CHAPTER 9

Subjective sleep disturbance in patients with partial epilepsy: a questionnaire-based study on prevalence and impact on quality of life


Al de Weerd¹, Sanne de Haas², Andreas Otte², Dorothée Kastelein-Nolst Trenité ⁴, Gerard van Erp ⁵, Adam Cohen², Marieke de Kam², Joop van Gerven²

¹ Centre for Sleep & Wake Disorders, Medical Centre Haaglanden, Westeinde Hospital, The Hague, The Netherlands
² Centre for Human Drug Research (CHDR), Leiden, The Netherlands
³ International Medical Research, Pfizer Group Pharmaceuticals, Freiburg, Germany
⁴ Epilepsy Centre ‘Meer en Bosch’, Heemstede, The Netherlands
⁵ Epilepsy Centre ‘Kempenhaeghe’, Heeze, The Netherlands
ABSTRACT

Purpose: This study was designed to assess whether sleep disturbance is more frequent among patients with partial seizures and what impact on quality of life (QoL) sleep disturbance may have on patients with partial seizures.

Methods: Questionnaire booklets were mailed to 1183 patients from four Dutch clinics. Each patient was asked to find two matched controls to complete the same set of questionnaires (Sleep Diagnosis List [SDL], Medical Outcomes Study [MOS]-Sleep Scale, Groningen Sleep Questionnaire, Epworth Sleepiness Scale and the SF-36™ Health Survey). The prevalence of sleep disturbance, based on the SDL, was compared between those with partial epilepsy and controls. Mean scores on sleep and the SF-36 Physical (PCS) and Mental (MCS) Component Summary scales were compared.

Results: Responses from 486 patients and 492 controls were analysed. Respondents with partial epilepsy had a highly significant, 2-fold higher prevalence of sleep disturbance compared with controls (38.6% vs. 18.0%; p<0.0001). Most sleep-disturbance subscales showed significant abnormalities in respondents with epilepsy, compared with controls. Mean SF-36 Total Mental and Physical Health summary scores were significantly lower in respondents with epilepsy compared with controls in both the strata with sleep disturbance and without (all p<0.05). The presence of a sleep disturbance in respondents with epilepsy was associated with the greatest impairment in QoL.

Conclusions: Sleep disturbance is over twice as prevalent in persons with partial epilepsy compared with controls, and most domains of sleep are significantly disturbed. Persons with partial epilepsy have significant QoL impairment, and sleep disturbance further compounds this.

156 PHARMACOLOGICAL DIFFERENCES OF GABAERGIC COMPOUNDS: A PHARMACODYNAMIC CHARACTERIZATION
INTRODUCTION

An often stigmatizing, unpredictable and disabling illness, epilepsy, affects 0.5-1% of people [1,2], of whom 60% are estimated to have partial epilepsy (focal epilepsy) [3,4]. The WHO 2000 study found that the global physical, social, economic consequences of epilepsy are high, accounting for 0.5% of the whole burden of diseases in the world [5]. Improving quality of life is increasingly being recognized as an important goal of epilepsy treatment [6]. Sleep disturbance is known to be associated with impairment of quality of life both in people with chronic illnesses [7] and in those without [8,9]. There are many possible relationships between sleep disturbances and epilepsy. These include sleep disorders related to psychosocial and mood disturbance that are associated with epilepsy [10,11] medication effects [12], nocturnal seizures [11,13] and daytime seizures [13]. Conversely, sleep disturbances can contribute to impairment of seizure control [13].

Given the prevalence of partial epilepsy and the quality of life impairment associated with epilepsy and the interrelationships between epilepsy and sleep disturbance, it is surprising that the clinical relevance of sleep disturbance has not been well studied. Here we describe the results of a cross-sectional study conducted in The Netherlands that sought to determine the prevalence and characteristics of subjective sleep disturbance in people with partial epilepsy and the impact this might have on quality of life.

METHODS

Participants

Men or women ≥ 18 years of age, diagnosed as having partial epilepsy with or without secondarily generalised seizures, taking one or two antiepileptic drugs (AEDs), were selected from two Dutch epilepsy clinics (Meer en Bosch and Kempenhaeghe) and two Dutch neurology outpatient clinics (Medical Centre Haaglanden, Westeinde Hospital and Leiden University Medical Centre) and requested by mail to take part in the survey. It was thought that by including patients on one or two AEDs and not including more severely ill patients would provide a study sample most representative of patients with partial seizures in the general population. In addition, by excluding the more severely ill patients on three or more AEDs, who could be expected to experience increased drug side-effects and might be expected to have more sleep problems than less severely ill patients, the extent of sleep disturbance in the partial epilepsy sample was not confounded by
these factors. Each patient was asked to find two people of the same age (within 5 years) and gender to take part, who were not partners or cohabitants who did not have epilepsy, and were not taking AEDS for any indication.

Survey methods

Questionnaire booklets, that included instructions for completing questionnaires, were posted to a total of 1183 patients. The Medical Ethics Committee of the Leiden University Medical Centre approved the study protocol and agreement was obtained from all participating centres. Letters from the responsible physician of each centre, explaining the purpose of the study to the patient and to age-matched controls, accompanied the booklets. Feedback was requested within 2 weeks (stamped addressed envelopes supplied), also if no age-matched controls were found. Patients, but not controls, were sent a reminder if they did not return the questionnaire within 3 weeks. Consent was inferred if the questionnaire was returned. Subjects with incomplete questionnaires were telephoned, if they agreed to be contacted for further information. The study was closed 5 weeks after mailing the questionnaires. All questionnaires were reviewed by an epileptologist to ensure inclusion criteria were met and to check for completeness of questionnaires. Patients were selected from outpatient databases at the clinicians based on having partial epilepsy. However, if insufficient information was available from questionnaires to ensure confirmation of a diagnosis of partial epilepsy, patients were contacted by phone to elaborate on their seizure symptomatology.

Questionnaires

The patient booklet included the following questionnaires: demographic and short health questionnaire previously used in the Dutch population [14], WHO epilepsy questionnaire [15], Sleep Diagnosis List [16] derived from the Sleep Diagnosis Questionnaire [17], Medical Outcomes Study (MOS)-Sleep Scale [18], Groningen Sleep Questionnaire (GSQ) [19-21], Epworth Sleepiness Scale (ESS) [22,23] and SF-36™ Health Survey [24,25]. All questionnaires were validated in Dutch or have been employed as research tools in The Netherlands for over 10 years. Patients and controls received identical booklets. The WHO epilepsy questionnaire was included in the control group booklet to exclude history and presence of epilepsy.

The SDL, which consists of 75 randomly distributed questions about six common sleep disturbances (e.g. insomnia, sleep apnea, periodic leg movements, daytime sleepiness) in the past 6 months,
was answered on a five-point scale from 1=never to 5= very often or always. A total mean score ≥ 3 in a category indicated the presence of a sleep disturbance. The MOS-Sleep Scale evaluated sleep in the past 4 weeks and included 12 questions about sleep, answered on a six-point scale from 1=all of the time to 6=none of the time, as well as perceived duration of sleep and sleep latency. Optimal sleep was defined as 7-8 hours/night. The GSQ included 14 questions about sleep the previous night, answered Yes (=1) or No (=0). A total score of ≤ 8 indicated disturbed sleep during the previous night. The ESS asked eight questions about how often a person dozed during day-to-day activities, answered on a four point scale from 0=never doze to 3=high chance of dozing. A total score ≥ 10 is generally taken to represent daytime sleepiness.

The SF-36 is a multidimensional questionnaire composed of 36 items, divided in 8 dimensions (Physical function, Role Limitations due to Physical Function, Bodily Pain, General Health, Vitality, Social Function, Role Limitations due to Emotional Function and Mental Health) and evaluates the negative health aspects (disease or illness) and the positive aspects (well-being). Mental and Physical Component Summary scores can be derived from the eight SF-36 scales. These component summaries have been found to discriminate among levels of severity in a variety of chronic diseases with a standardized mean score of 50 [26].

Statistical analysis

As this was an exploratory study, no power calculations were performed to determine the sample size as this was an exploratory study. Complete (sections of) questionnaires of subjects who matched inclusion criteria were used for analysis. MOS-Sleep subscales and GSQ score were missing if one item was missing. For the analysis of the SDL, 90% completion of a section was considered sufficient in the analysis. For the SF-36 subscale scores, missing values were substituted with group mean values in accordance with the instructions in the SF-36 manual.

The primary comparison was between patients with partial epilepsy and controls with respect to the prevalence of subjective sleep disturbance in the past 6 months (SDL) and the characteristics of subjective sleep disturbance, based on the SDL, MOS Sleep Scale and GSQ. All other analyses were secondary.

The proportions of respondents with sleep disturbance (SDL), suboptimal sleep (MOS-Sleep) and poor sleep the previous night (GSQ) were compared between groups using Fisher’s exact test. Logistic regression and a Wald Chi-square test established the influence of epilepsy, gender, shift/night work, marital status and social status
(based on demographic questionnaire) on these variables. The influence of centre (two epilepsy vs. two outpatient neurology clinics) and of AED use (monotherapy vs. polytherapy) was also examined using Fisher’s exact test.

Data were not normally distributed and therefore all sleep subscale scores were log-transformed for statistical analysis. Mean subscale scores on the SDL, MOS-Sleep Scale (except optimal sleep), GSQ and ESS were compared between the partial epilepsy and control groups using multiple ANOVA. To correct for potential imbalance in factors contributing to sleep disturbance, other than epilepsy, a factorial ANOVA was done with gender, shift or night work, marital status and social status as factors and age as covariate. The relationship between sleep disturbance (SDL) and quality of life (SF-36 mental health component (MCS) and physical health component (PCS) summary scores was examined using a 2-way ANOVA.

RESULTS

Participants

At the close of the study 625/1183 (53%) patients and 549 controls had returned questionnaires. We did not determine how many controls were asked to complete questionnaires by patients. Responses from 139 respondents with partial epilepsy were not included in the analysis because criteria for partial epilepsy or AED use were not met (22 not taking AEDs) or due to insufficient information. Responses from 57 controls were not included in the analysis because they had (a possible history of) epilepsy (30), were taking AEDs (3) or because of insufficient information (15).

Of the remaining questionnaires, 486 from patients and 492 from matched controls were sufficiently complete to be included in at least one of the analyses of sleep disturbance. The completion rates for each of the questionnaires are shown in table 1. The baseline demographic characteristics of patients and controls included in the analyses were generally similar (table 2), as was the history of medical illness, except for epilepsy. A history of psychiatric illness was identified in 30 respondents with epilepsy and 13 controls.

A greater proportion of epilepsy patients were single, lower proportions were employed and had received higher education. Of the 486 patients, 58% were taking AED monotherapy. The most common AEDs used by patients were as follows: carbamazepine (27%), lamotrigine (10%), oxcarbazepine (9%), valproate (6%), carbamazepine + lamotrigine (7%), carbamazepine + benzodiazepine (6%), carbamazepine + valproate (2.5%).
Prevalence of sleep disturbance

In the primary analysis of the SDL, the prevalence of subjective sleep disturbance in the past 6 months was significantly greater among respondents with partial epilepsy than among controls (38.6% vs. 18.0%; p<0.001; figure 1). In this analysis, all incomplete SDL subscale scores were excluded as indicated previously, but the difference remained present, if these incomplete items were analyzed as ‘not sleep disturbed’. In patients with sleep disturbance similar proportions were taking one AED (40.5%) and two AEDs (36.1%; p=0.4). In addition, there was no significant difference between the two epilepsy centres and the two neurology outpatient clinics in the prevalence of sleep disturbance on the SDL (p=0.2).

The prevalence of sleep disturbance during the previous night (GSQ) was also significantly greater among epilepsy patients than controls (27.3% vs. 15.5%; p<0.001). An average of less than 7 to 8 hours sleep per night (sub-optimal sleep on MOS optimal sleep subtest) in the past 4 weeks was reported by 39% of the patients compared to 32% of the controls (p=0.031). However, the odds ratio control/epilepsy corrected for gender, shift/night work, marital status and social status was 1.2 (p=0.206).

Characteristics of sleep disturbance

Mean scores on each of the six SDL subscales were statistically significantly higher in epilepsy patients compared with controls (table 3) after correction for associated factors mentioned in the statistical analysis section. The largest differences in mean scores between the two groups were in excessive daytime sleepiness (13.8%) and psychiatric sleep disorder (14.1%) and the smallest difference was in sleep apnoea (5.8%). These findings were corroborated by the mean scores on three of the six MOS-Sleep subscales (sleep disturbance, sleep adequacy and somnolence) and the overall sleep problems index (summary of 9 items), which also showed significantly greater sleep disturbances in partial epilepsy (table 3). The mean ESS score for daytime sleepiness was higher for the respondents with epilepsy, but this did not reach statistical significance (table 3).

Sleep disturbance and quality of life

Respondents with epilepsy had significantly lower mean scores for both the MCS and PCS scores of the SF-36, compared with controls (p<0.001; figure 2). The presence of a sleep disturbance over the past 6 months was also associated with quality of life impairment in both epilepsy patients and controls on both SF-36 summary scales.
Comparison between respondents with and without sleep disturbance within the stratum of respondents with partial epilepsy yielded mean differences of -9.6 (-11.49, -7.79) and -6.4 (-8.2, -4.6) on the Total Mental and Physical Health summary scales, respectively. Similar differences in quality of life were found, when all incomplete SDI-subscale scores were not excluded, but analyzed as ‘not sleep disturbed’.

**DISCUSSION**

This questionnaire-based, cross-sectional survey conducted by four Dutch epilepsy/neurology clinics indicates that subjective sleep disturbance is twice as prevalent among respondents with partial epilepsy than among matched controls. No specific type of subjective sleep disturbance was linked to this higher prevalence, since most types of subjective sleep disturbances were significantly more frequent in epilepsy patients. We also found that quality of life was significantly impaired in respondents with partial epilepsy, and that sleep disturbance was associated with even further significant and meaningful decrement in quality of life, in both controls and respondents with epilepsy.

The results of this survey seem to be representative for the population of patients with partial epilepsy. We selected patients taking one or two AEDs and excluded more severely ill patients inclusion of a not so severely ill sample was thought to be generalizable to the broader population with partial epilepsy, a assumption that concurs with the findings of others [27-29]. The demographic composition of responders in the patient group was quite similar to the characteristics among non-responders. The proportions of patients who were single, employed and had received higher education were similar to those in a follow-up study in newly diagnosed epilepsy patients [27]. Results were similar among patients attending specialized epilepsy clinics and general neurology clinics.

In total, 625 of the 1183 patients (53%) with partial epilepsy responded to the posted questionnaires. It is important to address response rates and their possible impact on findings in any questionnaire based study. Even with a high response rate, a representative sample is not guaranteed [30]. Templeton et al. concluded that some significant differences were identified, indicating the presence of non-response bias in studies with low-response [31]. A low response rate needs not affect the validity of the data collected, but it is still necessary to test for non-response effects and make corrections to the original data in order to maximize validity. In our study we compared age and male/female ratio which...
was not different between total study population and non-responders. The effect of different selection methods cannot be accurately predicted, but should nonetheless lead to cautious interpretation of small differences between the two groups. However, the response rate was adequate (52% 44-60% for each clinic), the group sizes were considerable (486 patients and 492 controls), and the differences in sleep disorder frequencies were large (any sleep disorder in 38.6% of the patients and 18.0% of the controls). Therefore, the study seems to provide a reliable indication for differences in sleep patterns, between patients with partial epilepsy and healthy controls. In addition, this 52% response rate is similar to the Dutch component of a questionnaire-based study on the quality of life in people with epilepsy (57%) [32].

Each patient was asked to find two acquaintances of the same age and gender, who were not partners or cohabitants, to complete an identical set of questionnaires. This was done to ensure that controls would be from the same social class, their sleeping patterns were unknown to the patients and that gender bias would not be introduced. Patient motivation to complete the questionnaires was probably greater than controls, because of concern for their health problem, although the exact number of controls who were actually asked to complete questionnaires is not known. Having sleep problems may have given greater impetus to respond but this would be applicable to both patients and controls and therefore was unlikely to confound the comparisons of sleep patterns between groups.

All questionnaires have been used previously in the Dutch population. There is a paucity of literature on the prevalence of subjective sleep disturbance in patients with epilepsy, but the prevalence rate observed in controls (18%), as determined by the SDL, is consistent with the rate reported in the Dutch general population (15%) by others [33]. In this study the prevalence of subjective sleep disturbance, determined in from the primary endpoint, the SDL questionnaire, was 38.6% in respondents with partial epilepsy, a statistically significant, two-fold higher prevalence than among controls (18%). Similarly, a significantly greater almost 2-fold higher prevalence of sleep disturbance during the previous night was found in respondents with partial epilepsy compared in the analysis of the GSQ (27% vs. 15%). In the analysis of sleep questionnaires there were no statistically significant effects related to centre (neurology or epilepsy clinic) or AED use.

We were unable to identify specific reasons, unrelated to partial epilepsy, for the higher prevalence rate of sleep disturbances among respondents with epilepsy. It remains uncertain how, or if, partial epilepsy causes sleep disturbances. The relationships may be complex, considering the interactions between nocturnal seizures and sleep architecture, sleep stages and interictal epileptiform
activity, exacerbation of seizures by disrupted sleep, the effects of AEDs on sleep architecture and daytime vigilance [13], mood disorders associated with epilepsy [10], and the underlying causes of epilepsy itself.

One of the greatest differences between the groups was on the psychiatric sleep disorder subscale of the SDL, a subscale that is particularly sensitive to the influence of mood disorders on sleep. In this sample, this may reflect a higher burden of mood disturbance that has been reported in people with epilepsy [34], but on the other hand, disturbed sleep itself can lead to psychiatric disturbances [35]. In this study a history of psychiatric disturbances was more frequent among those with partial epilepsy (6.2%) than among controls (2.6%), further suggesting that disordered sleep and psychiatric illness in partial epilepsy might be linked. The frequency of psychiatric disturbances was low, and could not account for the observed differences between groups in the prevalence of sleep disturbance.

It is important to note that the results of the questionnaires were generally similar, although there were some discrepancies. Epilepsy was significantly associated with excessive daytime sleepiness (SDL) and somnolence (MOS-Sleep). However, here was no significant association observed on the ESS. This inconsistency is difficult to explain as daytime somnolence associated with disturbed sleep and AED medication was expected in this sample. The finding is in agreement with a previous lack of excessive daytime sleepiness found in people with epilepsy using the ESS [36], and may show the limitations of this questionnaire in the epilepsy population, particularly as issues in the evaluation of daytime sleepiness have been observed by others [37]. One of the eight items of this questionnaire evaluates sleepiness during driving a car, which for a large number of epilepsy patients is not a common daily activity. The SDL may also have some misleading questionnaire items for this patient group. The subscores for narcolepsy were 10.3% higher in epileptic patients than in controls, although in absolute number the difference was small. This was unexpected and suggests that some SDL-items were unable to differentiate clearly between some epileptic and narcoleptic symptoms [38]. This clearly shows that for epilepsy some questionnaire items may be misleading. The lack of a significant difference between groups on the snoring subscale, may be related to the higher proportion of people who were single (and did not have a bed partner to provide feedback) among the respondents with partial epilepsy.

The SF-36, which has been validated in Dutch and as a psychometric measure in epilepsy [39], was used to explore the impact of partial epilepsy and sleep disturbance on the quality of life. The results in controls, and the influence of epilepsy or sleep disorders...
on the quality of life were all in agreement with previous studies. Normative SF-36 data determined in international settings, including The Netherlands [25,40], are comparable to our scores in the control group. The mean scores on the SF-36 subscales epilepsy patients in this study (data not shown) are consistent with findings in Dutch epilepsy patients in a European cross-sectional postal survey [32], and in other epilepsy studies [41]. Others have also found that the quality of life is significantly impaired in people treated for epilepsy [42] and in people with sleep disturbance in the general population [8]. In addition to these findings, our study showed that sleep disturbances occur frequently in partial epilepsy, and affect quality of life, both independently and significantly. The effect of sleep disturbance alone on mental health in those with partial epilepsy patients is comparable to the effect in patients with other chronic disorders such as asthma, back problems, arthritis, depression, congestive heart failure, recent myocardial infarction, diabetes and hypertension [7,34]. The effect of both the epilepsy and sleep disturbance, is comparable to the decrease in mental health associated with a disorder such as depression [7]. For physical health, the effect of a sleep disturbance in those with epilepsy was larger than the decrement observed in the chronic disease states mentioned above. This contrasts with other chronic disease states, where the disorder itself appears to have greater negative effect on the physical health than the associated sleep disturbance.

The clinical relevance of the statistically significant differences in SF-36 summary scales deserves comment. Mean MCS and PCS scores in patients with epilepsy were approximately one-half a standard deviation lower than controls. A difference of this magnitude is likely to be clinically meaningful [7]. Comparison between respondents with and without sleep disturbance within the stratum of respondents with partial epilepsy yielded mean differences of -9.6 (-11.49, -7.79) and -6.4 (-8.2, -4.6) on the Total Mental and Physical Health summary scales, respectively. These differences exceed the thresholds for minimally important changes in patients with epilepsy [43]. Thus, we propose that sleep disturbance in patients with partial epilepsy, whatever the aetiology, has a significant negative association with quality of life beyond that attributable to epilepsy and its treatment alone.

The results of this study extend our understanding of the prevalence and impact of subjective sleep disturbance in people with partial epilepsy. We wish to suggest that the recognition and management of sleep disturbance is an important and distinct consideration in patients with partial epilepsy. Further research of the psychological, pathophysiological and pharmacological interactions that may underlie the variety of sleep disturbances in epilepsy is warranted.
Table 1  Percentages of respondents* completing each of the questionnaires

<table>
<thead>
<tr>
<th></th>
<th>Partial epilepsy</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDL (all subscales complete)</td>
<td>409</td>
<td>438</td>
</tr>
<tr>
<td>GSQ</td>
<td>439</td>
<td>472</td>
</tr>
<tr>
<td>MOS (optimal sleep subscale)</td>
<td>477</td>
<td>485</td>
</tr>
<tr>
<td>SF-30</td>
<td>444</td>
<td>467</td>
</tr>
<tr>
<td>SDL (all subscales) + SF36</td>
<td>378</td>
<td>420</td>
</tr>
</tbody>
</table>

* Follow-up telephone calls were made to 19.8% of people with partial epilepsy and 16.7% of controls to complete questionnaires.

Table 2  Respondent characteristics and AED use

<table>
<thead>
<tr>
<th></th>
<th>Partial epilepsy</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>N</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>486</td>
<td>492</td>
</tr>
<tr>
<td>Single</td>
<td>145 (30%)</td>
<td>119 (24%)</td>
</tr>
<tr>
<td>Employed</td>
<td>355 (73%)</td>
<td>427 (87%)</td>
</tr>
<tr>
<td>Shift/night worker</td>
<td>20 (4%)</td>
<td>46 (9%)</td>
</tr>
<tr>
<td>Mean age (range), years</td>
<td>45 (19-81)</td>
<td>43 (18-81)</td>
</tr>
<tr>
<td>Mean (SD) alcohol intake, units/week</td>
<td>3 (5.2)</td>
<td>5 (6.8)</td>
</tr>
<tr>
<td>Lower secondary education or less</td>
<td>170 (34%)</td>
<td>124 (25%)</td>
</tr>
<tr>
<td>Pre-university education or higher</td>
<td>77 (16%)</td>
<td>150 (31%)</td>
</tr>
<tr>
<td>AED monotherapy</td>
<td>279 (58%)</td>
<td>492</td>
</tr>
</tbody>
</table>
Table 3  Mean (SD) SDL and MOS-Sleep subscale and GSQ and ESS scale scores

<table>
<thead>
<tr>
<th></th>
<th>Partial epilepsy</th>
<th>Controls</th>
<th>P group effect††</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><em>SDL</em> (Insomnia)</em>*</td>
<td>2.2 (0.79)</td>
<td>1.9 (0.63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Periodic leg movement syndrome</td>
<td>1.6 (0.74)</td>
<td>1.5 (0.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Excessive daytime sleepiness</td>
<td>1.8 (0.72)</td>
<td>1.6 (0.50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Narcolepsy</td>
<td>1.3 (0.44)</td>
<td>1.1 (0.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Apnoea</td>
<td>1.9 (0.70)</td>
<td>1.8 (0.62)</td>
<td>0.013</td>
</tr>
<tr>
<td>Psychiatric sleep disorder</td>
<td>2.1 (0.74)</td>
<td>1.8 (0.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>MOS-Sleep Scale†</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>28.0 (22.70)</td>
<td>20.6 (17.94)</td>
<td>0.007</td>
</tr>
<tr>
<td>Snoring</td>
<td>39.7 (32.07)</td>
<td>33.0 (28.24)</td>
<td>0.070</td>
</tr>
<tr>
<td>Awakening short of breath</td>
<td>16.7 (23.13)</td>
<td>12.1 (16.76)</td>
<td>0.141</td>
</tr>
<tr>
<td>Sleep quantity</td>
<td>30.3 (5.60)</td>
<td>29.8 (3.95)</td>
<td>0.577</td>
</tr>
<tr>
<td>Sleep adequacy</td>
<td>63.7 (25.33)</td>
<td>69.6 (21.51)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Somnolence (daytime)</td>
<td>30.0 (22.83)</td>
<td>21.4 (16.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall sleep problems index (9 items) §</td>
<td>28.9 (19.07)</td>
<td>21.7 (13.79)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>GSQ ¶</strong></td>
<td>10.4 (3.80)</td>
<td>11.3 (2.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>**ESS **</td>
<td>3.5 (2.70)</td>
<td>3.2 (2.04)</td>
<td>0.429</td>
</tr>
</tbody>
</table>

SDL: Partial seizures n=400-478 Controls n=436-488 across subscales. Score range on each subscale 1-5  †MOS-Sleep: Partial seizures n=465-477 Controls n = 479-488 across subscales. Score range on each subscale 0-100. ††Higher score = better sleep ‡MOS overall sleep problems index includes 9 questions regarding sleep latency, sleep disturbance, adequacy and somnolence § GSQ: Partial seizures n=439 Controls = 472. Possible score range 0-14 ‡‡ESS: Partial seizures n=470 Controls n=483. Possible score range 0-24 ††P value based on multiple ANOVA (SDL, MOS) and logistic regression (GSQ, ESS) including factors epilepsy, gender, marital status, social status, shift or night work with age as the covariate
Figure 1  Prevalence of sleep disturbance\textsuperscript{*} according to three sleep questionnaires

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1}
\caption{Prevalence of sleep disturbance\textsuperscript{*} according to three sleep questionnaires}
\end{figure}

\textsuperscript{*} The prevalence of sleep disturbance on the \textit{Sf-36} was the primary endpoint. The prevalence of sleep disturbance on the MOS-Sleep scale and Gsq were secondary endpoints.

Figure 2  Mean (95\% CI) \textit{Sf-36} PCS and MCS scores (Quality of Life) for all respondents and according to presence or absence of sleep disturbance\textsuperscript{*}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2}
\caption{Mean (95\% CI) \textit{Sf-36} PCS and MCS scores (Quality of Life) for all respondents and according to presence or absence of sleep disturbance\textsuperscript{*}}
\end{figure}

\textsuperscript{*} Presence of sleep disturbance defined as \textit{Sf-36} score $\geq$ 3 on any of the six \textit{Sf-36} subscales

\textbf{v68  PHARMACOLOGICAL DIFFERENCES OF GABAERGIC COMPOUNDS: A PHARMACODYNAMIC CHARACTERIZATION}
REFERENCES


