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The nature of excessive sleepiness and sudden sleep onset in Parkinson's disease

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ABSTRACT

Objectives: Excessive daytime sleepiness (EDS) and sudden sleep onset (SOS) episodes are frequent in Parkinson's disease (PD). The objectives are to identify clinical characteristics and factors associated with EDS and SOS episodes.

Methods: Clinical demographic data were recorded ($N=100$, mean age$=65.0\pm10.4$). EDS was identified by the Epworth Sleepiness Scale (ESS>10) and SOS episodes were registered. Disease severity was evaluated by the Unified Parkinson's Disease Rating Scale (UPDRS, I, II, and III), sleep disturbances by the Parkinson's Disease Sleep Scale (PDSS<100), depressive symptoms by the Beck Depression Inventory (BDI>10) and rapid eye movement (REM) sleep behavior disorder (RBD) by the REM sleep behavior scale. Levodopa equivalent dose was measured.

Results: PD patients with EDS (67%) were predominately male (73.1%) and had worse disease severity (UPDRS II and III $p=0.005$); SOS episodes (39%) were associated with disease duration, diabetes, sleep disturbances (PDSS Scale), disease severity (UPDRS I, II, III) and RBD symptoms ($p<0.05$). Stepwise regression analysis showed that EDS was independently associated with motor-symptoms severity (UPDRS III scale, $p=0.003$). SOS episodes were independently associated with disease duration ($p=0.006$) and sleep disturbances (PDSS scale, $p=0.03$): patients had more uncomfortable immobility at night, tremor on waking and snoring or difficult breathing.

Discussion: EDS and or SOS episodes are frequent and manifest a differential pattern in PD. SOS episodes are associated with longer disease duration, diabetes, sleep disturbances and RBD symptoms indicating that these "sleep attacks" are of multifactorial origin and probably influenced by brain structural abnormalities.

1. Introduction

Parkinson's disease (PD) presents with classical motor manifestations that include tremor, rigidity, akinesia and postural instability [1,2]. Several non-motor abnormalities, including sleep alterations, such as, excessive daytime sleepiness (EDS), "sleep attacks" or episodes of sudden onset of sleep (SOS), insomnia, restless legs syndrome and rapid eye movement sleep behavior disorder (RBD) have been described [3,4]. Importantly, EDS and SOS episodes greatly affect patients and caregiver's routine and potentially increase the risk of accidents [5]. To date, these alterations remain a challenge to

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treatment as there is not enough evidence to make a recommendation for the management of these sleep-wake abnormalities [6]. Possibly, sleep and wake abnormalities contribute to the heterogeneous clinical manifestations of PD and to the common daytime oscillations of symptoms. Thus, modifying factors that influence EDS and SOS episodes may contribute to improve therapy.

Previous evidences indicate that EDS and SOS episodes have a different pattern of manifestation in PD. For instance, EDS is frequently found [7]; otherwise, SOS is less common and manifests somewhat similar to narcoleptic events [8]. Of note, the extent and severity of SOS in PD is variable: some patients and caregivers inform long duration episodes with atonia while others report episodes of short duration without motor changes. Reports also suggest two distinct types of events: those of sudden onset without warning and those of slow onset with prodrome drowsiness [9]. Classical cataplectic symptoms as occurs in narcolepsy have not been observed in PD patients. Interestingly, a significant higher narcolepsy score in PD patients has been previously observed [10].

Clarifying whether clinical factors and associated comorbidities influence the manifestation of EDS and SOS episodes in PD may contribute for patient care. The objectives of this study are to characterize the clinical symptoms and to identify factors contributing to the presence of EDS and SOS in PD patients.

2. Material and methods

2.1. Study design

This is an observational cross-sectional study of consecutive patients with PD from an outpatient unit at a University Hospital in the city of Fortaleza, Brazil. The study involved 100 patients recruited among a population of 152 patients: 28 were too old or had difficulty with verbal communication, 10 refused to collaborate and 14 were considered as poor-compliant patients. Evaluations were performed over a period of 12 months (July 2010 to July 2011). Subjects were selected consecutively as part of a large cohort of patients with PD being followed in a longitudinal study [Sleep-For-PD study]. Specific questionnaires were all measured concurrently in a face-to-face interview by two trained medical staff. Patients were excluded if they had any severe comorbidity and were not competent to provide their informed consent. The protocol was analyzed and approved by the Ethics Committee (HU-UFC No. 045.0607).

2.2. Measures

Demographic data, habits and comorbidities were recorded using a standardized questionnaire. Daytime somnolence was assessed by the Epworth Sleepiness Scale (ESS), a questionnaire containing eight items that ask about the expectation of dozing in eight hypothetical situations. An ESS score ≥ 10 indicates EDS [11]. Patients and family or caregivers were interrogated about the presence of SOS or “sleep attacks”. We used the Parkinson's Disease Sleep Scale (PDSS), a 15-item visual analog scale that quantifies several aspects of nocturnal disabilities and sleep problems in PD; this scale has also been validated in Brazil [12]. A PDSS score ≤ 100 defined troublesome nocturnal symptoms and a cut-off of <5 for each item indicated sleep impairment. Disease severity was evaluated by the Unified Parkinson's Disease Rating Scale (UPDRS) Parts I, II, III, IV and V. Depressive symptoms were evaluated by the Beck Depression Inventory (BDI) and were defined as present if the score was BDI ≥ 10 [12]. The RBD scale that indicates clinically probable RBD was administered to all patients. The Levodopa Equivalent Dose was measured.

2.3. Statistical analysis

Descriptive statistics are presented as mean $\pm$ standard deviation, range and frequency (% values). Fisher's exact test for categorical variables, Mann–Whitney U test for continuous variables and Student's t-test for normally distributed data with equal variances were performed to compare between patients regarding the presence/absence of EDS and SOS episodes. Logistic regression analysis examined each factor associated with EDS or with SOS episodes. A forward stepwise multiple regression analysis was later performed: variables with historical evidence of influence on sleepiness and/or with a $p<0.10$ were all included; a $p<0.05$ was required for a variable to be retained in the final model. Statistical analysis was carried out using SPSS for Windows, version 16.0. Statistical significance was set at $p<0.05$.

3. Results

Patient characteristics according to the presence of EDS and to SOS episodes are depicted in Table 1. Individuals with EDS were predominately of male gender and had worse disease severity as evaluated by UPDRS II and III. Patients with SOS episodes had longer disease duration and worse severity of symptoms as evaluated by the UPDRS I, II and III. They also had more symptoms related to RBD (RBD scale). Logistic regression analysis confirmed an association between EDS and symptom severity (UPDRS II and III). Sudden sleep onset episodes were associated with disease duration, diabetes, sleep disturbances (PDSS Scale), disease severity (UPDRS I, II and III) and RBD symptoms (Table 2). Patients with SOS episodes had more EDS (67%, Fisher's exact test, $p=0.02$). Stepwise analysis showed that EDS was independently associated with motor symptoms severity (UPDRS III scale). SOS episodes were independently associated with disease duration and sleep disturbances (PDSS scale) (Table 3). Analysis of sleep disturbances showed that patients with SOS episodes had more night symptoms related to uncomfortable immobility, tremor on waking and snoring or difficult breathing (Fig. 1).

4. Discussion

Our data confirm that EDS and SOS episodes are frequent in PD. SOS episodes affected nearly 40% of patients and this is in agreement with a recent study involving a large number of PD