in healthy controls. During cuff inflation, the observed pain increase from fifth to 10th pulse was less than the increase from first to fifth pulse in healthy controls. In contrast, this effect was not seen in the chronic WAD group. This may explain why TS of pressure pain (i.e., pain increase from the first to 10th pressure pulse) was significantly different between both groups during cuff inflation, while no significant difference in TS effect was observed between patients with chronic WAD and healthy controls prior to heterotopic pain stimulation. In addition, the lack of significant pain increase from the fifth to 10th pressure pulse in healthy controls during counterstimulation could be equally interpreted.

CPM was found to be more effective in reducing C-fiber-mediated second pain than A-delta fiber-mediated first pain [63]. Ischemic and constant pain provoked by occlusion cuff predominantly involves C-fiber conduction [64]. Efficient CPM can modulate wind up of wide dynamic dorsal horn neurons leading to an inhibition of TS of second pain. In cases of impaired CPM, wind up or TS of second pain may be facilitated. This results in an increased transmission to supraspinal sites (e.g., thalamus, anterior cingulate cortex, and somatosensory cortex) via ascending pathways and an increase in pain perception [26]. We propose that impaired or less efficient CPM accounts for the findings in the chronic WAD group in the present study (i.e., similar TS of pressure pain prior to and during cuff inflation).

Different neurological and physiological mechanisms contribute to CPM. Besides activation of a spino-bulbospinal loop which modulates the noxious input at spinal level and which has been suggested as the key mechanism of CPM, brainstem structures (e.g., periaqueductal gray matter and rostral ventromedial medulla), and endogenous opioid release in pain-sensitive brain areas are engaged in descending pain inhibition [65, 66]. Cortical as well as subcortical areas are involved in descending pain modulatory pathways [67–70]. It will be an interesting issue for future research to specifically address the contribution of these factors to CPM in patients with chronic WAD.

The perception of pain is a multidimensional phenomenon influenced by various factors such as previous experiences, emotions, cognitions, and sociocultural beliefs, in addition to sensory input [71]. Various cognitive-emotional factors may be associated with development and maintenance of chronic WAD [72]. Results of earlier pain research demonstrated the effect of negative thinking about pain, hypervigilance to pain, depressive thoughts, and stress on pain perception [73–76]. In the present study, scores of Pain Catastrophizing Scale, Pain Vigilance Awareness Questionnaire, Beck Depression Inventory, and Impact of Event Scale were significantly different between patients with chronic WAD and healthy controls. However, the most important study findings remained even when data were controlled for pain hypervigilance, post-traumatic stress, depressive feelings, and catastrophic thoughts. Hence, cognitive and emotional factors do not account for impaired CPM as seen in patients with chronic WAD in this study.

This is in contrast to several other studies. Cathcart et al. [43] found for example that CPM was associated with depression in patients with chronic tension-type headache. Others demonstrated a relationship between pain catastrophizing and TS of pain; persons who catastrophize showed a greater pain increase in response to repetitive noxious stimulation [77–79]. However, a recent study reported that catastrophizing was unrelated to TS of nociceptive flexion reflex in healthy controls, suggesting that catastrophic thoughts causes enhanced pain perception via supraspinal processes rather than spinal processes [80]. Since subjective pain ratings were used to measure TS of pressure pain, we surprisingly found no correlations between psychological factors (including pain catastrophizing) and the outcome parameters (i.e., TS of pressure pain and CPM on TS of pressure pain).

Firstly, this suggests that psychological factors could play a role, but are not the only determinants of enhanced TS and altered pain modulation in patients with chronic WAD. Secondly, this could be explained by the time frame or way of psychological evaluation. Dixon et al. [81] showed that catastrophic thoughts evaluated during experimental pain assessment (i.e., in vivo), and not standard catastrophic thoughts measured prior to experimental pain testing, was associated with pain perception and pain tolerance. Others found that TS of pain was correlated with situation-specific catastrophizing (measured immediately after a specific painful event) but not with trait pain catastrophizing (i.e., catastrophic thoughts measured prior to pain testing and related to painful experiences in general) [80]. In the present study, questionnaires were administered prior to conducting experimental pain assessment and were proposed to measure thoughts and beliefs related to painful experiences in general

(i.e., not situation specific). Results of the present study need to be interpreted in view of these differences. In addition, it is recommended to take this into account when constructing future study designs.

Finally, it is important to note that most of abovementioned studies examined healthy subjects. Findings concerning the relationship between psychological factors and sensory responses in WAD are inconsistent. A significant correlation between catastrophizing and hypersensitivity to cold stimuli, but not between catastrophizing and nociception reflex responses (pain and thresholds), was found [82]. Thermal pain thresholds, but not pressure pain thresholds, were correlated with psychological variables in WAD [22, 24, 82, 83]. These findings support the hypothesis that psychological factors play a role but are not the only or main factors responsible for the complex clinical picture of chronic WAD. The relationships between psychological factors and measures of TS and CPM in WAD have not been explored. Although it was not a specific aim of this study to investigate such relationship, findings suggest that psychological factors, including pain catastrophizing, hypervigilance to pain, depressive thoughts, and post-traumatic stress have no (strong) impact on descending pain modulation in chronic WAD. Further investigation in this field is warranted.

A few study limitations merit attention. First, the contribution of attention to CPM effect cannot be ruled out. Provoking an intense and persistent pain stimulus by occlusion cuff inflation may attract the attention. However, it has been recently suggested that CPM and distraction underlie separate and independent mechanisms [84]. Second, the observation account for mechanical stimuli solely. Further study of CPM to chemical, electrical, and thermal stimuli is warranted. Third, the nature of the conditioning stimulus could have an influence as well. Studies investigating pain-modulating effect of other conditioning stimuli than cuff inflation are required. Finally, the patients with chronic WAD included in this study were not segregated in subgroups based on injury severity as proposed by the Quebec Task Force classification system [5]. However, classification of injury severity proposed by the Quebec Task Force in 1995 [5] still remains under debate [85–87]. Relying on this classification system does not provide any information concerning the nature or underlying mechanism. Despite the fact that some authors declared that the Quebec Task Force classification system provides a reasonable estimate of risk [88–90], others found no association between the Quebec Task Force classification and outcome [86].

In conclusion, this study demonstrates dysfunctional endogenous pain inhibition, and in particularly impaired CPM, in patients with chronic WAD. The observations are independent from pain hypervigilance, post-traumatic stress, depressive feelings, or catastrophic thoughts. Dysfunctional descending pain inhibitory pathways are likely to contribute to central sensitization in patients with chronic WAD.

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