

# Persistent genital arousal disorder: a review of the literature and recommendations for management. BASHH special interest group for sexual dysfunction

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**Summary:** Persistent genital arousal disorder is a newly recognized condition that is poorly understood. There is a paucity of research in this area and there are concerns as to the validity of the results of what little research there has been. This article aims to draw together current literature on this topic and provide readers with guidance on the management of this condition. This includes a working definition, an exploration of possible aetiologies within the confines of current knowledge, practical advice regarding assessment, management and auditable outcomes of practice.

## Q1 Keywords:

## INTRODUCTION

Female sexual arousal can be classified into subjective and genital arousal. Until recently the term sexual arousal disorder had been used to denote absent or diminished response of genital or subjective sexual arousal which evokes distress in the woman.<sup>1</sup>

In 2001 Leiblum and Nathan<sup>2</sup> published details of five women who rather than having low or absent genital arousal appeared to complain of persisting heightened genital arousal. They described the condition as persistent sexual arousal syndrome (PSAS). In fact Riley<sup>3</sup> in the UK had published details of a woman with a similar clinical picture some years earlier, and it is possible that Soranus of Ephesus alluded to the condition in the text 'Midwifery and diseases of women' in the second century AD.

In 2004, PSAS was recognized as a clinical entity by an International Definitions Committee.<sup>1</sup> Leiblum subsequently renamed it as the persistent genital arousal disorder (PDAD) (see below). PGAD had until recently been rarely reported,<sup>4</sup> implying it is a rare condition. However, a recent study of its prevalence in young women would suggest that as many as 1% of young women have the full-blown syndrome (L Garvey, personal communication). Sexual dysfunction is a sensitive issue and one that may be difficult to talk about. Recent population studies have highlighted low rates of women seeking medical or psychological help for sexual dysfunction despite reporting a high prevalence.<sup>5-7</sup> This may well be for sociocultural and economic reasons.<sup>7</sup> Women suffering from

PGAD may have feared being labelled as 'mad' by clinicians unfamiliar with the condition and thus not have sought help.

In this light, we wish to present here the data published to date on PGAD and give recommendations as to how such women may be best clinically managed.

## DEFINITION

A diagnosis of PGAD is at present based on the women's *subjective description of her symptoms*, which may include terms such as 'engorgement', which imply an objective vascular hyperaemia. In most cases in the literature such vulval and clitoral appearances have not been assessed.

A working definition of PGAD was initially formulated by Leiblum *et al.*<sup>8</sup> in 2005, but was described more fully in a later paper.<sup>9</sup> We have altered this slightly in order to accentuate that the definition is based on Symptoms.

For a diagnosis of PGAD to be made, we would suggest the presence of the following:

- (1) Symptoms characteristic of sexual arousal (genital fullness/swelling and sensitivity with or without nipple fullness/swelling) that persist for an extended period of time (hours or days) and do not subside completely on their own;
- (2) Symptoms of physiological arousal that do not resolve with ordinary orgasmic experience and may require multiple orgasms over hours or days to remit;
- (3) Symptoms of arousal are usually experienced as unrelated to any subjective sense of sexual excitement or desire;
- (4) The persistent genital arousal may be triggered not only by a sexual activity, but seemingly also by non-sexual stimuli or by no apparent stimulus at all;

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- (5) Symptoms are experienced as unbidden, intrusive and unwanted;
- (6) The symptoms cause the woman at least a moderate degree of distress.

The presence of distress is of some importance in that Leiblum's web survey results suggest that there is a group of women who have spontaneous genital arousal that persists to some extent, and that these women either see this in a neutral light or indeed welcome it.<sup>10</sup> A recent survey of young women attending a sexual health clinic found that up to a third recognized some degree of persisting genital arousal in the absence of desire but were not distressed by this (L Garvey, personal communication). To further complicate matters some women may be distressed by their persistent arousal some of the time, but at other times see it with equanimity or indeed find it pleasurable. Also of major importance is the absence of sexual desire in association with the PGAD – so that hypersexual states such as mania, so-called sexual addictions and being on stimulant social drugs, would exclude the women from being diagnosed with PGAD.

## AETIOLOGY

Because PGAD is a newly recognized condition, as well as there being very few published cases in the world literature, good data on aetiology, derived for instance from prospective cohort or even cross-sectional population, are not available. The evidence available consists of rather biased web surveys and case reports. One therefore needs to be circumspect in attributing causation based on the literature to date. Organic and psychological factors will overlap and interact in any individual case. Women of all ages can be affected by PGAD.

## Psychological

Leiblum and her colleagues have published three studies,<sup>8,11,12</sup> where they derived data from women who responded to invitations to take part in web surveys posted on three Internet women's sexuality or women's health websites. Women were asked to take part in the surveys if they felt that they might be experiencing persistent genital arousal. Critics of her methodology<sup>13,14</sup> have pointed out how biased these surveys are, with respondents likely being members of self-selected, self-help groups, where the symptoms of PGAD may merely represent epiphenomena of one or more underlying pathologies. In none of the three studies<sup>8,11,12</sup> is there a control group where women do not complain of persistent genital arousal. While acknowledging these limitations, the authors point out that this was the most efficient method of collecting data on as many women with PGAD as possible.

In the first of these studies, 53% of the 103 responders in fact had the full syndrome. Current trigger events were masturbation and sexual stimulation (37% and 53%, respectively), stress and anxiety (46% and 34%, respectively).<sup>8</sup> The second survey consisted of 388 women, 206 of whom endorsed the full picture of PGAD, the remainder being described as having 'non-PGAD' (they had at least some but not all of the features of PGAD). More PGAD women than non-PGAD women reported depression (45% versus 34%), anxiety (35% versus 21%), obsessive compulsive symptoms (24% versus 16%) and somatizing stress (70% versus 63%).<sup>11</sup> In the final

study,<sup>12</sup> 76 subjects had PGAD and 48 non-PGAD, with similarly high rates of anxiety and depression. In all, 60% versus 40% had depression in the PGAD and non-PGAD groups, respectively ( $P = 0.03$ ), and 32% versus 15% for panic attacks ( $P = 0.05$ ). There was an extremely high rate of past sexual abuse in the PGAD group (53% abused as a child and 36% as an adult), which was higher but not statistically significantly greater than in the non-PGAD group. In terms of which came first, PGAD or psychiatric illness, subjects with PGAD reported that in 64% and 78% of cases, the anxiety and depression, respectively, came some time before the onset of the genital problem. Chronic fatigue was found significantly more commonly in the PGAD compared with non-PGAD group (11% versus 0%,  $P = 0.05$ ).

A number of the case reports (13 in all) of PGAD in the literature document patients with moderate to severe anxiety, depression or obsessive compulsive disorders.<sup>4,9,15-17</sup> These include patients on or withdrawing from antidepressants,<sup>9</sup> which in itself may be an aetiological factor (see below).

Leiblum and Chivers<sup>10</sup> have put forward biologically and psychologically plausible explanations as to why these psychiatric states may be associated with PGAD. There may be a marked discordance between a woman's psychological and physiological (genital) state of sexual arousal. Women are capable of rapid genital responses both to visual sexually erotic material as well as to a broad range of more non-specific cues, e.g. sexual violence and primate sex.<sup>18,19</sup> Anxiety itself, under certain circumstances may increase genital engorgement,<sup>20</sup> as well as enhancing cognitive narrowing (increasing attention to threatening or unpleasant sensations).<sup>21</sup> Leiblum and Chivers<sup>10</sup> argue that sensations of genital arousal are detected and then appraised by the PGAD sufferer as negative for instance either because of past sexual assault or because of other catastrophic misinterpretation of the sensations (e.g. because of their personal take on the morality of sex). This negative appraisal produces more anxiety which in turn causes further cognitive narrowing and enhanced local genital responses. Depression often overlaps with anxiety, and somatization in terms of clinical features; hence many patients labelled as having depression would also fit into the above explanation.<sup>22</sup> Patients with chronic fatigue syndrome also appear to exhibit a greater degree of attentional bias to health threatening cues compared with controls,<sup>23</sup> hence their possible overrepresentation in the PGAD group compared with non-PGAD groups.<sup>12</sup>

## Role of antidepressants

Of the first 364 women who took part in the above web surveys,<sup>8,11,12</sup> five clearly identified the onset of PGAD with selective serotonin reuptake inhibitor (SSRI) antidepressant usage or withdrawal in response to the question 'what do you believe may have contributed to the initial development of your PGAD?'.<sup>9</sup> The authors acknowledge that clinical details of these women are incomplete.<sup>9</sup> In three of the cases, the PGAD onset was contemporaneous with venlafaxine withdrawal (in one of these only lasting for a few weeks), in another secondary to sertraline withdrawal, and in the fifth woman the PGAD occurred in sequential response to being on fluoxetine, venlafaxine, sertraline and escitalopram.

A brief letter from a PGAD sufferer reported that 10 of 15 women using the PSAS chat room on line had suffered PSAS

(sic) after coming off SSRI antidepressants.<sup>24</sup> A further case reported PGAD symptoms while on high-dose (350 mg per day) venlafaxine for depression. She was also taking the anti-psychotic quetiapin, which may have been implicated in that it has alpha adrenergic blocking activity.<sup>15</sup> Some features of PGAD may overlap with clitoral priapism. This may be precipitated by the use of trazodone, citalopram, nefazodone or olanzapine.<sup>4</sup> Cessation of trazodone associated with non-priapism PGAD has been reported to cause marked improvement of PGAD in one case.<sup>4</sup>

The mechanism of antidepressants causing PGAD, in particular the SSRIs, might be part of a withdrawal syndrome upon stopping them.<sup>9</sup> Another hypothesis is an increase in atrial natriuretic peptide (a profound vasodilator) that is produced on cessation of SSRI antidepressants.<sup>25</sup>

### Miscellaneous

The symptoms of PGAD have been described in association with a number of miscellaneous conditions such as genital prolapse,<sup>4,16</sup> pelvic arteriovenous fistula<sup>4</sup> and arising after brain surgery for a cerebral arteriovenous fistula.<sup>4</sup> More recently, a case of PGAD of five months duration was described in association with a dilated and incompetent left ovarian vein in a woman with 'pelvic congestion syndrome'.<sup>26</sup> Marked reduction of symptoms followed venous embolization. One case of PGAD appeared to display florid features of lichen sclerosus (no biopsy undertaken).<sup>16</sup> A further case of PGAD was reported to be associated with high soya intake in a postmenopausal woman – her symptoms subsided after dietary modification.<sup>27</sup> Very rarely somatosensory epileptic auras or temporal lobe epilepsy may masquerade as PGAD.<sup>28</sup> Wylie *et al.*<sup>29</sup> A reported case of sleep exacerbation of PGAD. Although they demonstrated increased vaginal pulse amplitude (VPA) in light sleep, this does not necessarily explain the aetiology as increased VPA also occurs in normal women at rapid eye movement sleep.<sup>30</sup> A comprehensive review of sleep-related abnormal sexual behaviours would suggest that most result in increase in sexual desire and semi-conscious sexual actions rather than PGAD.<sup>31</sup> Finally, a complex cardiological case with an atrial septal defect, symptoms suggestive of autonomic neuropathy and PGAD that came on after starting fludrocortisone has been described.<sup>32</sup>

PGAD may be caused by clitoral priapism; however, this commonly causes pain rather than PGAD symptoms.<sup>4</sup> The causes of this rare condition are discussed in the comprehensive article by Goldstein *et al.*<sup>4</sup> These authors have also suggested neurological, vascular, pharmacological, idiopathic and hormonal pathophysiological processes in some detail which might explain PGAD.

### Exacerbating and relieving factors

A wide variety of triggers and exacerbating factors are reported. In the web survey data,<sup>8,11,12</sup> current triggers that lead to the onset of PGAD in a third or more of the women were sexual stimulation (53%), masturbation (36%), stress (46%) and anxiety (34%). Exacerbating factors included pressure against the genitals (67%), 'something sexy you see' (59%), vibrations from a car or motorcycle (57%), stimulation by partner (55%) and intercourse (46%). The most frequently reported (6 cases in all) exacerbating factor in the case reports appears to have

been travelling in a car or train.<sup>9,16,17,26,29</sup> Although masturbation/orgasm gave some relief in about a half of the web survey cases,<sup>8</sup> this appeared to only afford very temporary relief in eight case reports where the clinical pictures appeared to be severe.<sup>2,4,9,27,33</sup> Web survey data suggested that 39% felt some relief was obtained by distraction.<sup>8</sup>

### PGAD symptomatology

Web survey data of women who complain of the full PGAD syndrome reported the following genital symptoms: clitoral tingling (86%), vaginal congestion (80%), vaginal wetness (77%), vaginal contractions (71%) and vaginal tingling (71%). Clitoral pain was reported in 20%. Nipple erection, however, was reported at a statistically much higher rate in the 'non-PGAD' group (57%) compared with the PGAD group (39%).<sup>11</sup>

### Differential diagnosis

As already mentioned, clitoral priapism is a rare condition, the presentation of which can potentially overlap with PGAD.<sup>4</sup> However, it should be possible to differentiate these two conditions based on history and examination. Women presenting with priapism will complain of significant pain and there should be accompanying clitoral engorgement visible on examination. If clitoral priapism is suspected, the authors advise an urgent referral to a gynaecologist.

### PATIENT ASSESSMENT

An overarching theme in the clinical management is the need for an eclectic and multidisciplinary approach.

### History

Exact symptoms should be assessed, along with exacerbating and relieving factors. A psychological and psychiatric history should be taken with particular emphasis on a history of anxiety, depression, obsessive compulsive illness or personality. Exclusion of a manic or hypomanic state, 'sexual addiction' or mental states altered by social drugs are all important – in these scenarios the sexual arousal is secondary to increased desire and therefore PGAD is not the diagnosis. A careful and compassionate enquiry into the past sexual assault and associated post-traumatic stress disorder is important. A neurological history, including any possible ictal episodes, should also be taken and enquiry made into genital trauma or surgery. A full history of medications, both current and past, particularly antidepressants, oestrogens and soy products is imperative.

### Examination

Detailed and careful examination of the external genitalia should be undertaken with particular emphasis on the presence of labial hyperaemia or dermatoses. Of particular importance is the presence of clitoral engorgement and note should be made of any labial or vulval varicosities. The absence of engorgement does not exclude a diagnosis of PGAD. A bimanual examination should be undertaken to exclude pelvic masses.

A mental state psychiatric examination should also be undertaken and, where appropriate, a detailed neurological and cardiac examination.

### Investigations

A full blood count should be undertaken and a haemoglobinopathy screen done if clitoral priapism is suspected. All patients should have a pelvic ultrasound to exclude intrapelvic masses.

- Q3** For pelvic varicosities should be considered. Incompetent veins to be diagnosed the varicosities need to be shown to have poor flow within them<sup>34</sup> for which a dynamic technique is needed. Per vaginal or transabdominal ultrasound is likely to delineate large veins (this simple screening tool picked up the abnormal veins in the case of the woman who had PGAD),<sup>26</sup> and Doppler measurement in the Valsalva manoeuvre can confirm backflow or stasis. Structural and dynamic flow problems can be confirmed using a magnetic resonance imaging (MRI) scan enhanced with gadolinium.<sup>34</sup> A neurological assessment may indicate the need for a brain and cord MRI.

### Treatment

All the treatment measures detailed below are based on case reports – there are no well-conducted treatment trials.

#### General measures

These include avoiding any factors that consistently appear to induce or exacerbate the PGAD. Most patients will have discovered these for themselves. Masturbation can lead to at least very temporary relief in many sufferers. Those with mild PGAD may have found that one or two orgasms relieves their symptoms but in the more severe cases repeated orgasms only appear to perpetuate the symptoms. (Earlier studies found that in normal women vaginal engorgement may persist for up to 15 minutes after orgasm).<sup>35,36</sup> Simple procedures such as using ice packs on the area may be helpful.<sup>4,29</sup>

#### Specific measures

On the basis of the data presented above, these would include stopping antidepressants such as trazodone if there is a temporal relationship with their use and the onset of the PGAD, treatment of a genital dermatosis, surgical repair of genital arteriovenous fistulas, management of haemoglobinopathies if present, cessation of high intake of phytoestrogens (soya), management of ictal events, repair of genital prolapses and embolization of ovarian veins.

#### Psychological therapies

Moderate to severe anxiety, depression, obsessive compulsive disorders and a past history of sexual assault will probably contribute to how the women experience their PGAD symptoms. Managing these conditions may induce reduction of genital symptoms and distress.

Cognitive behaviour therapy (CBT) and other psychological therapies including couple therapy may help to reduce symptoms.<sup>33</sup> A CBT approach would aim to address maladaptive beliefs and dysfunctional cognitions about sexual expression and genital changes. Negative and judgemental thoughts are

common in PGAD sufferers, many of whom are very distressed at the sexual nature of their symptomatology. Such negative thoughts contribute to the disruption of physiological responses and hence to the cognitive narrowing described above. By restructuring belief systems about the meaning of genital sensations, introducing self-management of intrusive arousal experiences and learning to decrease repetitive behaviours, such as self-stimulation, the woman can increase her coping skills and self-confidence. Anxiety management and relaxation techniques are a useful component of a cognitive approach, as these can actively reduce stress, as well as offering a form of distraction from the symptoms. If the partner of a PGAD sufferer is affected in a way that is detrimental to the relationship, psychosexual therapy for the couple can provide them with increased understanding and alternative patterns of relating, both emotionally and physically, that are less likely to exacerbate the symptoms.

Mindfulness meditation has been found to be helpful in the management of a number of organic and psychological conditions in that it significantly reduces the emotional and distress components of symptoms and makes sufferers more accepting of their chronic problems.<sup>37-40</sup> Thus, the emotional aspects of the distress of PGAD may be more accepted, colouring the women's life in a less judgemental and more positive way. It has also been shown in an early study to be useful in women with sexual dysfunction.<sup>40</sup> We have anecdotally found it useful in our clinical practice with patients with PGAD.

#### Psychotropic medications

Although PGAD has been reported on cessation of SSRI antidepressants,<sup>24</sup> in the web survey this was reported in just over 1% of women and thus appears to be a rare cause of PGAD.<sup>9</sup> Anecdotal case reports demonstrate that antipsychotics<sup>29</sup> and SSRI/SNRIs antidepressants,<sup>16</sup> rather than being a cause of PGAD, if used judiciously, may in fact be extremely helpful in controlling the symptoms of PGAD, as well as decreasing anxiety, depression and obsessive-compulsive disorder, and thus lessening the genital focusing. We have found this to also be the case in other as yet unreported cases in our routine practice. It would seem unwise to use trazodone as this antidepressant can cause vaso-engorgement. In two cases in the literature who have had severe depression, electroconvulsive therapy (ECT) was helpful in relieving both the depression **Q4** as well as the symptoms of the PGAD.<sup>17</sup> In other cases of severe depression and PGAD, ECT has not been successful in controlling the genital symptoms (I Goldstein, personal communication). It would seem unwise to treat the associated anxiety with benzodiazepines because of the potential for addiction and tolerance. To date there is no evidence that antiepileptics given as treatment for neuropathic pain (e.g. pregabalin or gabapentin) are useful.

### AUDITABLE OUTCOME MEASURES

- (1) All patients diagnosed with PGAD should have had a psychiatric history taken;
- (2) All patients diagnosed with PGAD should have had a full medical history documented including medications;
- (3) All patients diagnosed with PGAD need to have had a comprehensive genital and pelvic examination;
- (4) A pelvic ultrasound is the very minimum of investigation needed in all cases of suspected PGAD.

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