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Florent El Grabli, François Quesque, Céline Borg, Michael Witthöft, George A. Michael, et al.. Interoception and social cognition in chronic low back pain: a common inference disturbance? An exploratory study. *Pain Management Nursing*, 2022, 12 (4), pp.471-485. 10.2217/pmt-2021-0090 . hal-03773938

HAL Id: hal-03773938

<https://hal.science/hal-03773938v1>

Submitted on 9 Sep 2022

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Interoception and social cognition in chronic low back pain: a common inference disturbance? An exploratory study

Published in Pain Management (ISSN1758-1869), 2021 Dec 11.

doi: 10.2217/pmt-2021-0090.

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Abstract

Aim: Lower interoceptive abilities are a characteristic of chronic pain conditions. Social support plays an important role in chronic low back pain (cLBP) but social cognitive skills have rarely been investigated. This study aimed to characterize interoceptive and social cognitive abilities in cLBP and to study the relationship between both domains that have been brought closer together by brain predictive coding models. **Materials & methods:** Twenty-eight patients with cLBP and 74 matched controls were included. Interoceptive accuracy (Heart Beat Perception Task), sensibility/awareness (Multidimensional Assessment of Interoceptive Awareness) and mental-states inference abilities (Mini-Social cognition and Emotional Assessment) were assessed. **Results:** cLBP Patients had lower interoceptive accuracy and mentalizing performance. **Conclusion:** Less efficient interoceptive accuracy and mentalizing abilities were found in cLBP patients without correlation between these performances.

Lay abstract

Aim: Interoception, allowing to perceive body sensations such as heartbeats, has been reported to be decreased in chronic pain. This ability has been recently related to social cognition, because we need inferential mechanisms to decode others' emotions or our own sensations. The link between interoception and social cognition in chronic pain, however, is unknown. **Materials & methods:** We aimed to study key interoceptive & social abilities in 28 participants with chronic low back pain and 74 control participants. **Results:** Participants with chronic low back pain had lower performance in some interoceptive and social cognitive dimensions, but performances in these domains were unrelated. **Conclusion:** Interoception should be a target for therapeutic interventions.

Keywords: chronic pain • emotion recognition • interoception • low back pain • social cognition

Introduction

Low back pain is a very common symptom and the leading cause of disability in the world [1]. Symptoms range from a dull ache to a stabbing or shooting sensation, leading to various difficulties including moving or standing up straight, which deeply impact the patients' quality of life. Over 60–70% of people are estimated to experience an episode of low back pain during their lives and the pain is considered to be chronic when persisting for more than 3 months [2]. In contrary to acute pain, chronic pain lacks the acute warning function of physiological nociception and has such been conceptualized beyond a purely biomedical view. In particular, chronic low back pain (cLBP) has been long envisaged as a 'biopsychosocial' condition [3], where social and psychological factors play a considerable role, acting as significant modulators of pain at the cognitive [4] and neural level [5]. This underscores that pain is a complex process, encompassing sensory, emotional and cognitive components [6].

The neural signature of pain has recently been described in a new theoretical framework [7]. Within this framework, the prediction, perception and generation of pain strongly relate to interoception [6,8]. Defined as the sense of the body's internal physiological state, interoception allows us to infer, perceive and predict our own physiological state through the integration of multimodal sensory inputs arising from the body and environment [9]. A significant literature supports the relationship between pain processing and interoception and its most recent developments suggest that chronic pain syndromes in particular are characterized by lower interoceptive abilities [8]. In this context, interoception has been proposed as a key aspect for the future development of treatments for chronic pain [10]. However, because the topic is still young, designing therapeutic interventions that would consider interoception requires to better characterize the interoceptive abilities in chronic pain conditions. In cLBP specifically, only three studies [11–13] have been conducted on interoception: two reported a

decrease of interoceptive accuracy (i.e., the ability to perceive interoceptive signal, such as heartbeat [11,12]) and one reported abnormal interoceptive sensibility/awareness (i.e., interoception measured through self-reported questionnaires [13]). To emphasize the role of interoception in the therapy or management of cLBP, these findings have to be confirmed and extended.

Because interoception relies on constant inferences and perceptions about one's own internal state [14], there has been a strong interest in the role interoception could have in emotion processing and other's mental-state inference [15]. Interoception, formulated under active inference, is indeed increasingly considered to play a key role in such processes [16]. Regarding emotions, the substantial overlap between the neural substrates of both mechanisms [17] aligns with the most modern theoretical views that consider interoception and emotional states within a common predictive coding system [18]. The conceptualization of the brain as a 'prediction machine,' generating constant inferences about the inner and outer environment and adjusting their validity against incoming sensory or cognitive evidence, also provide a similar insight into the assumed overlap between interoception and mentalizing, the ability to infer other's mental states, also called theory of mind. Mentalizing is an important ability in daily social interactions as inferring other's feelings, thoughts or perspectives is critical for good social adaptation, adequate communication and, in a context of chronic condition, efficient social support. While it has only been recently pointed out, the relationship between interoception, emotion processing and mentalizing through a common predictive coding mechanism has already received support from a number of experimental and clinical studies [19,20], showing, in sum, a correlated decrease in interoceptive and social cognitive domains (i.e., mentalizing [15], empathy [21], emotion recognition [19]).

Whether the impairment of a common inference mechanism could explain the concomitant decline of interoception and

social cognition is an important theoretical question, having the potential to enrich the predictive coding framework, while deepening our understanding of interoception and its proposed fundamental role in body ownership and selfhood [22]. Clinically, as social support plays an important role in chronic pain syndrome, and cLBP in particular [23], it is of utmost importance to know if social cognitive skills are preserved or not, as they shape interpersonal relationships. We believe that it is indeed a critical dimension to consider in the management of pain, as social skills are relevant in the relationships with health professionals or within the patients' social circles. However, among the clinical populations considered in the past when investigating interoception and social cognition, chronic pain conditions and cLBP in particular have been left behind. Investigations of social cognition in chronic pain population in general have been scarce (though see, Shin *et al.* [24] and Sohn *et al.* [25]) and no previous study investigated social cognition (emotion processing, mentalizing) in cLBP. Although studies of interoceptive abilities in cLBP suggest that some abnormalities could exist regarding the perception or inference of internal states [11,12], the question remains if patients with cLBP also suffer from a lower ability to perceive or infer other's internal states, and if both abilities are indeed related.

In this context, we conducted this study with the aim to: characterize interoception and other's mental-state inference abilities in cLBP, in delineating interoceptive abilities into accuracy and sensibility/awareness as well as social inference into emotion recognition and mentalizing; study the relationship between interoception and other's mental-state inference. We hypothesized to observe a decrease of interoceptive accuracy but not sensibility/awareness in cLBP, with the first being correlated to normal or subnormal social cognitive performances.

Materials & methods

Participants

A total of 102 participants were included in this study, including 28 participants (n = 18 women) with a diagnosis of cLBP and 74 healthy control participants (n = 41 women) matched on age, gender, education level and BMI. Patients were recruited from the pain clinic of the Lille University hospital from February 2019 to April 2021 with the following inclusion criteria: be aged between 25 and 75 years; have received a diagnosis of cLBP from a pain specialist, following the French National Authority for Health guidelines; be hospitalized in the pain clinic of the Lille University hospital; and the following exclusion criteria: the presence of severe cognitive impairments – as measured by the Montreal Cognitive Assessment [26] (MoCA– that could negatively impact the administration of the proposed tests); the intravenous use of a psychoactive product (e.g., tricyclics, lidocaine, ketamine) within the 3 months before the study. All patients were volunteers and gave their informed consent prior to the participation in the study. Healthy control participants were seen in different centers. For the heart beat perception task (HBPT, n = 27), they were included as part of a previous study on interoception, originally seen at the Johannes Gutenberg- University Mainz in Germany [27]. Trained clinicians administered the Structured Clinical Interview for DSM-IV to ensure that no control participant fulfilled the diagnostic criteria for a current DSM-IV axis I disorder. For the Multidimensional Assessment of Interoceptive Awareness (MAIA, n = 21), control participants were seen at the Saint-Etienne University Hospital in France [28]. For the Mini-Social cognition and Emotional Assessment (mini-SEA, n = 26), control participants were seen at the Pitié-Salpêtrière University Hospital in France and had normal cognitive efficiency testing. All controls were recruited through leaflets, local press releases or newsletters, had no prior psychiatric or neurologic antecedents or complain, and were only seen at the hospital for the purpose of the study. Local ethics committees have approved the

study for all control participants, who all signed informed consents.

Procedure

All patients received a neurological and general examination prior to the study's assessment. When they engaged in the study, a general question on their cognitive well-being was asked: 'Does your pain affect your memory or cognition in your daily life?' Responses were recorded into yes/no. This was followed by an assessment of global cognitive efficiency using the MoCA. After the cognitive screening, a standardized assessment about their pain and anxious or depressive state was performed. Treatments used were recorded. Finally, we administrated an evaluation of interoception and social cognition abilities. The assessments related to pain, interoception and social cognition are described below in details. All assessments were performed in French, with validated version of tests or scales.

Pain evaluation

Brief pain inventory

This self-report questionnaire [29] assesses pain's severity and its impact on functioning. Answers are given across a 10-point Likert scale, from 0 (no severity/impact) to 10 (worse severity/maximum impact).

Roland–Morris questionnaire

The Roland–Morris questionnaire is a short self-survey [30], aiming to measure the functional impact of low back pain specifically. It has been validated in cLBP [31] and is composed of 24 items related to activities of daily living. Total score ranges from 0 (no impact) to 24 (maximum impact).

Thymic evaluation

Hospital anxiety & depression scale

The hospital anxiety and depression (HAD) scale [32] was used to assess anxiety and depression through 14 questions focused on

anxious (seven questions allowing the calculation of anxiety subscore) or depressive (seven questions allowing the calculation of depression subscore) symptoms. Anxiety and depression are considered as doubtful (subscores $\geq 8/21$) or certain (subscores $\geq 11/21$).

Interoception assessment

Heart beat perception task

This mental tracking heartbeat task assesses interoceptive accuracy [33]. After a 5-min rest period (in which patients must close their eyes and focus on their heartbeat), the participants are required to mentally count their heartbeats, without being able to take their pulse. Three heartbeat-counting trials of different duration (25, 35 and 45 s) are performed, separated by silent periods of 30 s. The beginning and end of each trial is indicated by a short audio recording asking the patient to 'count' or 'stop,' respectively. Then, patients report the number of heartbeats they counted. These estimated numbers are respectively compared with their actual numbers of heartbeats during these periods. Concerning the actual heartbeats, they are determined using a 12-channel Mortara 250c electrocardiogram (ECG). Five electrodes are used to record the ECG signal: two are placed at the shoulder and two on the wrist and one on the chest (fifth intercostal space in the mid-clavicular line). The ECG electrodes are placed before the rest period of 5 min. For each heartbeat-counting trial, the actual heartbeats are noted in parallel by the experimenter. Patients are not informed about their actual performance, nor about their actual number of heartbeats or about the duration of each trial. Accuracy is measured through a 'perception score' calculated from the relative difference between the actual and the counted number of heartbeats,

$$\text{perception score} = 1 - \frac{1}{3} \sum \left(\frac{|\text{recorded heartbeats} - \text{counted heartbeats}|}{\text{recorded heartbeats}} \right)$$

perfect detection yields perception score of 1, whereas under-reporting or over-reporting the actual number of heartbeats yields perception

score below 1. The 'number of correct responses' with one point by trial for which the calculated heartbeat is equal to the measured heartbeat ± 2 is also collected as a performance indicator.

MAIA questionnaire

The MAIA [34] was used to assess interoceptive sensibility/awareness. In this questionnaire, participants are required to score, on a 0–5 Likert scale (0 = never, 5 = always), the frequency to which each one of the listed circumstances happens (e.g., I notice changes in my breathing, such as whether it slows down or speeds up). The 32 items are distributed in eight scales: Noticing (awareness of uncomfortable, comfortable and neutral body sensations); Not distracting (not ignoring or distracting oneself from sensations of pain or discomfort); Not worrying (not worrying or experiencing emotional distress with sensations of pain or discomfort); Attention regulation (ability to sustain and control attention to body sensation); Emotional awareness (awareness of the connection between body sensations and emotional states); Self-regulation (ability to regulate psychological distress by attention to body sensations); Body listening (actively listening to the body for insight); and Trusting (experiencing one's body as safe and trustworthy). The total score corresponds to the mean of all subscores.

Interoceptive trait prediction error

In line with Garfinkel *et al.* [35], we computed an Interoceptive trait prediction error (ITPE) for each patient to investigate the influence of the divergence between perceived and objective interoception. The ITPE was defined as the difference between subjective interoceptive sensibility/awareness (MAIA score) and objective interoceptive accuracy (performance at the HBPT). These scores were converted to standardized Z-values. ITPE values were then calculated as the difference between interoceptive sensibility/awareness and interoceptive accuracy, with positive values indicating a propensity to overestimate

interoceptive ability, and negative values a propensity to underestimate interoceptive ability.

Facial emotion recognition

The facial emotion recognition test from the mini-SEA [36] is composed from 35 faces originated from the Picture of Facial Affect set [37], which are presented sequentially to the participants. For each face, the participants have to identify which emotion is expressed by choosing, among a list of seven different labels presented below the photograph, between fear, sadness, disgust, surprise, anger, happiness and neutral. The maximum transformed score is 15.

Mentalizing

The modified faux pas test from the mini-SEA, adapted from [38], is composed from ten written stories that are presented sequentially to participants after one example story. The participants have to read each story. After each reading, they have to report the presence (or absence) of a faux pas (i.e., someone involuntarily said something rude that they would not have said if they had access to the other character's knowledge) and, if they reported one, explain it through six specific questions. A faux pas is present in five stories. The maximum transformed score is 15.

Statistical analysis

All analyses were performed using IBM's SPSS 20. Data were plotted using GraphPad Prism 9. Normality of the data for interoception and social cognition tests was assessed with Kolmogorov–Smirnov and Shapiro–Wilk tests, both showing normal distributions (all $p > 0.2$). Intergroup differences were then explored using univariate analysis of variance (ANOVA). Age, education and gender were considered as covariates for all analyses. For the analyses that involved interoception scores, BMI was also added as a nuisance covariate considering its known impact on interoception. Eta-squared (η^2) were computed as effect sizes for group differences. Interquartile range (IQR) was used

to describe the non-Gaussian data. In the patient group, to study the relationship interoception and emotion recognition or

mentalizing, Pearson's partial correlations were used with age and education and gender set as nuisance variables.

Table 1. Demographics of participants and BMI.

	Patients (n = 28)	All controls (n = 74)	HBPT controls (n = 27)	MAIA controls (n = 21)	Mini-SEA controls (n = 26)	p-value
Age, mean (SD)	48.9 (12.2)	44.9 (11.1)	41.7 (12.5)	47.3 (9.7)	46.5 (10.2)	N.S.
Gender, number of women (proportion)	18 (64%)	41 (56%)	16 (59%)	15 (71%)	20 (77%)	N.S.
Education in years, median (IQR)	14.5 (14–17)	14.9 (13–18)	13 (13–18)	15 (14–16)	15 (14–18)	N.S.
BMI (kg/m ²), median (IQR)	26.4 (22–34.6)	23.5 (22.3–26.9)	23.0 (22.1–26.4)	25.6 (22.3–30.5)	N.A.	N.S.

Values are expressed as number (%) unless otherwise indicated.
HBPT: Heart beat perception task; IQR: Interquartile range; N.A.: Nonavailable; N.S.: Nonsignificant; SD: Standard deviation.

Results

Demographics & clinical data

Patients (mean age [years]: 48.9 ± 12.2 ; age range: 27–73, see Table 1) did not differ significantly from the control's population (mean age [years]: 50.0 ± 11.0 ; age range: 21–69) or subgroups. No difference was observed on the median education level (in years) between patients (14.5; IQR = 14–17) and for controls (15; IQR = 13–18). The median BMI for cLBP patients was 26.4 kg/m^2 (IQR = 22–34.6) and did not significantly differ from controls median BMI, which was 23.5 kg/m^2 (IQR = 22.3–26.9). The gender ratio did not differ between the groups and was of 64% of women in patients versus 56% in controls.

Mean MoCA score for patients was 26.4 (1.8). Regarding the question relative to their cognitive well-being, 19 (68%) patients reported that pain impacts their cognitive performance negatively.

Pain evaluation

The severity of pain was rated 5.7 in average by patients at the brief pain inventory (BPI; SD = 1.2) and interfered with their daily life at 5.7 (SD = 1.7). The pain was rated as having a moderate effect on their relationships with others, with a median of 4 (IQR = 1.8–5). The median Roland–Morris score of patients was

15 (IQR = 14–17), indicating the disabling nature of low back pain.

Thymic evaluation

According to the HAD scale, six (21%) patients had questionable anxiety symptoms and 13 (46%) patients had certain anxiety symptoms. Regarding depression, ten (36%) patients had a doubtful symptomatology and six (21%) had a definite symptomatology (see Table 2).

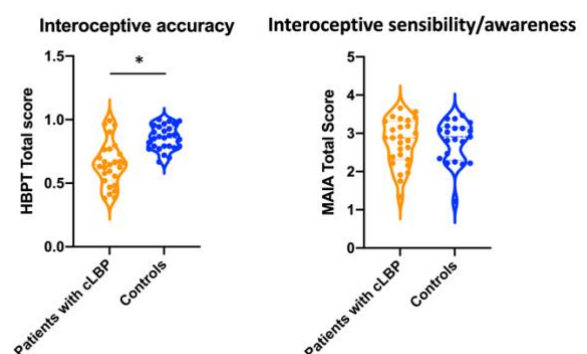


Figure 1. Performance of interoception abilities in chronic low back pain patients (orange) and controls (blue). Interoceptive accuracy was assessed with the heart beat perception task (HBPT, left panel). Interoceptive sensibility/awareness was explored with the Multidimensional Assessment of Interoceptive Awareness (MAIA, right panel). In the violin plots, the dotted line represents the interquartile segment; group median is indicated by a broken line. * Indicates $p < .001$

Interoceptive functioning

Regarding interoception accuracy, the mean score of patients with CLBP ($m = 0.65$, $SD = 0.18$) at the HBPT was significantly lower ($F = 32.58$; $p < 0.001$, $\eta^2 = 0.399$) than in controls ($m = 0.87$, $SD = 0.10$, see [Figure 1](#)). This result was very similar when the BMI was not considered in the model, and confirmed by a bootstrapping procedure (showing no overlap in the confident intervals between groups). Patients also had a lower median number of

correct responses (0; $IQR = 0-0.5$) as compared with controls (2; $IQR = 1-2$). In more detail, patients were $n = 20$ (74%) to have zero correct answers, $n = 4$ (15 %) to have one correct answer, and $n = 3$ (11 %) to have three correct answers compared with the controls who were $n = 24$ (89%) to have two correct answers and $n = 3$ (11%) to have three correct answers. All percentages have been rounded up.

Table 2. Patient's clinical characteristics.

	Patients (n = 28)
Etiology of pain	Failed back surgery syndrome, 18 (64%) Herniated nucleus pulposus, 6 (21%) Scoliosis, 1 (6%) Spondyloarthropathy, 1 (6%) Idiopathic, 1 (6%)
Duration of the cLBP in years, median (IQR)	2.8 (2–5.6)
Brief pain inventory	
Severity dimension, mean (SD)	5.7 (1.2)
Worst pain in the last 24 h	8 (8–9)
Least pain in the last 24 h	4 (3–5)
Pain on average	7 (5–7.3)
Pain right now	6 (5–7)
Effect of treatment	4 (2.8–6)
Interference dimension, mean (SD)	5.7 (1.7)
General activity	7 (6–8)
Mood	5 (2.8–7)
Walking ability	7 (4.8–8)
Normal work (including housework)	7 (6.8–8)
Relations with other people	4 (1.8–5)
Sleep	7 (6–9)
Enjoyment of life	2.5 (1.8–5)
Roland–Morris questionnaire	
Total score, mean (IQR)	15 (14–17)
Hospital anxiety and depression scale	
Total score, mean (SD)	17.8 (6.6)
Anxiety subscore, mean (SD)	9.9 (4.1)
Depression subscore, mean (SD)	7.9 (3.5)
Medications	
Analgesics	24 (86%)
Paracetamol	15 (54%)
NSAIDs	3 (11%)
Nefopam	2 (7%)
Tramadol	13 (46%)
Morphine	5 (18%)
Antiepileptic	12 (43%)
Psychiatric medications	20 (71%)
Antidepressants	18 (64%)
Benzodiazepine	4 (14%)
Cognitive screening	
Cognitive complaint	19 (68%)
Sleep complaint	21 (75%)
MoCA, mean (SD)	26.4 (1.8)
Values are expressed as median (IQR) unless otherwise indicated. Brief pain inventory (0 meaning – no severity or interference and 10 meaning – worse intensity or complete interference); Roland–Morris questionnaire (Echelle d'Incapacité Fonctionnelle pour l'Evaluation des Lombalgies) (evaluation from 0 meaning no impact, to 24 meaning maximum impact); Hospital anxiety and depression scale (anxiety and depression are considered as doubtful if subscores ≥ 8 or certain if subscores ≥ 11); cLBP: Chronic low back pain; IQR: Interquartile range; MoCA: Montreal cognitive assessment (score ≥ 26 is considered as normal); NSAID: Nonsteroidal anti-inflammatory drug; SD: Standard deviation.	

Regarding interoception sensibility/awareness, there was no significant difference ($F = 0.008$; $p > 0.93$; $\eta^2 < 0.005$) in the MAIA total mean score between controls ($m = 2.76$, $SD = 0.60$) and patients ($m = 2.61$, $SD = 0.60$). No statistical differences were observed for any subscores of the scale.

These findings were replicated when demographics or BMI were not considered as nuisance covariates. Similar results were indeed found for groups comparison on the HBPT ($F = 29.427$, $p < 0.0001$, $\eta^2 = 0.36$) or MAIA ($F = 0.017$; $p = 0.89$; $\eta^2 = 0.0001$) scores.

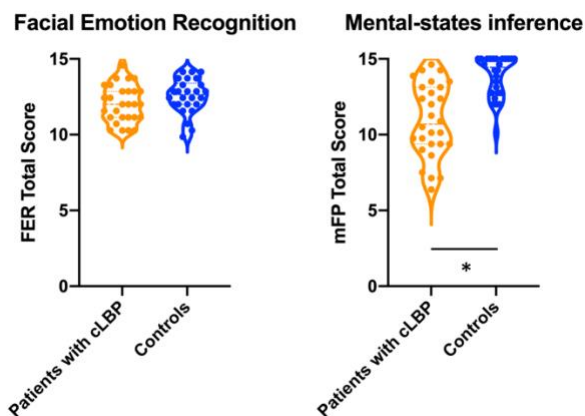


Figure 2. Performance in social cognition abilities in chronic low back pain patients (orange) and controls (blue). Facial emotion recognition (FER, left panel) was assessed with the FER test from the mini-SEA. Mental-state inference or mentalizing (mFP, right panel) was explored with the modified faux pas test from the same battery. In the violin plots, the dotted line represents the interquartile segment; group median is indicated by a broken line. * Indicates $p < .001$

Emotion recognition & mentalizing

No differences ($F = 2.26$; $p = 0.14$; $\eta^2 = 0.044$) were observed in the recognition of emotions from facial expression, with patients having a mean score of 12.05 ($SD = 1.2$) versus 12.5 ($SD = 1.2$) in control participants (see Figure 2). No differences were observed when groups were contrasted on each emotion in a post hoc analysis. Regarding mentalizing abilities, as measured with the modified faux-pas test, the

total score was significantly lower ($F = 25.76$; $p < 0.001$; $\eta^2 = 0.345$) on average in patients with cLBP ($m = 10.9$, $SD = 2.4$) in comparison to controls ($m = 13.7$, $SD = 1.4$ [see Figure 2]). Here again, when no covariates of nuisance were considered, we observed no difference between the groups on facial emotion recognition ($F = 1.153$; $p = 0.35$; $\eta^2 = 0.23$) and a similar difference regarding mentalizing ($F = 2.754$; $p < 0.005$; $\eta^2 = 0.68$).

Relationship between interoception (accuracy, sensibility/awareness) & social cognition (emotion recognition, mentalizing) in patients with cLBP

No significant relationships (nor statistical trends: minimum $p > 0.13$) were observed between interoception dimensions (either accuracy, measured with the HBPT or sensibility/awareness explored with the MAIA) and social cognition scores (emotion recognition or mentalizing) when tested through correlation analyses in cLBP (see Figure 3). This remained true with and without considering age, education, gender and BMI as a set of covariates. No significant relationship (nor statistical trends) were neither observed between interoception measures nor between social cognition measures.

Post hoc analysis: impact of pain level, disease duration, anxiodepressive symptoms & medication

No significant correlations were observed between interoceptive dimensions (accuracy, sensibility/awareness), social cognitive performance (emotion recognition, mentalizing) and the severity/impact of pain (BPI total score), its functional impact (Roland–Morris total score), the duration of disease (in years). Interestingly, the performance at the HBPT was correlated to anxiodepressive symptoms. More specifically, it correlated both with the anxiety and depression subscales of the HAD ($R = 0.47$; $p < 0.05$ and $R = 0.45$; $p < 0.05$, respectively, see Figure 4).

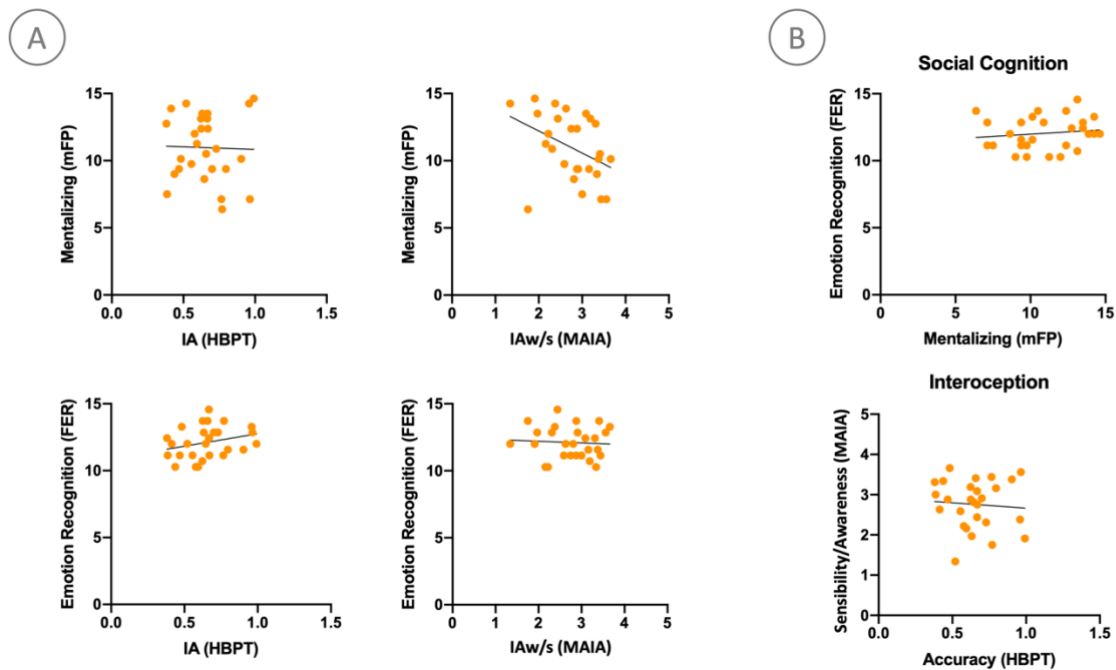


Figure 3. Statistical relationship in patients with cLBP between interoceptive and social cognitive measures, through (A) between-domain plots with interoceptive accuracy (IAc), interoceptive sensibility/awareness (IAw/s), mentalizing and emotion recognition; (B) within-domain plots. No correlations were found to be significant. Note that the plots do not reflect the consideration of nuisance covariates.

We also observed a moderate correlation between the severity/impact of pain (BPI total score) in the one hand and, in another, the duration of disease ($R = 0.46$; $p < 0.05$), the amount of depressive symptoms ($R = 0.50$; $p < 0.05$) and the functional impact of pain ($R = 0.45$; $p < 0.05$).

Finally, in order to control for potential effect of medication, additional analyses were conducted, comparing patients with and without paracetamol / acetaminophen treatments. No difference was retrieved (p 's > 0.21).

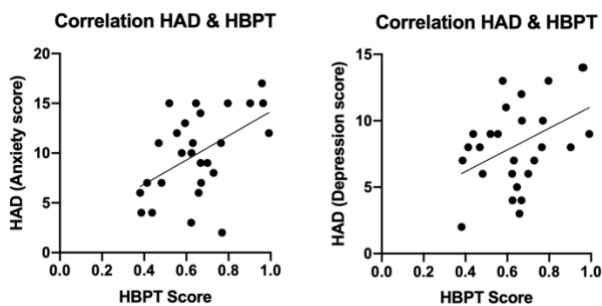


Figure 4. Statistical relationship in patients with cLBP between interoceptive accuracy (HBPT) and the severity of anxio-depressive symptoms (HAD scale).

Discussion

This study aimed to explore interoceptive and social cognitive abilities in a group of patients with cLBP. Given the significant links discussed in the literature between interoception and emotion recognition or mentalizing, we also aimed to study the statistical relationship between those dimensions, assuming that the variability of a common inference mechanism may impact the measures of both domains. Overall, this study identified a lower interoceptive accuracy performance and lower mentalizing abilities in patients with cLBP as

compared with controls. By contrast, interoceptive sensibility/awareness and emotion recognition performance did not differ between the groups. Although it was hypothesized, no statistical correlation between interoceptive and social cognitive abilities was retrieved.

So far, lower interoceptive abilities have previously been reported in patients with cLBP across three studies [11–13]. Patients with cLBP were found to present a lower accuracy in their perception of muscle contraction, underestimating the levels of their own muscle tension [11,12]. In the present study, we chose to explore interoceptive accuracy through another physiological dimension, relying on heartbeats perception. Using the HBPT was a novel but informed choice, as it was used in the same purpose with other chronic pain populations [39], such as fibromyalgia [40], noncardiac chest pain [41], multisomatoform disorder [42], but never in cLBP. Observing significant difficulties to estimate their heartbeats across the different trials, our study confirmed that patients with cLBP present lower interoceptive accuracy abilities than control participants. Overall, three patients out of four failed to all HBPT trials, which is in stark contrast with the performance observed in the control group, where all participants succeeded at least two of the three trials. We believe that relying on another physiological measure to explore interoceptive accuracy allowed us to extend the current limited knowledge in cLBP regarding interoceptive abilities. Given that our exclusion criteria have ruled out a cognitive general decline in patients, it is unlikely that the differences observed here could be caused by an undetected general cognitive deficit. Our study rather supports the notion that a lower interoceptive accuracy may be a hallmark of chronic pain syndrome [8].

Following the theoretical framework consensually adopted in the field of interoception [43], ‘accuracy’ has been distinguished from ‘sensibility’ or ‘awareness’ in our study. Accuracy represents the ability to detect internal body sensations (in our study, heartbeats). Sensibility refers to a self-

evaluation of subjective interoception and awareness represents the global sense of the physiological body, which we view as equivalent or at least overlapping concepts. We thus decided to use these two terms in our study to account for the diversity of the theoretical frameworks on interoception (Di Lernia *et al.* [8]). Here, we did not observe any difference between patients with cLBP and controls at the MAIA, a scale consensually used to assess interoceptive sensibility/awareness. Interestingly, this contrasts with the single past exploration of this dimension conducted in patients with LBP [13]. This last study did, however, include patients with LBP without specifying their level of pain chronicity that were compared with ‘mind–body’ trained participants (i.e., teachers of mind–body approaches such as yoga). This particularity could explain the difference with our findings alongside with other points discussed elsewhere [8]. The dissociation we observed here between interoceptive accuracy and sensibility/awareness in cLBP seems congruent with findings obtained in control participants [44] as well as in patients with depression [45].

As compared with interoception, social cognition has been even more scarcely investigated in cLBP. Both domains were considered together in our study given the numerous theoretical, anatomical, experimental and clinical links retrieved, pointing out a possible common inferential mechanism at play [18,46]. With the aim to provide a more detailed exploration of social cognition performance in cLBP, we chose to assess both emotion recognition and mentalizing performance. While we did not find any difference between patients and controls on the ability to recognize emotions, a lower ability to infer others’ mental states was observed in patients with cLBP. Similar results (i.e., lower mentalizing performance) have been observed in patients suffering from chronic somatoform pain [47] and severe migraine [48]. Contrasting with our present findings, emotion recognition abnormalities have been reported in complex regional pain syndrome [49].

In our study, the consideration of emotion recognition and mentalizing allowed us to distinguish between a low level and a high level of mental-state inference, respectively [50]. While the recognition of an emotion *in real life* does involve complex inference mechanisms, classical facial emotion recognition tests (such as the one we used in this study) only involve limited levels of inference, as the physical clues associated with each emotion are prototypical and static. In addition, the set of available answers were written below the photograph through the test, and no context was presented. By contrast, to explore mentalizing abilities, we relied on the modified faux pas test, which is based on stories that strongly rely on context analysis, social expertise and the integration of different mental perspectives in the absence of any physical clues, thus involving a higher level of inference. The fact that we observed, in patients with cLBP, lower performance in mentalizing but not in emotion recognition could be congruent with the notion that a common mechanism is at stake in interoception and mentalizing, as both rely on a high level of inference regarding internal states that are not directly accessible [46]. However, the absence of correlation between interoceptive accuracy and mentalizing remains an obstacle to an interpretation favoring the role of a common inferential mechanism. In this context, it would be purely speculative to bring any definitive interpretation for the lower performances retrieved in our study in both domains, especially as the literature is relatively new and inconclusive regarding this point. Chronic pain could indeed inherently involve interoceptive abnormalities associated to nociceptive disturbances. But, on the contrary, people with lower interoception could be at a greater risk for chronic pain given their difficulties to predict or interpret internal signals. Without clear answers so far, complementary questions could be asked regarding mentalizing: in other words, does chronic pain directly (through a shared-interoceptive component) or indirectly (through the negative evolution of the patients' social role, e.g., [51]) impact mentalizing abilities? To bring some elements of answer in cLBP, future studies should compare patients' groups defined on different

duration of disease, pain intensity and social support. In our study, however, post hoc analyses revealed that duration of disease and pain intensity had no significant effect on interoceptive or social cognitive abilities. Brain imaging investigations in cLBP could also provide the regional functional or structural correlates of both interoceptive and mentalizing abilities in cLBP.

Regarding this last point, at the neuroanatomical level, a possible interpretation of the concomitant mentalizing and interoceptive difficulties observed here could rely on the functional and structural abnormalities of the insular cortex, which have been reported in recent studies in cLBP [52,53]. Numerous studies pointed the role of this region in a wide range of cognitive abilities, and especially those related to the integration of internal and external states such as interoception and social cognition [54,55]. However, with no imaging data available, our study could not directly test the link between insular functioning and social cognitive or interoceptive abilities. Furthermore, although functional specificity has been described within the different regions of the insula, the lack of correlation retrieved in our study would rather support the notion that different networks are at play in both domains.

We observed a positive correlation between the severity of anxiodepressive symptoms and interoceptive accuracy. Anxiety and depression are common co-morbidities in patients treated in pain clinic [56], partly because of the dysfunction of the serotonergic and noradrenergic systems. A recent meta-analysis [57] suggested that depression has a complex relationship with interoceptive accuracy: while moderate depression seems to lower interoception accuracy performance, severe depression seems to have indeed a paradoxical effect by normalizing interoception accuracy performance. Interestingly, some randomized controlled trials (RCT) performed in the field of psychiatry and psychosomatic disorders found that interventions with interoception were effective in ameliorating symptoms [58]. These RCTs used different techniques (e.g., cognitive behavioral therapy with interoceptive training

or mindfulness) targeting different aspects of interoception. Future studies should focus on this issue by comparing strategies targeting interoceptive accuracy (e.g., therapy based on biofeedback [59,60]) or sensibility (e.g., mindfulness [61,62]) to determine the most efficient treatments.

In our study, the fact that control participants were recruited in different centers may constitute a confound for intergroup comparisons. However, as the current literature mostly supports the cultural universality of embodiment and associated representations of internal body states [63], we believe that the probability of a cultural influence on interoceptive measures remains low. Another limit of our methodology is the limited sample size of the groups considered. Although exploratory, we believe that this study has several notable strengths such as relying on a multidimensional assessment of interoception and social cognition, through the use of well-established measures. In addition, these two domains were here explored in a context where severe cognitive impairments are ruled out, as compared with other clinical population where both domains have been investigated together (i.e., [64]). Put in other words, in contrast to these previous settings, it is unlikely that in our study, a general cognitive decline had impacted interoceptive and mentalizing performance of patients with cLBP, although future studies should definitely rule out this possibility. Other limitations could be acknowledged given the preliminary nature of our study, and will need to be overcome in future studies. For example, use of the HBPT could be criticized mainly because participants may perform the task by estimating the time and using their knowledge of their heart rate rather than counting their felt heartbeats [65,66]. Moreover, we considered many confounding factors during the statistical analyses, which may have impacted the results negatively. Although we performed additional analyses to confirm that they had no significant effect on our results, which tend to support their robustness, future studies should therefore take this point into account in their design. For example, as paracetamol has been shown to impact empathy [67], registering its

use in control participants in future studies – which was not possible in our study – would be recommended. More generally, the effect of medications on interoception, mentalizing or emotion recognition is so far unclear and should be a relevant subject in future investigations.

From a clinical point of view, this study offers perspectives for innovative interventions in cLBP regarding interoception. Cognitive behavioral therapy has been recommended in the last evidence-based clinical guidelines for the treatment of cLBP given its impact to reduce the level of pain [68]. Cognitive relearning focusing on fear-avoidance and pain-perception are effective in the treatment of cLBP [69]. Because methods such as interoceptive exposure are classically employed in other disorders (e.g., panic disorder), interoception is not an unknown tool for psychologists. However, to our knowledge, interoceptive modeling treatments or therapy have been rarely theorized and developed from a practical point of view so far [8], despite encouraging results in irritable bowel syndrome [62] or in a pilot study in chronic pain patients [70]. Similarly, interoceptive abilities are still poorly taken into account in the evaluation of chronic pain patients. In parallel, activities such as yoga or mindfulness-based stress reduction [71,72] are often cited as a second-line or adjunctive treatment option for chronic pain [73] and are thus increasingly proposed by algologists, or requested by patients. There is increasing evidence that these approaches produce functional effects leading to an increase of body awareness and a decrease of pain [70,74,75] through insular neuroplasticity [61]. Taken together, significant elements support the association between body awareness, pain management and interoceptive abilities. This suggests that the effectiveness of these aforementioned approaches depends on, at least in part, an improvement of interoceptive abilities [76]. Interoception should thus be one of the focus among the future therapeutic approaches for cLBP. In this line, biofeedback-based interoceptive training [77] and mindfulness-based interoceptive exposure task [70] have been recently proposed as promising options.

Given that our study is the first to uncover mentalizing difficulties in cLBP, it seems too preliminary to advocate targeting social cognition abilities in therapy or educational training. First, it will be crucial to replicate and deepen these findings as well as to explore the variables that modulates these difficulties (in our study, post hoc analyses revealed no effect of pain intensity or its impact on these measures). The topic is, however, not trivial as social cognition difficulties have been already observed in chronic pain syndromes, and has the potential to provide key knowledge relevant to the patients' social functioning, an essential aspect of coping strategies and therapeutic intervention in chronic pain and cLBP in particular.

Conclusion

This study retrieved less efficient interoceptive accuracy and mentalizing abilities in cLBP patients without any correlation between these two performances. We believe that our study provides some interesting theoretical contribution, but above all, has a clinical usefulness. If our results on social cognition are

replicated, health practitioners dealing with chronic pain conditions should first ensure that the patients' mental-states inference skills are not reduced, and conduct their communication more explicitly if they are. Finally, our study underlines that interoception should be envisaged as a target or an approach for future treatments in chronic pain conditions. This domain would offer innovative path of interventions, at the interface between the mind and the body.

Acknowledgments

F Quesque is supported by the Région Haut de France.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Summary points

- Chronic low back pain (cLBP), the leading cause of disability in the world, has historically been envisaged as a 'biopsychosocial' condition, where social and psychological factors play a considerable role.
- Lower interoceptive abilities have recently been proposed to be a characteristic of chronic pain conditions and interoception is increasingly envisaged to be a central aspect of therapeutic interventions.
- Predictive coding models of the brain recently brought interoception closer to mental-state inferences mechanisms at play in social cognition, which received support from experimental and clinical studies.
- However, whether a common cognitive inference mechanism supports both interoception processing and mental-states decoding remains an open question.
- By administering a multidimensional assessment of interoception and social cognition, this study aimed to characterize the performance of patients with cLBP and to explore the relationship between both domains.
- We identified lower interoceptive accuracy and mentalizing abilities in patients with cLBP, as compared with controls.
- By contrast, interoceptive sensibility/awareness and emotion recognition performance did not differ between patients and controls.
- There was no statistical correlation between interoceptive and social cognitive abilities.

Ethical conduct of research

that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Data sharing statement

Data available on request due to privacy/ethical restrictions.

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