



Pain Severity and Depressive Symptoms in Endometriosis Patients: Mediation of Negative Body Awareness and Interoceptive Self-Regulation

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Abstract: Endometriosis-related pain may be associated with depressive symptoms. Although a growing body of evidence supports this association, the underlying mechanisms are still largely unclear. Impaired perceptions of bodily external and internal stimuli may be involved in this process. This study aims to assess the mediating role of 2 facets of interoception—the awareness of negative body signals and interoceptive self-regulation—in the association between pain severity and depressive symptoms among women with endometriosis. A total of 301 patients who reported a diagnosis of endometriosis were recruited from an endometriosis and chronic pelvic pain outpatient university clinic and through patient associations and completed self-reported instruments. A parallel mediation analysis was conducted. Almost half of women (48.2%) reported depressive symptoms above the self-rating scale cutoff values. Pain severity significantly predicted depressive symptoms ($\beta = .39$, 95% bootstrap confidence interval [CI] [.719, 1.333]). Negative body awareness ($\beta = .121$, 95% bootstrap CI [.174, .468]) and interoceptive self-regulation ($\beta = .05$, 95% bootstrap CI [.035, .252]) partially mediated this relationship. Our findings indicated that pain may interfere with the perception of the body as a source of calmness and safety, limiting the individual's ability to effectively regulate emotions. Future research should further explore these mechanisms and evaluate the efficacy of interventions focusing on interoceptive sensibility to enhance the psychological well-being of endometriosis patients.

Perspective: This article investigates for the first time the potential role of 2 facets of interoceptive sensibility in the relationship between pain severity and depressive symptoms in women with endometriosis. These findings may contribute to advancing knowledge about the mechanisms involved in the complex pain-depression cycle.

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Key words: Endometriosis, chronic pelvic pain, body awareness, depression, interoception

Endometriosis is a chronic inflammatory estrogen-dependent disease characterized by endometrium-like tissue outside the uterus,^{1,2} which affects between 2 and 10% of women of reproductive age, and up to 50% of women with chronic

pelvic pain (CPP) or infertility.^{3,4} The most frequent symptom of endometriosis is CPP,⁵ described as persistent or recurrent pain in the lower abdomen or pelvis lasting for at least 6 months,^{6,7} encompassing both cyclical (ie, dysmenorrhea) and noncyclical pelvic pain experiences.^{6,8-10}

Endometriosis-related pain symptoms are not always directly related to the disease's extent and location and tend to return after treatments even without lesion recurrences.^{1,11,12} Moreover, the nonspecific presentation of symptoms often delays the diagnosis,¹³ worsening the impact on quality of life and mental health.¹⁴⁻¹⁶

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2 The Journal of Pain

Following the biopsychosocial model,¹⁷⁻¹⁹ pain is viewed as a subjective experience resulting from the interaction among biological, psychological, and social factors.²⁰ Unlike acute pain, which serves as a protective warning and typically resolves shortly after tissue injury, chronic pain involves complex pathophysiological mechanisms that may produce or exacerbate pain, leading to chronic pain syndrome. These processes include neuroplasticity, visceral hypersensitivity,^{18,21} and alterations in pain-related sensory pathways in the peripheral and central nervous system, namely central sensitization,²² often resulting in increased pain severity and reduced responsiveness to medications.²³

Studies have found that endometriosis patients with severe CPP exhibit higher levels of depressive symptoms compared to those without pain, indicating a strong association between pain and psychological distress.²⁴⁻²⁶ It has been proposed that both pain and depressive symptoms may stem from shared underlying factors, including sensitization processes,^{7,27} Hypothalamic-pituitary-adrenal axis alterations,^{28,29} augmented inflammatory processes,³⁰⁻³² and altered immunity.^{33,34} However, pain improvement alone does not necessarily lead to a reduction in depressive symptoms,^{35,36} suggesting a complex interplay with cognitive, emotional, and social factors in influencing pain experiences and psychological distress.^{37,38} For instance, pain acceptance, psychological flexibility, self-efficacy, and social support have been positively associated with psychological well-being in chronic pain patients,³⁹⁻⁴³ while catastrophizing was related to heightened pain and depressive symptoms.⁴⁴⁻⁴⁶

CPP can also affect patients' body perception,⁴⁷ impairing the processing of bodily external and internal stimuli.⁴⁸⁻⁵⁰ Interoceptive sensibility refers to the subjective perception of visceral afferent information (ie, heart, lung, and stomach) and the ability to accurately perceive it.^{51,52} In other populations, altered interoceptive sensibility has been associated with both increased pain severity^{51,53,54} and depression.⁵⁵⁻⁵⁷ In this vein, it may serve as a significant variable within the biopsychosocial framework, further explaining the chronic pain impact on psychological distress. Interoceptive sensibility is usually measured by using self-report questionnaires like the Body Perception Questionnaire (BPQ)⁵⁸ and the Multidimensional Assessment of Interoceptive Awareness (MAIA),⁵⁹ involving different facets of this construct. In particular, the Awareness subscale of the BPQ provides a measure of the subjective experience of one's negative bodily signals. Higher scores on this scale are associated with somatosensory amplification,⁴⁸ higher pain intensity,⁶⁰ and increased levels of depressive symptoms.⁶¹ The MAIA self-regulation subscale, instead, captures the ability to regulate emotions by focusing attention on body sensations.⁶² Higher scores on this scale are related to enhanced pain tolerance,⁶³ less pain-catastrophizing,⁶⁴ and lower depressive symptoms.⁶⁵

Although the influence of CPP severity on depression³⁷ and the associations between interoceptive sensibility and both pain and emotional well-being are well-known,^{49,52,55} no studies investigated the role of

The Role of Interoceptive Sensibility in Endometriosis

interoceptive sensibility in the CPP-depression relationship in endometriosis patients. We hypothesize that altered interoceptive sensibility (measured by negative body awareness and interoceptive self-regulation) will mediate the relationship between pain severity and depressive symptoms. In particular, we expect that pain severity will be positively associated with negative body awareness, which in turn will be associated with depressive symptoms. Moreover, pain severity will be negatively related to interoceptive self-regulation, which in turn will negatively predict depressive symptomatology.

Methods

Participants and Procedures

Participants included 301 women diagnosed with endometriosis, recruited at the Endometriosis and Chronic Pelvic Pain Outpatient Service of Policlinico Umberto I University Hospital of Rome and through social media thematic groups on endometriosis. Eligible patients were women who reported being diagnosed with endometriosis through gynecological examination, pelvic ultrasounds, magnetic resonance imaging, or surgery. Patients had to be over 18 years old and able to speak and understand fluently Italian. Exclusion criteria were current pregnancy and menopause.

All participants took part voluntarily in the study and were not remunerated. At the time of recruitment, women received information about the aims of the study and signed an informed consent. The study was approved by the Institution Review Board of the Psychology Department, Sapienza University of Rome (Prot. N. 0000800).

Measures

Sociodemographic Data and Clinical Information

Patients were asked to report sociodemographic information, including age, education, marital status, and occupation. Clinical data such as height, weight, age at symptom onset, age at diagnosis, previous surgery, type of hormonal therapy, characteristics of endometriosis (ovarian endometrioma and/or deep endometriosis), and menstrual characteristics (ie, characteristics of the menstrual cycles, presence of amenorrhea due to hormonal therapy) were also recorded. Additionally, participants were asked to provide data about endometriosis-related pelvic pain symptoms experienced over the previous 3 months. These symptoms included dysmenorrhea, dyspareunia, acyclic pelvic pain, dyschezia, and dysuria, which were rated on a 0 to 10 numerical rating scale (0 = "no pain," 10 = "the worst imaginable pain"). Consistent with previous clinical studies, values above 5 were considered indicative of the presence of moderate pain.^{66,67}

Pain Severity

Pain severity was measured by using the Pain Severity subscale of the West Haven-Yale Multidimensional Pain

Inventory,^{68,69} in line with previous studies on CPP patients.⁷⁰⁻⁷²

This subscale consists of 2 items regarding patients' perceptions of one's pain intensity: "On average, how severe has your pain been during the last week?" and "How much suffering do you experience because of your pain?". Responses to each question are scored on a 7-point rating scale ranging from 0 (No pain) to 6 (Extreme Pain) and averaged to produce an overall score, with higher scores reflecting greater pain severity.

Interoceptive Awareness

Body awareness of uncomfortable or threatening body signals. The Body Awareness domain of the Body Perception Questionnaire—Short Form (BPQ)^{58,73} was used to assess the subjective experience of information arising from within the body. Items refer to sensations primarily linked to stress reactions in organs that are innervated by the autonomic nervous system. An example item is "I feel my mouth is dry" with responses evaluated on a 5-point Likert scale from 1 (Never) to 5 (Always). Higher scores correspond to higher levels of body-related sensations' awareness.

Interceptive Self-Regulation

The 4-item Self-Regulation Subscale of the MAIA^{62,74} was used to evaluate the ability to regulate negative emotions by attention to body sensations. An example item is "I can use my breath to reduce tension," with responses scored on a 6-point Likert scale ranging from 0 (Never) to 5 (Always). Higher scores indicate higher interoceptive sensibility.

Depressive Symptoms

Depressive symptoms were captured through the Depression Subscale of the Hospital Anxiety and Depression Scale.^{75,76} The questionnaire investigates the presence of depressive symptoms over the past week. An example item is "I can laugh and see the funny side of things (reversed score)" with responses scored on a 4-point Likert scale ranging from 0 to 3. Total scores range from 0 to 21, with higher scores representing more severe depressive symptoms. A cutoff score of ≥ 8 indicates clinically significant depressive symptoms.⁷⁷

Statistical Analyses

Data analyses were conducted using IBM SPSS Statistic version 26 (SPSS Inc, Armonk, NY). The demographic, clinical, and psychological variables were described by their means (M) \pm standard deviations or by the number of participants (N) with the percentage in parenthesis.

The distribution of continuous variables was investigated using descriptive statistics, considering skewness and kurtosis (values ranging between -1 and $+1$ were considered acceptable). Pearson correlations were conducted to examine the associations between study variables, and all results were reported as Pearson's r and P value.

A power analysis using Monte Carlo power analysis for indirect effects⁷⁸ indicates a minimum sample of 153 participants is required to detect medium effects (effect size = .30) with a power of .95 using a mediational model with parallel mediators ($\alpha = .05$).

A parallel multiple-mediation path analysis model was used to examine whether body awareness and interoceptive self-regulation would mediate the relationship between pain severity and depressive symptoms. Parallel multiple-mediation path analysis allows testing multiple mediators simultaneously while accounting for any confounding variables controlled for as covariates.⁷⁹ Hayes⁷⁹ PROCESS macro for SPSS was used to conduct the mediational path analyses through model 4, which provided bootstrapping confidence intervals (CIs), model estimations, and conditional and direct effect computations.⁸⁰ The method included 5,000 bootstrap samples for coefficient and indirect estimation and 95% bias-corrected CIs for the indirect effect. The hypothesized model was built with pain severity (Multidimensional Pain Inventory) as the independent variable, body awareness (BPQ) and interoceptive self-regulation (MAIA) as mediators, and depressive symptomatology (Hospital Anxiety and Depression Scale) as the dependent variable. Variables that significantly correlated with the predictor, the mediators, or the outcome were entered as covariates, as suggested by Meyvis and Van Osselaer.⁸¹

We reported the standardized effect size (β) and the 95% bias-corrected CI for the indirect effect model. The mediation effect is significant if the 95% CI does not include 0.

Results

Women's ages ranged from 18 to 51 years (mean 35.3 ± 7.6). Most women were employed (73.7%), had a high school diploma (40.9%), and were in a stable relationship (62.4%). The majority of women were Caucasian (98.3%) and only a few were from other ethnicities (1.7%). Overall, 73.7% of women were undergoing hormonal therapy and 50.7% were in amenorrhea due to progestin or continuous oral contraception treatments. Regarding the presence of endometriosis, 38.2% of women reported having ovarian endometrioma, 43.2% deep-infiltrating endometriosis, and 18.6% both ovarian and deep-infiltrating endometriosis lesions. A large proportion of women (51.8%) had undergone previous surgery. The mean diagnostic delay was 10.2 (standard deviation 8.3). Out of 301 patients, 48.2% exceeded the cutoff for depression on the self-report questionnaire. Sociodemographic and clinical characteristics are reported in detail in [Tables 1 and 2](#).

[Table 3](#) reports the bivariate correlations among the variables of interest. The results showed that pain severity was positively correlated with diagnostic delay ($r = .17$, $P = .004$), Body Mass Index ($r = .17$, $P = .004$), depression ($r = .37$, $P < .001$), and body awareness ($r = .38$, $P < .001$), and negatively correlated with education ($r = -.12$, $P = .031$), and interoceptive self-regulation ($r = -.17$, $P = .003$). Depressive symptomatology was positively

Table 1. Sociodemographic Characteristics of the Patients (n = 301)

VARIABLE	M ± SD OR N (%)
Age	35.3 ± 7.6
Education	
High school diploma	123 (40.9%)
Bachelor's degree	69 (22.9%)
Master's degree	48 (15.9%)
Postgraduate courses	35 (11.6%)
Middle school certificate	25 (8.3%)
Elementary school certificate	1 (.3%)
Marital status	
Married/committed relationship	188 (62.4%)
Single	106 (35.2%)
Divorced	7 (2.3%)
Employment status	
Employed	222 (73.7%)
Unemployed	40 (13.3%)
Student	39 (13.0%)
Nationality	
Italian	291 (96.7%)
Other	10 (3.3%)

Abbreviation: SD, standard deviation.

correlated with Body Mass Index ($r = .13$, $P = .026$), amenorrhea due to hormonal therapy ($r = .13$, $P = .029$), and body awareness ($r = .37$, $P < .001$), and negatively correlated with interoceptive self-regulation ($r = -.35$, $P < .001$). Diagnostic delay positively correlated with both body awareness ($r = .13$, $P = .036$) and interoceptive self-regulation ($r = -.15$, $p = .011$).

We examined the indirect effect of pain severity on depressive symptoms through negative body awareness and interoceptive self-regulation, with amenorrhea due to hormonal therapy, education, diagnostic delay, and Body Mass Index inserted as covariates. Preacher and Hayes⁸⁰ bootstrapping estimates of indirect effects were employed for the mediation analysis. The overall model was significant ($F_{(6, 295)} = 19.174$, $P < .001$, adj. $R^2 = .335$). Fig 1 displays the standardized regression coefficients among the model variables. The mediational model (Fig 1) revealed a significant indirect effect of the impact of pain severity on depressive symptoms through negative body awareness ($\beta = .121$, 95% bootstrap CI [.174, .468]) and a significant indirect effect of the impact of pain severity on depression through interoceptive self-regulation ($\beta = .05$, 95% bootstrap CI [.035, .252]). Findings support the total effect of pain severity on depression ($\beta = .39$, 95% bootstrap CI [.719, 1.333]). Furthermore, the direct effect of pain severity on depressive symptoms in the presence of the mediators was also significant ($\beta = .21$, 95% bootstrap CI [.267, .856]). Hence, both body awareness and interoceptive self-regulation partially mediated the relationship between pain severity and depressive symptoms.

Conclusions

The present study aimed to examine the impact of pain severity on depressive symptoms in women with endometriosis, while also investigating the mediating

Table 2. Clinical Characteristics of the Patients (n = 301)

VARIABLE	M ± SD OR N (%)
Menstrual cycle characteristics	
Amenorrhea due to hormonal treatment	152 (50.7%)
Between 21 and 30 d	105 (35.0%)
< 21 d of duration	18 (6.0%)
Between 31 and 35 d	16 (5.3%)
> 35 d of duration	9 (3.0%)
Obstetrics history	
Nullipara	232 (77.1%)
Age at first childbirth	30.2 ± 4.7
Live birth (≥1)	69 (22.9%)
Miscarriage (≥1)	52 (17.3%)
Previous endometriosis surgical treatment	
Yes	145 (51.8%)
No	156 (48.2%)
Age at diagnosis	29.2 ± 7.4
Age at onset of pain symptoms	19.1 ± 8.9
Diagnostic delay	10.2 ± 8.3
Hormonal therapy	
Yes	222 (73.7%)
No	79 (26.3%)
Type of therapy	
Progestins	165 (54.8%)
Estrogen-progestins	39 (13.0%)
Type of endometriosis	
Ovarian endometrioma	115 (38.2%)
Deep endometriosis	130 (43.2%)
Both ovarian and deep	56 (18.6%)
Endometriosis-related pelvic pain symptoms	
Dysmenorrhea*	6.6 ± 2.9
Dysmenorrhea ≥5	122 (40.5%)
Dyspareunia†	5.1 ± 3.1
Dyspareunia ≥5	184 (61.7%)
Acyclic pelvic pain	6.8 ± 2.7
Acyclic pelvic pain ≥5	244 (81.1%)
Dyschezia	3.6 ± 3.3
Dysuria	1.9 ± 2.6
Body Mass Index	23.1 ± 4.4
Pain severity (MPI)	3.8 ± 1.5
Depressive symptoms	
HADS	7.7 ± 3.8
HADS ≥8	145 (48.2%)
Interoception	
MAIA_Self regulation	2.3 ± 1.2
BPQ_Awareness	80.7 ± 15.1

Abbreviations: SD, standard deviation; MPI, Multidimensional Pain Inventory; HADS, Hospital Anxiety and Depression Scale.

*Measured only in individuals with regular period (49.3%).

†Measured only in individuals who had intercourse in the last 3 months (61.4%).

role of interoceptive sensitivity (ie, body awareness for uncomfortable or threatening stimuli and interoceptive self-regulation). Our hypothesis posited a direct influence of pain severity on depressive symptoms, along with an indirect relationship mediated by both negative body awareness and interoceptive self-regulation. Consistent with our hypothesis, the findings indicated that pain severity positively predicted depressive symptoms, with both negative body awareness and interoceptive self-regulation partially mediating this relationship. To our knowledge, the current study is the first to highlight the

Table 3. Matrix of Correlations

VARIABLE	1	2	3	4	5	6	7	8	9	10
1. Age	-									
2. Education	.06	-								
3. Diagnostic delay	.17^{***}	.12[*]	-							
4. Body Mass Index	.15^{**}	-.10	.03	-						
5. Hormonal therapy	-.09	.04	-.12[*]	.02	-					
6. Amenorrhea	-.08	-.04	-.01	-.01	.58^{**}	-				
7. Parity	.39[*]	-.06	.06	.09	-.01	-.04	-			
8. Pain severity	-.05	-.13[*]	.17[*]	.17[*]	-.01	-.06	.05	-		
9. Depressive symptoms (HADS)	-.01	-.10	.07	.13[*]	.09	.13[*]	.05	.37^{**}	-	
10. Body awareness (BPQ)	-.05	-.08	.13[*]	.07	-.01	-.01	-.01	.38^{**}	-.37^{**}	-
11. Self-regulation (MAIA)	.08	.08	.15[*]	.02	.01	.01	-.01	-.17^{**}	-.35^{**}	-.05

Abbreviation: HADS, Hospital Anxiety and Depression Scale.

* < .05.
** < .01.

mediational role of these 2 facets of interoceptive sensibility in the relationship between pain severity and depressive symptoms in endometriosis patients.

The Relationship Between Pain Severity and Depressive Symptoms

Our findings highlight a high frequency of depressive symptoms in women with endometriosis, in line with the prevalence reported in previous research.^{24,26,37} Consistently with the literature,⁸²⁻⁸⁴ a positive direct association between pain severity and depressive symptomatology has also emerged.

Different pathways may lead to increased depressive symptomatology. Endometriosis-related pain triggers or exacerbates psychological distress, negatively affecting physical, sexual, and social domains of quality of life.^{26,84,85} On the reverse path, literature has shown that depressive symptomatology amplifies pain perception in chronic pain patients^{86,87} and in patients with

endometriosis,²⁴ creating a vicious cycle that exacerbates both conditions. Within a biopsychosocial approach, various psychosocial factors (ie, cognitive tendencies and strategies, social support, etc) have been previously reported to interplay with psychophysiological and biological processes in shaping the experience of pain and the associated mental health symptomatology differently. Findings from the present study provide initial evidence of 2 underexplored processes that may play a role in maintaining the pain-depression cycle: heightened awareness of uncomfortable or threatening body signals and reduced interoceptive self-regulation. In this sense, endometriosis-related pain severity may contribute to the development or worsening of depressive symptomatology through these mechanisms.

The Mediating Role of Negative Body Awareness

The positive association between pain severity and body awareness of uncomfortable or threatening

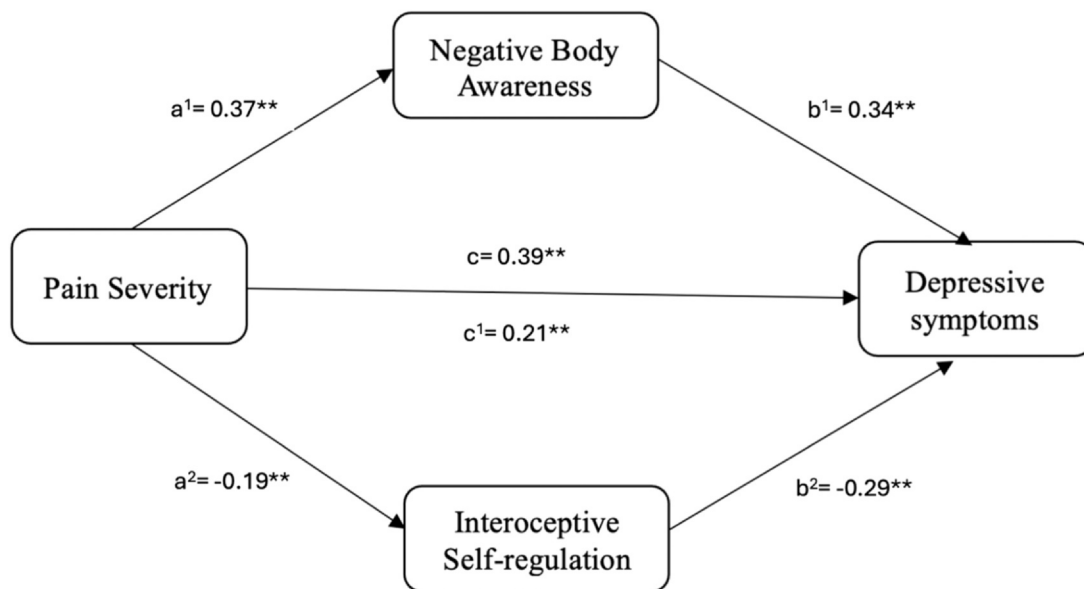


Figure 1. The parallel mediational model. Note: **P < .001.

stimuli, reported in our findings, extends previous studies conducted in nonendometriosis populations,^{51,61} which showed that chronic pain patients tend to be more attuned to negative bodily sensations.^{49,88,89} Patients with fibromyalgia, for example, reported greater body awareness of pain-related stimuli compared with healthy controls,⁶⁰ suggesting that this fostered focus on body signals may be an attempt to monitor and manage pain.^{60,90} Nonetheless, a heightened awareness of somatic information may be potentially maladaptive,⁹¹ increasing concerns, rumination, or feelings of helplessness, all common symptoms of depression.^{55,92} Consistently, in our study, negative body awareness significantly mediated the relationship between pain severity and depressive symptoms.

The Mediating Role of Interoceptive Self-Regulation

A mediation of the ability to regulate negative emotions through conscious attention to body sensations was also found. Indeed, pain may interfere with the possibility of perceiving the body as a place of safety and calmness, leading the individual to be less body-connected and less able to benefit from its processes (ie, breathing) as a source of regulation. Congruently, previous studies on nonendometriosis patients showed that individuals with chronic pain reported impaired interoceptive self-regulation.⁹³ Reduced occasions to experience relief through body processes may, in turn, contribute to increased vulnerability to emotional distress, including depressive symptoms^{51,94,95} both directly and through heightened dysfunctional regulation strategies (eg, rumination, catastrophizing, etc).^{52,64,94,96} It may be important that future studies evaluate the interaction of interoceptive self-regulation with these processes.

Overall, our study provides a preliminary insight into 2 processes that may play a role in the complex relationship between pain severity and depressive symptoms in endometriosis patients, namely body awareness of threatening or unpleasant stimuli and interoceptive self-regulation. It is conceivable that pain triggers a process where individuals heighten their attention to negative body signals. Perceiving these stimuli as threatening and, in an attempt, to cope with them, individuals may avoid recurring to the body and its functions as a source of relief. Indeed, interventions working on the reappraisal of the pain sensations as nonthreatening through a combination of cognitive, mindfulness-based, emotional, and somatic techniques demonstrated their efficacy in managing pain in patients with several chronic pain conditions, including chronic back pain,^{21,97,98} migraine,⁹⁹ irritable bowel syndrome,¹⁰⁰ and endometriosis.¹⁰¹ Acknowledging the mediational role of negative body awareness and interoceptive self-regulation emerged in the present study, sheds some light on the potential paths that may be involved in the efficacy of the above-described interventions.

Despite the valuable insights provided by this study, several limitations need to be considered when

interpreting these findings. First, it is not possible to make causal inferences from the cross-sectional design and to determine the temporal order of the observed relationship. The dynamic interactions over time between pain severity, negative body awareness, interoceptive self-regulation, and depression symptoms warrant further investigation. Intervention studies aimed to modify body awareness of threatening or unpleasant stimuli and interoceptive self-regulation may shed light on these relationships. Second, considering the methodological issues, the use of self-report questionnaires raises the risk of response bias and may not fully capture the complexity of the constructs under investigation. Including objective measures, like physiological assessments or clinician-rated evaluations, could improve the validity of the findings. In conducting the mediational analysis, we used multiple hierarchical regression analyses through the macro PROCESS. Although this method holds merit for estimating mediation and conditional processes in regression-based models involving observed variables,⁷⁹ future research could benefit from accounting also for measurement errors (ie, structural equation models), thereby providing unbiased structural coefficients.¹⁰²

Third, additional clinical information that could have improved the generalizability of our findings may not have been recorded. This could have included a measure of pain days per month and opioid use, along with the prevalence of other pain-related comorbidities and chronic pain syndromes (eg, irritable bowel- or painful bladder syndrome). Including data on pelvic floor spasms and myofascial trigger points could have additionally contributed to a more precise understanding of how pain experience impacted mental health. Our gynecologists could ascertain the diagnosis of endometriosis only for women recruited at the hospital outpatient service. Women recruited online stated that they had previously received a diagnosis of endometriosis from other clinicians/gynecologists through gynecological examinations, imaging results, or surgical procedures. However, the confirmation of the diagnosis by our gynecologists was not possible, as the women came from different regions of the country, and asking all of them to access the outpatient service would not have been feasible.

Fourth, the generalizability of the findings is also limited by the specific characteristics of the sample, primarily composed of women of Caucasian origin. The low percentage of women from other ethnicities partly reflects the lower presence of foreigners in Italy compared with other European countries and partly may be due to the inclusion criterion of speaking Italian. Moreover, it may also result from the greater lack of disease awareness and reduced access to diagnostic examinations among ethnic minority groups. Future studies should consider representative samples involving local minority communities and adopting ad hoc measurement instruments including language-adapted questionnaires.

Finally, based on previous research on the association of interoceptive sensibility with pain severity or

intensity,⁵¹ we focused only on how pain severity may alter body perceptions. We did not include pain interference as a variable in the model, as it evaluates more generally the consequences of pain on daily, work, and leisure activities. Nevertheless, future studies may investigate how psychosocial factors interact with pain interference and different aspects of quality of life to influence depressive symptoms.

Notwithstanding these limitations, our study underscores the importance of considering body awareness, and interoceptive self-regulation, as factors that influence the relationship between pain severity and depressive symptoms in endometriosis patients. These findings contribute to integrating body-mind connections more explicitly into current theoretical biopsychosocial models. Addressing interoceptive sensibility may offer promising possibilities for developing targeted interventions to alleviate the psychological distress experienced by individuals with endometriosis. Further research is warranted to explore these mechanisms in greater detail and to evaluate the efficacy

References

1. Becker CM, Bokor A, Heikinheimo O, et al. ESHRE guideline: endometriosis. *Hum Reprod Open* 2022(2):hoac009, 2022. <https://doi.org/10.1093/hropen/hoac009>
2. Zondervan KT, Becker CM, Missmer SA: Endometriosis. *N Engl J Med* 382:1244-1256, 2020. <https://doi.org/10.1056/NEJMra1810764>
3. Shafir AL, Farland LV, Shah DK, et al. Risk for and consequences of endometriosis: a critical epidemiologic review. *Best Pract Res Clin Obstet Gynaecol* 51:1-15, 2018. <https://doi.org/10.1016/j.bpobgyn.2018.06.001>
4. Meuleman C, Vandenabeele B, Fieuws S, Spiessens C, Timmerman D, D'Hooghe T: High prevalence of endometriosis in infertile women with normal ovulation and normospermic partners. *Fertil Steril* 92(1):68-74, 2009. <https://doi.org/10.1016/j.fertnstert.2008.04.056>
5. Agarwal SK, Chapron C, Giudice LC, et al. Clinical diagnosis of endometriosis: a call to action. *Am J Obstet Gynecol* 220(4):354.e1-354.e12, 2019. <https://doi.org/10.1016/j.ajog.2018.12.039>
6. Uppal T, Amarasekara C, Kaushik V: Chronic pelvic pain. *Australas J Ultrasound Med* 14(1):24-27, 2011. <https://doi.org/10.1002/j.2205-0140.2011.tb00182.x>
7. Lamvu G, Carrillo J, Ouyang C, Rapkin A: Chronic pelvic pain in women: a review. *JAMA* 325(23):2381-2391, 2021. <https://doi.org/10.1001/jama.2021.263>
8. Won HR, Abbott J: Optimal management of chronic cyclical pelvic pain: an evidence-based and pragmatic approach. *Int J Womens Health* 2:263-277, 2010. <https://doi.org/10.2147/IJWH.S7991>
9. de Las Mercedes Villa Rosero CY, Mazin SC, Nogueira AA, et al. Prevalence of chronic pelvic pain and primary dysmenorrhea in women of reproductive age in Ecuador. *BMC Womens Health* 22(1):363, 2022. <https://doi.org/10.1186/s12905-022-01948-y>
10. Latthe P, Mignini L, Gray R, Hills R, Khan K: Factors predisposing women to chronic pelvic pain: systematic review. *BMJ* 332(7544):749-755, 2006. <https://doi.org/10.1136/bmj.38748.697465.55>
11. Porpora MG, Pallante D, Ferro A, Crisafi B, Bellati F, Benedetti Panici P: Pain and ovarian endometrioma recurrence after laparoscopic treatment of endometriosis: a long-term prospective study. *Fertil Steril* 93(3):716-721, 2010. <https://doi.org/10.1016/j.fertnstert.2008.10.018>
12. Vercellini P, Fedele L, Aimi G, Pietropaolo G, Consonni D, Crosignani PG: Association between endometriosis stage, lesion type, patient characteristics and severity of pelvic pain symptoms: a multivariate analysis of over 1000 patient. *Hum Reprod* 22(1):266-271, 2007. <https://doi.org/10.1093/humrep/del339>
13. Pino I, Belloni GM, Barbera V, et al. Endometriosis treatment Italian Club, ETIC. "Better late than never but never late is better", especially in young women. A multicenter Italian study on diagnostic delay for symptomatic endometriosis. *Eur J Contracept Reprod Health Care* 28(1):10-16, 2023. <https://doi.org/10.1080/13625187.2022.2128644>
14. Laganà AS, La Rosa VL, Rapisarda AMC, et al. Anxiety and depression in patients with endometriosis: impact and management challenges. *Int J Womens Health* 9:323-330, 2017. <https://doi.org/10.2147/IJWH.S119729>
15. Culley L, Law C, Hudson N, et al. The social and psychological impact of endometriosis on women's lives: a critical narrative review. *Hum Reprod Update* 19(6):625-639, 2013. <https://doi.org/10.1093/humupd/dmt027>
16. Simoens S, Dunselman G, Dirksen C, et al. The burden of endometriosis: costs and quality of life of women with endometriosis and treated in referral centres. *Hum Reprod* 27:1292-1299, 2012. <https://doi.org/10.1093/humrep/des073>

of targeted interventions that may improve the well-being of individuals living with endometriosis.

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17. Engel GL: The need for a new medical model: a challenge for biomedicine. *Science* 196(4286):129-136, 1977.
18. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC: The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull* 133(4):581-624, 2007. <https://doi.org/10.1037/0033-2909.133.4.581>
19. O'Donnell KF: Preoperative pain management education: a quality improvement project. *J Perianesth Nurs* 30(3):221-227, 2015.
20. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain* 161(9):1976-1982, 2020.
21. Afshar YK, Gordon A, Schubiner H, et al. Effect of pain reprocessing therapy vs placebo and usual care for patients with chronic back pain: a randomized clinical trial. *JAMA Psychiatry* 79(1):13-23, 2022. <https://doi.org/10.1001/jamapsychiatry.2021.2669>
22. Guo SW, Wang Y: The prevalence of endometriosis in women with chronic pelvic pain. *Gynecol Obstet Invest* 86(4):337-348, 2021. <https://doi.org/10.1159/000093019>
23. Evans S, Moalem-Taylor G, Tracey DJ: Pain and endometriosis. *Pain* 132(Suppl 1):S22-S25, 2007. <https://doi.org/10.1016/j.pain.2007.07.006>
24. Facchin F, Barbara G, Saita E, et al. Impact of endometriosis on quality of life and mental health: pelvic pain makes the difference. *J Psychosom Obstet Gynaecol* 36(4):135-141, 2015. <https://doi.org/10.3109/0167482X.2015.1074173>
25. Gambassi G: Pain and depression: the egg and the chicken story revisited. *Arch Gerontol Geriatr* 49(Suppl 1):103-112, 2009. <https://doi.org/10.1016/j.archger.2009.09.018>
26. Van Barneveld E, Manfers J, van Osch F, et al. Depression, Anxiety and Endometriosis: a systematic review and meta-analysis. *J Womens Health* 31(2):219-230, 2022. <https://doi.org/10.1089/jwh.2021.0021>
27. Li T, Mamillapalli R, Ding S, et al. Endometriosis alters brain electrophysiology, gene expression and increases pain sensitization, anxiety and depression in female mice. *Biol Reprod* 99(2):349-359, 2018. <https://doi.org/10.1093/biolre/iy035>
28. Wingenfeld K, Hellhammer DH, Schmidt I, Wagner D, Meinlschmidt G, Heim C: HPA axis reactivity in chronic pelvic pain: association with depression. *J Psychosom Obstet Gynecol* 30(4):282-286, 2009. <https://doi.org/10.3109/01674820903254732>
29. Pagàn-Busigò J, Lòpez-Carrasquillo J, Appleyard C, Torres-Reveròn A: Beyond depression and anxiety: a systematic review about the role of corticotropin-releasing hormone antagonists in diseases of the pelvic and abdominal organs. *PLoS One* 17(3):e0264909, 2022. <https://doi.org/10.1371/journal.pone.0264909>
30. Graziottin A, Skaper SD, Fusco M: Mast cells in chronic inflammation, pelvic pain and depression in women. *Gynecol Endocrinol* 30(7):472-477, 2014. <https://doi.org/10.3109/09513590.2014.911280>
31. Hu C, Yang H, Zhao Y, et al. The role of inflammatory cytokines and ERK1/2 signaling in chronic prostatitis/
- The Role of Interceptive Sensibility in Endometriosis
- chronic pelvic pain syndrome with related mental health disorders. *Sci Rep* 6:28608, 2016. <https://doi.org/10.1038/srep28608>
32. Galandrini R, Porpora MG, Stoppacciaro A, et al. Increased frequency of human leukocyte antigen-E inhibitory receptor CD94/NKG2A-expressing peritoneal natural killer cells in patients with endometriosis. *Fertil Steril* 89(5):1490, 2008. <https://doi.org/10.1016/j.fertinstert.2007.05.018>
33. Nasyrova RF, Sotnikova LS, Baystrukova NV, et al. Psychoimmune interactions in women of reproductive age with endometriosis. *Bull Exp Biol Med* 152(1):93-97, 2011. <https://doi.org/10.1007/s10517-011-1463-0>
34. Porpora MG, Scaramuzzino S, Sangiuliano C, et al. High prevalence of autoimmune diseases in women with endometriosis: a case-control study. *Gynecol Endocrinol* 36(4):356-359, 2020. <https://doi.org/10.1080/09513590.2019.1655727>
35. Lerman SF, Rudich Z, Brill S, Shalev H, Shahar G: Longitudinal associations between depression, anxiety, pain and pain related disability in chronic pain patients. *Psychosom Med* 77(3):333-341, 2015. <https://doi.org/10.1097/PSY.000000000000158>
36. Cagnacci A, Della Vecchia E, Xholli A: Chronic pelvic pain improvement: impact on quality of life and mood. *Gynecol Endocrinol* 35(6):502-505, 2019. <https://doi.org/10.1080/09513590.2018.1540571>
37. Gambadauro P, Carli V, Hadlaczky G: Depressive symptoms among women with endometriosis: a systematic review and meta-analysis. *Am J Obstet Gynecol* 220(3):230-241, 2019. <https://doi.org/10.1016/j.ajog.2018.11.123>
38. Kalfas M, Chisari C, Windgassen S: Psychosocial factors associated with pain and health-related quality of life in Endometriosis: a systematic review. *Eur J Pain* 26(9):1827-1848, 2022. <https://doi.org/10.1002/ejp.2006>
39. Gentili C, Rickardsson J, Zetterqvist V, Simons LE, Lekander M, Wicksell RK: Psychological flexibility as a resilience factor in individuals with chronic pain. *Front Psychol* 10:2016, 2019. <https://doi.org/10.3389/fpsyg.2019.02016>
40. McCracken LM: Learning to live with pain: acceptance of pain predicts adjustment in persons with chronic pain. *Pain* 74(1):21-27, 1998. [https://doi.org/10.1016/S0304-3959\(97\)00146-2](https://doi.org/10.1016/S0304-3959(97)00146-2)
41. Facchin F, Barbara G, Dridi D, et al. Mental health in women with endometriosis: searching for predictors of psychological distress. *Hum Reprod* 32(9):1855-1861, 2017. <https://doi.org/10.1093/humrep/dex249>
42. Adams LM, Turk DC: Psychosocial factors and central sensitivity syndromes. *Curr Rheumatol Rev* 11(2):96-108, 2015. <https://doi.org/10.2174/1573397111666150619095330>
43. Sundström FT, Lavefjord A, Buhman M, McCracken LM: Associations between psychological flexibility and daily functioning in endometriosis-related pain. *Scand J Pain* 24(1):20220157, 2024.
44. Zarbo C, Brugnera A, Frigerio L, et al. Catastrophizing moderates the relationship between pain severity and depressive symptomatology among women with endometriosis. *Psychol Health Med* 12(1):1-13, 2023. <https://doi.org/10.1080/13548506.2023.2235737>

45. McPeak AE, Allaire C, Williams C, Albert A, Lisonkova S, Yong PJ: Pain catastrophizing and pain health-related quality-of-life in endometriosis. *Clin J Pain* 34(4):349-356, 2018. <https://doi.org/10.1097/AJP.0000000000000539>
46. Linton SJ, Buer N, Vlaeyen J, Helsing AL: Are fear-avoidance beliefs related to the inception of an episode of back pain? A prospective study. *Psychol Health* 14(6):1051-1059, 2000. <https://doi.org/10.1080/08870440008407366>
47. Tsay A, Allen TJ, Proske U, Giummarra MJ: Sensing the body in chronic pain: a review of psychophysical studies implicating altered body representation. *Neurosci Biobehav Rev* 52:221-232, 2015. <https://doi.org/10.1016/j.neubiorev.2015.03.004>
48. Borg C, Chouchou F, Dayot-Gorlero J, et al. Pain and emotion as predictive factors of interoception in fibromyalgia. *J Pain Res* 11:823-835, 2018. <https://doi.org/10.2147/JPR.S152012>
49. Di Lernia D, Serino S, Riva G: Pain in the body. Altered interoception in chronic pain conditions: a systematic review. *Neurosci Biobehav Rev* 71:328-341, 2016. <https://doi.org/10.1016/j.neubiorev.2016.09.015>
50. Solcà M, Park HD, Bernasconi F, Blanke O: Behavioral and neurophysiological evidence for altered interoceptive bodily processing in chronic pain. *Neuroimage* 217(1):116902, 2020. <https://doi.org/10.1016/j.neuroimage.2020.116902>
51. Mehling WE, Daubenmier J, Price CJ, Acree M, Bartmess E, Stewart AL: Self-reported interoceptive awareness in primary care patients with past or current low back pain. *J Pain Res* 6:403-418, 2013. <https://doi.org/10.2147/JPR.S42418>
52. Critchley HD, Garfinkel SN: Interoception and emotion. *Curr Opin Psychol* 17:7-14, 2017. <https://doi.org/10.1016/j.copsyc.2017.04.020>
53. Duschek S, Montoro CI, Reyes Del Paso GA: Diminished interoceptive awareness in fibromyalgia syndrome. *Behav Med* 43(2):100-107, 2017. <https://doi.org/10.1080/08964289.2015.1094442>
54. Preston C, Gilpin HR, Newport R: An exploratory investigation into the longevity of pain reduction following multisensory illusions designed to alter body perception. *Musculoskelet Sci Pract* 45:102080, 2020. <https://doi.org/10.1016/j.msksp.2019.102080>
55. Harshaw C: Interoceptive dysfunction: toward an integrated framework for understanding somatic and affective disturbance in depression. *Psychol Bull* 141(2):311-363, 2015. <https://doi.org/10.1037/a0038101>
56. Paulus MP, Stein MB: Interoception in anxiety and depression. *Brain Struct Funct* 214(5-6):451-463, 2010. <https://doi.org/10.1007/s00429-010-0258-9>
57. Singh Solorzano C, Grano C: Predicting postpartum depressive symptoms by evaluating self-report autonomic nervous system reactivity during pregnancy. *J Psychosom Res* 174:111484, 2023. <https://doi.org/10.1016/j.jpsychores.2023.111484>
58. Porges SW. Body Perception Questionnaire. Laboratory of Developmental Assessment. University of Maryland. 1993;10:2009.
59. Mehling WE, Price C, Daubenmier JJ, Acree M, Bartmess E, Stewart A: The Multidimensional Assessment of Interoceptive Awareness (MAIA). *PLoS One* 7(11):e48230, 2012. <https://doi.org/10.1371/journal.pone.0048230>
60. Martínez E, Aira Z, Buesa I, et al. Embodied pain in fibromyalgia: disturbed somaterepresentations and increased plasticity of the body schema. *PLoS One* 13(4):e0194534, 2018. <https://doi.org/10.1371/journal.pone.0194534>
61. Mehling WE, Gopisetty V, Daubenmier J, Price CJ, Hecht FM, Stewart A: Body awareness: construct and self-report measures. *PLoS One* 4:e5614, 2009. <https://doi.org/10.1371/journal.pone.0005614>
62. Mehling WE, Acree M, Stewart A, Silas J, Jones A: The Multidimensional Assessment of Interoceptive Awareness, version 2 (MAIA-2). *PLoS One* 13(12):e0208034, 2018. <https://doi.org/10.1371/journal.pone.0208034>
63. Weiss S, Sack M, Henningsen P, Pollatos O: On the interaction of self-regulation, interoception and pain perception. *Psychopathology* 47(6):377-382, 2014. <https://doi.org/10.1159/000365107>
64. Park YL, Hunter J, Sheldon BL, et al. Pain and interoceptive awareness outcomes of chronic pain patients with spinal cord stimulation. *Neuromodulation* 24(8):1357-1362, 2021. <https://doi.org/10.1111/ner.13318>
65. Cavaggioni G, Lia C, Resta S, et al. Are mood and anxiety disorders and alexithymia associated with endometriosis? A preliminary study. *Biomed Res Int* 2014:786830, 2014. <https://doi.org/10.1155/2014/786830>
66. Bourdel N, Alves J, Pickering G, Ramilo I, Roman H, Canis M: Systematic review of endometriosis pain assessment: how to choose a scale? *Hum Reprod Update* 21(1):136-152, 2015. <https://doi.org/10.1093/humupd/dmu046>
67. Wickström K, Edelstam G: Minimal clinically important difference for pain on the VAS scale and the relation to quality of life in women with endometriosis. *Sex Reprod Healthc* 13:35-40, 2017. <https://doi.org/10.1016/j.srhc.2017.05.004>
68. Kerns RD, Turk DC, Rudy TE: The West Haven-Yale Multidimensional Pain Inventory (WHYMPI). *Pain* 23(4):345-356, 1985. [https://doi.org/10.1016/0304-3959\(85\)90004-1](https://doi.org/10.1016/0304-3959(85)90004-1)
69. Ferrari R, Novara C, Sanavio E, Zerbini F: Internal structure and validity of the multidimensional pain inventory, Italian language version. *Pain Med* 1(2):123-130, 2000. <https://doi.org/10.1046/j.1526-4637.2000.00020.x>
70. Barnack JL, Chrisler JC: The experience of chronic illness in women: a comparison between women with endometriosis and women with chronic migraine headaches. *Women Health* 46(1):115-133, 2007. https://doi.org/10.1300/J013v46n01_08
71. Li PS, Peng XM, Niu XX, et al. Efficacy of acupuncture for endometriosis-associated pain: a multicenter randomized single-blind placebo-controlled trial. *Fertil Steril* 119(5):815-823, 2023. <https://doi.org/10.1016/j.fertnstert.2023.01.034>
72. Hawkins RS, Hart AD: The use of thermal biofeedback in the treatment of pain associated with endometriosis: preliminary findings. *Appl Psychophysiol Biofeedback* 28(4):279-289, 2003. <https://doi.org/10.1023/a:1027378825194>

10 The Journal of Pain

73. Poli A, Maremmani AGI, Chiorri C, *et al.* Item reduction, psychometric and biometric properties of the Italian version of the body perception questionnaire-short form (BPQ-SF): the BPQ-22. *Int J Environ Res Public Health* 18(7):3835, 2021. <https://doi.org/10.3390/ijerph18073835>
74. Cali G, Ambrosini E, Picconi L, Mehling WE, Committeri G: Investigating the relationship between interoceptive accuracy, interoceptive awareness, and emotional susceptibility. *Front Psychol* 6:1202, 2015. <https://doi.org/10.3389/fpsyg.2015.01202>
75. Zigmond AS, Snaith RP: The hospital anxiety and depression scale. *Acta Psychiatr Scand* 67:361-370, 1983. <https://doi.org/10.1111/j.1600-0447.1983.tb09716.x>
76. Iani L, Lauriola M, Costantini M: A confirmatory bifactor analysis of the Hospital Anxiety and Depression Scale in an Italian community sample. *Health Qual Life Outcomes* 12:84, 2014. <https://doi.org/10.1186/1477-7525-12-84>
77. Nnoaham KE, Hummelshoj L, Webster P, *et al.* World Endometriosis Research Foundation Global Study of Women's Health consortium. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril* 96(2):366-373, 2011. <https://doi.org/10.1016/j.fertnstert.2011.05.090>
78. Schoemann AM, Boulton AJ, Short SD: Determining power and sample size for simple and complex mediation models. *Soc Psychol Pers Sci* 8(4):379-386, 2017. <https://doi.org/10.1177/1948550617715068>
79. Hayes AF: *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach (Methodology in the Social Sciences)*. 2nd ed. The Guilford Press; 2018
80. Preacher KJ, Hayes AF: Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav Res Methods* 40(3):879-891, 2008. <https://doi.org/10.3758/BRM.40.3.879>
81. Meyvis T, Van Osselaer SMJ: Increasing the power of your study by increasing the effect size. *J Consumer Res* 44(5):1157-1173, 2018.
82. Fourquet J, Báez L, Figueroa M, Iriarte RI, Flores I: Quantification of the impact of endometriosis symptoms on health-related quality of life and work productivity. *Fertil Steril* 96(1):107-112, 2011. <https://doi.org/10.1016/j.fertnstert.2011.04.095>
83. Casalechi M, Vieira-Lopes M, Quessada MP, Araújo TC, Reis FM: Endometriosis and related pelvic pain: association with stress, anxiety and depressive symptoms. *Minerva Obstet Gynecol* 73(3):283-289, 2021. <https://doi.org/10.23736/S2724-606X.21.04704-3>
84. Vitale SG, Petrosino B, La Rosa VL, Rapisarda AMC, Laganà AS: A systematic review of the association between psychiatric disturbances and endometriosis. *J Obstet Gynaecol Can* 38(12):1079-1080, 2016. <https://doi.org/10.1016/j.jogc.2016.09.008>
85. Warzecha D, Szymusik I, Wielgos M, Pietrzak B: The impact of endometriosis on the quality of life and the incidence of depression-a cohort study. *Int J Environ Res Public Health* 17(10):3641, 2020. <https://doi.org/10.3390/ijerph17103641>
86. Ishak WW, Wen RY, Naghdechi L, *et al.* Pain and depression: a systematic review. *Harv Rev Psychiatry* 26(6):352-363, 2018. <https://doi.org/10.1097/HRP.0000000000000198>
87. Jaracz J, Gattner K, Jaracz K, Górna K: Unexplained painful physical symptoms in patients with major depressive disorder: prevalence, pathophysiology and management. *CNS Drugs* 30(4):293-304, 2016. <https://doi.org/10.1007/s40263-016-0328-5>
88. McDermid AJ, Rollman GB, McCain GA: Generalized hypervigilance in fibromyalgia: evidence of perceptual amplification. *Pain* 66(2-3):133-144, 1996. [https://doi.org/10.1016/0304-3959\(96\)03059-X](https://doi.org/10.1016/0304-3959(96)03059-X)
89. Hollins M, Walters S: Experimental hypervigilance changes the intensity/unpleasantness ratio of pressure sensations: evidence for the generalized hypervigilance hypothesis. *Exp Brain Res* 234(6):1377-1384, 2016. <https://doi.org/10.1007/s00221-015-4541-0>
90. Borsook D, Moulton EA, Schmidt KF, Becerra LR: Neuroimaging revolutionizes therapeutic approaches to chronic pain. *Mol Pain* 3:25, 2007. <https://doi.org/10.1186/1744-8069-3-25>
91. Abramowitz JS, Schwartz SA, Whiteside SP: A contemporary conceptual model of hypochondriasis. *Mayo Clin Proc* 77(12):1323-1330, 2002. <https://doi.org/10.4065/77.12.1323>
92. Ciaramella A, Pozzolini V, Scatena E, Carli G: Can interoceptive sensitivity provide information on the difference in the perceptual mechanisms of recurrent and chronic pain? Part I. A retrospective clinical study related to multidimensional pain assessment. *Scand J Pain* 23(2):308-317, 2023. <https://doi.org/10.1515/sjpain-2022-0040>
93. De Jong M, Lazar SW, Hug K, *et al.* Effects of mindfulness-based cognitive therapy on body awareness in patients with chronic pain and comorbid depression. *Front Psychol* 7:967, 2016. <https://doi.org/10.3389/fpsyg.2016.00967>
94. Herbert BM, Herbert C, Pollatos O: On the relationship between interoceptive awareness and alexithymia: is interoceptive awareness related to emotional awareness? *J Pers* 79(5):1149-1175, 2011. <https://doi.org/10.1111/j.1467-6494.2011.00717.x>
95. Paolucci T, Zangrando F, Iosa M, *et al.* Improved interoceptive awareness in chronic low back pain: a comparison of Back school versus Feldenkrais method. *Disabil Rehabil* 39(10):994-1001, 2017. <https://doi.org/10.1080/09638288.2016.1175035>
96. Bair MJ, Robinson RL, Katon W, Kroenke K: Depression and pain comorbidity: a literature review. *Arch Intern Med* 163(20):2433-2445, 2003. <https://doi.org/10.1001/archinte.163.20.2433>
97. Eggart M, Valdés-Stauber J: Can changes in multidimensional self-reported interoception be considered as outcome predictors in severely depressed patients? A moderation and mediation analysis. *J Psychosom Res* 141:110331, 2021. <https://doi.org/10.1016/j.jpsychores.2020.110331>
98. Roberts RL, Ledermann K, Garland EL: Mindfulness-oriented recovery enhancement improves negative emotion regulation among opioid-treated chronic pain patients by increasing interoceptive awareness. *J Psychosom Res* 152:110677, 2021. <https://doi.org/10.1016/j.jpsychores.2021.110677>

99. Tesarz J, Leisner S, Gerhardt A, et al. Effects of eye movement desensitization and reprocessing (EMDR) treatment in chronic pain patients: a systematic review. *Pain Med* 15(2):247-263, 2014. <https://doi.org/10.1111/pme.12303>
100. Wertheim B, Aarts EE, de Roos C, van Rood YR: The effect of eye movement desensitization and reprocessing (EMDR) on abdominal pain in patients with irritable bowel syndrome (IBS): a study protocol for a randomized controlled trial (EMDR4IBS). *Trials* 24(1):785, 2023. <https://doi.org/10.1186/s13063-023-07784-1>
101. Moreira MF, Gamboa OL, Pinho Oliveira MA: A single-blind, randomized, pilot study of a brief mindfulness-based intervention for the endometriosis-related pain management. *Eur J Pain* 26(5):1147-1162, 2022. <https://doi.org/10.1002/ejp.1939>
102. Sarstedt M, Hair JF, Nitzl C, Ringle CM, Howard MC: Beyond a tandem analysis of SEM and PROCESS: use of PLS-SEM for mediation analyses!. *Int J Market Res* 62(3):288-299, 2020. <https://doi.org/10.1177/1470785320915686>