Cognitive, Psychophysical, and Neural Correlates of Vulvar Pain in Primary and Secondary Provoked Vestibulodynia: A Pilot Study

Katherine Sutton, PhD,* Caroline Pukall, PhD,* Conor Wild, PhD,* Ingrid Johnsrude, PhD,* and Susan Chamberlain, MD*†

*Queen's University, Kingston, Ontario, Canada; †Kingston General Hospital, Kingston, Ontario, Canada

DOI: 10.1111/jsm.12863

ABSTRACT

Introduction. Provoked vestibulodynia (PVD) is a common condition characterized by localized, provoked pain that can be present since first vaginal penetration attempt (primary) or can develop after a period of pain-free penetration (secondary). Research has demonstrated psychosocial and psychophysical differences between women with these subtypes of PVD, but the question of whether neural responses to pain also differ remains to be investigated.
Aim. This study aims to examine whether cognitive, psychophysical, and neural responses to vulvar pressure pain differ between women with PVD1 and PVD2.
Methods. Women with PVD1 and PVD2 were compared for group differences using multiple modalities, including questionnaires, psychophysical testing, and neuroimaging. Pain ratings were held constant across groups, rather than amount of pressure applied.
Main Outcome Measures. Demographics, sexual functioning, four questionnaires examining anxiety and catastrophizing, quantitative sensory testing at the vulvar vestibule using a vulvalgesiometer, and functional and structural magnetic resonance imaging (MRI).
Results. Findings suggest that women with PVD1 are more anxious and that they catastrophize more about their vulvar and nonvulvar pain than women with PVD2. Overall, MRI results demonstrated structural and functional similarities to other chronic pain findings for both groups of women. Gray matter (GM) density also differed between groups: women with PVD1 showed significant decreases in GM throughout areas associated with pain processing. Functionally, between-groups differences were found during painful vulvar stimulation despite lower pressures applied to the vulva for women with PVD1 because of their heightened sensitivity; the determination of the level of vulvar pressure to elicit pain was based on subjective ratings.
Conclusions. Findings are limited by sample size and liberal alpha values; however, future research is certainly warranted based on the preliminary findings of this study suggesting both similarities and differences between PVD1 and PVD2. Overall, women with PVD1 seem to fare worse on several pain-related and psychosocial variables compared with women with PVD2. **Sutton K, Pukall C, Wild C, Johnsrude I, and Chamberlain S. Cognitive, psychophysical, and neural correlates of vulvar pain in primary and secondary provoked vestibulodynia: A pilot study. J Sex Med 2015;12:1283–1297.**

Key Words. Provoked Vestibulodynia; Neuroimaging; Sensory Testing; Psychosocial

Introduction

Provoked vestibulodynia (PVD) is characterized by provoked pain localized to the vulvar vestibule [1]. The pain of PVD can be present since the first vaginal penetration attempt (primary/lifelong; PVD1) or can develop after a

The study was funded by the Canadian Institutes of Health Research (CIHR) FRN#79472 and the National Vulvodynia Association. Dr. Sutton received a SSHRC grant during a portion of her Ph.D., of which this study was part.

period of pain-free penetration (secondary/acquired; PVD2). The prevalence of these subtypes is thought to be about equal [2]. They are characterized by different demographic, psychosocial, and pain variables. Women with PVD1 are more likely to be single [3,4] and nulliparous [5]. Many studies have found that women with PVD1 report more severe pain symptoms and more psychological and sexual problems, though some evidence exists to the contrary [6]. For example, women with PVD1 tend to be more likely to be dysmenorrheic [5,6], to have a family history of dyspareunia [2], and to report heightened anxiety around body exposure during sexual activity, as well as lower levels of social and emotional functioning [7]. Multiple studies have found that women with PVD report more severe pain with first and subsequent intercourse attempts [2,7] and that PVD1 status accounts, in part, for intercourse pain scores [8]. In contrast, Brotto et al. found that women with PVD2 self-reported more severe symptoms and higher sexual distress than women with PVD1 [6]. In another study, women with PVD1 displayed heightened experimental pain sensitivity, including lower heat pain tolerance at a nonvulvar site, as well as lower heat detection and heat pain thresholds at the vulvar vestibule [7]. Women with PVD1 have been shown to have greater nerve fiber density and thickness at the vestibule, but women with PVD2 show more inflammation [9], suggesting the possibility of differing pain mechanisms in these two groups, which may have treatment implications. To support this statement, it appears that women with PVD1 and PVD2 also differ in treatment response, with higher success rates for surgical [10,11] and multidisciplinary [8] treatments for women with PVD2. Despite evidence of these important differences, these subtypes are not typically analyzed separately in most studies, including neuroimaging protocols.

Gray matter (GM) density was investigated in women with PVD (PVD1 and PVD2 subtypes combined) and healthy control women [12]. In contrast to patterns found in chronic pain patients, women with PVD had significantly *higher* GM density in pain modulatory and stress-related areas [12]. The authors hypothesized that the young age of the PVD sample could explain this unexpected pattern. They also suggested there might be bidirectional changes in GM density in chronic pain patients, as noted in some psychiatric conditions. Longer pain duration and increased age may be associated with increased levels of stress hormones resulting in decreased GM density. Increases in younger pain patients may be due to microglial proliferation associated with excess neural activity in areas of pain modulation [12]. In another study, evidence of augmented neural activity in areas involved in pain modulation was found in women with PVD (subtypes combined) [13]. These increases occurred during mild and moderate pain applications and provide evidence of allodynia in PVD [13]. Both studies demonstrate that women with PVD display alterations in pain processing areas of the brain; however, neither study contrasted PVD1 and PVD2. Another functional magnetic resonance imagining (fMRI) study found greater activation in a heterogeneous group of women with vulvodynia (including PVD) as compared with healthy control women [14]. Higher brain activations were found in the posterior cingulate cortex in women with primary as compared with secondary vulvodynia when painful pressure was applied to the thumb but not the vulva. Given the potential importance of subtyping women with vulvar pain, we examined whether women with PVD1 and PVD2 differ in brain structure or function in response to pain and touch stimuli.

Methods

Participants

This study represents a focused analysis of PVD1 and PVD2 within a larger MRI study examining women with and without PVD. Ethical approval for these studies was obtained from both university and hospital research ethics boards. Female participants were recruited through a university lab database and through flyers distributed in the community. Inclusion and exclusion criteria are published online.

Women who were deemed eligible following the telephone screening interview were scheduled for an appointment in the Department of Obstetrics & Gynecology at the university hospital. A female research assistant obtained informed consent and was present throughout the assessment. The same gynecologist assessed all participants using a standardized gynecological examination protocol to determine whether participants met criteria for the PVD or control groups. The research assistant and gynecologist were blind as to whether the women were classified as having PVD1 or PVD1. The main inclusion criterion for the PVD group was an average pain rating of greater than 3/10 on the cotton-swab exam of the vulvar vestibule. The cotton-swab exam is the main diagnostic test for