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HAL Authorization

## Original Experimental

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# Endometriosis diagnosis buffers reciprocal effects of emotional distress on pain experience

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### Abstract

**Objectives:** Emotional profile is involved in the experience of chronic pain related to endometriosis. Following the Örebro Model of Behavioral Emotion Regulation of Pain, the aim of this study was to understand the processes involved in the psychological adaptation to pain experienced during menstruations in women either diagnosed or not diagnosed with endometriosis.

**Methods:** The study was conducted on a sample of 545 women, either diagnosed with endometriosis or not, during their menstruations. Functional repercussions and intensity of pain, catastrophic thinking, difficulties in emotional regulation and emotional distress were assessed through an online questionnaire. Structural equation modeling (SEM) was carried out.

**Results:** Women diagnosed with endometriosis experience more suffering than women who have not had such a diagnosis. The model we adapted from Örebro's model fits the data well. A differential effect is observed regarding the retroactive effect of depression on pain. Although emotional distress increases functional repercussions among women both with and without the diagnosis, growing pain intensity only occurs among those without.

**Conclusions:** A woman presenting pain during menstruation faces emotional regulation issues that make her more vulnerable to the development of emotional distress. Pain impacts emotional distress, but emotional distress does not impact pain among women for whom the origin of the pain was known (i.e., a diagnosis of endometriosis). Having a diagnosis allows women to externalize the origin of their pain, attributing it to the disease and not to their psychological state.

**Keywords:** emotional distress; emotional regulation; endometriosis; pain.

## Introduction

Endometriosis is a progressive, incurable gynecological disease with a broad spectrum of clinical symptoms that greatly affect women's quality of life and mental health [1–4]. The disease causes chronic pain conditions such as vulvodynia, bladder pain syndrome, and inflammatory bowel syndrome that have disabling consequences in women's daily lives [5]. Since these symptoms are not specific to endometriosis, its prevalence is likely underestimated. Although 2–3% of women are diagnosed and treated, estimates indicate that the disease affects 6–10% of women of reproductive age [5]. Consequently, some women may suffer from menstrual pain for a decade or more before being diagnosed, all the while experiencing or anticipating ostracism, criticism, and attempts to trivialize or dismiss their dysmenorrhea from partners, colleagues, and health professionals [6]. As a result, the women can normalize the symptom pathogenicity [7]. Consequently, without diagnoses, it is difficult to differentiate those women experiencing endometriosis from those experiencing dysmenorrhea only. Some previous studies have shown that biomedical variables cannot fully describe the complex experiences of endometriosis or dysmenorrhea, revealing the important need to assess the psychological and associated cognitive-emotional vulnerability [8, 9]. Indeed, the lack of recognition of this

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disease, as well as the persistence of menstrual pain, induces physiological, emotional, and behavioral processes resulting, for some women, in a negative psychological adjustment to the disease [1, 10].

The biopsychosocial model has highlighted the central role of psychological factors in the development and maintenance of chronic pain and disability. Thus, the literature identifies several risk factors, e.g. depression, [11–13]; anxiety disorders, [14–16]; catastrophic thinking [17, 18], and different models put forward to explain how they contribute to chronic pain, e.g. fear-avoidance model, [19]. These factors are targeted by interventions aimed at preventing the development of prolonged disability. However, the management of these pain comorbid factors was still in its infancy due to (1) poor prognostic value if these factors were taken individually [20] and (2) a lack of a clear theoretical understanding of the mechanisms involved [21]. Thus, a transdiagnostic approach has recently been the focus of a growing body of research in the field of chronic pain. This literature highlights the central role of emotional regulation in the development and maintenance of comorbidity between chronic pain and emotional problems, primarily in a population of patients with musculoskeletal disorders [22–24].

Emotional regulation consists of the conscious or unconscious attempts to influence one's emotions, their appearance, and their expression or feeling, in order to maintain emotional homeostasis [25, 26]. Emotional processes are essential in the development and maintenance of pain [11, 27, 28], which are conceptualized in the "Örebro Model of Behavioral Emotion Regulation of Pain". This model emphasizes the recurrent cyclical nature of both conditions, triggered by "flare-ups". Pain patients are thus subject to alternating periods of feeling relatively well and periods of recurrence of pain and/or depressed moods. This alternation would trigger negative feelings, reactivating catastrophic ideas related to previous experiences and, in turn, generating an increase in negative mood (or a decrease in positive mood) that finally results in higher pain intensity. These episodes would trigger the emotional regulation system. Thus, if the regulation is appropriate, negative emotions are managed and pain is less intense. Conversely, if regulation is inadequate, negative affects will increase and trigger emotional distress and pain. A vicious circle thus develops, including negative affects, emotional dysregulation that increases the levels of distress, and pain itself [11]. The Örebro Model is particularly relevant to the clinical application of this knowledge as it highlights the core role of emotional regulation to explain the reciprocal relationships between pain intensity and emotional distress [11]. It may, therefore, be transferable to

the context of endometriosis, and more broadly to that of dysmenorrhea, although the latter was not taken into account in this context.

## Objectives

A growing body of evidence supports the evaluation of an emotional profile as part of a rational approach to pain, especially when considering the chronic pain experienced in endometriosis [29]. Following the Örebro Model, the aim of this study was to better understand the processes (i.e., catastrophic thinking, emotional regulation, or emotional distress) involved in the psychological adaptation to pain experienced during menstruations in women either diagnosed or not diagnosed with endometriosis.

## Methods

An observational study was conducted on a representative sample of women, either diagnosed with endometriosis or not, during their menstruations.

### Participants

The study included adult women with and without diagnosis of endometriosis. The population was subdivided into two groups: 1/The first group, called "diagnosed" (D) comprised women diagnosed with endometriosis diagnosed by a physician; 2/The second group "not diagnosed" comprised women who did not have an established diagnosis. Women who were under 18-years old, menopausal, or under protective custody were excluded from the study.

### Procedure

An online questionnaire was distributed using social network platforms where the general public can communicate about endometriosis, such as "Endogirls", "Endocorp's", "Superendogirl". A consent form informing participants of their rights and the implications of their participation was approved by each participant. Protocol was ethically reviewed and approved by the Institutional Review Board of University of Nantes (no: IORG0011023).

### Measures

**Functional repercussions of pain:** The Brief Pain Inventory (BPI) [30, 31] uses visual analogue scales to measure general pain and its functional repercussions (on general activity, mood, ability to walk, usual work, relationships, sleep, and will to enjoy life). The validated version focuses on pain experienced over the past week but, in this study, we chose to adapt the scale to the past month in order to account for hormonal cycles (28 days).

**Catastrophic thinking:** The Pain Anxiety Symptoms Scale (PASS-20) [32] is a 20-item measurement scale designed to assess pain-related beliefs. It has four subscales, including a cognitive dimension involving catastrophic thoughts ( $\alpha = 0.92$ ), which was used in this study.

**Difficulties in emotional regulation:** The Difficulties in Emotional Regulation Scale - Short Form (DERS-SF), is composed of 18 items rated on Likert scales and has five dimensions. The French validation of this scale [33], like other validations of this scale before it [34–36], revealed that the “awareness” dimension should be excluded from the model and the calculation of the total score of the DERS-SF. Values of Cronbach’s alpha for the scales range from 0.92 to 0.95.

**Emotional distress:** The Hospital Anxiety and Depression Scale (HADS) is a self-evaluation scale, validated in French, that assesses the severity of anxious and depressive symptomatology [37–39]. The HADS includes two subscales: one focusing on anxiety symptoms ( $\alpha = 0.82$ ) and one focusing on depression symptoms ( $\alpha = 0.83$ ). Following the literature, only the depressive subscale was used to assess emotional distress in the present study.

## Statistical analysis

**Statistical analyses were performed using Jamovi and R software:** Chi-square and Student’s *t*-tests were used to assess homogeneity of the diagnosed and non-diagnosed groups for frequency and mean comparisons, respectively. When appropriate, Welch approximations

for heteroskedasticity (Levene’s  $p < 0.05$ ) or Mann-Whitney Wilcoxon tests for non-normal distributions (Shapiro’s  $p < 0.05$ ) were performed.

Structural equation modeling (SEM) was carried out with the *Lavaan* R package [40]. A non-recursive model was first identified in view of the Örebro framework, conceptualizing pain and functional repercussions over catastrophic thinking, catastrophic thinking over emotional regulation and, lastly, emotional regulation over emotional distress in a sequential manner. Potentially, depression can have a retroactive effect on both pain intensity and functional repercussions. We used Yuan–Bentler  $\chi^2$  robust maximum likelihood to estimate the model because there was a significant violation of multivariate normality (Mardia  $p < 0.05$ ) [41]. The model was tested for the whole sample and by using multigroup SEM to compare the women with and without diagnoses of endometriosis. According to Hu and Bentler (1999) [42], a model demonstrates a good fit when the Root Mean Square Error of Approximation RMSEA  $\leq 0.06$ , Standardized Root Mean Square Residual SRMR  $\leq 0.08$  and Comparative Fit Index (CFI) or Tucker-Lewis Index (TLI)  $\geq 0.95$ . These thresholds are only guidelines, and decisions must be taken regarding the pattern of adjustment and closeness of values to the standards [43].

## Results

A total of 545 women were included in the study: 253 women with a diagnosis of endometriosis and 292 without. Table 1 presents the descriptive characteristics of the sample depending on whether or not the women had been diagnosed with endometriosis prior to the study.

**Table 1:** Descriptive statistics.

	Diagnosed		Not diagnosed		<i>p</i> .
	M	(sd)	M	(sd)	
Age	30.51	7.797	27.58	9.421	<0.001
Family status	N	%	N	%	
Single	83	15.2	134	24.6	0.003
Part of a couple	169	31	158	29	0.003
Widow	1	0.2	0	0.0	0.003
Professional status					
Managers	17	3.1	30	5.5	<0.001
Employee	43	7.9	31	5.7	<0.001
Student	48	8.8	152	27.9	<0.001
Salaried	84	15.4	59	10.8	<0.001
Unemployed	33	6.1	6	1.1	<0.001
Self-employed	15	2.8	7	1.3	<0.001
Other	13	2.4	7	1.3	<0.001
Children					
Yes	64	11.7	68	12.5	0.585
No	189	34.7	224	41.1	0.585
Menstrual pain					
Chronic pelvic pain	251	46.1	2	0.4	<0.001
Low back pain	222	40.7	31	5.7	<0.001
Deep pain during sexual intercourse	188	34.5	65	11.9	<0.001
Absenteeism	151	37.7	102	18.7	<0.001

## Differential impact of diagnosis on pain and psychological measures

As shown in Table 2, women diagnosed with endometriosis experience more suffering than women who have not had such a diagnosis. Women diagnosed with endometriosis have significantly higher scores on levels of pain intensity and functional repercussions. In addition, they have significantly higher scores on scales measuring pain anxiety symptoms, difficulties in emotional regulation, and catastrophic thinking.

### Path model

The model we adapted from Örebro's model fits the data well, as shown by the robust goodness-of-fit indices for both the single model:  $\chi^2(3) = 15.8$ ,  $p = 0.001$ , CFI = 0.983, TLI = 0.943, SRMR = 0.033, RMSEA = 0.099 [0.054, 0.149], and the multigroup model  $\chi^2(6) = 13.82$ ,  $p = 0.032$ , CFI = 0.983, TLI = 0.945, SRMR = 0.030, RMSEA = 0.079 [0.022, 0.134]. Standardized estimates for the model are given in Figure 1. First, the correlation between pain and functional repercussion is shown significant for both women with and without diagnosis of endometriosis ( $\beta_{D.} = 0.35$ ,  $p < 0.001$ ;  $\beta_{ND.} = 0.55$ ,  $p < 0.001$ ). As depicted, pain anxiety symptoms are significantly predicted by pain intensity among women diagnosed ( $\beta_{D.} = 0.24$ ,  $p < 0.001$ ) or not diagnosed ( $\beta_{ND.} = 0.21$ ,  $p < 0.01$ ) with endometriosis. Impact of functional repercussions on pain anxiety symptoms is also significant regardless of whether endometriosis was diagnosed ( $\beta_{D.} = 0.41$ ,  $p < 0.001$ ;  $\beta_{ND.} = 0.31$ ,  $p < 0.001$ ). In the same way, pain anxiety symptoms are also positively linked to subsequent difficulties in

emotional regulation ( $\beta_{D.} = 0.31$ ,  $p < 0.001$ ;  $\beta_{ND.} = 0.27$ ,  $p < 0.001$ ), which, in turn, result in greater emotional distress ( $\beta_{D.} = 0.45$ ,  $p < 0.001$ ;  $\beta_{ND.} = 0.39$ ,  $p < 0.001$ ). A differential effect is observed regarding the retroactive effect of depression on pain. Although emotional distress increases functional repercussions among women both with and without the diagnosis ( $\beta_{D.} = 0.33$ ,  $p < 0.001$ ;  $\beta_{ND.} = 0.36$ ,  $p < 0.001$ ), growing pain intensity only occurs among those without ( $\beta_{D.} = 0.10$ ,  $p = 0.15$ ;  $\beta_{ND.} = 0.25$ ,  $p < 0.001$ ).

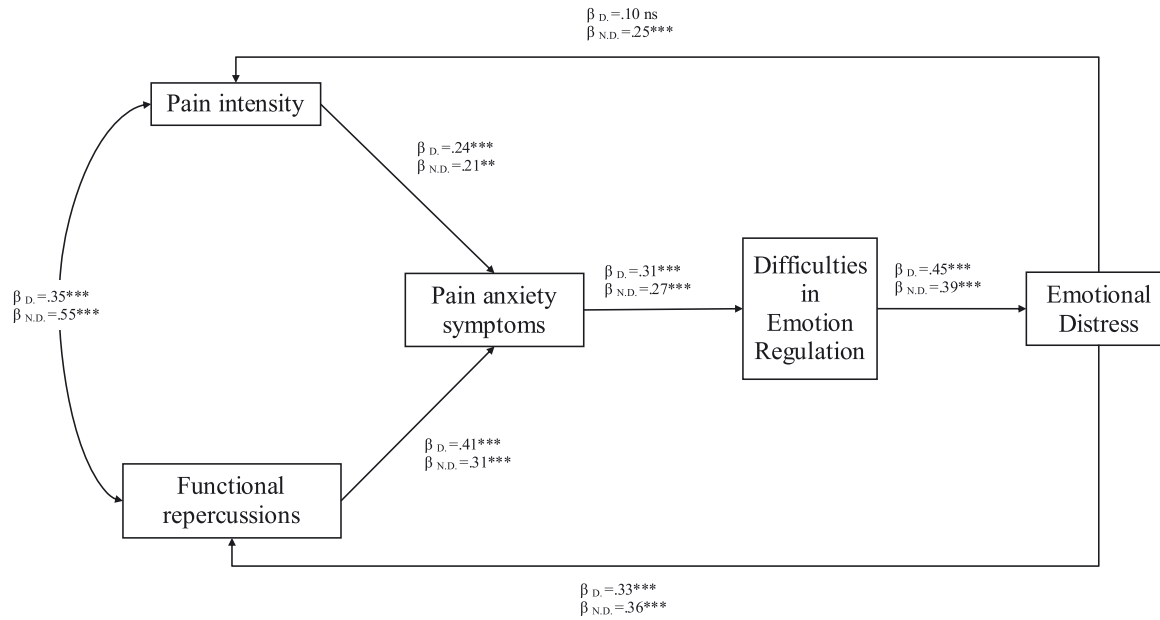
## Discussion

This study focused on the processes involved in the psychological adaptation to pain experienced during menstruation by women with and without a diagnosis of endometriosis. The Örebro model of chronic pain was applied for women with and without endometriosis during menstruation.

Our present results show that the women diagnosed with endometriosis report a greater level of disability during their periods than women without this diagnosis. Indeed, painful and irregular periods have repercussions for women's social and professional lives [44]. These women reported higher levels of catastrophic thoughts related to pain during menstruation, problems in emotion regulation and emotional distress. Women with endometriosis are more prone to develop comorbidities like depression or anxiety [45, 46]. A rationale for this comorbidity between pain and psychopathology could be the common cognitive and emotional processes. The catastrophic thinking associated with the pain and the emotion regulation can lead to the development of anxious and emotional distress [1].

**Table 2:** Differential impact of diagnosis on pain and psychological measures.

	Diagnosed		Not diagnosed		<i>t</i>	<i>p.</i>	Cohen's <i>d</i>
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>			
Pain intensity	7.771	1.459	4.753	2.49	-17.52	<0.001	-1.478
Functional repercussions of pain							
General activity	5.86	2.617	3.388	2.908	-10.014	<0.001	-0.894
Mood	6.217	2.652	4.423	2.981	-7.180	<0.001	-0.636
Ability to walk	5.728	2.83	2.239	2.844	-10.262	<0.001	-0.915
Usual work	5.728	2.83	3.249	3.03	-9.443	<0.001	-0.845
Relationships	5.339	2.894	2.759	2.759	-10.226	<0.001	-0.913
Sleep	5.915	2.921	3.379	3.123	-9.467	<0.001	-0.839
Life enjoyment	4.774	3.283	1.770	2.699	-11.137	<0.001	-0.999
Pain anxiety symptoms	11.395	3.945	8.616	3.873	-8.281	<0.001	-0.711
Difficulties in emotional regulation	40.70	13.30	38.29	12.02	-2.198	0.028	-0.189
Catastrophic thoughts	17.89	5.016	13.38	5.464	-9.971	<0.001	-0.856



**Figure 1:** Predictive paths linking pain, pain-related functional repercussions and depression through pain anxiety symptoms and emotional regulation.

D. = diagnostic of endometriosis; N.D. = No diagnostic of endometriosis. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

The Örebro model explains these links. This study shows its ecological relevance whether or not women have been diagnosed and whether they suffer from moderate or high pain intensity. Thus, a woman presenting pain during menstruation faces emotional regulation issues that make her more vulnerable to the development of emotional distress.

One of the strongest results of this study is the absence of a retroactive association between pain intensity and emotional distress, which was found only in women for whom the origin of the pain was known (i.e., a diagnosis of endometriosis). Pain impacts emotional distress but emotional distress does not impact pain, contrary to what is usually observed for chronic pain [47]. There are several possible explanations for these results. First, the variability in pain intensity during menstruation was different between women with and without a diagnosis of endometriosis, as shown by the percentages of variation of 9.2 and 52%, respectively. Pain is so pervasive in the daily lives of these women that the response process may have been impacted and the scores saturated. Second, having a diagnosis allows women to externalize the origin of their pain, attributing it to the disease and not to their psychological state. If pain indirectly generates emotional distress, the impact of emotional distress on pain would be short-circuited for those women who do not have feelings of guilt or hold themselves responsible for their perceived pain.

Emotional distress has exogenous and endogenous parts. Concerning the exogenous part, studies stress that

women experience or anticipate ostracism, criticism, and attempts to trivialize or dismiss their dysmenorrhea from partners, colleagues and physicians [6, 48–50]. As endometriosis is still poorly recognized, the chronic nature of the pain and the difficulties related to its management contribute to the emergence of emotional distress. Concerning the endogenous part, women may live for years without being aware of the pathogenicity of their symptoms. Thus, in the absence of any medical or rational explanation, women are more likely to internalize the problem and make themselves responsible for their perceptions of the symptoms. This perception refers to an inability to tolerate and cope with symptoms that are considered mild and normal for menstruating women. The emotional distress in this context leads to a focus on the pain and increases its impact. Once a diagnosis is made, women can still have emotional distress due to the pain and its repercussions for daily living repercussions. However, they may be freed from the negative thoughts implying their own responsibility in their pain experience, i.e., the endogenous part of emotional distress that formerly exacerbated the pain.

A well-established diagnosis should find the source of emotional distress. However, it is clear that women's complaints about intense and chronic pelvic pain during menstruations are not always listened to or recognized by general practitioners or gynecologists. Potentially, only 2–3% of existing endometriosis is correctly diagnosed and managed [51]. Societal work based on the development of

research and interventions targeting the illness representation is therefore necessary, especially research dealing with the causal attribution of the symptoms. This will help to reduce diagnostic wandering and thus allow women to stop blaming themselves for their suffering and to better cope with their condition. Different actors can be involved: politicians and public health authorities by working on the recognition of the status (through actions such as the assumption of the costs of care); companies by recognizing menstrual pain through the implementation of a menstrual leave and work time/place accommodations (resting space, flexible hours, time dedicated to gynecological consultation); education from an early age on menstrual pain and improving physician training (particularly in listening skills and recognition of women's complaints). This calls for a study of the means that are available to the actors to address the problem.

## Perspectives and limitations

The reality of endometriosis symptoms is not yet sufficiently recognized and the disease remains trivialized. In the absence of clear symptomatology, it is tempting to normalize and even psychologize the suffering of women affected by painful periods by making their psychological state the cornerstone of any explanation of the symptoms. Although the link between pain sensitivity and psychological state is thought to be reciprocal [52], our results tend to only support this hypothesis among non-diagnosed women, i.e., that physiological state unidirectionally predicts psychological state. Further research should examine those aspects in greater depth and compare the top-down and bottom-up hypotheses explaining the relationship between medical and psychological variables. In this regard, future longitudinal studies supported by cross-lagged panel models could be useful to compare the two predictive paths of the association between pain and psychological state.

Choice of sampling method in this study should also be discussed. This study comes up against the complexity inherent in the clinical reality of endometriosis. It is difficult to establish a diagnosis of endometriosis. And among the non-diagnosed women, it is quite possible that several are living with latent endometriosis for which they perceive a lower pain intensity for a number of reasons (e.g., effective medical treatment, functional coping strategy, desensitization to pain over the years, a less-painful period at measurement time, etc.). Pain is a warning but not the main indicator. This is why we rely on the medical diagnosis and why our inclusions are based on the clinical

interview with the physician and the diagnosis established by thorough examinations. This statement leads us to consider the development of an adapted instrument for pain assessment in such a population with intense and fluctuating levels of suffering.

## Conclusions

Care programs depend on an appropriate diagnosis, regardless of the pathology or mechanisms responsible for the pain. It seems clear that much remains to be done to understand and acknowledge endometriosis. Future research in this field may be particularly beneficial in helping to understand what renders endometriosis so characteristic, both from a medical standpoint and from a psychological point of view. This would improve diagnosis and overall care of women living with the disease.

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**Author contributions:** MLB was responsible for the project management and supervision. LG created the Internet survey, conducted the data collection. LG and GB performed the statistical analysis. All authors wrote the first draft of the manuscript and approved the final manuscript. All authors discussed the results and commenting on the manuscript. All authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Competing interests:** Authors state no conflict of interest.

**Informed consent:** Informed consent has been obtained from all individuals included in this study.

**Ethical approval:** Research involving human subjects complied with all relevant national regulations, institutional policies and is in accordance with the tenets of the Helsinki Declaration (as amended in 2013) and has been approved by the Institutional Review Board of University of Nantes (n°: IORG0011023).

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