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# Sexual functions in women with focal epilepsy. A preliminary study

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**ABSTRACT –** We analyzed sexual function in 29 women suffering from focal epilepsy using the Female Sexual Function Index, Beck Depression Inventory, Beck Anxiety Inventory and a battery of laboratory tests were performed to find possible correlations and differences. A total FSFI score lower than the predefined cut-off score was found in 20.7% women and the presence of at least one subtype of sexual dysfunction was found in 51.7% of them. The most frequent dysfunction was lack of lubrication, which occurred in 34.5% of patients. A higher depression score was significantly correlated with a worse total score of Female Sexual Function Index and with decreased score of lubrication, satisfaction and pain. Patients who were seizure-free had better total score of Female Sexual Function Index and score of lubrication, orgasm and pain in comparison to patients who were not seizure-free. A higher anxiety scale was correlated only with lower satisfaction. We found a statistically significant correlation of reduced desire and use of carbamazepine and with lower dehydroepiandrosterone sulphate and free-androgene index. Reduced arousal was also correlated with the use of carbamazepine and lower dehydroepiandrosterone sulphate. Patients with a combination of complex partial and generalized tonic-clonic seizures had a worse total sexual function score and pain score than those with complex partial and generalized tonic-clonic seizures only. Sexual dysfunctions are relatively common problems in epileptic women with focal epilepsy. Prospective studies, including a control group, are needed.

**Key words:** epilepsy, focal, sexual dysfunction, depression, seizure-freeness

The quality of life of women patients suffering from epilepsy is, as in male patients, affected by many factors of which sexual function is also an important one. Actual studies show that the incidence of sexual dysfunction (SD) in women with epilepsy is from 20 to 30% (Harden 2006; Morrell 2002). While sexual dysfunction was recognized as a relatively common problem in men with epilepsy from the 1960's, in women the same issue was studied rather marginally. Thus knowledge of the incidence, various types and possible mechanisms of sexual dysfunction in women with epilepsy was very poor. More studies oriented towards women were repeated in the 1980's (Ndgegwa *et al.* 1986). Early research work did not discriminate between different subtypes of female sexual dysfunction, their mechanisms and specific causes. The evaluation of female sexual dysfunc-

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tion was based on self-reporting. Later on, standardized scales targeted on one or more dimensions of sexual dysfunction were used. A great deal of attention was paid to psychosocial factors. The neurophysiological basis of sexual dysfunction started to be taken into account in the 1990's. For example a study evaluating and comparing genital blood flow during audiovisual erotic stimulation in epileptic and non-epileptic men and women was performed (Morrell *et al.* 1994) with significantly worse results for epileptic patients despite equal subjective arousal level.

There are several known or presumed etiologic factors responsible for female sexual dysfunctions. The question remains as to the proportion of the possible influence of each of these factors, the exact pathophysiological mechanism and its possible solution. One of the most discussed factors is the effect of antiepileptic medication, which can contribute to sexual dysfunction by both direct cortical effects and by changes in hormone profiles mediated by induced or inhibited liver metabolism. Adversely, hormone secretion can be altered by epileptic activity itself. Carbamazepine (CBZ), phenytoin (PHT), barbiturates and of the new antiepileptic drugs (AEDs) topiramate (TPM) increase the liver synthesis of sexual hormone binding globuline (SHBG), which lowers the active free fraction of blood hormones (Ramsay and Slater 1998 ; Stoffel-Wagner *et al.* 1998). As liver enzyme inducers they also reduce the efficacy of contraception (Coulam and Annegers 1979; Penovich 2000; Lambert 2001). Valproate (VPA) as a liver metabolism inhibitor may increase blood levels of estrogen and testosterone, which can additively contribute to hyperandrogenism and polycystic ovary syndrome with amenorrhoea more often seen in women with epilepsy (Margraf and Dreifuss 1981; Isojarvi *et al.* 1993 and 1996; Sharma and Jacobs 1997; Morrell *et al.* 2003). Gabapentin (GBP) treatment may induce reversible anorgasmia (Drabkin and Calhoun 2003). As to the believed role of altered blood hormone levels in lowered sexual functions, some studies do not prove this association. However androgens seem to be responsible for sexual desire in both men and women (McEwen 1992; Rubinow and Schmidt 1996; Herzog 1999), but the exact relationship is not known.

Often repeated are the psychological and social factors – depression, anxiety, poor self-esteem and absence of a stable partner. The last factor was evaluated as an important risk factor for impaired sexual arousal, lubrication, orgasm and dyspareunia even in non-epileptic women (Artilles Perez *et al.* 2006).

Epilepsy itself and its compensation remains an important factor to be considered as a cause of sexual dysfunction. This can be seen well on the example of studies proving improvement in sexual functioning in seizure-free patients after epilepsy surgery despite continuing AED therapy (Walker and Blumer 1975; Cogen *et al.* 1979; Lambert 2001). Epileptic activity may influence the secretion of luteinizing hormone (LH) (Herzog, 1982) and prolactin (PRL) that were associated with a lack of sexual desire in a study performed on women (Herzog *et al.* 1986).

In the study by Morrell and Guldner (Morrell and Guldner 1996), sexual function and arousability together with anxiety, depression and sexual behavior was evaluated in 116 women with focal or generalized epilepsy. In spite of normal sexual experience, both groups reported less sexual arousability, and women with focal epilepsy reported more sexual anxiety. Women with focal epilepsy reported significantly more dyspareunia, vaginismus, arousal insufficiency and sexual dissatisfaction, while in women with idiopathic generalized epilepsy (IGE) more frequent anorgasmia and sexual dissatisfaction was seen. Sexual dysfunction was not related to depression, seizure frequency or any AED, and women with dyspareunia had higher depression scores.

The Female Sexual Function Index (FSFI), developed and published in 2000 (Rosen *et al.* 2000), is as a female version of the "International Inventory of Erectile Function". It was the first questionnaire screening and analyzing all types of female sexual dysfunction separately. According to the classification used in FSFI, sexual dysfunction in females is divided into 6 subtypes – desire, arousal, lubrication, orgasm, satisfaction and pain, taking in account possible different mechanisms concerned in each subtype and their possible specific etiologic factors. Our study was designed to evaluate the occurrence and types of sexual dysfunction in women with focal epilepsy treated with antiepileptic mono or polytherapy by the means of FSFI, and to evaluate an association with possible variables (depression and anxiety scores, epilepsy compensation and antiepileptic medication - classical versus new AEDs). Our aim was to achieve a more detailed analysis of the possible impingement of all these factors on separate types of sexual dysfunction.

## Methods

### Demographic data

In our study we analyzed sexual functions, depression and anxiety scores and blood hormone levels in 29 women suffering from focal epilepsy. The women were recruited from the outpatients attending the neurological department. The age of our group ranged from 20 to 43 years with an average of 32.6 ± 6.5 years. The onset of epilepsy ranged from 3 to 38 years with an average of 17.9 ± 10.4 years.

Only patients with a stable sexual partner for at least 3 months were included in the study (15 were married, 14 lived in a couple, the average duration of partnership was 14.0 ± 5.5 years). The number of pregnancies in our series ranged from 0 to 5, with an average of 1.45 ± 1.1. The number of children ranged from 0 to 3, with an average 0.9 ± 0.81. The inclusion criteria comprised absence of severe gynecological, urological or other condi-

tions, which could be potentially responsible for the sexual dysfunction. Nine out of 29 patients took hormonal contraception.

### Epilepsy type, seizure type

Nineteen patients had been treated for temporal lobe epilepsy and 10 for extratemporal epilepsy (of which 8 had frontal lobe epilepsy and 2 had epilepsy with onset at the parieto-occipital region). The diagnosis was made on the basis of seizure semiology, EEG and MRI findings. Symptomatic brain lesions were found in 16 patients, 8 of them had mesiotemporal sclerosis, and 2 of them low grade glioma. In the 6 remaining patients the following types of lesions were revealed: post-traumatic lesions, dysembryoplastic neuroepithelial tumour, malformation of cortical development, cavernoma, arachnoid cyst and post-inflammatory lesions. 7 out of the whole group underwent resective surgery in the treatment of their epilepsy.

The duration of epilepsy ranged from 1 to 31 years with an average of 14.6 ± 9.2 years. In the life course in 15 out of the whole group only complex partial seizures (CPS) occurred, while 4 patients suffered from generalized tonic clonic seizures (SGTCS) only and 10 had a combination of both types.

Ten patients have been seizure-free for a period longer than 3 months and 19 patients have experienced seizures in this period. In patients who have not been seizure-free the average frequency of seizures counted on the basis of the preceding 3 months was 4.1 ± 5.8 seizures per month (ranged from 0.3 to 24 seizures per month). The average frequency of partial seizures was 4.1 ± 5.9 seizures per month, while the average frequency of generalized tonic clonic seizures was 0.4 ± 0.7 seizures per month.

### Antiepileptic drug treatment

All of the patients have been treated by the use of AEDs. Thirteen patients were treated by the use of monotherapy (lamotrigine [LTG] – 7 patients, CBZ – 4 patients, levetiracetam [LEV] and pregabalin [PGB] – 1 patient). Thirteen patients were treated by a combination of 2 AEDs (1 patient with a combination of CBZ and VPA, 1 with CBZ and clonazepam [CLN], 8 patients treated with combination of VPA, CBZ or oxcarbazepine [oxCBZ] with one newer AED and 2 patients with a combination of 2 newer AEDs). There were 3 patients treated with a combination of 3 AEDs – one was treated with CBZ and VPA in combination with one newer AED, 2 out of them treated with combination of CBZ with 2 newer AEDs.

For the purpose of analysis we distinguished between classical AEDs (CBZ, oxCBZ, VPA, CLN) and new AEDs (LTG, LEV, PGB, TPM).

The AED therapy had to be stable at least 3 months prior to the study. In all patients the serum levels of lamotrigine and classical AEDs were verified to exclude noncompliance.

### Assessment of patients' sexual function

For the assessment of patients' sexual function we used the Czech version of FSFI which evaluates 6 particular domains of sexual function separately – desire, arousal, lubrication, orgasm, satisfaction and pain. This questionnaire consists of 19 questions. Two questions evaluated desire, 4 questions arousal, 4 questions lubrication, 3 questions orgasm, 3 questions satisfaction and 3 questions concerned pain. To rectify the disproportion in the number of questions among the subtypes the score for each subtype has a specific factor to be multiplied by. The end score for each subtype then varies from 0 to 6 with the exception of desire where it varies from 1.2 to 6. The maximum total score is 36. Wiegel *et al.* (2005) used a cut-off score of 26.55 which we also employed in our study. This means that the total FSFI score of 26.55 marks the borderline for global dysfunction. As cut-off scores for particular subtypes have not been established, we used a cut-off equal to 1 standard deviation below the mean of a normal population as reported by Rosen *et al.* (2000).

### Other assessments

To evaluate depression and anxiety in our patients we used the Czech versions of the standardized Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI).

In all of the patients, the following blood tests were performed: quantitative assessment of blood levels of prolactin (PRL), total testosterone (total-T), free androgen index (FAI), sex hormone-binding globulin (SHBG), estradiol (E2), dehydroepiandrosterone sulphate (DHEAS), progesterone (PRG), follicle stimulating hormone (FSH), luteinizing hormone (LH) and hCG to exclude pregnancy. PRL, E2, PRG, LH and FSH levels were determined using immunoanalysis assays (Advia Cantaur analyzer, Bayer). Total-T, SHBG, hCG and DHEAS levels were determined by electrochemiluminiscence assay with Elecsys 2010 analyzer (Roche). FAI was calculated according to following formula: FAI = testosterone x 100 / SHBG.

Blood levels of triiodethyronine (T3), free thyroxine (fT4) and thyroid-stimulating hormone (TSH) were assessed by the use of Microparticle Enzyme Immunoassay (MEIA) – (AxSym analyzer, Abbott).

Blood was taken in the early follicular phase to obtain the most comparable results.

Both total FSFI scores and FSFI subscale scores for each particular type of sexual function were correlated with age, duration of sexual partnership, number of pregnancies, number of children, duration of epilepsy, type and lateralisation of epilepsy, seizure frequency, laboratory findings and depression and anxiety scores (BDI and BAI).

The study was approved by the local ethics committee at St. Anne's Hospital, Brno. All of the patients signed an informed consent.

### Statistics

A statistical analysis was performed independently by an expert in biostatistics from an independent academic institution. The Pearson correlation test, Kruskal-Wallis test and Mann-Whitney test were used for the statistical analysis. A p value < 0.05 was considered to be statistically significant.

## Results

### Incidence of sexual dysfunctions *(figure 1)*

A total FSFI score lower than the predefined cut-off score (26.55) was found in 6 out of 29 evaluated women (20.7%). Three were found dysfunctional in all subtypes, 2 were dysfunctional in five of 6 subtypes and 1 was identified to have 2 abnormal subscores (for arousal and lubrication).

The presence of at least one subtype of sexual dysfunction was found in 15 out of 29 women examined (51.7%). Eight of them suffered from one isolated sexual dysfunction subtype (3 had lack of lubrication, 3 lack of desire, 1 suffered from dyspareunia, and 1 was not satisfied with her sex life), while other subscores were normal. Two women suffered from a combination of 2 types of dysfunction (lubrication + arousal deficit or lubrication + desire deficit). Two women suffered from a combination of 5 subtypes of sexual dysfunction and 3 women were dysfunctional in all 6 subtypes.

The most frequent dysfunction was lack of lubrication, which occurred in 10 out of 29 patients (34.5%). The lack of lubrication was present in combination with other types of sexual dysfunction in 7 patients, while in 3 patients it was seen in isolation.

A lack of desire was found in 8 out of 29 patients (27.6%). The lack of desire was present in combination with another type of sexual dysfunction in 5 patients, and in 3 patients it was an isolated disorder.

Dyspareunia was found in 6 out of 29 patients (20.7%). Dyspareunia was present in combination with another type of sexual dysfunction in 5 patients and in 1 patient it was an isolated disorder.

An arousal deficit was found in 6 out of 29 patients (20.7%). It was present always in combination with another type of sexual dysfunction.

Orgasm was impaired in 5 out of 29 patients (17.2%). It was also always present in combination with another type of sexual dysfunction.

Finally a lack of satisfaction with sex life was noted also in 5 out of 29 patients (17.2%). In 4 cases it was present in combination with another type of sexual dysfunction and in 1 case it was an isolated dysfunction.

### Incidence of depression and anxiety *(figure 2)*

The average BDI score was 11.3 ± 8.4. 16 out of 29 examined women had some degree of depression evaluated by the BDI score (55.2%). According to BDI score range the depression was mild in 9, moderate in 5 and severe in 2 patients.

The average BAI score was 14.6 ± 11.8. Seven out of 29 women examined had some degree of anxiety evaluated by BAI score (24.1%). According to the BAI score range the anxiety was moderate in 5, and severe in 2 patients.

Neither the total FSFI score nor the scores of all the subscales of FSFI (desire, arousal, lubrication, orgasm, satisfaction and pain) were influenced by age, duration of epilepsy, the age of onset of epilepsy, number of pregnancies, number of children, duration of the partnership with the sexual partner, being married or not and the usage of contraception. Correlation analysis did not show a statistically significant correlation between sexual functions defined by FSFI

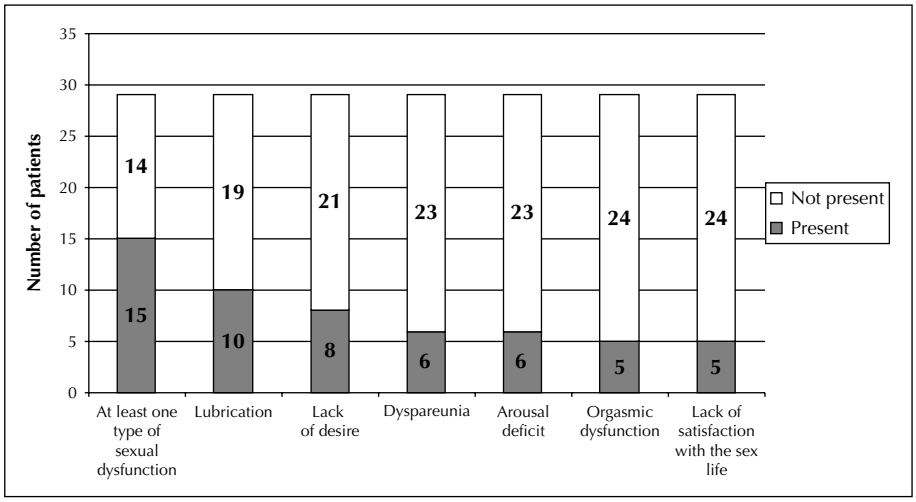


**Figure 1.** Incidence of sexual dysfunction.

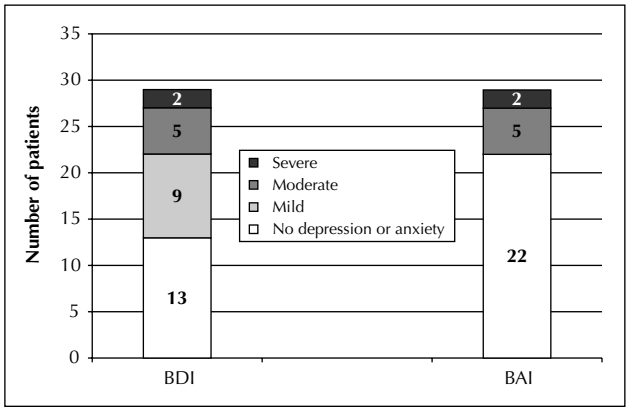


**Figure 2.** Incidence of depression and anxiety.

and localization of seizure onset (temporal *versus* extratemporal), lateralisation of seizure onset, etiology (symptomatic versus cryptogenic), frequency of both generalized and complex paritial seizures and number and type of AEDs (classical versus newer antiepileptic drugs). The following statistically significant findings were noticed.

### Total score of FSFI

Total score of FSFI was significantly correlated with the following variables: Patients who were absolutely seizure-free had a better total score of FSFI in comparison with patients who were not (30.8 ± 2.6 *vs* 26.3 ± 3.1; p = 0.046). Also the type of seizure in patients past history significantly influenced the total FSFI score. Patients who experienced the combination of CPS and SGTCS had the worst total score in comparison to patients who experienced only CPS and only SGTCS in their past history (CPS+SGTCS – 25.3 ± 7.5; CPS only – 28.4 ± 5.1; SGTCS only – 32.3 ± 2.1; p = 0.042). A lower BDI score was positively correlated with a lower total score (p = 0.042), which means that the lower the depression scale was, the lower the sexual functions were. No other statistically significant correlations and differences were found in terms of total FSFI score *(table 1)*.

### Sexual desire

The lower score of sexual desire was significantly correlated with lower blood levels of DHEAS and lower values of FAI (p = 0.01 respectively 0.008). Nevertheless other

**Table 1.** Statistically significant correlations and differences between sexual dysfunctions and other variables.

| | Correlations (Pearson correlation test) | | | | Differences between groups (Kruskal-Wallis and Mann-Whitney tests) | | |
|---|---|---|---|---|---|---|---|
| | **BDI** | **BAI** | **DHEAS** | **FAI** | **Seizure-free *vs* not seizure-free** | **Type of seizures (GTCS + CPS/ CPS only/ oGTCS only)** | **Type of AEDs treatment (only newer/ newer + conventional/ conventional only)** |
| Total score of FSFI | p = 0.042 | NS | NS | NS | 30.8 ± 2.6 *vs* 26.3 ± 3.1 p = 0.046 | 25.3 ± 7.5 *vs* 28.4 ± 5.1 *vs* 32.3 ± 2.1 p = 0.042 | NS |
| Desire | NS | NS | p = 0.01* | p = 0.008* | NS | NS | 6.5 ± 1.8 vs 4.6 ± 1.9 *vs* 5.5 ± 1.2 p = 0.042 |
| Arousal | NS | NS | p = 0.033* | NS | NS | NS | NS |
| Lubrication | p = 0.046 | NS | NS | NS | 18.7 ± 1.6 *vs* 14.7 ± 4.7 p = 0.004 | NS | NS |
| Orgasm | NS | NS | NS | NS | 13.8 ± 1.7 *vs* 11.2 ± 3.4 p = 0.02 | NS | NS |
| Satisfaction | p = 0.049 | p = 0.045 | NS | NS | NS | NS | NS |
| Pain | p = 0.042 | NS | NS | NS | p = 0.067** | 11.3 ± 3.7 *vs* 13.9 ± 3.2 *vs* 14.25 ± 1.5 p = 0.017 | NS |

* Positive correlation with lower DHEAS and FAI and CBZ treatment; ** borderline significance; NS: not significant.

analyses showed an association with antiepileptic drug treatment. Patients with a decrease in sexual desire were treated with CBZ either in monotherapy or in polytherapy in 61.9%, whereas patients who were not experienced lower sexual desire only in 12.5% (p = 0.003). The type of the AED treatment influenced sexual desire as well. A higher score of sexual desire was found in patients treated only by new AEDs either in monotherapy or in polytherapy than in patients treated by a combination of conventional and newer AEDs or only by conventional AEDs (newer AEDs – 6.5 ± 1.8; conventional + newer AEDs – 4.6 ± 1.9; only conventional AEDs 5.5 ± 1.2; difference between groups – p = 0.042). No other significant correlations or differences were found *(table 1)*.

**Sexual arousal**

The lower score of sexual arousal was significantly correlated with lower blood levels of DHEAS (p = 0.033). Also here the association with antiepileptic drug treatment was noticed. Patients with a decrease of sexual arousal were treated with CBZ either in monotherapy or in polytherapy in 62.5%, whereas patients who had not experienced lower sexual arousal only in 38.5% (p = 0.037). No other statistically significant correlations and differences were found *(table 1)*.

**Lubrication**

The disturbance of lubrication was significantly correlated with seizure-freeness. Patients who were seizure-free during a pre-defined time period had a better lubrication score in comparison with those patients who were not (18.7 ± 1.6 in seizure-free patients *vs* 14.7 ± 4.7 in non seizure free patients; p = 0.004). A lower BDI score was positively correlated with a lower score of lubrication (p = 0.046), which means that the lower the depression scale was, the worse the lubrication. No other statistically significant correlations and differences were found *(table 1)*.

**Orgasm**

The disturbance of orgasm was significantly correlated with seizure freedom. Patients who were seizure-free during a pre-defined time period had a better orgasm score in comparison to those patients who were not (13.8 ± 1.7 in seizure-free patients *vs* 11.2 ± 3.4 in non seizure-free patients; p = 0.02). No other statistically significant correlations and differences were found *(table 1)*.

**Satisfaction with sex life**

Satisfaction with sex life was not significantly correlated with seizure freedom, although patients who were seizure-free were more satisfied with their sex lives in comparison with patients who were not (p = 0.103). Nevertheless lower satisfaction with sex life was correlated with both depression and anxiety (defined by BDI and BAI). A significant lower satisfaction with sex life was positively correlated with lower BDI and BAI scales (p = 0.049 and p = 0.045). No other significant correlations or differences were found *(table 1)*.

**Pain**

Pain during sexual intercourse was not significantly correlated (borderline significance) with seizure freedom, although patients who were seizure-free had a better pain score in comparison with patients who were not (p = 0.067). The score of pain during sexual intercourse was statistically significantly correlated with the BDI scale. The worse the BDI scale was, the worse was the score of the pain (p = 0.042). Also the type of seizures previously experienced significantly influenced the pain score. Patients who experienced a combination of CPS and SGTCS had a worse pain score in comparison to patients who experienced only CPS and only SGTCS in their past history (CPS + SGTCS – 11.3 ± 3.7; CPS only – 13.9 ± 3.2 SGTCS only – 14.25 ± 1.5; p = 0.017). No other significant correlations or differences were found *(table 1)*.

## Discussion

According to all the available literature, sexual dysfunction had been reported in 14-86% of women with epilepsy (Walker and Blumer 1975; Jensen *et al.* 1992; Morrell *et al.* 2003; Lambert 2001). This suggests a great diversity in perception and evaluation of sexual dysfunction in the earlier studies. Early research work based on verbally self-reported sexual dysfunction could have been biased by an unawareness of SD more frequently described in patients with epilepsy (Shukla *et al.* 1979) and by selecting more sexually open patients willing to answer. Thus the incidence of SD could have been underestimated. On the contrary the higher percentage of patients with SD in some older studies might be attributed to the selection of patients with intractable epilepsy through recruitment of hospitalized inpatients. Another factor responsible for non-consistence of earlier data is probably the lack of complexity in earlier comprehension of sexual dysfunction and thus variable interpretation often limited to one or more aspects of sexuality. Harden (2006) reports the occurrence of some degree of sexual dysfunction (including libido, arousal and orgasm impairment) in 20-30% of women with epilepsy.

For the evaluation of SD and its specific subtypes, the type of epilepsy seems also to be an important factor - greater incidence of SD has been documented in focal epilepsies than in IGE (Gastaut and Collomb 1954 ; Shukla *et al.* 1979). Another study (Morrell and Guldner 1996) showed a different pattern of particular types of SD in focal epilepsy and IGE. In patients with focal epilepsy it was more frequent dyspareunia, vaginismus, arousal insufficiency

and sexual dissatisfaction. More sexual anxiety was found in focal epilepsy patients, but this was not correlated with the SD. In patients with idiopathic generalized epilepsy (IGE) more frequent global anorgasmia and sexual dissatisfaction was found. Also the presence or absence of a stable partner seems to be predictive of the quality of sexual functions. There is work showing a bimodal distribution of sexual interest in women with epilepsy dependent on whether they have a stable sexual partner (Duncan *et al.* 1997).

In our present study only patients with focal epilepsy and with a stable partner were included. As there was a surprisingly good acceptance of our research with only a negligible minority of women unwilling to complete the questionnaires we think it unlikely selection bias has influenced our results. We used the FSFI questionnaire, which allowed us to evaluate a wide spectrum of SD subtypes. We found that 51.7% out of our 29 female epileptic patients suffered from at least one type of SD. The total FSFI score was evaluated deficient in 20.7% of our patients. The relatively high number of patients having at least one type of SD correlates with an expected better sensitivity of FSFI to each aspect of sexual function. The relatively low number of women with a deficient total score may be attributed to the relatively high proportion of seizure-free patients who may be slightly deficient in one separate subscore but have good total scores.

The most frequent type of sexual dysfunction found in our study was deficient lubrication and lack of desire, followed by arousal deficiency and dyspareunia. A possible link between arousal, lubrication and dyspareunia was suggested but not proved in the work by Morrell and Guldner (1996), who also found a higher rate of these particular dysfunctions in patients with focal epilepsy. In our work arousal deficit, lack of lubrication and dyspareunia were found together either in women suffering from all types of SD at once or we found the 3 types rather individually with no obvious particular link among them. This might suggest different mechanisms of cause of each, but it is due to too small a sample that we are can't draw conclusions.

As to altered desire, the results of many investigations remain contradictory. Despite having quite a small sample of patients (all of them living in a stable partnership), we have proved a relatively high incidence of lowered desire which some recent studies have not shown (Duncan *et al.* 1997). We have noted the occurrence of impaired desire either individually with no other concomitant dysfunction or clustered with a greater number of them. Our study design allowed us to evaluate effectively the association of each of the factors with sexual dysfunction and its subtypes.

We found a significant correlation between reduced desire and exposure to CBZ, lower DHEAS and lower FAI. Reduced arousal was also correlated with use of CBZ and lower DHEAS. This finding is consistent with the accepted causal association of enzyme-inducing AEDs with typical hormonal changes (increased SHBG, lowered FAI and DHEAS and lowered E2) as proved by many primordial analyses performed on male and also female subjects (Mattson RH *et al.* 1985; Isojarvi 1990; Duncan *et al.* 1997; Murialdo *et al.* 1998). Traditionally androgens had been considered to play an important role in sexual functions, particularly in maintaining sexual desire and arousal (McEwen 1992; Rubinow and Schmidt 1996; Herzog *et al.* 2003). Nevertheless whether impaired sexual functions are really caused by decreases in androgen levels has always been a controversial issue. Even in the non-epileptic population some research works have shown an association between higher DHEAS and better sexual functions in women (Spark 2002; Arlt *et al.* 2000), while others dispute this effect (Davis *et al.* 2005). More recent research confirms the positive effect of DHEAS supplementation treatment on sexual function in women with adrenal androgen insufficiency (Panjari and Davis 2007). In epileptic patients the situation is even more complicated due to the fact that AED therapy is probably not the sole factor influencing hormonal levels and sexual functions. Some of the studies performed on the epileptic population dispute the impact of CBZ therapy either on sexual functions (Bergen *et al.* 1992; Duncan *et al.* 1999) or even on androgen levels (Bauer *et al.* 2000), while others prove an association (Toone *et al.* 1983). However in our work the discussed association seems to be evident. The contradictory results may be due to an absence of distinction between the subtypes of SD in many previous investigations and due to different design and statistical methodology used. Thus many etiologic factors responsible for other subtypes of SD might have interfered and the study might have failed to show the difference between the patients treated and not treated with inducing AEDs. Our study design enabled us to concentrate on impaired desire and search for the statistical correlations and possible etiologic factors among the variables. In conclusion it remains controversial whether the usage of CBZ leads to decrease of FAI and DHEAS and whether this metabolic change influences arousal and desire or whether this is an accidental finding.

With regard to other hormones, we have not shown any other changes and associations with sexual functions in our patients. However available results of clinical research suggest other possible relations – for example low estradiol was also found to be correlated to sexual dysfunction in epileptic women (Morrell *et al.* 2005).

Seizure freedom turned out to be one of the most evident and statistically significant factors for better female sexual functioning no matter whether the subject had undergone epilepsy surgery. Seizure freendom was significantly correlated with a better total FSFI score. Moreover it was also significantly correlated with better scores of lubrication and orgasm (in orgasm it was the sole evaluated significant factor). Seizure freedom was also positively correlated

with a better score of pain, although it does not reach statistical significance *(table 1)*. On the other hand in patients still having seizures there was no statistically significant correlation between seizure frequency and SD. There are controversial results concerning the association of seizure frequency and the incidence of sexual disturbances in men and women in the literature. Some authors have found no correlation between "hyposexuality" and seizure frequency in women (Morrel and Guldner 1996). On the other hand, the work by Christianson *et al.* (1995) revealed that patients who were seizure-free had a higher level of sexuality in comparison to these patients who were not. Some studies revealed an association between severity of epilepsy and SD. Jensen *et al.* (1990) noticed the increase of SD in periods of more frequent seizures and Duncan *et al.* (1997) confirmed decreased libido with increased seizure frequency in women with epilepsy. Summarizing the data from the literature and the data from our study we can conclude that although the seizure frequency and severity may have some important impact on sexual dysfunction, seizure freedom appears to be the most important factor to influence sexual behavior.

We did not notice any correlation between both the total score of FSFI and FSFI subscores regarding subtypes of sexual dysfunction and age, duration of epilepsy, the age of onset of epilepsy, number of pregnancies, number of children, duration of the partnership with the sexual partner, being married or not and the use of contraception. Bergen *et al.* (1992) and Morrell and Guldner (1996) did not reveal a positive association between the age of onset or duration of epilepsy and sexual dysfunction n epileptic women. On the other hand, Demerdash *et al.* (1991) found a positive correlation between longer duration of epilepsy and the incidence of sexual dysfunction in women.

From the other evaluated factors BDI scores turned out to be the most often evaluated as significant. Worse BDI scores were statistically significantly correlated with worse total FSFI scores and with worse lubrication, lack of satisfaction with sex life and dyspareunia. These data are very interesting because there are many controversies in relation to depression and sexual dysfunction in epileptic women. Morell and Guldner (1996) reported no significant correlation between BDI score and sexual dysfunction in 116 women with both focal epilepsy and IGE. Nevertheless the sub-analysis of their results showed that women with dyspareunia had a higher BDI score in comparison to women without this disturbance. These data correlate with our present data. We found a statistically significant correlation between higher BDI and worse pain score. It is known that sexual function may be influenced by mood and other factors. One study showed that sexual dysfunctions are mainly influenced by depression, overall wellbeing and negative experiences in sexual relationships (Laumann *et al.* 1999). Another study revealed a positive correlation between depression and sexual dysfunction (Morrell *et al.* 2005). They reported that sexual dysfunction assessed by the Sexual Behavior Inventory and Sexual Arousability Inventory was more common in women with self-reported symptoms of mild depression from the use of the BDI.

A worse anxiety score in the BAI was significantly correlated with impaired satisfaction with sex life in our work. Other types of sexual dysfunction and the total score of FSFI were not correlated with the BAI score. Similar results were reported in the literature (Morrel and Guldner, 1996).

The type of seizures experienced in the course of the epilepsy was found to be statistically significant for sexual function. Patients with a combination of CPS and SGTCS had a worse total sexual function score than those with CPS or SGTCS alone. A combination of both the seizure types was also significantly more frequent in patients with dyspareunia when compared to patients with only CPS or SGTCS. Total FSFI score was influenced not only by the seizure type but also by BDI and seizure-freeness. We did not notice any significant differences between the groups of patients with temporal and extratemporal epilepsy although a higher incidence of sexual dysfunction in patients with epilepsy arising from the temporal lobe has been reported (Demerdash *et al.* 1991).

We conclude that our study shows a relatively high incidence of distinct subtypes of SD and relatively low incidence of global SD. Thus there must be a point in distinguishing and evaluating sexual dysfunctions separately as well as in searching for specific etiologic factors.

By evaluating statistical associations in a group of patients with ill-defined and distinguished types of dysfunction some important factors may be neglected. We think that this is due to distinguishing desire and arousal from other SD subtypes where we have shown an association of classic antiepileptic medication use and hormonal changes with worse sexual desire and arousal. There was no statistical association with other SD subtypes in our study.

To conclude, our study indicates several major factors influencing sexual function in women with epilepsy. Seizure freedom and depression score seem to be the most important factors for most aspects of sexual function as well as for the total score of SD. New data show a relationship of type of seizures experienced in the course of life to SD. □

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