

# Quality of sleep in primary focal dystonia: a case–control study

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**Background:** Sleep disturbances are common in patients with movement disorders. Evaluating quality of sleep is of primary importance because of the effect that nocturnal and daytime sleep abnormalities exert on general health status. However, quality of sleep has never been addressed in detail in patients with dystonia. The aim of this case–control study was to analyse quality of sleep in patients with the two most common forms of primary focal dystonia, blepharospasm (BSP) and cervical dystonia (CD).

**Methods:** We evaluated quality of sleep (Pittsburgh Sleep Quality Index, PSQI) and excessive daytime sleepiness (Epworth Sleepiness Scale, ESS) in 98 patients with focal adult-onset dystonia (52 with BSP; 46 with CD) and in a group of 56 age- and gender-matched healthy subjects. The Beck Depression Inventory (BDI) was used for the evaluation of depressive symptomatology.

**Results:** Quality of sleep was impaired (significantly higher PSQI scores) in both groups of patients. However, differences in PSQI scores between patients with CD and control subjects were partly confounded by BDI scores, whereas differences in PSQI scores between patients with BSP and control subjects were not influenced by BDI. Excessive daytime sleepiness was not significantly more frequent than in control subjects in either patients with BSP or patients with CD.

**Conclusions:** This study suggests that the assessment and treatment of insomnia-related complaints should be considered in global management plans of patients with focal dystonia, particularly in those affected by BSP.

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## Introduction

Sleep disturbances have recently been recognized as frequent comorbidities in movement disorders, particularly in patients affected by Parkinson's disease (PD) [1,2]. The disturbances include insomnia, abnormal movements during sleep [e.g. periodic leg movements, rapid eye movement (REM) sleep behaviour disorder] and excessive daytime sleepiness. The frequency of insomnia increases with advanced motor stages of PD suggesting that slowed movements during the night, difficulties in turning in bed or adjusting blankets, pain, cramps, nocturnal and early morning dystonia are likely to be the main causes of this sleep disturbance [3]. On the other hand, REM sleep behaviour disorder is a frequent and early clinical sign of PD and sometimes

precedes motor signs [4]. Excessive daytime sleepiness (EDS), instead, has been suggested to be a treatment-related phenomenon in PD [5], although it has been speculated that it might also be because of lesions in the arousal systems of the brain (for a review see: De Cock *et al.* [3]).

Dystonia is a movement disorder characterized by sustained muscle contractions that give rise to abnormal postures or involuntary movements [6,7]. A few polysomnographic studies showed changes in spindle activity and fragmented sleep in patients with generalized dystonia [8,9], impaired sleep efficiency and reduced slow and REM sleep in patients with cranial dystonia [10]. Overall, these findings raised the possibility that quality of sleep is abnormal in dystonic patients. Although the evaluation of quality of sleep is of primary importance in assessing the influence that nocturnal and daytime sleep abnormalities exert on general health status, satisfaction with life, mood and work performance [11], to our knowledge, quality of sleep has never been addressed in details in dystonia.

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In this study, therefore, we analysed quality of sleep and excessive daytime sleepiness in patients with the two most common forms of primary adult-onset dystonia, that is blepharospasm (BSP) and cervical dystonia (CD), and in healthy subjects.

## Methods

Patients fulfilling international standard criteria [12] for primary adult-onset BSP and for primary adult-onset CD were consecutively recruited amongst outpatients periodically seen at the movement disorder clinics of the Universities of Bari and Genoa, Italy, over a 4-month period. Patients with BSP and CD were compared to age-matched healthy volunteers (normal controls, NC), recruited in the same time period amongst non-consanguineous spouses of neurological outpatients affected by BSP, CD or hemifacial spasm who periodically received botulinum toxin treatment in the two centres. Diagnoses were confirmed by the senior neurologist with long-standing experience in movement disorders at each centre. Exclusion criteria in all groups were the presence of other neurological abnormalities, prior exposure to neuroleptics and other forms of secondary dystonia. Informed consent was obtained for all subjects according to the declaration of Helsinki, and the study was approved by the institutional review boards of the University of Genoa and Bari.

All subjects were screened through a semi-structured interview for the assessment of presence/absence of coffee or alcohol exposure, and concomitant cardiovascular, pulmonary or urological diseases. The quality of sleep was measured by means of the Pittsburgh Sleep Quality Index (PSQI), a self-rated questionnaire that assesses a variety of factors related to sleep quality [13]. PSQI is a valid, reliable instrument, widely used amongst healthy adults and patients with different neurological disorders, including different types of movement disorders [5,13–18]. The PSQI differentiates 'poor' from 'good' sleepers by measuring seven areas, which are all self-rated by the patient: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction during the last month. The scores on each item are based on a 0 to 3 scale, whereby three reflects the negative extreme. A global sum of '5' or greater indicates a 'poor' sleeper. Excessive daytime somnolence (EDS) was measured by means of the Epworth Sleepiness Scale (ESS). The ESS is a questionnaire intended to measure daytime sleepiness. The subject is asked how likely he is to doze off or fall asleep in a variety of situations such as reading, watching TV, driving a car, etc. The patient's self-judgment refers to

his/her usual way of life in recent times. The scores on each item are based on a 0 (no chance of dozing) to 3 (high chance of dozing) scale. A score of 10 or more is considered suggestive of excessive sleepiness [19]. The Beck Depression Inventory (BDI) was used for the evaluation of depressive symptomatology. A BDI score > 10 is suggestive of depression [20]. Severity of dystonia was rated by means of the Burke–Fahn–Marsden (BFM) rating scale. All patients with BSP and CD were periodically treated with botulinum toxin injections, and assessments were always performed at least 3 months following their last botulinum toxin injection.

For the statistical analysis, data were entered in two different non-parametric analyses comparing: (i) BSP with NC and (ii) CD with NC. For categorical variables, differences between the groups were assessed by  $\chi^2$ . For continuous variables, because data were not normally distributed (according to the Kolmogorov Smirnov statistical test), differences between the groups were assessed by the Mann–Whitney *U* test. A linear regression analysis was performed to correlate PSQI mean value with BFM value and disease duration. The association between the PSQI score and case–control status was analysed using logistic regression models, which were always adjusted for main confounding factors, i.e. age, gender and BDI score. Two stepwise logistic regression models were separately constructed to perform the following comparisons: BSP versus NC and CD versus NC. A standard statistical package computed odds ratios (ORs), two-sided 95% confidence intervals (CIs) and *P* values; *P* < 0.05 was considered to be significant. All statistical analyses were performed by using spss 13.0.

## Results

### Demographic and clinical features of cases and controls

As shown in Fig. 1, six subjects (two cases and four controls) were excluded. Ninety-eight patients with focal adult-onset dystonia (52 with BSP and 46 with CD) and 56 NC entered the study, and their participation rate was 100%.

Because patients with CD were younger than patients with BSP, amongst the 56 NC, we selected two different groups of control subjects, GROUP 1 (comprising all the 56 subjects) and GROUP 2 (comprising 46 of the 56 subjects), frequency-matched by age and gender to the group of patients with CD and to the group of patients with BSP, respectively. The main demographic and clinical features of the study sample are summarized in Table 1.

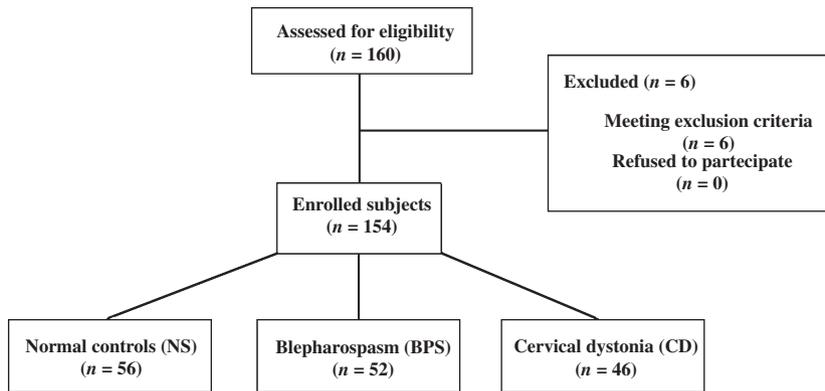


Figure 1 Flow diagram of the study.

	BSP (n = 52)	NC (n = 46)	CD (n = 46)	NC (n = 56)
Age	67 (44–84)	61 (56–84)	59.5 (29–87)	60 (40–84)
Gender (M/F)	13/39	17/29	15/31	21/35
Disease duration (year)	6 (1–24)	–	10.5 (1.5–32)	–
Alcohol (yes/no)	16/36	22/24	19/27	26/30
Coffee (yes/no)	38/14	39/7	33/13	48/8
BDI	9 (0–30)	6 (0–25)	10.5 (0–44)**	6 (0–25)
BFM	8 (2–19.5)	–	7 (3–56.5)	–

Table 1 Characteristics of subjects

BSP, Blepharospasm; NC, normal controls; CD, cervical dystonia; BDI, beck depression inventory; BFM, Burke–Fahn–Marsden rating scale.  
Median (range); \*\* $P < 0.01$ .

Age, gender, exposure to alcohol and coffee consumption were comparable between patients and their respective control subjects. The mean BDI score was significantly higher in patients affected by CD than in the respective healthy control group ( $P = 0.007$ ) (Table 1), whereas it did not differ between patients with BSP and their NC group (Table 1). Data from the semi-structured interview did not yield a significant difference from NC in the frequency of cardiovascular, pulmonary and urological diseases for both patients with BSP and patients with CD (data not shown).

#### Quality of sleep and excessive daytime somnolence

The mean PSQI score was significantly higher in patients with BSP than in their respective NC group ( $P < 0.001$ ; Table 2). Patients with CD scored higher on the PSQI than their respective healthy control subjects ( $P = 0.002$ ; Table 2).

The analysis of the subcomponents of the PSQI scale showed that patients affected by BSP had significantly higher scores in components 2 (sleep latency), 3 (sleep duration), 4 (sleep efficiency) and 6 (medication) compared to NC (Table 2). Patients affected by CD had significantly higher scores only in component four (sleep efficiency) compared to their healthy control group (Table 2). Considering the cutoff level of '5', 75%

Table 2 Quality of sleep and excessive daytime sleepiness

	BSP (n = 52)	NC (n = 46)	CD (n = 46)	NC (n = 56)
Sleep quality	1 (0–3)	1 (0–3)	1 (0–3)	1 (0–2)
Sleep latency	1 (0–3)*	1 (0–3)	1 (0–3)	1 (0–3)
Sleep duration	1 (0–3)*	0 (0–3)	1 (0–3)	0 (0–3)
Sleep efficiency	1 (0–3)**	0 (0–3)	1 (0–3)**	0 (0–3)
Sleep disturbances	1 (0–4)	1 (0–2)	1 (0–3)	1 (0–2)
Sleeping medication	0 (0–3)*	0 (0–3)	0 (0–3)	0 (0–3)
Daytime dysfunction	0 (0–3)	0 (0–2)	1 (0–3)	0 (0–2)
PSQI score	7.5 (2–21)**	5 (0–15)	7 (0–16)**	4 (0–15)
Number of subjects with overall PSQI score > 5 (%)	39 (75%)*	24 (52%)	33 (72%)*	27 (48%)
ESS (% of subjects with score > 10)	7.7%	4.3%	8.7%	8.9%

Median (range); \* $P < 0.05$ ; \*\* $P < 0.01$ .

BSP, Blepharospasm; NC, normal controls; CD, cervical dystonia; PSQI, Pittsburgh sleep quality index; ESS, Epworth sleepiness scale.

of patients with BSP and 72% of patients with CD were classified as 'poor sleepers' (Table 2). There was no significant correlation between PSQI value and severity of dystonia (assessed by means of the BFM rating scale) in BSP patients (standardized beta = 0.18,  $P = 0.19$ ), whilst a significant relationship was found between PSQI and BFM in patients with CD (standardized beta = 0.49,  $P = 0.001$ ). However, after having

adjusted for BDI score, the correlation between PSQI score and BFM score in patients with CD lost its significance (standardized beta = 0.26,  $P = 0.086$ ). Also, there was no significant correlation between PSQI value and disease duration in patients with BSP (standardized beta = 0.14,  $P = 0.32$ ), whilst a significant relationship was found between PSQI and disease duration in patients with CD (standardized beta = 0.33,  $P = 0.028$ ). However, after having adjusted for BDI score, the correlation between PSQI score and disease duration in patients with CD lost its significance (standardized beta = 0.24,  $P = 0.054$ ). In all the groups evaluated (CD patients, BSP patients and their respective NC), the mean ESS score was always < 10, and the percentage of subjects with ESS > 10 was similar in all the groups evaluated (Table 2). Accordingly, the  $\chi^2$  statistical analysis failed to show any difference between groups (BSP versus NC  $P = 0.49$ , CD versus NC  $P = 0.9$ ).

### Logistic regression analysis

Univariate logistic regression analysis showed that age and gender and BDI were not significantly associated with the diagnosis of BSP (age: OR = 1.03,  $P = 0.25$ ; gender: OR = 0.57,  $P = 0.20$ ; BDI: OR = 1.05,  $P = 0.16$ ) when compared to NC. Furthermore, we observed a significant and positive association between PSQI score and diagnosis of BSP (Table 3). The latter association remained significant after having adjusted for age, gender and BDI score (Table 3).

Univariate logistic regression analysis showed that age and gender were not significantly associated with a diagnosis CD (age: OR = 0.98,  $P = 0.22$ ; gender: OR = 0.80,  $P = 0.61$ ) when compared to NC, whilst the BDI score was associated with a diagnosis of CD (OR = 1.09,  $P = 0.004$ ). Univariate logistic regression

**Table 3** Logistic regression analysis of the association between PSQI score and blepharospasm or cervical dystonia

	OR	<i>P</i> value	95% CI
BSP versus NC			
PSQI	1.23	0.002	1.08–1.40
Adjusted for age	1.22	0.002	1.08–1.39
Adjusted for age, gender	1.22	0.003	1.07–1.39
Adjusted for age, gender, BDI score	1.27	0.002	1.09–1.48
CD versus NC			
PSQI	1.19	0.004	1.05–1.33
Adjusted for age	1.20	0.002	1.07–1.36
Adjusted for age, gender	1.20	0.003	1.07–1.36
Adjusted for age, gender, BDI score	1.13	0.097	0.98–1.3

BSP, Blepharospasm; CD, cervical dystonia; NC, normal controls; PSQI, Pittsburgh sleep quality index; BDI, Beck depression inventory.

analysis yielded a significant association between PSQI score and a diagnosis of CD when compared to NC. However, the association was not confirmed by stepwise logistic regression analysis because of a significant confounding effect of BDI score (Table 3).

Subitems' case-control analysis revealed that subitems 3 (sleep duration) (OR = 1.65,  $P = 0.038$ ), 4 (sleep efficiency) (OR = 1.73,  $P = 0.11$ ) and 6 (medication) (OR = 1.55,  $P = 0.40$ ) mainly contributed to the significant association between overall PSQI score and BSP.

### Discussion

The present study is, to the best of our knowledge, the first to assess quality of sleep and daytime sleepiness in patients affected by primary adult-onset BSP and CD. The demographic and clinical features of our case population were consistent with those typically observed in patients with primary adult-onset cranial/cervical dystonia. Direct comparison between groups showed worse quality of sleep compared to control subjects in patients with both forms of primary adult-onset dystonia, with a percentage of 'poor sleepers' (PSQI > 5) higher than 70% amongst both patients with BSP and patients with CD. In the BSP group, logistic regression analyses showed that the diagnosis of BSP was significantly associated with a higher PSQI score; age, gender and BDI score were not associated with BSP and also failed to exert any significant effect on the PSQI odds ratio. In the CD group, BDI score was significantly associated with the diagnosis of CD and also confounded the estimate of PSQI odds ratio, leading to the lack of its statistical significance. The analysis of the subcomponents of the PSQI scale also showed different profiles of CD and BSP groups: patients with CD had abnormal scores in sleep efficiency, whilst patients with BSP had abnormal scores in sleep duration, latency and efficiency. These subcomponents were shown to differentiate normal subjects from patients with primary insomnia [14], suggesting that insomnia might be a comorbidity issue in patients with cranial/cervical dystonia. Finally, we observed that, despite the poorer quality of sleep, excessive daytime sleepiness was not significantly more represented amongst patients with dystonia than amongst control subjects.

It is unclear whether dystonic movements persist during sleep [10,21,22]. If so, the presence of abnormal movements could, in some way, interfere with sleep. However, the lack of correlation between PSQI scores and dystonia severity scores in patients with BSP did not support this hypothesis. Likewise, PSQI scores correlated with dystonia severity in patients with CD in the single variable linear regression model, but this

appeared to be because of a confounding effect of the BDI score.

The observed association between poor quality of sleep and BSP might alternatively suggest an implication of physiological mechanisms of sleep in the pathophysiology of BSP. Abnormal excitability of brainstem circuits has been demonstrated in both BSP [23] and in a number of sleep disturbances including cataplexy and periodic limb movements of sleep [24,25]. Obviously, there are limits to the broad interpretation of sleep quality based on subjective sleep interviews, and abnormalities of brainstem circuitries may be more accurately related to sleep patterns using objective measures of sleep architecture as polysomnographic recordings.

Unlike for patients with BSP, the poorer quality of sleep in patients with CD was mostly accounted for by the higher degree of depressive symptomatology detected in this group of patients. Comorbid depression has been repeatedly reported in patients with CD [26–29]. Our findings confirm previous observations that depression may be a frequent problem in CD [26–29], but the causal relationship between depression and quality of sleep still remains uncertain.

The poor quality of sleep of our dystonic patients did not seem to have an impact on daytime sleepiness (both considering the daytime dysfunction domain of the PSQI and the ESS score). ESS has been demonstrated to be a good tool in measuring daytime sleepiness distinguishing normal subjects from patients belonging to various diagnostic groups. However, some disorders related to impaired alertness, such as idiopathic or psychophysiological insomnia, are not associated with abnormal scores on the ESS [19]. This is consistent with evidence that such patients have a low sleep propensity, even when they are able to relax [30]. Overall, in line with the pattern of PSQI subscore changes, the lack of excessive daytime somnolence supports the possibility that primary insomnia might be a comorbid sleep disturbance in patients with these forms of primary adult-onset dystonia.

Some limitations of the study deserve discussion. First, the aim of the present study was limited to the evaluation of quality of sleep in patients with cranial and cervical dystonia and did not systematically assess the diagnosis of co-occurring sleep disturbances. The PSQI is commonly used in clinical practice and is a useful clinical instrument, designed to differentiate good from poor sleepers. The measure that this questionnaire provides is characterized by high internal homogeneity and consistency, test-retest reliability and validity for primary insomnia [14]. However, it has a poor correlation with polysomnographic parameters [13,31]. In fact, sleep complaints measured by PSQI may often be more indicative of general dissatisfaction than of any

specifically sleep-related disturbances, and PSQI appreciably correlates with sleep diary variables but not with any actigraphic variables [31]. Further work based on neurophysiologic analyses (e.g. polysomnographic and actigraphic recordings) is needed to expand upon the pattern of abnormal physiology of sleep in patients with primary dystonia. Second, we did not consider the exposure to pharmacological treatments except the ones for insomnia, which have been evaluated in the last part of the PSQI questionnaire. Indeed, some medications have been associated with insomnia such as certain over-the-counter cold and asthma preparations and medications for high blood pressure [32]. However, a previous study showed that dystonic patients have exposure rates for the most frequent general medical conditions that are comparable to those from the general population, including antecedent diabetes, thyroid diseases, anxiety, depression and other diseases [33]. In addition, a retrospective analysis of patients' records did not show a significant incidence of cardiovascular, pulmonary and urological diseases in both the groups evaluated. Third, we did not re-assess quality of sleep in our patients during the period of maximal botulinum toxin-induced benefit to avoid a potential learning effect related to the questionnaire. Nevertheless, the possibility that changes in symptom severity are paralleled by changes in sleep quality seems unlikely, given the lack of correlation between severity of dystonia and PSQI scores.

In conclusion, this study suggests that insomnia-related complaints may be present in patients with dystonia, at least in those affected by primary adult-onset BSP. Assessment and treatment of such complaints should be included in global management plans of patients with adult-onset dystonia, at least of those affected by BSP.

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