



Sexual quality of life in epilepsy: Correlations with sex hormone blood levels

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ABSTRACT

Seventy-nine consecutive inpatients of an epilepsy center (34 women, 45 men) who had either generalized epilepsy, temporal lobe epilepsy, focal epilepsy of other origin, or no epilepsy completed the Derogatis Interview for Sexual Function—Self-Report Inventory. Quantitative assessments of blood levels were performed for prolactin, total testosterone, sex hormone-binding globulin, estradiol, dehydroepiandrosterone sulfate, luteinizing hormone, and follicle-stimulating hormone. In men, increasing sex hormone-binding globulin levels and duration of epilepsy decreased sexual quality of life. Sex hormone-binding globulin level in men was related to enzyme-inducing antiepileptic drugs and age. In women, we found no associations between blood hormone levels and sexual quality of life. Our results suggest that sexual quality of life is affected by sexual hormone blood levels in men, but not in women with epilepsy. Avoiding enzyme-inducing antiepileptic drugs may lower the risk of raised sex hormone-binding globulin levels and, thus, of lowered sexual quality of life in men with epilepsy.

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1. Introduction

Epilepsy is related to an increased rate of sexual dysfunction in women and men [1–3]. The etiology of sexual dysfunction in epilepsy is multifactorial [4]. Endocrinological, neurological, psychological, and social factors may add to a decrease in sexual function in epilepsy [5–9]. In this study, we addressed the influence of sexual hormone blood levels on sexual well-being in epilepsy. Epilepsy may be related to altered sex hormone blood levels, leading to sexual dysfunction [7,10,11]. Bioactive testosterone correlates with sexual function in men and women, and patients with epilepsy have less bioactive testosterone than healthy persons [3,7,11–13]. Furthermore, raised levels of follicle-stimulating hormone (FSH) or sex hormone-binding globulin (SHBG) and decreased levels of dehydroepiandrosterone sulfate (DHEAS) may correlate with sexual dysfunction in men with epilepsy [13]. In women with epilepsy, decreases in estradiol or DHEAS have been reported to correlate with sexual anxiety and dysfunction [7]. In this study, we tested the influence of sex hormone blood levels on sexual quality of life in women and men with epilepsy. We hypothesized that the levels of total testosterone (TT), FSH, SHBG, DHEAS, estradiol (E2), prolactin (PRL), and luteinizing hormone (LH) may

influence sexual quality of life in epilepsy. This should especially be the case in men with epilepsy (compare [12,14–16]).

Sexual dysfunction in epilepsy may also be iatrogenic [3,17]. Enzyme-inducing antiepileptic drugs (AEDs) influence sex hormone blood levels. A possible explanation is that enzyme-inducing AEDs raise estradiol blood levels by conversion of testosterone to estradiol via aromatase. Elevated estradiol levels would then induce SHBG synthesis, thereby further decreasing the amount of bioactive testosterone [18,19], which may then lead to sexual dysfunction. Therefore, in this study we tested whether patients taking enzyme-inducing drugs would show altered sex hormone levels (especially raised SHBG levels) and lower sexual quality of life than patients taking medication that is neutral with respect to enzyme induction.

The term *sexual dysfunction* refers to such different aspects of sexual activity as erectile function and libido. In this study we documented sexual well-being with a comprehensive questionnaire covering several sexual functions and aspects in women and men [20,21] and we therefore use the term *sexual quality of life* (SQOL) [22]. SQOL encompasses at least six different domains: (1) interest, desire, and libido; (2) satisfaction with or quality of sexual experiences such as ejaculation and orgasm and pain or discomfort with sex; (3) sufficient excitement and arousal as shown, for example, by morning erection or sufficient lubrication for intercourse; (4) the ability to achieve an orgasm; (5) attitudes or behaviors of the person and his or her partner such as feelings of avoidance and embarrassment and change in frequency of sexual intercourse; (6) the impact of sexual functioning on the relationship [21,22].

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2. Methods

2.1. Patients

This study received prior approval from the ethics committee of the Protestant Hospital Alsterdorf and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Each participant gave informed consent to the study. Seventy-nine consecutive inpatients of the Epilepsy Center Hamburg were included in this study (34 women, 45 men). Thirteen of these patients had neither epilepsy nor any psychiatric disorder. Diagnoses in this group encompassed sleep disturbances and syncope due to nonneurological reasons. We used these patients as a control group. Seventeen patients had generalized epilepsy, 34 patients had temporal lobe epilepsy, and 15 patients had focal epilepsy with foci outside the temporal lobe. Inclusion criteria were age between 18 and 65 and fluency in German. Furthermore, patients had to be willing to participate in the study and had to have completed questionnaires (see Procedures). Exclusion criteria were psychiatric diagnoses other than depression or anxiety disorder and verbal intelligence quotient below 75. Crystallized verbal intelligence quotient (IQ) was estimated with the German vocabulary test Wortschatztest (words of increasing difficulty have to be recognized among phonologically similar nonsense words) [23]. In addition, patients with diabetes mellitus, high blood pressure, liver or kidney diseases, and hypothyroidism were excluded from the study. In addition, patients taking medication other than AEDs, including antidepressant medications, were also excluded from the study.

2.2. Procedures

All patients admitted to the Epilepsy Center Hamburg between February 2006 and March 2007 were asked to participate in the study if they were between 18 and 65 years old, fluent in German, and had no learning disability as evident from patient history and direct communication. Sixty-two of 199 patients we intended to include in the study (31%) refused to take part or did not return the questionnaires. Of these patients, 3 had generalized epilepsy, 34 had focal epilepsy, 12 had a psychiatric diagnosis, 9 had diagnoses other than epilepsy or psychiatric illness, 2 had epilepsy of unclear etiology, and in two patients the diagnosis remained unclear even after intensive video/EEG monitoring. Thirty patients were women, and 32 were men. Mean age was 37 years ($n = 62$; $SD = 12$). Of the remaining 137 patients, we further excluded 58 patients for the following reasons. Forty-eight patients had a psychiatric disorder other than depression or anxiety disorder (e.g., substance or alcohol abuse, borderline disorder, anterograde amnesia). Twenty-three patients had a neurological diagnosis other than epilepsy (e.g., severe head injury, stroke): 13 had a diagnosis of substance abuse, 1 had a urological diagnosis, 3 had thyroid disease, 3 had heart disease, and 7 had other diagnoses (e.g., asthma). Please note that many patients had two or more reasons that led to exclusion.

Patients received the questionnaire during the first 3 days of their stay at the Epilepsy Center, as the items on the questionnaire relate to the preceding 4 weeks. Blood samples were taken on the morning of the second day of their stay in the Epilepsy Center, when no significant medication changes had been performed yet (for further details see below). Medication information at the time of admission was taken from the patients' files. Patients were blind to their blood hormone levels when completing the questionnaire.

2.3. Assessment of SQOL

We employed the German version of the Derogatis Interview for Sexual Function—Self-Report Inventory (DISF-SR) [20,21,24]. The

inventory includes separate versions for women and men, both composed of 25 items assessing five domains: Cognition and Fantasy (abbreviated Fantasy, 5 items), Arousal (5 items), Behavior and Experience (abbreviated Experience, 5 items), Orgasm (6 items), and Drive and Relationship (abbreviated Relationship, 4 items). In the domains Fantasy, Experience, and Relationship, the questionnaire items are identical for women and men. In the domain Arousal, all items differ between the versions for women and men; and in the domain Orgasm, two items differ. To sum up, 7 of 25 items differ between the versions for women and men. Items are answered on either a 4- or 8-point scale. The 4-point scale ranges from “not at all” to “very much so.” One 8-point scale ranges from “not at all” to “4 times a day or more often,” and the second 8-point scale ranges from “could not be worse” to “could not be better.” The DISF-SR has proven reliability (internal consistency, test–retest and interrater reliability) and construct validity [21] and provides gender-keyed norms. Higher scores represent better SQOL. We report Area T scores for women and men for the five subscales and the overall score as provided by the test manual. Area T scores are normalized percentile rankings. A value of 50 designates the normal mean, with a SD of 10. Norms are based on several hundred nonpatient community respondents.

2.4. Assessment of blood hormonal profiles

Morning blood samples were drawn between 8 and 9 AM after an overnight fast. They were centrifuged, and hormonal assays were performed the same day or the next day after overnight storage of the sample in a refrigerator. The following quantitative assessments of blood levels were performed: PRL, TT, SHBG, E2, DHEAS, LH, and FSH. PRL, TT, E2, DHEAS, LH, and FSH were determined with electrochemiluminescence immunoassays (Roche); SHBG was determined with a chemoluminescence immunometric assay (Diagnostic Products Corp.). Two sets of controls with different concentration levels were used within each assay run. Free androgen index (FAI) was calculated according to the equation $FAI = TT \times 100 / SHBG$. For women, the day of the menstrual cycle was documented.

2.5. Diagnostic workup

All patients underwent a diagnostic workup with 24- to 72-hour video/EEG monitoring and were investigated by structural magnetic resonance imaging (MRI). The diagnosis of temporal lobe epilepsy (TLE) was based on seizure semiology (e.g., epigastric or déjà vu aura, alimentary or hand automatisms, dystonic arm posturing during seizures, duration of seizures 1–5 min, gradual termination, postictal confusion, amnesia or partial amnesia) and interictal or ictal EEG abnormalities. Auras and seizure semiology were documented either as reported by the patient or witnesses or by videotelemetry or video/EEG monitoring [25–27]. Idiopathic generalized epilepsy was defined by typical semiology of juvenile myoclonic epilepsy, absence seizures, or primary generalized tonic-clonic seizures and generalized EEG patterns during video/EEG monitoring. For the purpose of this study, seizure frequency was operationalized as rare (≤ 1 /year), often (>1 /year, but ≤ 1 /week), or very often (>1 /week).

2.6. Mono- versus polytherapy, enzyme-inducing AEDs

Patients taking only one AED were classified as receiving “monotherapy,” and patients taking more than one AED were classified as receiving “polytherapy.” Patients receiving phenytoin, carbamazepine, or primidone were classified as “taking an enzyme-inducing AED”; patients taking all other AEDs were classified as “taking a non-enzyme-inducing AED.”

2.7. Statistical methods

We tested differences in demographic and clinical variables and blood hormonal levels between groups using *t* tests, analyses of variance (ANOVAs), Mann–Whitney *U* tests, Kruskal–Wallis ANOVAs, and χ^2 tests. When subgroup sizes were small, we recalculated results with parametric and nonparametric statistics. If the results differed, we described both parametric and nonparametric tests (see Tables 3 and 4); otherwise, we described parametric results. Relationships between hormones and SQOL were analyzed by correlations and multiple regression analysis using the DISF-SR overall score. Correlations with subscales are reported only when variables correlated with the overall score, to avoid inflation of significance tests. We also employed partial correlations to test the relationship of age, duration of epilepsy, and sex hormone blood levels to the DISF-SR overall score.

3. Results

Comparisons of the different patient groups and of women and men, with respect to demographic and clinical data, are provided in Tables 1 and 2, respectively.

3.1. Influence of hormones on SQOL

Hormone levels of the different patient groups are summarized in Table 3 (women) and Table 4 (men). In the first step, we analyzed the influence of hormones on SQOL. We calculated correla-

tions between hormone levels and the DISF-SR overall score. For women, we excluded three postmenopausal women (at least 1 year without monthly periods). We further excluded three perimenopausal women (44, 46, and 47 years old) with FSH levels >25 U/L (reference interval for ovulation phase is 4.7–21.5 U/L, postmenopausal reference interval starts at >25 U/L; calibration: 2nd WHO Reference Standard IRP 78/549), resulting in $n = 28$ (see Table 3). We excluded post- and perimenopausal women to avoid confounding factors and exclude alternative explanations of the results. TT showed a trend toward a negative correlation with DISF-SR overall score ($r = -0.33$, $P = 0.09$). After female control participants were excluded, no correlations were found ($n = 24$). For men ($n = 45$), DISF-SR overall score correlated with levels of PRL ($r = -0.42$, $P = 0.006$), LH ($r = -0.38$, $P = 0.01$), FSH ($r = -0.37$, $P = 0.01$), DHEAS ($r = 0.34$; $P = 0.03$), TT ($r = -0.33$, $P = 0.03$), and SHBG ($r = -0.50$, $P = 0.001$). When male control participants were excluded ($N = 37$), all reported correlations remained significant (P 's < 0.02), except for TT ($r = -0.32$, $P = 0.06$). We included the variables correlating with DISF-SR overall score as independent variables in a forward regression analysis with the dependent variable DISF-SR overall score using an inclusion criterion of $F > 3.0$ and an exclusion criterion of 0. The resulting regression model included SHBG ($\beta = -0.42$ (SD = 0.14), $t(41) = -2.9$, $P = 0.006$) and PRL ($\beta = -0.26$ (SD = 0.14), $t(41) = -1.8$, $P = 0.08$). The model explained 28% of the variance of SQOL (corrected R^2 , $F(3,41) = 8.1$, $P < 0.001$). When control participants were excluded, the same regression analysis included SHBG only, explaining 25% of variance ($F(1,35) = 11.5$, $P = 0.002$).

Table 1
Comparison of different patient groups with respect to demographic and clinical information.

Variable	GE ($n = 17$)	Focal epilepsy ($n = 15$)	TLE ($n = 34$)	Controls ($n = 13$)	<i>P</i>
Sex (women/men)	8/9	7/8	14/20	5/8	0.95 ^a
Age ^b	28 (9)	37 (12)	38 (11)	32 (11)	0.02 ^c
MRI finding (positive/negative/no MRI)	2/8/7	2/11/2	18/15/1	0/13/0	<0.001 ^a
Verbal IQ ^b	91 (8)	101 (14)	96 (12)	99 (9)	0.12 ^c
Body mass index ^b	29 (6)	26 (4)	26 (6) $n = 31$	27 (4)	0.26 ^c
<i>DISF T scores^b</i>					
Overall	51 (14)	43 (16)	42 (19)	53 (9)	0.07 ^c
Fantasy	50 (9)	47 (10)	48 (14)	54 (7)	0.40 ^c
Arousal	50 (19)	44 (17)	46 (20)	56 (14)	0.23 ^c
Experience	45 (15)	45 (15)	42 (14)	51 (11)	0.30 ^c
Orgasm	51 (12)	43 (17)	39 (15)	52 (5)	0.007 ^c
Relationship	52 (8)	40 (12)	42 (15)	53 (6)	0.004 ^c
<i>Patient characteristics</i>					
Duration of epilepsy, median (quartiles)	10.0 (6; 24)	5.5 (2; 26)	14.5 (7; 28)		0.39 ^d
Seizure frequency (rare/often/very often)	5/4/8	3/5/7	5/13/11 $n = 29$		0.79 ^a
Polytherapy/monotherapy/no AEDs	5/10/2	4/5/6	15/15/4	0/1/12 ^e	0.12 ^a
Enzyme-inducing AEDs (no/yes)	14/1	7/2	21/9		0.62 ^a
<i>AED</i>					
Lamotrigine	8	4	10 + 1		
Valproate	5	0 + 1	5 + 4		
Carbamazepine	1	1	7 + 1	1	
Phenytoin	0 + 1	0 + 1	1		
Oxcarbazepine	1	2 + 1	7 + 1 + 1		
Topiramate	0 + 1	0 + 1	2 + 2		
Gabapentin	0 + 1	0	0 + 1		
Levetiracetam	0 + 1	0	0 + 3 + 2		
Primidone	0 + 1 + 1	0	0 + 1 + 1		
Zonisamide	0	0	0 + 1		
Ethosuximide	0	0 + 0 + 1	0		
Clonazam	0	0	0 + 0 + 1		
Hormonal contraception (yes/no)	1/7	1/6	5/9	3/2	0.22 ^a

^a χ^2 test.

^b Mean (SD).

^c ANOVA.

^d Kruskal–Wallis ANOVA.

^e Controls were not included in the inference statistical test. One control patient received carbamazepine.

Table 2

Comparison of women and men with respect to demographic and clinical information.

Variable	Women (n = 34)	Men (n = 45)	P
Diagnosis (GE/ETLE/TLE/controls)	8/7/14/5	9/8/20/8	0.95 ^a
Age ^b	33 (12)	35 (11)	0.44 ^c
Verbal IQ ^b	98 (10)	95 (13)	0.38 ^c
Body mass index ^b	26.5 (6.5) n = 34	26.9 (4.2) n = 42	0.73 ^c
<i>DISF T scores^b</i>			
Overall	44 (17) ^d	48 (16)	0.34 ^c
Fantasy	48 (12) ^d	50 (10)	0.49 ^c
Arousal	43 (15) ^d	52 (19)	0.02 ^c
Experience	45 (14) ^d	45 (15)	0.92 ^c
Orgasm	43 (13) ^d	45 (15)	0.54 ^c
Relationship	45 (14) ^d	46 (12)	0.55 ^c
<i>Patient characteristics</i>			
Duration of epilepsy, median (quartiles)	n = 29 10 (4;24) n = 29	n = 37 15 (4;26) n = 35	0.36 ^e
Seizure frequency (rare/often/very often)	4/10/13 n = 27	9/12/13 n = 34	0.64 ^a
Polytherapy/monotherapy/no AEDs	9/13/7	15/17/5	0.49 ^a
Enzyme-inducing AEDs (yes/no)	4/18 n = 22	8/24 n = 32	0.55 ^a

^a χ^2 test.^b Mean (SD).^c ANOVA.^d Excluding 3 perimenopausal and 3 postmenopausal women (n = 28), we found the following values: DISF Overall T (mean, SD) = 46 (17); DISF Fantasy T = 49 (13); DISF Arousal T = 44 (15); DISF Experience T = 46 (14); DISF Orgasm T = 44 (13); DISF Relationship T = 45 (14). Significance levels did not change, except for Orgasm T, on which women and men no longer differed significantly (P = 0.05).^e Kruskal Wallis ANOVA.

For men, SHBG correlated positively with PRL ($r = +0.36$, $P = 0.02$) and negatively with all DISF-SR subscales (r 's < -0.34 , P 's < 0.03).

At this point, it is important to note that the power to find correlations differs between women and men, because the sample size for men (n = 37) was approximately one-third larger than that for women (n = 24). This may also explain the absence of relationships between hormone levels and SQOL in women. However, please note that even when considering statistical trends ($0.10 < P \leq 0.05$) as meaningful, we could not detect any correlations between SQOL and hormones in women with epilepsy. The one trend of a negative correlation in women reported above is even counterintuitive, as it would suggest that more TT would lead to lower SQOL in women. Please note further that FAI did not correlate with SQOL, in either women or men. Summing up, we found no influence of sex hormone blood levels on DISF-SR overall score in women and a negative influence of SHBG on DISF-SR overall score and subscale scores in men.

3.2. Relationship of SHBG level, age, duration of epilepsy, and SQOL in men

SHBG correlated with duration of epilepsy ($r = 0.31$, $P = 0.08$) and age ($r = 0.41$, $P = 0.02$). When age was partialled out, SHBG no longer correlated with duration of epilepsy ($r = 0.10$, $P = 0.59$). On the other hand, when duration of epilepsy was partialled out, SHBG no longer correlated significantly with age ($r = 0.30$, $P = 0.11$). Thus, only age and duration of epilepsy combined seem to negatively influence SHBG blood levels.

Table 3

Blood hormone levels in women (excluding 3 peri and 3 postmenopausal women).

Variable	GE (n = 8)	Focal epilepsy (n = 5)	TLE (n = 11)	Controls (n = 4)	P
Day of cycle	7.0 (6.7) n = 8	14.3 (11.6) n = 3	18.9 (8.7) n = 11	20.3 (3.5) n = 3	0.02
Hormonal contraception (yes/no)	1/7	1/4	5/6	3/1	0.14
Prolactin (μ g/L)	15.0 (7.2)	26.7 (16.2)	16.3 (8.9)	14.5 (8.0)	0.18
LH (U/L)	5.8 (3.3)	6.3 (3.1)	7.1 (8.7)	3.5 (4.7)	0.81
FSH (U/L)	5.3 (0.84)	6.1 (2.4)	4.6 (3.5)	3.0 (3.3)	0.38
E2 (ng/L)	73.6 (21.0)	65.6 (56.4)	105.6 (73.3)	69.0 (98.1)	0.58
DHEAS (μ mol/L)	2.3 (1.2)	1.8 (0.7)	1.4 (0.9)	1.5 (0.5)	0.18
TT (μ g/L)	0.5 (0.2)	0.4 (0.2)	0.4 (0.2)	0.3 (0.3)	0.66
SHBG (nmol/L) ^a	90.9 (79.3)	122.7 (124.4)	182.5 (126.1)	330.7 (212.9)	0.05
	68.4 (33.0;180.0)	72.6 (52.0;100.0)	142.0 (65.0;298.0)	384.0 (179.0;484.5)	0.14
FAI (%) ^a	1.1 (1.1)	0.6 (0.3)	0.3 (0.3)	0.2 (0.1)	0.04
	0.7 (0.2;1.8)	0.6 (0.5;0.8)	0.2 (0.1;0.5)	0.1 (0.1;0.3)	0.09

^a Where parametric and nonparametric test results differ, we report median values in addition to the means.**Table 4**

Blood hormone levels in men.

Variable	GE (n = 9)	Focal epilepsy (n = 8)	TLE (n = 20)	Controls (n = 8)	P
Prolactin (μ g/L)	13.9 (4.9)	12.6 (3.9)	17.3 (16.7)	11.2 (7.2)	0.62
LH (U/L) ^a	6.3 (2.3)	4.5 (1.8)	6.5 (4.1)	4.0 (1.5)	0.17
	5.3 (4.7;7.6)	4.7 (3.0;5.8)	4.8 (3.5;8.7)	4.1 (2.7;4.5)	0.07
FSH (U/L)	3.6 (2.8)	5.5 (3.9)	7.4 (6.9)	4.8 (3.9)	0.32
E2 (ng/L)	30.2 (15.3)	29.6 (9.0)	29.0 (8.8)	33.4 (10.9)	0.81
DHEAS (μ mol/L) ^a	4.2 (1.6)	2.0 (1.2)	3.8 (6.0) ^b	4.3 (1.8)	0.70
	4.2 (3.4;5.3)	2.1 (0.8;3.3)	2.1 (1.6;3.7)	4.6 (2.6;5.6)	0.03
TT (μ g/L)	4.0 (1.1)	5.2 (1.3)	5.7 (1.6)	4.5 (2.1)	0.05
SHBG (nmol/L)	20.2 (9.1)	52.7 (16.8)	52.7 (29.5)	26.3 (9.5)	0.002
FAI (%) ^a	20.2 (12.9)	11.0 (5.0)	12.5 (4.8)	18.5 (8.1)	0.04
	18.9 (12.4;26.4)	9.6 (7.0;14.3)	13.2 (8.6;16.0)	19.2 (14.5;23.1)	0.07

^a Where parametric and nonparametric test results differ, we report median values in addition to the means.^b One outlier (28.0 μ mol/L) led to distortion of mean and SD and, thus, to very different results in parametric and nonparametric statistics. After exclusion of this outlier, parametric tests also showed a significant result (P = 0.008).

Controlling for the influence of age, SQOL remained related to duration of epilepsy ($r = -0.48$, $P = 0.006$) and SHBG level ($r = -0.44$, $P = 0.01$). On the other hand, SQOL did not correlate with age.

3.3. Influence of enzyme-inducing drugs on SHBG levels and SQOL in men

In the next step, we compared male patients taking enzyme-inducing or non-enzyme-inducing AEDs with respect to SHBG blood levels. Patients taking enzyme-inducing AEDs had higher SHBG levels ($n = 8$, median = 63.0, quartiles = 39.0; 122.0) than patients taking non-enzyme-inducing AEDs ($n = 24$, median = 39.3, quartiles = 18.5; 51.2, Mann–Whitney U test, $P = 0.03$). Poly or monotherapy had no influence on this relationship. We also found a nonsignificant trend toward a lower DISF-SR overall score in patients taking enzyme-inducing AEDs ($n = 8$, median = 36.5, quartiles = 19.0; 50.0) compared with patients taking non-enzyme-inducing AEDs ($n = 24$; median = 52.0; quartiles = 33.5; 61.5; Mann–Whitney U test, $P = 0.06$). Table 3 reveals that in our patient sample, duration of epilepsy, enzyme-inducing drugs, and diagnosis were confounded. Patients with TLE had the longest mean duration of epilepsy compared with the other groups; also, a large proportion of patients with TLE were taking carbamazepine. It may thus be that the correlation between SHBG or duration of epilepsy and SQOL is confounded with the diagnosis of TLE.

4. Discussion

In this study, we found that SHBG level influences SQOL in men with epilepsy. Increasing SHBG levels and longer duration of epilepsy decreased SQOL in men. Furthermore, an increased SHBG level in men was related to intake of enzyme-inducing AEDs and age. In women, we found no associations between blood hormone levels and SQOL.

Our results expand on other studies demonstrating an association between SHBG level and sexual function in men with epilepsy [13]. Explanations of this relationship differ. Some authors assume SHBG reduces SQOL via reduction of free testosterone and/or albumin-bound testosterone [18,19]. However, a recent study reported increased SHBG levels in hyposexual patients with normal serum testosterone [28]. Together with the results of this study, this points to an independent effect of SHBG on SQOL. Another explanation worth mentioning is that SHBG may induce synthesis of estradiol, which is assumed to reduce SQOL in men. Still, as serum estradiol did not differ between diagnostic groups in this study, this explanation also is not sufficient. The way in which increased SHBG levels influence SQOL in men with epilepsy must be further examined in future studies.

In this study, we found that duration of epilepsy negatively influenced SQOL in men. A possible explanation is that in men with epilepsy, the increased SHBG levels caused by enzyme-inducing AEDs and the physiological increase in SHBG with age [e.g., 29] interact and lead to a steeper increase in SHBG levels in men with epilepsy over the years, thus resulting in lower SQOL with increasing duration of epilepsy. In this study we used a more comprehensive questionnaire to describe sexual dysfunction than was used in former studies. This may explain why we found a correlation between duration of epilepsy and SQOL when a previous study could not detect this relationship [3]. Those authors found an accelerated decrease in bioavailable testosterone over three decades (ages 20–50) in patients with TLE taking enzyme-inducing drugs, as well as in untreated patients with focal epilepsy, suggesting a cumulative influence of epilepsy on blood hormone levels [3].

Our study suggests that SHBG level is related to enzyme-inducing AEDs in men. In addition, we noted a relationship between en-

zyme-inducing AEDs and lowered SQOL, which just missed statistical significance. These results are in line with studies that have reported sexual dysfunction in men with epilepsy treated with enzyme-inducing AEDs [e.g., 3].

We could not find a relationship between hormonal blood levels and SQOL in women. This may be due to the fact that we did not standardize the day of the menstrual cycle on which blood samples were drawn, as is the gold standard procedure. Blood samples had to be drawn during the stay of the patients in the epilepsy clinic and before medication regimens were changed. Therefore, standardization of the day of the cycle was not possible in this clinical study. This is an important issue for the meaningful analysis of data. There are substantial differences between follicular, periovulatory, and luteal phase testosterone levels in women and these differences may have prevented us from demonstrating an existing relationship between testosterone levels and SQOL in women as compared with men. However, the lack of correlations between sex hormones and SQOL in women that we report in this study is in line with a recent study in which blood samples were drawn on standardized days 3–7 of the menstrual cycle. The authors describe little influence of sex hormones on SQOL in women with epilepsy, and report lower correlations of sexual dysfunction with hormone levels in women with epilepsy than in healthy controls [11]. Another former study could not find an influence of hormone blood levels on sexual activity and attitudes in women with epilepsy [30]. A more recent study found correlations between estradiol and DHEAS and different subscales of sexual dysfunction in women. However, correlations were low (0.24–0.31) and the authors had run multiple correlation analyses, raising the risk of chance findings [7]. Also, they mixed healthy controls and patients with epilepsy, and did not report correlations for patients with epilepsy alone. In this study, we found many and high correlations between SQOL and sex hormones in men and only few such correlations in women. This is in line with the overall picture in the literature, where more correlations between sexual dysfunction and sex hormones are reported for men than for women [e.g., 3,13,16].

Our conclusion that endocrinological factors may have a more substantial influence on SQOL in men than in women is in line with a study that found an impact of biological factors in men, whereas in women sexual problems were associated with psychological factors [31]. Similarly, poor health has been found to be a risk factor for a number of sexual problems in men, but only for sexual pain in women. In women, sexuality may be more strongly related to emotional well-being [32]. Together with the findings of this study, these results suggest that physiological variables in general seem to be more important for SQOL in men than in women.

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