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Psychogenic causes of Chronic Pelvic Pain and impact of CPP on psychological status
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Psychogenic causes of Chronic Pelvic Pain and impact of CPP on psychological status

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The good physician treats the disease, the great physician treats the patient who has the disease
William Osler, 1849-1919

Abstract

The paper updates the word ”psychogenic”; suggests a pathophysiologic reading of the psychogenic contribute to CPP, via the stress-induced **corticotropin-releasing factor (CRF) signaling pathways**, and differentiates predisposing, precipitating and maintaining factors; summarizes the pertinent evidence; focuses on the differential diagnosis between prominent “psychogenic” vs somatic etiology of CPP; highlights the common diagnostic mistakes with a focus on iatrogenic factors and nocebo effect; discusses the psychological and sexual consequences of CPP.

Introduction

Pain is a red traffic light calling for immediate attention on our physical and mental health. When chronic, pain shouts that the key causative factor(s) of pain have remained unaddressed in the shadow of the untold and/or of the diagnostic neglect. Overfocus on the somatic disease(s) causing CPP may often induce the physician to forget the patient as a human being with a story to tell, where psychological factor(s) causing chronic stress may hold the key of the multisystemic disruption contributing to the onset and/or the worsening of pain.

However, **three major problems** arise when discussing the psychogenic causes of CPP.

First, the concrete risk that the patient’s pain is dismissed as “invented”, “all in her head” , with a substantial neglect of its biological basis, for the still persisting Cartesian dualism that body and mind are two separate entities. As a consequence, only a few physicians respect psychogenic factors as solid biological contributors of pain.

Second, if psychogenic factors work on pain etiology and perception, they should do that through a biological pathway. How can we then recognize the key pathophysiologic steps that translate something “psychological” into a biological contributor of pain?

Third, how can we diagnose the subset of patients who really have a powerful and prominent psychogenic component of their pain?

And once CPP is rooted in the woman’s body, how will it impact on her psychosexual status?

The **key points** of the chapter will therefore be the:

- update of the word ”psychogenic”
- pathophysiologic, multisystemic reading on the biological correlates of psychogenic factors in CPP
- summary of the evidence that supports the role of psychogenic causes in CPP

- criteria for a differential diagnosis between a prominent "psychogenic" vs somatic etiology of CPP
- common diagnostic mistakes in the psychogenic domain with a focus on iatrogenic factors
- psychological and sexual consequences of CPP

What does "psychogenic" really mean?

Etymology, from the Greek "psyché" (mind), and "genic" (caused by), indicates something "generated" in the psychological domain. Psychogenic causes can be:

- **intrapsychic**. This includes mental disorders, such as psychosis, which may alter both the cognitive processes and self-perception of pain; major depression, which "speaks through the body" and is characterized by a variety of somatic pain-related complaints; trait anxiety, where a genetic predisposition to anxiety disorders and an up-regulated amygdala may increase the neurovegetative arousal response to pain and lower the central pain threshold. Personality disorders may as well increase the vulnerability to internal or environmental pain signals. All these disorders are "intrapsychic", but nonetheless they have a solid neurobiological basis; or
- **context-dependent, psychological/relational**. Environmental psychogenic factors may act through an **active physical damage**, such as in physical or sexual abuse, which may immediately trigger a variety of stress and trauma-induced physical responses, or a **deprivation damage**, such as in the persistent emotional neglect of institutionalized children, for examples, or of children of severely depressed mothers. In both cases, the psychological factors have a biological correlate, characterized by the neuroimmunendocrine changes typical of chronic stress, through the **corticotropin-releasing factor (CRF) signaling pathways** (Taché & Brunnhuer, 2008). This induces a persistent increase of glucocorticoids and a reduced activity of the serotoninergic and dopaminergic neurons and pathways, leading to depression, loss of vital energy, and increased inflammatory activity, with increased inflammatory markers.

In general, intrapsychic and context-dependent factors interact and potentiate each other over time, if not adequately addressed from a pharmacologic and/or psychotherapeutic point of view. This diagnostic omission or neglect may further increase the vulnerability to peripherally generated pain signals and facilitate the progression to CPP.

Key point: the word "psychogenic" will be maintained throughout the text, but should be considered in its close reciprocity with neuroimmunendocrine correlates.

How do psychogenic causes translate into physical pain?

The key question here is just one: **how can physical and/or sexual abuse concur or trigger CPP?** If abuse activates CPP, then there should be a pathophysiologic reading of the mechanism(s) of action of the psychogenic causes (Chapman et Al, 2008; Scott et Al,2008; Taché & Brunnhuer, 2008; Kemeny, 2009).

To put psychogenic causes in the proper neurobiological, endocrine and immune context, we need:

a) an **updated pathophysiologic re-reading of how psychogenic factors translate into biological ones**. The obsolete dualism body vs mind (that persists in the clinical setting every time physicians say: "Pain is all in your mind") is therefore to be definitely abandoned in favor of an integrated psychoneuroendocrine and immune view (Solms & Turnbull, 2002; Chapman et Al, 2008, Taché & Brunnhuer, 2008, Kemeny, 2009). Indeed, there exists a bidirectional network of interactions between the central and peripheral nervous system (including the pain system), the endocrine system and the immune system. The existence of these pathways allows stressful life experience to impact the immune, endocrine and nervous systems with important implications for health (Chapman, 2008,

Kemeny, 2009). CPP may be the final result of this complex multisystemic disruption induced by any stressor, from the prominently psychogenic to the strictly biological (**Fig. 1**). One powerful elicitor of changes in the autonomic, endocrine and immune systems is physical and emotional threat typical of sexual abuse. To detail its psychosomatic correlates is beyond the scope of this chapter. The professionals interested in the area are therefore referred to specific papers and books (McDonald, 1998; Solms & Turnbull, 2002; Chapman et Al, 2008, Taché & Brunnhuer, 2008, Kemeny, 2009).

The following example is suggested to transmit the sense of this line of thinking: when a child or a woman is physically or sexually abused, she undergoes a **violent acute stress response**, with a **huge neurovegetative physical and emotional arousal**. Indeed, any injurious event provokes autonomic, endocrine and immune processes as well as sensory signaling (Chapman et Al, 2008).This process will be **chronically up-regulated** if the abuse is **repeated** over time, and/or if frequent **nightmares** on the experience trigger at night the very same abrupt neurovegetative arousal, with all its psychological feelings of fear, anguish, horror, pain, helplessness and despair. A dysfunctional physical and emotional status, similar to what has been described as Post-Traumatic Stress Disorder (PTSD), may result:

- **In the brain**, this **persistent neurovegetative arousal**, characterized by chronic plasmatic **increase of glucocorticoids and inflammatory molecules**, will increase the activity of the amygdala (the cross road of the four basic emotions command system (Panksepp, 1998) and a key center for memories with high emotional impact. The up-regulated amygdala contributes to maintain the hyper-reactivity of the alarm system even to minor stimuli, through an increase of the so called long-term potentiation of neuronal activity (Solms & Turnbull, 2002). Moreover, in case of pain or stress of whatever etiology, the amygdala will immediately activate the maximal alert and arousal response. This contributes to: **a)** increase the "**free floating anxiety**", that will peak in women genetically predisposed to anxiety disorders; **b) reduce the central threshold of pain perception**; **c) re-activate a neurogenic increased production of pain and inflammatory signals** (that can be peripherally mediated through the mast cells) (Omoigui, 2007; Graziottin, 2009).

  Meanwhile, the identification of the **corticotropin-releasing factor (CRF) signaling pathways** contributes to a deeper understanding of stress-related endocrine (activation of pituitary-adrenal axis), behavioral (anxiety/depression, altered feeding), autonomic (activation of sympathetic nervous system), and immune responses present in all the situations where a psychogenic factor induces chronic stress (Taché & Brunnhuer, 2008). Furthermore, the chronic increase of glucocorticoids may have a specific downregulating effects on the dopaminergic neurons that mediate the seeking-appetitive lust-system (Panksepp, 1998). This will translate in the loss of vital energy, asthenia, fatigue, loss of sexual desire and, typically, the "**anhedonia**", the loss of the ability to perceive pleasure and joy in whatever activity, that is complained of in patients with CPP, more so in the subset of those with previous physical or sexual abuses. In parallel, the down-regulation of the serotoninergic system will contribute to *depression*, that will further increase the perception of pain signals, and the reduction the central pain threshold.
- **In the periphery**, the **neurogenic -stress-induced- up-regulation of mast cells** will increase the vulnerability of different mucosae (intestinal, vaginal, bladder) to the aggression of a variety germs, typical of the so called "Irritable Bowel Syndrome", or to local noxae, such us the endometrial shedding in endometriosis. This vulnerability requires the permitting presence of the mast cells as key mediators of the stress response, transforming an environmental stressor into a biological damage, as it has been well proven in the mast cell knocked-out mice. This also contributes to the re-reading of pain under a unifying

hypothesis, the so call "Law of pain" (Omoigui, 2007), suggesting that un upregulated inflammatory status, involving the inflammatory cells and/or the inflammatory molecules such as interleukins and tumor-necrosis factor alpha, is the common denominator of acute and chronic pain, independent of its been nociceptive or neuropathic, central or peripheral.

b) to have a **temporal reading of psychogenic factors as predisposing, precipitating and maintaining contributors of pain**. Instead of an "or psychogenic or medical" approach, the "psychogenic **and** biogenic" is more coherent with the real narrative experience of CPP, and the biology of pain.

Psychogenic causes in CPP

A huge bulk of literature suggests that psychogenic factors are specifically relevant in the clinical history of women with CPP (Latthe et Al, 2006, Field and Swarm, 2008). **Tab. 1** summarizes the review of Pallavi Latthe (2006), on controlled trials, to give the reader at glance the sense of power of those events. For example, anxiety and depression may contribute to and/or increase the perception of pain by an OR, respectively, of 2.28 and 2.69. Paranoia, ie the psychotic disruption of cognitive functions and self-perceptions, may predispose to CPP with an OR of 13.89. The post-traumatic stress disorder (PTSD) may increase the vulnerability to CPP with an OR of 5.47. Finally, eight controlled trials indicate that psychosomatic disruption may predispose to CPP with an 0R of 8.01.

Moreover, childhood physical abuse will predispose to CPP with an OR of 2.18. Ten studies suggest that childhood sexual abuse will increase the vulnerability to CPP with an OR of 1.51, while 11 trials suggest that adult/life sexual abuse seems to have a stronger predisposing effect with an OR of 3.49. Quite interestingly, disturbed puberty or painful early memories further increase the vulnerability of CPP with an OR of 3.77. Unsatisfactory relation with spouse may as well be consistent with a stressing experience predisposing to CPP with an OR of 4.01. Environmental psychological/relational factors such as alcoholism in one parent may further contribute with an OR of 2.69, while divorce in one parent may have an even stronger impact with an 0R of 3.68.

Potential psychogenic factors should therefore be investigated in every patient, in a respectful and tactful approach.

Key point: the physician should clarify that the attention to the psychogenic component is meant to recognize potential psychological contributors to maintain or worsen the woman's pain, but that all the physical/somatic factors will **in parallel** be thoroughly and rigorously investigated. And that he/she believes in and cares about the truth of her pain.

CAUTION!

"Psychogenic" does not mean that pain is "invented" or "all in her head"! It means that intrapsychic and/or context-dependent psychological-relational factors may: **a)** increase the production of pain signals through the chronic stress they cause; **b)** increase the vulnerability to pain signals produced in the pelvis through a reduction of both the gate control of painful stimuli at the posterior horn of the medulla and the central threshold of pain, and a chronic increase of glucocorticoids; **c)** increase anxiety and depression that may further contribute to increase pain perception and the vulnerability to pain syndromes; **d)** reduce dopaminergic and opiatergic pathways, thus reducing vital energy, sexual desire and the possibility to enjoy pleasure ("anhedonia").

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Criteria for the diagnosis of psychogenic pain

Key characteristics of psychogenic pain are summarized in **Tab. 2.** The differences between "prominent" psychogenic and somatic pain have been polarized to ease the reading of the key differences. In real life there is a continuous interaction between the two. Only a really minor subset of patient with CPP is having a prominent "psychogenic" pain. The vast majority has solid etiologies and frequent comorbidities, often misdiagnosed, neglected, overlooked for years. The psychological component may have grown as a result of the anguish, the sense of despair, the reactive depression, the worsening of the clinical picture itself, with more widespread and less differentiated pain. Understanding the psychogenic component, when present, in its various weight and impact is nevertheless essential to address the many contributors of pain in a comprehensive way. In this sense, in the multidisciplinary team of a pain clinic the psychologist/psychotherapist is precious in giving the patient the right and the setting to give words to her pain (Mombelli, 2003, Field and Swarm, 2008), while feeling well looked after – and therefore reassured that she is been rigorously evaluated - from the strictly medical point of view.

To ease the understanding of the potential psychogenic component of pain, key questions have been summarized in **Tab. 3** (Mombelli, 2003).The goal is to appreciate **if pain in disruptive in an otherwise "functioning" life**, or if it is the tip of the iceberg of a variably dysfunctional life. Then the psychogenic pain can serve different conscious or, more often, **unconscious purposes**, such as selected attention, secondary gains, use of dynamics of power or guilt or avoidance, or just calling for help for previous abuses the patient never found the courage, the words, or the adequate supportive listening to disclose .

The apparently neutral question about the **quality of sleep** is richly informative per se. As a general rule, nociceptive pain gets worse at night; pure neuropathic or psychogenic pain is usually silent during sleep. However patients with a psychogenic component of pain, specifically if associated to Post-Traumatic Stress Disorder, do report a poor quality of sleep, referred as light, disturbed, with frequent wake-ups, early wake, non-regenerating, and a morning sense of being "more tired than the evening before". All these changes are usually related to the hyper-arousal typical, for example, of previous abuses and/or Post-Traumatic Stress Disorders. The key point is that the disruption of sleep pattern is a major biological stress, which further contributes to the sense of physical and mental exhaustion, besides the parallel increase of inflammatory indexes. Moreover, the recurrence of nightmares, even with confused content, should alert about the concrete risks of previous physical and/or sexual abuses, with parallel recurrent hyperactivity of the adrenergic/alert system that may concur to amplify any signal of pain.

When asking about **stressful events**, is key to understand if there is any temporal and/or symbolic link with the onset/site of pain.

Quality of coping is another sensitive area. Patients with a significant psychogenic component of pain tend to have poor adaptive coping (Mombelli, 2003). The way they cope with life difficulties is inadequate; they may feel overwhelmed even by minor events. Catastrophizing coping is the most dangerous in terms of resolution of pain. Even in front of a self- reported pain diary indicating a clear improvement of pain, when asked: "How do feel now?" this patient will answer: "Awful, as usual". "But your diary clearly indicates a definite improvement…". "Yes, but if I get worse again?". This type of answer may suggest that her life has been increasingly structured around different negative painful experiences, and/or that she is non-confident about the resolution of her problem, or, also, that "losing" her pain may cause the loss of secondary advantages or gains.

In this perspective, the patient's opinion about her pain, the presence of guilty feelings, for example for a previous voluntary abortion in a religious patient, the timing or the characteristics of pain and their potential link with other

problems (ie professional or family-related) should be gently considered. Finally, the possibility that pain may carry any real or symbolic advantage, for example within the family (to convey the attention of otherwise overbusy parents or partner) or at work should be evaluated in a psychodynamic evaluation and psychotherapeutic intervention, sometimes extended to the partner, or to parents in case of adolescents (Fields and Swarm, 2008). The goal would be to obtain the same attention, or get healthier family dynamics, with a less self-destructive and painful unconscious strategies.

Common mistakes

- **Diagnostic neglect**: the vast majority of physicians do not routinely ask about previous harassment or abuse. For fear of a too intimate question, for feeling not sufficiently trained to work on it, or to avoid the risk of opening a time-consuming Pandora' vase of sorrow, tears and regrets. Only a minority (3% in a Canadian survey on gynecologists and family physicians) ask about previous violence or abuse.
  Key point: it is difficult to provide an effective intervention, if there is no mention of problem!
- **Diagnostic overfocus**: when sexual abuse is revealed, many physicians and psychologists alike tend to read everything as a consequence of it, with the opposite risk of missing significant correlated and/or independent comorbidities. The correct thinking should be "and... and", not "aut... aut" (or... or). Both the so called psychogenic area and the physical one should be explored in a balanced, respectful, informative way.
- **Inability to read the common neurobiological pathway that blends together abuse and CPP**, i.e. the complex emotions –fear, terror, anxiety, anguish, physical and emotional pain, panic, depression, loneliness, despair- that are triggered in both physical and sexual abuse, **and** in CPP. Specifically, both involve, directly and indirectly, **the area of the body with the highest emotional impact (sexual and reproductive, besides the sphincter control and the continence-related issues) and both have a high symbolic meaning**. The human being is a symbolic animal and the reading of life condensed through symbols goes beyond the limits of education, culture or race and becomes universal.
- **Failure to realize/admit that there are four iatrogenic abuses** (Graziottin, 2006), **inclusive of nocebo effects** (Benedetti et Al, 2007; Scotts et Al, 2008)*:*
  a) **the denial of the biological truth of pain**: every time a physician states that "pain is all in her head" he/she abuses the patients' trust, causing further negative emotional states, such as anxiety, depression, sense of unworthiness, loneliness and despair. But he/she can also trigger (further) domestic violence, physical, emotional and/or sexual, when the family and/or partner are told that she is "inventing" her pain. Many partners are frankly furious at the idea of keeping on travelling and spending on doctor shopping , and not having sex when CPP causes/includes dyspareunia, while she is having "nothing" and is just pretending she has pain. "If the doctor/professor said that, you must stop once and for all of complaining. Shut up! I'm fed up with your pain!";
  b) **the nocebo effect (" I will damage")**. Physicians are well familiar with the placebo effect, while only a few are aware of the powerful nocebo effect, inclusive of their verbal and non-verbal language. Every time we deny the truth of pain, or we state that the situation is more serious than it really is, every time we communicate a negative diagnosis without stressing the space of hope that should be maintained for every patients, particularly in the CPP domain, the nocebo effect is there, whereby expectation of a negative outcome may lead to the worsening of a symptom (Benedetti et Al, 2007). Increasing evidence suggests that the nocebo effect is neurobiologically based as the placebo one. Specifically, when **words (or behaviors) are painful**, there is an **increase in anticipatory anxiety**, and a **reduction in the**

serotoninergic, dopaminergic and opiatergic pathways, opposite to what has been documented when a placebo effect is in play (Benedetti et Al 2007; Scott et Al, 2008). Recent experimental evidence indicates that negative verbal suggestions induce anticipatory anxiety about the impending pain increase, and this verbally-induced anxiety triggers the activation of cholecystokinin (CCK) which, in turn, facilitates pain transmission. CCK-antagonists have been found to block this anxiety-induced hyperalgesia ("nocebo hyperalgesia"), thus opening up the possibility of new therapeutic strategies whenever pain has an important anxiety component (Benedetti et Al 2007).The **practical recommendation** is to be aware of the powerful emotional (and biological) effect of our wording and **communicate carefully and tactfully**, balancing the description of the severity of the case with the much needed attention to all that will be done to improve the condition and reduce pain;

c) **physical abuse**: 5,8% of my patients with lifelong dyspareunia and vulvar vestibulitis (unpublished data) reported as unique traumatic abusive experiences in their life the invasive diagnostic or therapeutic maneuvers in the genital area performed by physicians/ nurses, in the childhood or early adolescence, without care or appropriate analgesia. Exams such as urethral swab, cystoscopy, vaginal swabs, vaginal examination, sutures of genital minor traumas after injuries received while playing, manual separation of labia conglutination in case of lichen sclerosus, are recalled as traumatizing, violent, and fear triggering, increasing the anticipatory anxiety when a "white coat" is approaching the patient's body (Graziottin 2006). Again, a powerful, long lasting, neurobiologically based nocebo effect is in play;

d) **sexual abuse**: when the physician breaks the boundaries of appropriate doctor-patient relationship, and negative consequences may appear months or year after the abuse.

- **Lack of awareness that the first psychological intervention, with a powerful placebo/reassuring effect**, that every physician should use in his/her practice, is:
  a) **the empathic, respectful listening** of the personal history, inclusive of past negative experiences;
  b) the explanation to the woman – and the partner, when present! – **that her pain is real**, is not in her head, it has a name (the diagnosis), a number of causes – psychological and physical, that will be addressed in a balanced way- , a time to improve (the prognosis) and a multidisciplinary approach to accelerate the improvement;
  c) **the establishing of a good trusting doctor-patients relationships**, so critically important when CPP is in play (McDonald, 1998, Field and Swarm, 2008): "I felt I finally found the doctor who **would have taken care of me and my problem**. For the first time **I felt I was believed, and my anxiety melted away**". This is an example of a doctor-patient relationships where the physician becomes the first drug, with a powerful placebo effect, again neurobiologically based, as increasing evidence suggests (Benedetti et Al, 2007; Scott et Al, 2008).

Psychological and sexual consequences of CPP

Psychological and sexual consequences of CPP are modulated by a number of variables, including the duration of pain and the moment the diagnosis of CPP is made in the course of the natural history of it; its etiology, severity, type of comorbidities; the mental state before CPP and, last but not least, the quality of affective and emotional bonding in the couple/family and quality of medical support.

Anxiety, depression, loss of vital energy, fatigue, distress and sleep disorders may increase over time with increasing severity and worsening of pain. Specifically depressing factors are the feelings that pain is not considered "rigorously",

that its main etiology is missed, that physicians trivialize it as "psychogenic". Sexuality is among the most neglected areas when CPP is complained of (Graziottin, 2006).

Indeed , the majority of patients with CPP complain of a dysfunctional sexuality:

- **loss of sexual desire** and **poor mental arousal**, which may be caused by:
    a) the comorbidity with depression;
    b) the negative feedbacks from the genitals (Fig. 2) when poor genital arousal leading to vaginal dryness, and/or introital or deep dyspareunia are complained of (Graziottin, 2006, 2009);
- **poor genital arousal**, with vaginal dryness secondary to spontaneous or iatrogenic (treatment related) hypoestrogenic states;
- **dyspareunia**, depending on a number of factors (Graziottin, 2006, 2009):
    a) **genital pain**, that is the strongest reflex inhibitor of genital arousal and vaginal lubrication. It facilitates microabrasions of the introital mucosa contributing to vulvar vestibulitis, with hyperactive mast cells, proliferation of pain fibers and lifelong or acquired hyperactivity of the levator ani (Graziottin, 2009);
    b) **pelvic pain**, more often associated with: deep endometriosis, when located within the uterosacral ligament, in the posterior fornix/posterior vaginal wall, or in adenomyosis; pelvic inflammatory disease; irritable bowel syndrome; interstitial cystitis (Graziottin, 2006).
- **orgasmic difficulties**, specifically during intercourse, when low desire, vaginal dryness and/or dyspareunia are comorbid with CPP.

In the multidisciplinary approach, psychosexual consequences of CPP should be carefully evaluated and appropriate treatment plan should be proposed and discussed with the woman and the partner, when available.

Conclusions

Psychogenic factors can be powerful contributors of CPP, as predisposing, precipitating or maintaining factors of chronic stress. One of the currently most credited pathophysiologic reading is through the **corticotropin-releasing factor (CRF) signaling pathways**. Acknowledging the presence and relative weight of psychogenic factors should increase the diagnostic skill and empower the physicians' **attitude to cure the woman with CPP** and not only the disease or its somatic correlates. A multidisciplinary approach, with a psychotherapeutic/pharmacologic support (with anxiolytics or antidepressants) when indicated, in parallel to the medical treatment, will enhance the possibility of reducing the emotionally driven stress. Giving words to the emotional side of pain is key in a caring and curing perspective.

Finally psychosexual consequences should be evaluated and treated accordingly, from the medical and/or psychodynamic point of view, with a tailored approach. Overall, the caring physician should not say any more "pain is all in your head", but **"your psychological suffering (and previous abuses) speaks through your body"**. This is why we should give words to your emotional pain, with a psychological approach (when indicated) while curing all the physical causes of your CPP. I want you to feel better, to get better. To reduce your pain in all its components is my priority and our goal".

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SCIENCE RIVISITED

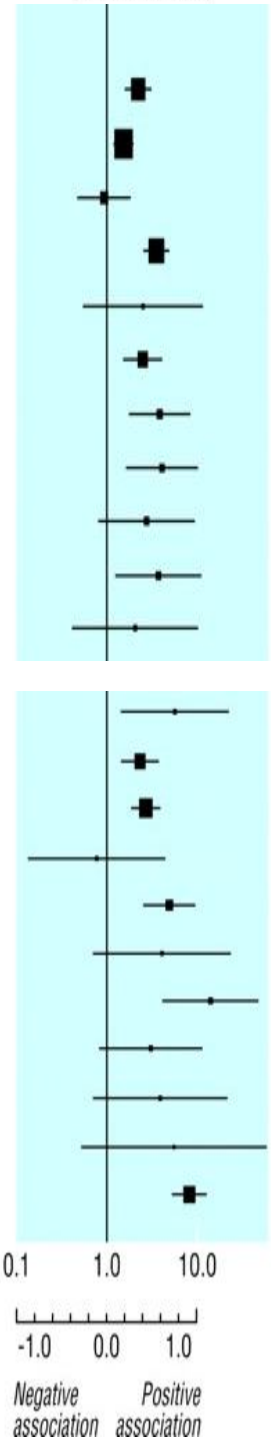
Fig. 1 Schematic reading of how psychogenic predisposing, precipitating and maintaining causes of CPP may increasingly modify the biological vulnerability to environmental pathogens or to endogenous noxae, inclusive of autoimmunity.

PSYCHOGENIC CAUSES OF CPP	BIOLOGICAL CORRELATES OF PSYCHOGENIC CAUSES	BIOLOGICAL ETIOLOGY OF CPP
PREDISPOSING - **Intrapsychic**: depression, anxiety, paranoia, personality disorders - **Context-related**: physical or sexual abuse, chronic emotional distress, alcoholism in one parent, marital conflicts, post-traumatic stress disorders...	**PREDISPOSING** Persistent neurovegetative arousal due to the psychogenic chronic stress leading to: **Corticotropin-releasing factor (CRF) signaling pathways with:** - chronic increase of glucocorticoids - amygdala up-regulation and increased anticipatory anxiety - down-regulation of the dopaminergic, serotoninergic and opiatergic system - hyperactivation of mast cell and of the pain system, peripheral and central ↓	**PREDISPOSING** Genetic vulnerability to: - anxiety and depression (inclusive of its somatic correlates) - up-regulation and degranulation of mast cells - allergies and autoimmunity
PRECIPITATING Acute emotional trauma, loss, stress, recurrent abuses	**PRECIPITATING** Increased biological vulnerability to endogenous and environmental pathogens ↓	**PRECIPITATING** - Environmental pathogens (virus, bacteria, fungi...) - Intercourse during vestibular inflammation or in non-aroused states - Endogenous damaging factors (endometrial shedding in endometriosis) - Autoimmunity
MAINTAINING Persistence of predisposing and/or precipitating factors Diagnostic omission / neglect Iatrogenic nocebo effect	**MAINTAINING** Up-regulation of the inflammatory, nervous, muscle systems, with chronic inflammation, neurogenic pain, muscle inflammation, chronic sleep disorders ↓	**MAINTAINING** Periodic endometrial shedding Recurrent intestinal, vaginal, bladder infections Chronic inflammation Neuropathic pain
	CHRONIC PELVIC PAIN	

EVIDENCE AT GLANCE

Tab 1. Meta-analysis of risk factors associated with non cyclical chronic pelvic pain, focusing on studies on abuse/psychological factors (all multiple studies are heterogeneous; ***P<0.001; **P<0.01)

Factor	No of trials	No of women: Cases	No of women: Controls	SMD (99% CI)	OR (99% CI)
Abuse/psychological factors					
Childhood physical abuse***	5	309	960	0.43 (0.24 to 0.62)	2.18 (1.55 to 3.06)
Childhood sexual abuse***	10	592	1472	0.23 (0.08 to 0.37)	1.51 (1.16 to 1.97)
Adult/lifetime physical abuse	5	157	363	-0.05 (-0.43 to 0.33)	0.91 (0.46 to 1.81)
Adult/lifetime sexual abuse***	11	664	966	0.69 (0.51 to 0.87)	3.49 (2.52 to 4.83)
Psychological abuse	1	36	43	0.50 (-0.34 to 1.33)	2.47 (0.54 to 11.24)
Any abuse	6	176	641	0.49 (0.21 to 0.77)	2.45 (1.47 to 4.06)
Disturbed puberty/painful early memories	4	223	71	0.73 (0.31 to 1.16)	3.77 (1.74 to 8.17)
Unsatisfactory relation with mother/spouse	3	135	44	0.77 (0.26 to 1.27)	4.01 (1.60 to 10.06)
Alcoholism in one parent	1	106	36	0.55 (-0.13 to 1.22)	2.69 (0.79 to 9.19)
Divorce in one parent	1	106	36	0.72 (0.11 to 1.33)	3.68 (1.23 to 11.08)
Death in one parent	1	106	36	0.39 (-0.49 to 1.28)	2.02 (0.40 to 10.13)
Disturbed pregnancy	1	32	25	0.95 (0.18 to 1.72)	5.58 (1.39 to 22.39)
Anxiety***	5	178	241	0.45 (0.19 to 0.72)	2.28 (1.41 to 3.70)
Depression**	8	410	376	0.55 (0.34 to 0.76)	2.69 (1.86 to 3.88)
Extroversion	1	35	9	-0.15 (-1.11 to 0.81)	0.76 (0.13 to 4.36)
Hysteria***	2	182	76	0.87 (0.51 to 1.23)	4.83 (2.50 to 9.33)
Neuroticism	1	35	9	0.77 (-0.20 to 1.73)	4.01 (0.70 to 22.99)
Paranoia	1	37	23	1.45 (0.77 to 2.13)	13.89 (4.02 to 48.02)
Borderline syndrome	1	106	36	0.61 (-0.11 to 1.33)	3.02 (0.82 to 11.08)
Current phobias	1	25	30	0.74 (-0.21 to 1.70)	3.86 (0.69 to 21.71)
Post-traumatic stress disorder	1	25	10	0.94 (-0.37 to 2.25)	5.47 (0.51 to 58.84)
Psychosomatic symptoms***	8	303	250	1.15 (0.90 to 1.39)	8.01 (5.16 to 12.44)



Latthe et Al, 2006, with permission

TIPS & TRICKS

TAB 2. Key differences between somatic vs psychogenic pain

Somatic pain	Psychogenic pain
The patient describes a more localized pain	The description of pain site is more elusive
Uses sensory words to qualify his/her pain	The wording to describe her pain is highly emotional
Accurately describes periodic and selective changes in his/her pain	Cannot identify any pattern of pain changes (ie circadian, menstrual, premenstrual, ovulatory...)
Can identify factors (such as posture, movements or even foods) that can increase or reduce pain	Stress is the most cited factor in worsening pain
Does not report major interpersonal difficulties	Usually reports interpersonal difficulties
Treats pain more as a symptom than as a disease per se	Clinical history indicates other psychosomatic diseases
Repeated consultations are mainly motivated by feeling of medical inaccuracy in addressing physical symptoms	Has a long history of doctor shopping, with lots of exams, motivated by the need of second/ third/forth opinions

Modified from F. Mombelli, 2003

TIPS & TRICKS

Tab. 3 Key questions to be asked when considering a **psychogenic component** of pain

1. How's the patient' life? Is it generally "working" or not?
2. Does the patient suffer from insomnia? How's the general quality of sleep?
3. Is there any stressful event – such as physical or sexual abuse, or emotional neglect - in the patient' life that can have a temporal or symbolic link with the pain onset or worsening?
4. How's the general quality of her *adaptive coping?*
5. What's the patient' opinion about her pain?
6. Are the timing or the characteristics of pain have any link with other problems (ie professional or family-related) of the patient' life?
7. Does pain carry any real or symbolic advantage?

Modified from F. Mombelli, 2003