

# Persistent Genital Arousal Disorder in 18 Dutch Women: Part I. MRI, EEG, and Transvaginal Ultrasonography Investigations

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## ABSTRACT

**Introduction.** Systematic blood analysis and electroencephalographic (EEG) and magnetic resonance imaging (MRI) study in women with persistent genital arousal disorder (PGAD) are needed to get more insight into the syndrome's etiology and pathogenesis.

**Aim.** To investigate possible causes of PGAD.

**Methods.** Eighteen women fulfilling all five criteria of PGAD were included in the study. In-depth interviews and routine blood and hormonal investigations, together with EEG and MRI scans of the brain and pelvis, were performed in all women. Transvaginal ultrasonography (TVUS) and MRI scans with contrast were performed in subjects who had indications of abnormalities on MRI scans.

**Main Outcome Measures.** Detailed descriptions of blood, neurophysiological, and (neuro)anatomical findings.

**Results.** The majority of women experienced PGAD symptoms during early menopause without existing laboratory abnormalities, besides those belonging to menopause. The EEG studies showed no severe diffuse or focal abnormalities. The MRI scans of the brain did not show any specific abnormalities, apart from an already known pericallosal aneurysm in one patient and postoperative findings of meningioma surgery in another patient. MRI scans of the pelvis showed clear to moderate-clear indications of pelvic varices in 55% of the women. TVUS confirmed the existence of pelvic varices in nine women; these had a mild, moderate, and severe extent in two, three, and four women. In three of the latter four patients, an additional MRI with gadolinium contrast disclosed mild to moderate dilation of ovarian veins; 39% of the women were known with varices of one or both legs.

**Conclusions.** The current study did not show overt pathology that could causally explain PGAD sensations. As pelvic varices are a common finding in adult women, the current findings do not allow the conclusion that PGAD is causally related to pelvic varices. However, the high prevalence of pelvic and lower limb varices in the current group of women warrants further research of their role in PGAD. **Waldinger MD, van Gils APG, Ottervanger HP, Vandenbroucke WVA, and Tavy DLJ. Persistent genital arousal disorder in 18 Dutch women: Part I. MRI, EEG, and transvaginal ultrasonography investigations. J Sex Med \*\*;\*\*\*:\*\*-\*\*.**

**Key Words.** PSAS; PGAD; MRI; EEG; TVUS; Pelvic Varices

## Introduction

Persistent sexual arousal syndrome (PSAS) or persistent genital arousal disorder (PGAD) is characterized by five diagnostic criteria: (i) involuntary genital and clitoral arousal that persists for

an extended period of time (hours, days, months); (ii) the physical genital arousal does not go away following one or more orgasms; (iii) the genital arousal is unrelated to subjective feelings of sexual desire; (iv) the persistent feelings of genital arousal feel intrusive and unwanted; and (v) distress is

associated with persistent genital arousal [1]. In 2001, the syndrome was for the first time reported in medical literature by Leiblum and Nathan [2]. It is thought to be a rare complaint that can negatively interfere with a patient's activities of daily living and social functioning [2–4]. The prevalence, etiology, and pathogenesis of the syndrome are unknown [2–4]. Current insight into PGAD is thus far limited by a lack of systematic research, despite a considerable number of case reports [2,5–13]. In the current study we report the results of a series of magnetic resonance imaging (MRI) and electroencephalogram (EEG) investigations conducted in 18 women who actively were seeking medical treatment for complaints of unwanted genital arousal sensations and who fulfilled the five diagnostic criteria for having PGAD [1].

### Material and Methods

The current study reports on 18 women with complaints of persistent unwanted feelings of genital arousal who visited the Outpatient Department of Neurosexology of the HagaHospital Leyenburg, The Hague, in the Netherlands, between October 2004 and July 2008, were diagnosed with PGAD, and who provided written informed consent. The women were not actively recruited but were either referred by their general physician, gynecologist, and sexologist or contacted the first author after Internet information on the PGAD research and treatment facilities in our Outpatient Department. According to the regulations of the medical ethical committee, official permission for study participation was not required as the study was not placebo controlled and experimental drugs were not taken. All patients were investigated by the first author, who followed a standard procedure. After a neuropsychiatric and medical sexological interview of about 1 hour, women who were clinically diagnosed as having PGAD underwent routine and hormonal laboratory testing, an MRI scan examination of the brain and pelvis, an EEG, and a transvaginal ultrasonography (TVUS) in case that MRI was suggestive for pelvic abnormalities.

### MRI of the Brain

MRI of the brain was performed on a 1.5-T system (Intera, Philips Medical Systems, Best, The Netherlands) by using a standard head coil. The protocol included initial acquisition of a scout image (repetition time msec/echo time msec, 15/5), followed by the following sequences: T1-weighted spin echo (500/14; section thickness, 6 mm; field

of view, 210 mm; matrix, 256 × 256), transverse T2-weighted fast spin echo (2,474/17–102; section thickness, 6 mm; field of view, 210 mm; matrix, 256 × 256), and coronal fluid-attenuated inversion recovery (repetition time msec/echo time msec/inversion time msec, 11,000/140/1,800; section thickness, 5 mm; field of view, 240 mm; matrix, 256 × 256). The acquired images were assessed by the second author for structural abnormalities, dilatation of lateral ventricles and temporal horn, and the presence of abnormal signal intensities, particularly of the temporal and parietal regions.

### MRI of the Pelvis

In the same session MRI of the pelvis without contrast was performed using a body phased-array coil. Axial, coronal, and sagittal high-resolution multishot turbo spin-echo sequences (repetition time msec/echo time msec, 1,600/100), with 3-mm slice thickness and 0.6-mm slice interslice gap and a 1,024 × 1,024 matrix were acquired of the pelvis, including the external and internal genitalia, the urethra, and sacrum. In addition all patients underwent T2-weighted imaging with inversion recovery sequences (repetition time msec/echo time msec/inversion time msec, 2,500/50/160) in sagittal and coronal planes with 5-mm-thick slices, a slice gap of 1 mm and a matrix of 512 × 512. Each pelvic study was assessed by the second author for the presence of clitoral enlargement, vaginal prolapse, urethral diverticula, uterine and ovarian abnormalities, and pelvic varicoceles as seen in pelvic congestion syndrome [14]. No additional procedures such as tilting or Valsalva were performed during the MRI examinations because of technical difficulties and the risk of inferior image quality.

### EEG

EEGs were performed on digital 32-channel Brainlab (OSG, Rumst, Belgium) machines with electrodes placed according to the 10/20 system. The sampling frequency was set to 500 Hz and filter settings were 0.16 to 70 Hz. Each recording included longitudinal bipolar, transverse bipolar, average reference, and source derivation montages. In addition, a transverse bipolar montage according to the “Maudsley electrode” system was used. In this system there is bilateral anterior temporal electrode placement, which gives more coverage of the basal temporal regions [15]. The EEG investigations were performed by the last author.

**TVUS**

Conventional TVUS of the uterus and adnexa was performed in both sagittal and oblique transverse planes with an 8.8-MHz probe (Xario-Toshiba, Toshiba Co., Tokyo, Japan). The presence on nonpulsatile flow in dilated veins was shown by Doppler ultrasound. Examinations were performed when the subjects were lying in the supine position with knees in 30- to 45-degree flexion. Gynecological examination on indication was performed by the third author. All TVUS investigations were conducted by the fourth author. A Valsalva procedure was not performed during the TVUS.

**Blood Sampling**

Routine blood analyses were performed in each woman. Endocrine assessments included prolactin, follicle stimulating hormone (FSH), luteinizing hormone (LH), total estradiol, progesterone, testosterone, sex hormone-binding globulin, free thyroxine, and thyroid stimulating hormone (TSH). In addition, vitamins and minerals were assessed; iron, iron-binding globulin, and iron saturation was calculated. Folic acid, vitamin B12, haptoglobin, and protoporphyrins were also assessed and reference ranges were used according to the manufacturer manuals. All laboratory tests used in this study were performed using commercially available assays.

**Statistics**

Descriptive statistics were computed for the measures used in the analyses of the baseline characteristics, and are reported as mean ± standard deviation. A two-tailed *t*-test was performed on endocrine blood analyses.

**Results**

The characteristics of the 18 women with PGAD are shown in Table 1. At presentation, women were on average (mean ± SD), 53.7 ± 9.7 years (median 55 years, range 30–70 years). Of all women with PGAD, 15 (83%) had a relationship with a male partner. Of them 12 (80%) was married. The mean ± SD duration of relationship was 24.7 ± 15.1 years. Of all women 12 (67%) were menopausal, which occurred at the mean ± SD age of 49.1 ± 3.9 years (median 50 years). Apart from the complaints of PGAD, all women were in good physical health. The genital symptoms started at the mean ± SD age of

**Table 1** Patient characteristics

Patient no.	Age of patient (year)	Marital status at intake	Age of partner (year)	Relationship (year)	No. of children	Illnesses	Age of menopause	Age of onset PGAD	Localization of PGAD
1	70	Married	76	50	2		53	67	Clitoris
2	68	Partner	77	20	2		48	68	Clitoris
3	61	Married	61	40	1	UE	50	57	Clitoris, vagina
4	61	—	—	—	—	UE	50	50	Vagina, labia
5	59	Married	60	38	2		38	59	Vagina
6	60	Married	60	41	2		50	50	Clitoris, vagina
7	58	Married	63	35	3	UE	52	57	Clitoris
8	56	Married	56	34	2	E, PS, RA, MYS	50	54	Clitoris
9	57	Married	61	3	2		50	52	Clitoris, vagina, labia
10	54	Married	54	18	2		52	52	Clitoris, vagina, groin
11	54	Married	50	11	2	SC	—	50	Clitoris
12	51	Partner	48	1	—	HP	50	48	Clitoris, vagina, labia, groin
13	52	Divorced	—	—	2	MS, EG	46	50	Clitoris, vagina, labia, labia
14	45	Married	49	27	2		—	44	Clitoris
15	46	Partner	34	6	4		—	20	Clitoris, vagina, labia
16	45	Married	45	24	3		—	42	Clitoris
17	43	Married	50	24	2	BS	—	43	Pubic bone
18	30	—	—	—	1		—	28	Vagina

E = epilepsy; RA = rheumatism; UE = uterus extirpation; EG = extraterine gravidity; HP = hypoparathyroidism; BS = bladder surgery; SC = cesarean section; MS = meningioma surgery; MYS = myoma surgery; PS = prolapse surgery.

**Table 2** Electroencephalogram investigations

Patient no.	Background rhythm	Focal	Paroxysmal	Interpretation
1	Mild slowing of alpha rhythm	Mild temporal slowing	None	Mild diffuse slowing and temporal slowing with medication
2	Normal alpha, generalized beta activity	Right temporal wicket spikes	None	Excessive beta, wicket spikes (benign variant)
3	Normal	None	None	Normal
4	Normal	Mild bitemporal slowing	None	Mild temporal slowing, diffuse normal; possibly age-related vascular abnormality
5	Mild slowing of alpha rhythm	Left temporal slowing	None	Left temporal slowing, mild diffuse abnormality ischemia
6	Normal	Mild bitemporal slowing	None	Mild temporal slowing, diffuse normal; possibly age-related vascular abnormality
7	Normal	None	None	Normal
8	Mild slowing of alpha rhythm	Mild temporal slowing	Generalized sharp diffuse charge	Mild diffuse and temporal abnormality
9	Normal, generalized beta	None	None	Normal, effect of benzodiazepines
10	Normal	None	None	Normal
11	Normal alpha, generalized beta activity	Sharp left occipital waves	Wicket spikes bilateral	Mild specific left occipital region
12	Normal	None	None	Normal
13	Normal	Delta left occipital	None	Focal slowing due to meningioma surgery, otherwise normal
14	Normal	None	None	Normal
15	Normal alpha, generalized beta activity	None	None	Normal, effect of benzodiazepines
16	Normal	None	None	Normal
17	Normal	None	None	Normal
18	Normal	None	None	Normal

49.5 ± 11.8 years (median 50 years). Of the 12 menopausal women, the mean ± SD age was 58.9 (5.7) years (median 58.5 years). In these women, PGAD started at 55.3 ± 6.6 years (median 53 years). The mean ± SD age of the six nonmenopausal women was 43.3 ± 7.1 years (median 54 years). In the latter women, PGAD started at 37.8 ± 11.4 years (median 50 years). The unwanted genital sensations were experienced at the clitoris, vagina, and labia in 14 (78%), 10 (55%), and 5 (28%) women, respectively; 8 (44%) women reported a combination of these localizations. One woman (5%) reported the sensations behind the pubic bone, and two women (11%) in the region of the groins. All women experienced the symptoms continuously during the day in severe to very severe degrees, which varied in the course of weeks and months. In 15 (83%) women the sensations were expressed as an imminent orgasm, persistently remaining on the verge of an orgasm without completion, i.e., without the pleasurable feeling of an orgasm.

Routine blood and additional iron analyses of all patients were normal. Also endocrine assessments, free thyroxin, and TSH were within the normal ranges. Of the 12 menopausal women, definite menopause was confirmed by high FSH and LH values and low estradiol

levels. In these women the mean ± SD levels of LH, FSH, estradiol, progesterone, and testosterone were 25.6 ± 9.8 U/L, 51.0 ± 21.7 U/L, 26.6 ± 13.3 pmol/L, 1.3 ± 0.6 nmol/L, and 1.1 ± 0.6 nmol/L, respectively. All six premenopausal women reported intact menstrual cycles. Their endocrine levels were 16.6 ± 19.6 U/L, 13.4 ± 9.6 U/L, 387.4 ± 187.2 pmol/L, 16.0 ± 20.5 nmol/L, and 1.2 ± 0.5 nmol/L, respectively.

The EEG studies overall showed no severe diffuse or focal abnormalities (Table 2). In three patients, mild diffuse and temporal slowing was noted which could be explained by the use of medication. Five of the 18 EEGs contained a few sharp waves mostly in the temporal regions. Wicket spikes were seen in one EEG. In one case, short lasting generalized epileptiform activity was present. Specific focal epileptiform activity in the temporal or parietal regions was not seen in the EEGs.

The MRI scans of the brain did not show any specific abnormalities, apart from a pericallosal aneurysm in one patient and postoperative findings of meningioma surgery in another patient. Both women were known with these lesions (Table 3).

The MRI scan of the pelvis showed no abnormalities of the clitoris and urethra. Besides three

**Table 3** Magnetic resonance imaging investigations of the brain

Patient no.	Atrophy	Abnormal signal intensities	Structural abnormalities
1	—	Minimal white matter intensities	—
2	—	—	—
3	—	—	—
4	—	—	—
5	—	Minimal white matter intensities	—
6	—	Minimal white matter intensities	—
7	—	—	Pericallosal aneurysm
8	—	—	—
9	—	Minimal white matter intensities	—
10	—	—	—
11	—	—	—
12	—	—	—
13	—	—	Postoperative changes after meningioma removal
14	—	—	—
15	—	—	—
16	—	—	—
17	—	—	—
18	—	—	—

Note: Dashes indicate absence of characteristic.

women with an ovarian cyst and two women with hysterectomy, there were no clitoral, urethral, uterine, and/or ovarian abnormalities. However, in 10 (55%) of the women, there were clear (30%) and moderate-clear (70%) indications of pelvic varices (Table 4).

An additional TVUS was performed in 12 women, whose MRI of the pelvis showed indications of pelvic varices or cysts (Table 5). TVUS confirmed the existence of pelvic varices in nine women; these had a mild, moderate, and severe extent in two, three, and four women. In three of the latter four patients, an additional MRI with gadolinium contrast was performed and disclosed

mild to moderate dilation of ovarian veins. Additional history interview revealed that 7 (39%) women were known with varices of one or both legs. Of these women, 5 (71%) subjects underwent varices surgery prior to the PGAD episode (Table 6).

**Discussion**

This is the first study of systematic blood analysis, MRI, EEG, and TVUS examinations in a series of women with PGAD. All 18 women included in this study met the five diagnostic criteria of PGAD. All women suffered from continuous

**Table 4** Magnetic resonance imaging investigations of the pelvis

Patient no.	Clitoral enlargement	Vaginal prolapse	Urethral diverticula	Uterine and ovarian abnormalities	Pelvic varices
1	—	—	—	Leiomyoma	—
2	—	—	—	—	+
3	—	—	—	Hysterectomy	+
4	—	—	—	Ovarian cyst	+
5	—	—	—	—	—
6	—	—	—	—	—
7	—	—	—	Hysterectomy	++
8	—	—	—	—	+
9	—	—	—	—	—
10	—	—	—	—	—
11	—	—	—	—	—
12	—	—	—	—	+
13	—	—	—	—	—
14	—	—	—	—	+
15	—	—	—	Ovarian cyst	—
16	—	—	—	Ovarian cyst	++
17	—	—	—	—	+
18	—	—	—	—	++

Note: Dashes indicate absence of characteristic. ++ = definite pelvic varices; + = mild pelvic varices.

**Table 5** Transvaginal ultrasonography investigations of the pelvis

Patient no.	Age	Parity	Menopausal	Uterus	Right adnexa	Left adnexa	Pelvic varices
2	72	2	Yes	Normal	Normal	Normal	++
4	63	0	Yes	Hysterectomy	Not visible	Cyst Ø 3.5 cm	±
7	60	3	Yes	Normal	Normal	Normal	++
8	56	2	Yes	Normal	Normal	Normal	++
9	57	2	Yes	Normal	Normal	Normal	-
10	54	0	Yes	Normal	Cyst Ø 2.5 cm	Normal	-
12	52	0	Yes	Myoma Ø 0.8 cm	Not visible	Normal	-
13	52	2	Yes	Myoma Ø 1.6 cm	Normal	Normal	±
14	49	2	No	Normal	Normal	Normal	+
16	46	3	No	Normal	Follicle < 2 cm	Follicle < 2 cm	++
17	43	2	No	Normal	Follicle < 2 cm	Normal	+
18	30	1	No	Normal	Cyst Ø 3 cm	Follicle < 2 cm	+

Pelvic varices: - (absent); ± (mild); + (moderate); ++ (severe).

undesired genital sensations, either at the clitoris, the vagina, or labia region in the absence of sexual fantasies or sexual desire. Prospective follow-up of a few years of most of these women showed a long-term cyclic pattern of complaints. The severity varied during many months with periods of diminished or increased PGAD symptoms of many weeks' durations. All women reported varying degrees of social withdrawal, desperate feelings, dysthymia, agitation, or depressed mood as a direct result of the persistency of the unwanted genital sensations. The EEG studies overall showed no severe diffuse or focal abnormalities. Mild temporal slowing was noted in 6 of the 18 patients. This finding is common in middle-aged and elderly individuals, and is considered to be of no clinical significance and is probably due to mild

vascular changes. Mild diffuse slowing was noted in three patients, which was likely caused by the use of medication. The findings of a few sharp waves in five cases are unspecific findings and can be attributed to normal variability or interference with atypical alpha morphology. The wicket spikes, which were seen in two cases, are considered variant within the normal range. One patient had sharp waves in the left occipital region possibly caused by subclinical ischemic changes, while in another case focal slowing was found after a meningioma operation. Specific focal epileptiform activity in the temporal or parietal regions was not seen in any of the EEGs.

It is well known that temporal lobe epilepsy or the use of antiepileptic drugs is associated with hyposexuality [16]. On the other hand, hypersexuality, e.g., increased sexual fantasies and desire, has been described in patients with bilateral temporal lobe lesions and in patients after temporal lobe resection for temporal epilepsy [17]. In light of the normal neuroradiological and mostly normal EEG findings in our patients, we have found no evidence that PGAD can be attributed to temporal lobe dysfunction.

The MRI studies of the brain showed no specific pathologies except in one woman with an aneurysm in the frontal lobe. The MRI investigation of the pelvis in seven women showed indications of the existence of pelvic varices and an additional three women showed definitive signs of dilated veins as seen in pelvic congestion syndrome [14]. Although pelvic varices are common in menopausal women, and may particularly occur in multipara, it is unknown whether they are involved in the pathogenesis of PGAD. Recently, a case report indicated an association of pelvic congestion syndrome with PGAD [13]. However, in contrast to the latter case report, the pelvic varices in

**Table 6** Pelvic varices according to magnetic resonance imaging (MRI) scan and transvaginal ultrasonography (TVUS) and history of varices legs

Patient no.	MRI scan pelvic varices	TVUS pelvic varices	Varices legs (surgery)
1	-		-
2	+	++	Yes (3 × surgery left)
3	+		-
4	+	±	-
5	-		-
6	-		-
7	++	++	Yes (1 × surgery l/r)
8	+	++	-
9	-	-	Yes (1 × surgery l/r)
10	-	-	Yes, l/r
11	-		-
12	+	-	-
13	-	±	-
14	+	+	Yes (2 × surgery r)
15	-		-
16	++	++	Yes, r
17	+	+	Yes (1 × surgery l/r)
18	++	+	-

- (absent); ± (mild); + (moderate); ++ (severe).

most of the women of the current study were only mild to moderate. Moreover, although pelvic varicose veins have been associated with chronic pelvic pain [18], none of the women in the current study complained of chronic pelvic pain. By additional interviewing it appeared that 39% of the women had varices of the legs and/or previously had surgery for these varices. This is in line with current knowledge that pelvic varices are commonly associated with lower extremity varices [19]. In a study of women with pelvic veins >5 mm in diameter, venous insufficiency of the lower limbs was reported in 70% of cases [19]. Pelvic varices are a well-recognized clinical entity. However, prevalence rates in the general female population are hardly known. In one of the few studies, performed in 273 healthy female kidney donors, 9.9% of the women were detected to have ovarian varices at preoperative abdominal aortography [20]. Interestingly, compared with the 9.9% prevalence of pelvic varices in the general population, the prevalence of 55% in the current group of women with PGAD is remarkably high. It suggests that PGAD may be associated with pelvic varices. However, as there are no data on the prevalence of PGAD complaints in menopausal women with pelvic varices, one should be cautious to ascribe PGAD solely to the presence of pelvic varices.

It should be noted that the current study also has some limitations. For example, although it is insofar the largest clinical study, which has systematically investigated PGAD by MRI scans, EEGs, and TVUS, the sample still is relatively small. Moreover, the MRI scan and TVUS of the pelvis have not been performed with tilting or Valsalva procedures, which may have resulted in an underreport of the extent of pelvic varices. For more robust confirmation of pelvic varices, venography would have been required. However, this is an invasive procedure with its own risks of bleeding and perforation.

### Conclusion

In the current series of women with PGAD, blood analysis, EEG of the brain, MRI scans of the brain, MRI scans of the pelvis, and TVUS did not show overt pathology that could causally explain the unwanted genital feelings of imminent orgasm. However, in 55% of the women, the MRI investigations of the pelvis showed indications of the existence of pelvic varices, which was confirmed by additional TVUS. In the majority of cases, the extent of the pelvic varices was rather mild. In

addition, 39% of the women had been known with varices of one or both legs. As the occurrence of pelvic varices is a rather common finding in gynecological investigations in adult women, the current findings do not allow the conclusion that PGAD is causally related to pelvic varices. However, our findings of a very high prevalence of pelvic varices may indicate an association of PGAD and pelvic varices and therefore warrants further research of the contribution of pelvic varices in PGAD. This is currently under investigation by our research group. In summary, the current study has not found clear electroencephalographic, cerebral, or pelvic anatomical abnormalities that may explain the symptoms of PGAD.

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