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## The Genito-Pelvic Pain/Penetration Disorder Paradigm and Beyond

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# CHAPTER

# 7

## **The Distinct Impact of Voluntary and Autonomic Pelvic Floor Muscles on Genito-Pelvic Pain/ Penetration Disorder**

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## ABSTRACT

While the debate on diagnostic distinction continues, the DSM-5 combined dyspareunia and vaginismus into the genito-pelvic pain/penetration disorder. Recent research into the pathophysiology of dyspareunia and vaginismus has focused mainly on general pelvic floor pathology, the experience of pain, and cognitive-affective factors, while ignoring female genito-pelvic reflexes. It has not been taken into account that the vaginal canal, with its surrounding musculature, is an active canal capable of genito-pelvic reflexes, and that several of these reflexes might be triggered separately and/or simultaneously during sexual activity. We hypothesize that vaginal reflexive contractions play a substantial role in the pathogenesis of genito-pelvic pain/penetration disorder and postulate the genito-pelvic reflex hypothesis, i.e. in acute dyspareunia, primarily voluntary contractions or inadequate relaxation of the pelvic floor muscles predominate to guard against the pain due to vaginal trauma/infection and/or stress/anxiety. In chronic dyspareunia, these voluntary contractions induce increasingly (sub)mucosal vaginal damage: contact- and pain receptors become more sensitive. The increased sensitivity of the contact receptors induces powerful autonomic reflexive contractions. These autonomic contractions provoke vulvar pain, which causes overreactive pelvic floor muscles. In lifelong vaginismus, autonomic reflexive contractions of the pelvic floor muscles predominate the entire disease process.

## INTRODUCTION

Vaginismus and dyspareunia are characterized by persistent and recurrent problems with vaginal penetration. In vaginismus, the key symptom is the inability to allow vaginal penetration; in dyspareunia, the central issue is pain during sexual intercourse.<sup>(1)</sup> Although accurate figures are lacking, the prevalence of vaginismus is approximately 0.5-1%,<sup>(2)</sup> while the prevalence of dyspareunia is believed to range from 12% to 21%.<sup>(3)</sup>

Over the past 15 years, there has been ongoing debate about whether vaginismus can be differentiated categorically or on a dimension of severity from dyspareunia/provoked vestibulodynia(PVD).<sup>(4)</sup> Discussions continue owing to the lack of valid and reliable diagnostic criteria for vaginismus and the notion that dyspareunia and vaginismus share many similarities. To a greater or lesser extent, these similarities are the presence of i) vulvar pain during (attempts to) vaginal penetration, ii) pelvic floor overreactivity, iii) fear and/or anxiety and iiiii) sexual, psychological and relational distress.<sup>(5)</sup>

In a recent functional MRI study, sexually asymptomatic women and women with either vaginismus or dyspareunia were exposed to penile-vaginal penetration stimuli and stimuli that elicited disgust. Similarities and overlap in brain activity were found between the three groups of women.<sup>(6)</sup> Although group differences in subjective sexual arousal were observed in one study,<sup>(7)</sup> Cherner & Reissing<sup>(8)</sup> did not find any difference in physiological genital arousal after exposure to erotic film excerpts between women with lifelong vaginismus and dyspareunia.

Notwithstanding the existing evidence of similarities, recent research that focused in particular on lifelong vaginismus in comparison with dyspareunia, has uncovered a number of specific differences between the two disorders. These differences could have clinical implications. Compared to women with dyspareunia, women with lifelong vaginismus were found to experience less subjective sexual arousal and show more negative reactions to sexual stimuli, which included fear of pain and fear of losing control of one's body during vaginal penetration.<sup>(8-9)</sup> One study reported stronger subjective disgust and heightened facial expressions of disgust towards sexual stimuli (measured by the facial levator labia superior muscle as a unique physiological marker of disgust) in women with lifelong vaginismus.<sup>(9)</sup> Perhaps not surprisingly, avoidance behaviour has been reported as a substantial differentiator between women with vaginismus and dyspareunia.<sup>(10)</sup> In women with vaginismus, it is possible that negative cognitions, emotions and a propensity for disgust induce them to avoid vaginal penetration and sexual behaviour in general. In contrast, women with dyspareunia are more likely to continue having sexual intercourse, despite the discomfort and/or pain, albeit with reduced frequency.<sup>(8-12)</sup>

Although the DSM-5 has combined the two disorders into the genito-pelvic pain/penetration disorder (GPPPD), the debate on diagnostic distinction continues.<sup>(13)</sup> Starting with the 1980 edition of the DSM, vaginismus was defined by a singular diagnostic criterion: recurrent or persistent involuntary spasm of the musculature of the outer third of the vagina that interferes with sexual intercourse.<sup>(14)</sup> In the DSM-5 “vaginal spasm” was removed in favour of “marked tension or tightening of the pelvic floor muscles during attempted vaginal penetration”.<sup>(13)</sup> The justification for this change was that vaginal spasm in previous iterations of the DSM had never been demonstrated as reliable or valid diagnostic criterion. However, it is questioned whether the rather vague notion of pelvic muscle tension or tightening in the current DSM-5 is an improvement. In our opinion, the original spasm criterion should be reconsidered and re-examined in terms of genito-pelvic reflexes. In this paper, we propose the genito-pelvic reflex hypothesis, which offers a new perspective on our understanding of vaginal penetration problems that interfere with sexual intercourse.

## **ANAL CANAL**

The idea for the genito-pelvic reflex hypothesis finds its origin in anorectal research. In 1985, Preston and colleagues described “paradoxical” reflexive contractions in the anal canal, which they named “anismus”, in a group of constipated patients during attempted defecation.<sup>(15)</sup> Anismus, recently renamed dyssynergic defecation, refers to failure of normal relaxation of the pelvic floor muscles during (attempted) defecation, i.e. unconscious voluntary external anal sphincter contraction occurs instead of relaxation. Interestingly, Preston drew already analogies between dyssynergic defecation and vaginismus in the 1990s. His theory was that in women with vaginismus, paradoxical reflexive contractions occur probably in the pubococcygeal muscle.<sup>(16-18)</sup>

In a study of Broens et al. it was demonstrated that an autonomic anal-external sphincter continence reflex can be solicited by stimulation of anal submucosal receptors. In the anorectum, overreaction of this anal-external sphincter continence reflex increased the basal anal sphincter pressure.<sup>(19)</sup> After anal injection of botulinum toxin this high anal basal pressure normalised.<sup>(20)</sup> Also an autonomic reflex of the puborectalis muscle has been found: the puborectal continence reflex. Autonomic reflexes are “involuntary” and occur unconsciously. This puborectalis reflex appears to be triggered by stretching of the puborectalis muscle and can cause a long-lasting contraction of the puborectalis muscle.<sup>(21)</sup>

## VAGINAL CANAL

The anal canal, the vaginal canal and the urethra have a common embryological origin. Based on this knowledge, Broens et al. recently theorized that the vaginal canal has a sort of canalicular sphincter (reflex) mechanism, analogous to the anal canal and urethra, and that this mechanism could be involved in GPPPD.<sup>(22)</sup> Intravaginal pressures and vaginal contractions in asymptomatic women were evaluated, using high resolution solid state circumferential catheters. In response to intravaginal stimulation, the vaginal canal was found to have deep and superficial high pressure zones. These zones were generated by voluntary contractions and (very strong) reflexive contractions. Even a very low pressure in the balloon triggered autonomic reflexive contractions in these two zones that by far exceeded the pressure and duration of maximal voluntary contractions. The authors suggests that it's possible that autonomic reflexive contractions are involved in the pathogenesis of vaginismus and dyspareunia. They theorized that the deep high-pressure zone represents a "deep vaginal sphincter," i.e., puborectalis muscle contraction, mediated by the vagino-puborectalis reflex. They further postulated that the superficial vaginal high-pressure zone represents a "superficial vaginal sphincter", i.e., bulbocavernosus muscle contraction, mediated by the superficial vagino-bulbocavernosus reflex.<sup>(22)</sup> The bulbocavernosus muscle, ischiocavernosus muscle, anal and urethral sphincters, and, possibly, also the puborectalis muscle, i.e. muscles that derive from the embryonic cloaca, are regulated by motoneurons in a special sacral motor neuronal pool termed Onuf's nucleus.<sup>(23-25)</sup> Onuf motoneurons have been suggested to be of a combined somatic and autonomic type.<sup>(26)</sup>

## PATHOGENESIS; PERIPHERAL AND CENTRAL SENSITIZATION

Minor vaginal submucosal damage could induce release of inflammatory mediators and neurogenic inflammation resulting in a reduction in the thresholds of nociceptors (peripheral sensitization). However, the pathogenesis of PVD cannot be exclusively ascribed to peripheral neurogenic inflammation. Neuronal inflammation may also be the effect of changes at central level.<sup>(27)</sup> A prevailing theory for PVD is the neuromatrix theory, suggesting that chronic pain can be the result of alterations in the widely distributed neural network, including the brain. It is believed that injury, pathology and even chronic stress can modulate this matrix.<sup>(28)</sup> According to this theory, somatic sensory input is only one component of the neuromatrix. Consequently, vulvar pain in PVD might be due to modifications in the neural network, in the absence of a physical cause. In summary, neurogenic inflammation and the accompanying pain are chronic sequels to central-

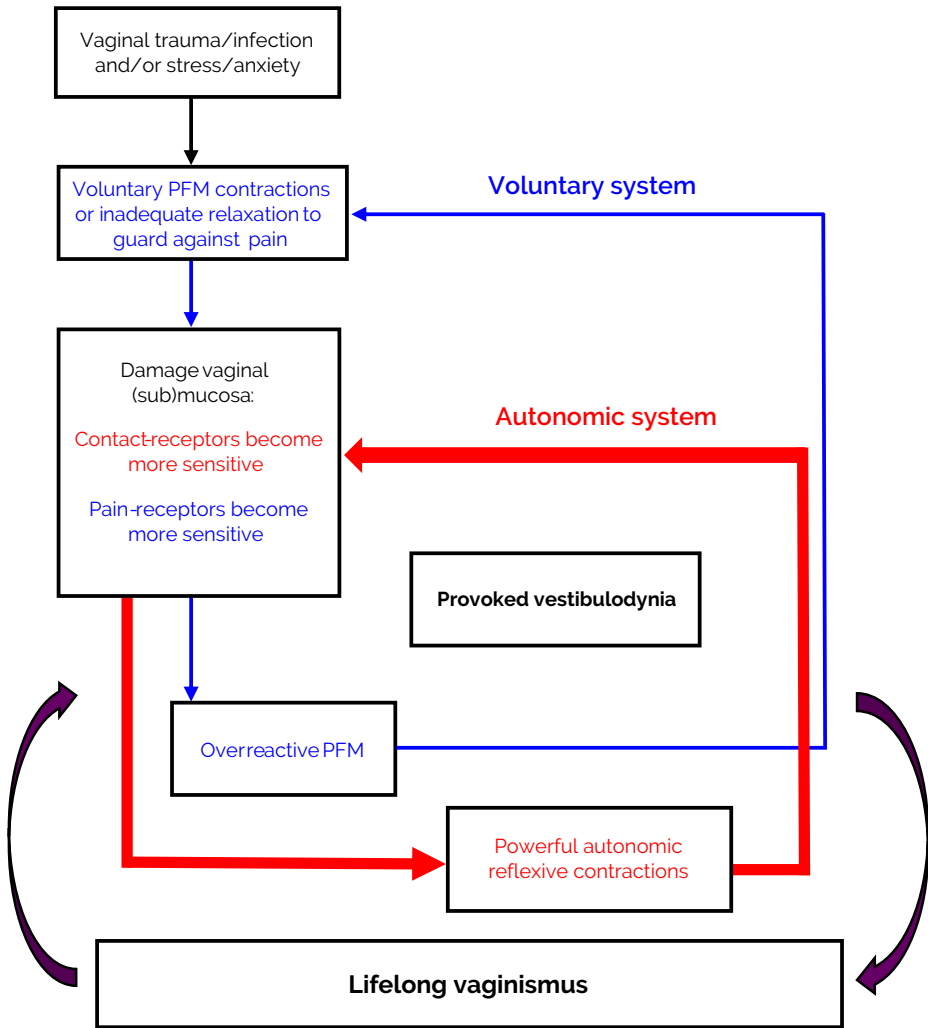
and peripheral sensitization, which results from the bidirectional influence of peripheral input and the nervous system.<sup>(1)</sup>

## GENITO-PELVIC REFLEX HYPOTHESIS IN GPPPD

According to our genito-pelvic reflex hypothesis, in dyspareunia, women inadequately relax or contract their pelvic floor muscles (PFM), while continuing vaginal penetration despite pain. Primarily, in acute dyspareunia, voluntary pelvic floor muscle contractions or inadequate relaxation occurs to guard against pain due to vaginal trauma/infection and/or stress/anxiety. In chronic dyspareunia, these PFM contractions induce increasingly (sub)mucosal damage: contact- and pain receptors become more sensitive. This increased sensitivity of the contact receptors induces powerful autonomic reflexive contractions. These powerful autonomic reflexive contractions provoke vulvar pain, which causes overreactive PFM. In contrast to the voluntary system, the autonomic system is not triggered by pain and its contractions are more powerful than the voluntary contractions.<sup>(22)</sup> Vulvar (sub)mucosal damage activates both the voluntary and autonomic system and this occurs simultaneously, suggesting that these systems are connected. However, in essence these systems are not coupled. Therefore, the willingness to relax PFM does not affect the autonomic circle. In contrast to women with dyspareunia, women with lifelong vaginismus are struggling with powerful autonomic reflexive contractions which dominate the entire disease process, which causes these women's inability to allow vaginal penetration. (see figure 1: *Genito-Pelvic Reflex Hypothesis in GPPPD*).

## GPPPD AND PELVIC FLOOR MUSCLES

Several pelvic floor study's support our hypothesis. Shafik and colleagues (2002) reported that in women with vaginismus, the basal EMG activity in the levator ani, puborectal and bulbocavernosus muscles was significantly higher than in control women.<sup>(29)</sup> Frasson performed a neurophysiological study and observed involuntary muscular activity in the levator ani, external anal sphincter and the bulbocavernosus muscle in women with vaginismus as well in patients with dyspareunia. He concluded that the "bulbocavernosus muscle reflex" was "hyperexcitable" in women with vaginismus.<sup>(30)</sup> In 2010, Gentilcore-Saulnier and her colleagues used surface EMG and a probe to measure superficial bulbocavernosus activity and deep pelvic floor activity respectively. Compared to a control group, the women with dyspareunia showed significantly higher contractility at rest in the superficial as well as deep layers.<sup>(31)</sup>



**Figure 1 | Genito-Pelvic Reflex Hypothesis in GPPPD.** Primarily, in acute dyspareunia, voluntary pelvic floor muscle (PFM) contractions or inadequate relaxation occurs to guard against pain due to vaginal trauma/infection and/or stress/anxiety. In chronic dyspareunia, these PFM contractions induce increasingly (sub)mucosal damage: contact- and pain receptors become more sensitive. This increased sensitivity of the contact- and pain receptors induces powerful autonomic reflexive contractions. These powerful autonomic reflexive contractions provoke vulvar pain, which causes overreactive PFM. In contrast to the voluntary system, the autonomic system is not triggered by pain and its contractions are more powerful than the voluntary contractions. Vulvar (sub)mucosal damage activates both the voluntary- and autonomic system and this occurs simultaneously, suggesting that these systems are connected. However, in essence these systems are not coupled. Therefore, the willingness to relax PFM does not affect the autonomic circle. In contrast to women with dyspareunia, women with lifelong vaginismus are struggling with powerful autonomic reflexive contractions which dominate the entire disease process, and causes these women's inability to allow vaginal penetration.



Our hypothesis finds also support in a recent review study of Thibault-Gagnon and Morin (2015), in which they describe active (contractile) and passive (viscoelastic) components of pelvic floor muscle tone in women with provoked vestibulodynia. Based on their review they suggest that pelvic floor muscle overreactivity may have a predominant influence on the pelvic floor muscle contractile capacities in women with PVD.<sup>(32)</sup> A recent study of Lahaie et al. (2015) found that vaginal muscle tension was significantly greater in a group of women with vaginismus compared to women suffering from dyspareunia/PVD.<sup>(33)</sup> Similar to other muscle groups, the pelvic floor musculature is indirectly innervated by the limbic system.<sup>(34)</sup> Therefore, it is very likely that the puborectal and bulbocavernosus muscles are reactive to emotional stimuli and states, such as stress, anxiety, fear or disgust. Both and her colleagues measured pelvic floor muscle activity and genital sexual arousal in sexually healthy women without pelvic floor dysfunction using a vaginal photoplethysmograph with built-in-surface electromyography. The results of their study were that vaginal pulse amplitude (VPA) increased in response to sexual film footage and EMG values were significantly higher in response to anxiety-evoking film footage. Higher EMG values in response to the anxiety film footage were associated with lower VPA.<sup>(35)</sup>

## **GPPPD AND TREATMENT MODALITIES**

The genito-pelvic reflex hypothesis gains further support when prevailing treatment modalities are taken into account. It is generally believed that GPPPD should be treated according to a multidimensional approach. Main components of this approach are: psychological interventions, pelvic floor physiotherapy and vestibulectomy. In case of therapy-resistance, transcutaneous electrical nerve stimulation (TENS) and botulinum toxin are sometimes added.<sup>(36)</sup> Ideally, treatment interventions target both the voluntary and autonomic system.

Some studies have been published on botulinum toxin-A treatment for pelvic floor overreactivity in women with dyspareunia and vaginismus.<sup>(37-40)</sup> Botulinum toxin is a potent neurotoxin produced by the bacterium *Clostridium botulinum*, a Gram-positive spore-forming organism. When injected for therapeutic purposes, it binds to peripheral nerve receptors and prevents the release of acetylcholine into the synaptic cleft, which leads to muscle paralysis.<sup>(41)</sup> In a recent study, multiple injections of botulinum toxin type A in women with pelvic floor muscle overreactivity provided significant relief from dyspareunia.<sup>(42)</sup> In a study by Ghazizadeh with 24 women with vaginismus, botulinum toxin A was injected into the puborectalis muscle at three sites bilaterally. At 1 week post-

treatment, the symptoms of vaginismus had diminished or disappeared completely in 23 (95%) of the women; 18 (75%) were able to have pain-free intercourse after one injection, while four (16.7%) experienced mild pain during intercourse. At one-year follow-up, no symptom recurrence was reported.<sup>(43)</sup>

TENS is suggested to have two mechanism for relieving pain: 1) inhibition of pain signals by stimulating non-nociceptive afferent neurons and 2) by supraspinal inhibition.<sup>(44)</sup> In a study of Vallinga et al. addition of transcutaneous electrical nerve stimulation (TENS) to a multidimensional approach reduced the level of vulvar pain and the need for vestibulectomy in women with PVD.<sup>(44)</sup> In vestibulectomy, an invasive and irreversible surgical technique, presumably pain receptors and/or pro-inflammatory molecules are removed. Success rates are reported, ranging from 61-94%.<sup>(45)</sup>

Pelvic floor physiotherapy targets also the proposed hypothesis.<sup>(6)</sup> Pelvic floor muscle exercises consist of voluntary contraction as well as relaxation, in order to reduce the resting tone, guarding reactions, and overreactivity of the pelvic floor muscles. Outcome studies reported successful treatment results in women with dyspareunia.<sup>(46-47)</sup> Only one retrospective outcome study is available on physiotherapy in women with vaginismus. While intercourse was reported to be possible at the end of therapy, the duration of treatment was significantly longer than that for dyspareunia.<sup>(48)</sup>

Ter Kuile et al. demonstrated that therapist-aided exposure to fear eliciting vaginal penetration objects was an effective treatment for lifelong vaginismus. The therapists facilitated the women to perform vaginal penetration exercises (i.e., with a finger and/or dilatator) in order to overcome avoidance behaviour and fear. Nearly all the women reported successful intercourse following treatment.<sup>(49)</sup> This supports that problematic sexual intercourse in women with lifelong vaginismus can be defeated without any form of 'invasive' intervention.

## CONCLUSIONS AND RECOMMENDATIONS

Although it has never been investigated systematically, vaginal spasm has been abandoned in the new DSM-combined diagnosis and replaced by an exceedingly vague criterion that potentially applies to vaginismus as well as dyspareunia: "Marked tensing or tightening of the pelvic floor muscles during attempted vaginal intercourse/penetration". In this paper we postulate that systematic investigation of deep- and superficial vaginal pelvic- and perineal muscle (reflex)activity is long overdue and essential to help clarify the role of pelvic pathology in vaginismus and dyspareunia.

A first step to test the genito-pelvic reflex hypothesis would be to measure vaginal reflexive contractions in sexually asymptomatic women under different conditions: at neutral-baseline, in response to negative emotions (e.g., disgust and threat) and most importantly, during exposure to erotic stimuli and disorder-specific stimuli (e.g., penile-vaginal penetration). Modern neurophysiological techniques are suitable to analyse and describe the components of the reflex arc. Ideally, a histological approach should be used to detect the exact anatomical locations of the (intra)vaginal receptors. In order to confirm the autonomic character of the reflexes, tests need to be replicated in different study groups under different circumstances, e.g., in asymptomatic women, under superficial and spinal anaesthesia, and in women with spinal cord lesions.<sup>(19)</sup> Vaginal reflexive contraction tests should also be applied to clinical populations, in particular to women with vaginismus and dyspareunia. It is of major importance to evaluate further the role of different emotional stimuli on pelvic floor muscle contractions in healthy subjects and in women with vaginismus and dyspareunia to pursue the hypothesis of a clear link with the limbic system/pelvic musculature.

More knowledge on genito-pelvic reflexes is urgently required to invigorate the scientific interest in PVD and lifelong vaginismus. Research focussing on the underlying pathophysiology of female sexual pain disorders will contribute to solve the diagnostic dilemma, and will provide more insight into the pathogenesis in order to develop differential and improved management protocols for women with these distressing disorders.

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# PART

Reflection

