# Primary Dysmenorrhea and Painful Sex: Canaries in the Coal Mine?

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## Abstract

**Objective:** Primary dysmenorrhea and provoked vestibulodynia (PVD) are common pain conditions in young women. The purpose of this study was to document the severity of dysmenorrhea in women with confirmed PVD to further clarify reports of comorbidity. Since central sensitisation (CS) of the nervous system is present in both conditions, diagnosis of either, but especially both conditions, may reflect past chronic stress.

**Methods:** We investigated this comorbidity in a sample of 63 women who met diagnostic criteria for PVD, and a comparison group of 89 women with low sexual desire and arousal but no pain during sex. All women completed questionnaires about the history and severity of their dysmenorrhea.

**Results:** Of the women with PVD, 28.6% recalled moderate and 34.9% severe dysmenorrhea. For women in the comparison group, these figures were 22.5% and 19.1%, respectively. Women with PVD reported that the periods they experienced as teenagers were more painful, longer, more debilitating, and persistently painful for more years than those recalled by women in the comparison group.

**Conclusions:** Our findings suggest that the origins of the early-onset CS require serious investigation. Research into the potential to reduce future chronic pain conditions through early effective treatment of primary dysmenorrhea is also needed.

**Keywords:** dysmenorrhea, chronic dyspareunia, past stress

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## Résumé

**Objectif :** La dysménorrhée primaire et la vestibulodynie provoquée (VDP) sont des pathologies fréquentes causant de la douleur chez les jeunes femmes. Cette étude visait à documenter la sévérité de la dysménorrhée chez les femmes atteintes de VDP confirmée afin de préciser le signalement de comorbidités. Étant donné que la sensibilisation centrale du système nerveux est présente dans les deux pathologies, le diagnostic de l'une ou l'autre, mais surtout des deux, peut dénoter un stress chronique antérieur.

**Méthodologie :** Nous avons étudié cette comorbidité dans un échantillon de 63 femmes qui satisfaisaient aux critères diagnostiques de VDP, et un groupe témoin de 89 femmes présentant une faible libido et peu d'excitation, mais aucune douleur pendant les rapports sexuels. Toutes les femmes ont rempli des questionnaires sur l'histoire et la sévérité de leur dysménorrhée.

**Résultats :** Parmi les femmes atteintes de VDP, 28,6 % ont déclaré avoir souffert de dysménorrhée modérée et 34,9 %, de dysménorrhée sévère. Chez les femmes du groupe témoin, ces chiffres étaient respectivement de 22,5 % et 19,1 %. En comparaison aux femmes du groupe témoin, les femmes atteintes de VDP ont signalé qu'à l'adolescence, leurs menstruations avaient été plus douloureuses, plus longues, plus débilitantes et que la douleur avait persisté pendant un plus grand nombre d'années.

**Conclusions :** Nos observations laissent supposer que les origines de la sensibilisation centrale à début précoce nécessitent une analyse sérieuse. Des recherches sur la possibilité de réduire les futures maladies chroniques douloureuses par un traitement précoce et efficace de la dysménorrhée primaire sont également nécessaires.



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## INTRODUCTION

Severe primary dysmenorrhea and provoked vestibulodynia (PVD) are common chronic pain conditions in young women. The onset of primary dysmenorrhea is typically 1–2 years after menarche. When severe, dysmenorrhea

is unresponsive to analgesics and is often managed by combined hormonal contraceptives.[1] Studies suggest some 10% to 20% of teens report severe primary dysmenorrhea.[2,3]

PVD is recurrent pain characterized by allodynia (pain from a non-noxious stimulus) of the vestibule, usually tested with touch from a cotton swab. The pain is provoked by any touch or contact and is without known cause.[4] Although typically elicited from sexual activity, the pain can be provoked by gynaecological examination or tampon insertion. PVD occurs in 8% to 10% of women and possibly twice that proportion in women under 20 years of age.[5,6] There is some evidence of genetic predisposition.[7]

Limited research confirms comorbidity between PVD and primary dysmenorrhea. Painful menses (severity not indicated) was identified in 86.8% of 50 women with primary PVD (pain at first attempt at any vaginal penetration) and 63.9% of women with secondary PVD.[8] Another study found 27 of 44 women with primary and 13 of 45 women with secondary PVD had dysmenorrhea (severity not clarified).[9]

Both primary dysmenorrhea and PVD are associated with other chronic pains, including temporomandibular joint pain, irritable bowel syndrome, fibromyalgia, and interstitial cystitis.[10] For both primary dysmenorrhea and PVD, their comorbidity with other chronic pain conditions is thought to reflect central sensitization (CS) of the central nervous system (CNS). CS is the phenomenon of abnormal sensory processing within the CNS, with functional and structural changes in the CNS arising from its inherent plasticity. These changes cause amplification of neural signaling to elicit pain hypersensitivity.

The changes of CS may occur from altered "top-down" signaling from the brain to the spinal cord or repeated afferent nocioceptor activity from the periphery to the spinal cord and brain. In keeping with the latter mechanism, monthly severe pelvic pain could cause sufficient afferent nocioception to encourage "bottom-up" causation of CS and therefore possible PVD, perhaps influenced by genetic predisposition. We therefore studied the prevalence of severe dysmenorrhea in women with PVD and compared its prevalence in women who have low sexual desire but lack any sexual pain.

We hypothesized that the prevalence of recalled severe dysmenorrhea in teenage years would be higher in women with PVD than in women with low sexual desire.

## METHODS

### Participants

Data for this study were obtained from the baseline assessment of participants in a recently completed clinical trial of psychological treatments for women with PVD (Anon., n.d.).[11] Participants (N = 130) met the following inclusion criteria: (1) a diagnosis of PVD confirmed by clinical history and a cotton-swab test carried out by a physician with expertise in sexual medicine and vulvovaginal conditions; (2) a duration of PVD of at least 6 months; (3) an ability to attend eight weekly treatment sessions; (4) aged 19 years or older and premenopausal; (5) fluent in English; and (6) willing to refrain from any new treatments for PVD for the duration of the study until the 6-month follow-up point. Exclusion criteria were (1) unprovoked vulvovaginal pain; (2) pelvic pain; (3) a vulvar skin condition; and (4) significant symptoms of dissociation (the study involved group psychological skills, and participant dissociation would have made participation challenging). Of this original sample of 130, 63 provided data on their dysmenorrhea history and were included in the present study. Women who did and did not provide dysmenorrhea data did not differ in demographic characteristics except for ethnicity: Women who provided dysmenorrhea data were more likely to be Caucasian than women who did not provide those data (78% vs. 56%; $\chi^2[2, N = 126] = 8.524$; $P = 0.014$).

The comparison group data were obtained from the baseline assessment of participants in an ongoing trial of psychological treatments for women with sexual interest/arousal disorder. Participants (N = 111) met the following inclusion criteria: They (1) were experiencing distressing sexual interest/desire and/or sexual arousal concerns; (2) were between the ages of 19 and 65; (3) were fluent in English; (4) anticipated attending all group sessions and completing homework; and (5) did not meet diagnostic criteria for borderline personality disorder. Exclusion criteria were as follows: (1) not experiencing distressing sexual interest/desire and/or sexual arousal concerns; (2) not between the ages of 19 and 65; (3) not fluent in English; (4) experiencing a psychiatric or medical condition that would interfere with group session attendance or homework completion; and (5) meeting diagnostic criteria for borderline personality disorder. Out of the original sample of 111, 89 provided data on dysmenorrhea history and were included in the present study. Women who provided dysmenorrhea data did not differ in demographic characteristics from women who did not provide those data.

The two groups of women (63 with PVD and 89 with sexual interest/arousal disorder but no sexual pain) were directly compared in this study.

### Procedure

After consenting to participation, women in both groups completed a dysmenorrhea questionnaire and demographics questionnaire developed by our teams. All

questionnaires were administered using SurveyMonkey, unless participants requested otherwise. When preferred, paper copies were mailed. The University of British Columbia Research Ethics Board approved both studies.

### Measures

Participants answered questions about their age, education, employment status, sexual orientation, relationship duration, number of children, and childbirth history.

#### *Dysmenorrhea questions*

Dysmenorrhea in women's teenage years was assessed with eight self-report questions developed by the research team and listed in Table 1. They included questions about the age of menarche, average menstruation duration, and six questions assessing pain: pain severity on a scale ranging from 0 = not painful to 3 = severely painful, pain onset during menstruation, and pain duration both within a menstruation period (in days) and across the life span (in years). The impact of pain on daily functioning was assessed by the question "Any painful periods you experienced as a teenager when not on hormonal birth control. . ." followed by five response options ranging from (1) "periods were not painful" to (5) "required some absences from work or school with insufficient relief from medication."

## RESULTS

Descriptive data for all demographic measures are reported in Table 2. There was a statistically significant difference in age between groups ($t[150] = -3.70$, $P < 0.001$), with women in the low-desire group being significantly older. Demographic variables related to age were also significantly different between the two studies: Women with low desire reported their primary relationship to be longer, had more children, and had more pregnancies. Those variables were then compared between the groups while controlling for age, and the differences were no longer significant, indicating that the differences were largely related to age. Women in the two studies did not differ in the distribution of employment, level of education, or sexual orientation (all $\chi^2$ statistics are nonsignificant and are reported in Table 2).

### Dysmenorrhea Questionnaire

A total of 28.6% of women with PVD recalled moderate and 34.9% recalled severe primary dysmenorrhea. The percentages were 22.5% and 19.1% in women with low sexual desire but without sexual pain ($\chi^2[3, N = 152] = 8.093$; $P = 0.044$), indicating that women with PVD were more likely to report a history of severe dysmenorrhea than women with low sexual desire.

Because of the difference in participant age between the studies, all analyses comparing menstruation- and dysmenorrhea-related variables were conducted using analysis of covariance with age as a covariate. The estimated marginal means and $F$ test values are reported in Table 3. Women in the two studies did not differ in mean age at menarche, the average length of the menstrual period (in days), or average age in years when painful menstruations began. For both groups, pain began around day 1 of menstruation.

Women with PVD reported a significantly higher intensity of menstrual pain compared with women with low desire, and pain lasted longer during menstruation for women with PVD than for women with low desire. Women with PVD also reported menstrual pain as lasting for more

**Table 1. Menstruation history questions**

| Menstruation history question | Answer options |
|---|---|
| How old were you when you first began menstruating? | Open-ended |
| How many days, on average, did your periods last? | 1, 2, 3, 4, 5 or more |
| Age in years when you first began experiencing these painful periods? | Open-ended |
| The periods you had as a teenager, when not on hormonal birth control (pill, patch, vaginal ring, etc.), were | 1 = Not painful; 2 = Mildly painful; 3 = Moderately painful; 4 = Severely painful |
| On which day of your cycle did the pain usually begin? | First, second, third, fourth, fifth, sixth day or later |
| For how many days did the pain usually last? | 1, 2, 3, 4, 5, 6 or more |
| Number of years you experienced this amount of pain? | Open-ended |
| Any painful periods you experienced as a teenager when not on hormonal birth control | 1 = Periods were not painful; 2 = Did not affect daily activity; 3 = Rarely affected daily activity and medication rarely required; 4 = Was relieved by pain medication so that absence from school or work was rarely required; 5 = Required some absences from work or school with insufficient relief from medication and possibly including experience of nausea, vomiting, and/or headache |

**Table 2. Demographic variables for PVD and low-desire studies**

| Measure | PVD group; n = 63 | Low-desire group; n = 89 | | *P* value | Total |
|---|---|---|---|---|---|
| Age in years, mean (SD) | 32.4 (8.6) | 39.2 (12.7) | $t = -3.70$ | <0.001 | 36.3 (11.7) |
| Length of relationship in months, mean (SD)[a] | 93.9 (80.6) | 146.7 (119.0) | $t = -3.03$ | 0.003 | 125.4 (108) |
| Number of children, mean (SD)[a] | 0.3 (0.7) | 0.7 (1.0) | $t = -2.87$ | 0.005 | 0.6 (1.0) |
| Number of children delivered, mean (SD)[a] | 0.3 (0.7) | 0.6 (1.0) | $t = -2.44$ | 0.016 | 0.5 (0.9) |
| Number of pregnancies, mean (SD)[a] | 0.5 (1.0) | 1.1 (1.4) | $t = -3.23$ | 0.002 | 0.9 (1.3) |
| Highest level of education, no. (%) | | | $\chi^2 = 2.432$ | 0.787 | |
| High school | 1 (1.6) | 3 (3.4) | | | 4 (2.6) |
| College/tech/trade school | 13 (20.6) | 19 (21.6) | | | 32 (21.2) |
| Undergraduate degree | 24 (38.1) | 32 (36.4) | | | 56 (37.1) |
| Master's degree | 15 (23.8) | 26 (29.5) | | | 41 (27.2) |
| Doctoral degree or MD | 2 (3.2) | 2 (2.3) | | | 4 (2.6) |
| Other | 8 (12.7) | 6 (6.8) | | | 14 (9.3) |
| Current employment, no. (%) | | | $\chi^2 = 2.981$ | 0.887 | |
| Full time | 29 (46.0) | 36 (40.4) | | | 65 (42.8) |
| Part time | 5 (7.9) | 12 (13.5) | | | 17 (11.2) |
| Self-employed | 7 (11.1) | 9 (10.1) | | | 16 (10.5) |
| Unemployed | 2 (3.2) | 4 (4.5) | | | 6 (3.9) |
| Retired | 0 (0.0) | 2 (2.2) | | | 2 (1.3) |
| Student | 10 (15.9) | 13 (14.6) | | | 23 (15.1) |
| Homemaker | 4 (6.3) | 5 (5.6) | | | 9 (5.9) |
| Other | 6 (9.5) | 8 (9.0) | | | 14 (9.2) |
| Sexual orientation, no. (%) | | | $\chi^2 = 4.941$ | 0.176 | |
| Heterosexual | 52 (83.9) | 65 (73.0) | | | 117 (77.5) |
| Homosexual | 1 (1.6) | 5 (5.6) | | | 6 (4.0) |
| Bisexual | 9 (14.5) | 15 (16.9) | | | 24 (15.9) |
| Other | 0 (0) | 4 (4.5) | | | 4 (2.6) |

[a] Difference between PVD and low-desire group for this variable becomes nonsignificant when age is controlled in the comparison.
PVD: provoked vestibulodynia.

**Table 3. Estimated marginal means of menstruation- and dysmenorrhea-related variables compared between PVD and desire studies while controlling for age**

| | Group; EMM (SE)[a] | | | | |
|---|---|---|---|---|---|
| Measure | PVD ; n = 63 | Low desire; n = 89 | *F* | *P* value | Partial eta squared |
| Age of menarche, y | 12.4 (0.4) | 13 (0.3) | 1.55 | 0.214 | .01 |
| Average duration of menses, days | 4.7 (0.1) | 4.8 (0.1) | 0.7 | 0.405 | .01 |
| Age of first painful periods | 14.2 (0.7) | 15.3 (0.6) | 1.3 | 0.250 | .01 |
| Intensity of menstrual pain as a teenager, when not on hormonal birth control (pill, patch, vaginal ring, etc.) | 2.8 (0.1) | 2.3 (0.1) | 6.6 | 0.011 | .04 |
| Cycle day on which pain usually began | 1.2 (0.1) | 1.3 (0.1) | 0.7 | 0.415 | .01 |
| Usual pain duration, days | 2.7 (0.2) | 2.1 (0.1) | 6.5 | 0.012 | .06 |
| Duration of this amount of pain, y | 15 (1.3) | 11 (1.1) | 5.1 | 0.026 | .05 |
| Interference with school and activities, presence of other physical symptoms with menses in teens when not on hormonal birth control | 3.5 (0.2) | 2.9 (0.2) | 6.4 | 0.013 | .04 |

[a] SE from analysis of covariance comparing the PVD and low-desire groups with age as a covariate.
EMM: estimated marginal means; PVD: provoked vestibulodynia; SE: standard error.

years throughout their life than did the women with low desire. Finally, women with PVD reported that menstrual pain affected their daily functioning to a higher degree than did women with low desire.

## DISCUSSION

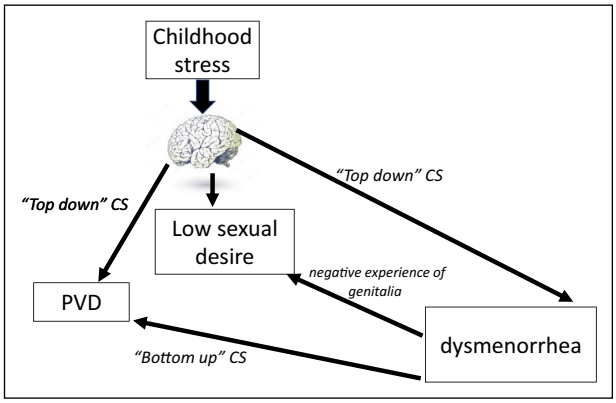
Our results support our hypothesis that women with PVD, when compared with a group of women with low sexual desire and arousal but no pain with sex, would give histories of more severe dysmenorrhea. Women with PVD recalled teenage menses to be more painful, to be of longer duration, to disrupt their daily lives more severely, and to remain painful for more years than was recalled by women with low desire. Among the women with PVD, 28.6% and 34.9%, respectively, reported past moderate and past severe dysmenorrhea. For women with low desire, these figures were 22.5% and 19.1%, respectively.

Our results were not unexpected given the evidence of CS in both PVD and primary dysmenorrhea. Women with PVD demonstrate both hyperalgesia and decreased pain thresholds in nongenital parts of the body.[12] Functional brain imaging has confirmed increased activation of pain circuits in women with PVD from painful stimuli applied to areas remote from the genitalia.[13] Similarly, severe dysmenorrhea was found to be associated with abdominal allodynia, reflecting CS in women with chronic pelvic pain.[14] Functional brain changes in women with severe dysmenorrhea persist outside of the menstrual phase.[15]

It has been suggested that primary dysmenorrhea may trigger the changes of CS via "bottom-up" signaling (Figure).[16,17] Severe teenage menstrual pain may be a "canary in the coal mine" for future chronic pain. Our confirmation of high comorbidity between severe dysmenorrhea and PVD encourages adequate monthly pain control to limit CS.

An additional mechanism underlying CS in PVD—"top-down" regulation from the brain to the spinal cord, sensitizing dorsal horn cells—might also be important. PVD can be apparent the first time tampon insertion is attempted, often soon after menarche and before establishment of ovulatory and potentially painful menses. For some women, factors in earlier years may be relevant in the etiology of their CS. Research has shown the adult hypothalamic-pituitary-adrenal (HPA) axis may become dysregulated by stressors earlier in life.[18] This dysregulation is linked to chronic pain in adult life,[19,20] including PVD.[21,22] Stress-associated reduction of descending inhibition of nocioceptive signals is a major way in which CS facilitates pain signals[23] and could underlie both severe dysmenorrhea and PVD (Figure).

**Figure. The compounding effects of stress on menstrual and sexual pain and sexual desire.**




Childhood stress may cause "top-down" development of central sensitization (CS). CS may lead to both provoked vestibulodynia (perhaps influenced by genetic predisposition) and to primary dysmenorrhea. The latter may cause "bottom-up" CS, increasing the risk of provoked vestibulodynia in those genetically predisposed. Childhood stress is a risk factor for adult low sexual desire and arousal. Any role of dysmenorrhea in negatively influencing adult sexual arousal and desire remains to be clarified.

Evidence supporting "top-down" regulation of pain circuits includes the finding of blunted cortisol awakening responses,[21] reflecting hyporesponsiveness of the HPA axis in women with PVD. The psychological stress from chronic anxiety states, perfectionism, ultra-conscientiousness, catastrophization, hypervigilance, and self-dislike, all associated with PVD, might underlie "top-down" modulation.[5,23,24] Women with primary dysmenorrhea also have findings reflective of hyporesponsiveness of the HPA axis and exhibit significantly lower mean cortisol levels than found in controls.[25] Limited research into mood, stress, and dysmenorrhea indicates that symptoms of anxiety and depression are positively related to pain severity.[26]

We also found that women with low desire recalled more dysmenorrhea relative to the general population. Recent work has linked adult hypoactive sexual desire disorder to dysregulation of the HPA axis compatible with previous chronic stress.[27] The low dehydroepiandrosterone sulfate (but not androgen) activity[26] repeatedly found in women with low desire is thought to reflect past stress and current HPA dysregulation.[29] That same stress may invoke CS with a propensity towards increased pain, but not towards PVD if genetic risk is absent. We suggest that via "top-down" modulation, childhood stress increases the risk of CS development, which may invoke dysmenorrhea and/or

PVD (the latter more likely in genetically susceptible women). The CS-invoked dysmenorrhea perpetuates the CS by "bottom-up" afferent signaling (Figure).

### Clinical Implications

PVD can be devastating for young women with its toll on sexual enjoyment, sexual self-image, relationship possibilities, and fertility. Understanding its etiology is urgent. Further confirmation of a link between PVD and primary dysmenorrhea encourages research into two questions. First, is primary dysmenorrhea causative of the CS documented in PVD and other chronic pain conditions? Second, are both severe menstrual pain and vestibular allodynia reflective of pre-existing CS? We join others in calling for more research into primary dysmenorrhea.[29,30]

## CONCLUSIONS

Our data confirm high comorbidity between PVD and dysmenorrhea. We advocate early, effective treatment of dysmenorrhea to prevent subsequent chronic pain conditions. However, given that the allodynia of PVD can predate dysmenorrhea, we suggest that childhood stress might initiate early development of CS, predisposing women to both conditions; therefore, both might be viewed as "canaries in the coal mine." We recommend addressing dysmenorrhea in both physical and mental health assessments.

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## REFERENCES

1. French L. Dysmenorrhea. Am Fam Physician 2005;71:285–91.
2. Davis AR, Westhoff CL. Primary dysmenorrhea in adolescent girls and treatment with oral contraceptives. J Pediatr Adolesc Gynecol 2001;14:3–8.
3. Durain D. Primary dysmenorrhea: assessment and management update. J Midwifery Women's Health 2004;49:520–8.
4. Bornstein J, Goldstein A, Coady D. 2015 Consensus terminology and classification of persistent vulvar pain. Available at: http://www.issvd.org/wp-content/uploads/2015/09/consensus-terminology-of-Vulvar-Pain-V5.pdf. Accessed on March 31, 2020.
5. Danielsson I, Sjoberg I, Wikman M. Vulvar vesitbulitis: Medical, psychosexual and psychosocial aspects, a case control study. Acta Obstet Gynecol Scand 2000;79:872–8.
6. Landry T, Bergeron S. How young does vulvo-vaginal pain begin? Prevalence and characteristics of dyspareunia in adolescents. J Sex Med 2009;1(6):927–35.
7. Gerber S, Bongiovanni A, Ledger W. Interleukin-1$\beta$ gene polymorphism in women with vulvar vestibulitis syndrome. Eur J Obstet Gynecol Reprod Biol 2003;107:74–7.
8. Brotto LA, Sadownik L, Thomson S, et al. A comparison of demographic and psychosexual characteristics of women with primary versus secondary provoked vestibulodynia. Clin J Pain 2014;30:428–35.
9. Granot M, Friedman M, Yarnitsky D, et al. Primary and secondary vulvar vestibulitis syndrome: systemic pain perception and psychophysical characteristics. Am J Obstet Gynecol 2004;191:138–42.
10. Reed BD, Harlow SD, Sen A, et al. Relationship Between vulvodynia and chronic comorbid pain conditions. Obstet Gynecol 2012;120:145–51.
11. Brotto LA, Bergeron S, Zdaniuk B, Driscoll M, Grabovac A, Sadownik LA, Smith KB, Basson R. A Comparison of Mindfulness-Based Cognitive Therapy Vs Cognitive Behavioral Therapy for the Treatment of Provoked Vestibulodynia in a Hospital Clinic Setting. J Sex Med 2019;16:909e923.
12. Sutton KS, Pukall CF, Chamberlain S. Pain ratings, sensory thresholds, and psychosocial functioning in women with provoked vestibulodynia. J Sex Marital Ther 2009;35:262–81.
13. Hampson JP, Reed BD, Clauw DJ, et al. Augmented central pain processing in vulvodynia. J Pain 2013;149:579–89.
14. Jarrell J, Arendt-Nielsen L. Allodynia and dysmenorrhea. J Obstet Gynecol Can 2006;38:270–4.
15. Cifre I, Sitges C, Fraiman D, et al. Disrupted functional connectivity of the pain network in fibromyalgia. Psychosom Med 2012;74:55–62.
16. Wei SY, Chao HT, Tu CH, et al. Changes in functional connectivity of pain modulatory systems in women with primary dysmenorrhea. Pain 2016;157:92–102.
17. Berkley KJ. Primary dysmenorrhea: an urgent mandate. Pain Clin Updates 2013;21:1–7.
18. van der Vegt EJM, van der Ende J, Kirschbaum C, et al. Early neglect and abuse predict diurnal cortisol patterns in adults: a study of international adoptees. Psychoneuroendocrinology 2009;34:660–9.
19. Clauw DJ, Crofford LJ. Chronic widespread pain and fibromyalgia: what we know and what we need to know. Best Pract Res Clin Rheumatol 2003;17:685–701.
20. Fries E, Hesse J, Hellhammer J, et al. A new view on hypocortisolism. Psychoneuroendocrinology 2005;30:1010–6.
21. Ehrström S, Kornfeld D, Rylander E, et al. Chronic stress in women with localized provoked vulvodynia. J Psychosom Obstet Gynaecol 2009;30:73–9.
22. Khandker M, Brady SS, Vitonis AF, et al. The influence of depression and anxiety on risk of adult onset vulvodynia. J Women's Health 2011;20:1445–51.
23. McEwan BS, Kalia M. The role of corticosteroids and stress in chronic pain conditions. Metabolism 2010;59:S9–15.
24. Payne KA, Binik YM, Amsel R, et al. When sex hurts, anxiety and fear orient attention toward pain. Eur J Pain 2005;9:427–36.
25. Vincent K, Warnaby C, Stagg CJ, et al. Dysmenorrhoea is associated with central changes in otherwise healthy women. Pain 2011;152:1966–75.
26. Dorn LD, Negriff S, Huang B, et al. Menstrual symptoms in adolescent girls: association with smoking, depressive symptoms, and anxiety. J Adolesc Health 2009;44:237–43.

27. Basson R, O' Loughlin JI, Weinberg J, et al. Dehydroepiandrosterone and cortisol as markers of HPA axis dysregulation in women with low sexual desire. Psychoneuroendocrinology 2019;104:259–68.

28. Basson R, Brotto LA, Petkau J, et al. Role of androgens in women's sexual dysfunction. Menopause 2010;17:962–71.

29. Berkley KJ, McAllister SL. Don't dismiss dysmenorrhea!. Pain 2011;152:1940–1.

30. Iacovides S, Avidon I, Baker FC. What we know about primary dysmenorrhea today: a critical review. Hum Reprod Update 2015;21:762–78.