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Sleep and Impulsivity in Parkinson's Disease

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Abstract

Background—Impulsive behavior and poor sleep are important non-motor features of Parkinson's disease (PD) that negatively impact the quality of life of patients and their families. Previous research suggests a higher level of sleep complaints in PD patients who demonstrate impulsive behaviors, but the nature of the sleep disturbances has yet to be comprehensively tested.

Methods—Consecutive idiopathic PD patients (*N*=143) completed the Minnesota Impulse Disorder Interview and a sleep questionnaire that assessed sleep efficiency, excessive daytime sleepiness, restless legs symptoms, snoring, dreams/nightmares, and nocturia. Patients were also given a Unified Parkinson's Disease Rating Scale motor examination and they completed cognitive testing.

Results—Impulsive PD patients endorsed more sleep complaints than non-impulsive PD patients. The group difference was primarily attributable to poor sleep efficiency (e.g., greater nocturnal awakenings), $p < .01$, and greater daytime sleepiness, $p < .01$, in the impulsive PD patients. Interestingly, restless legs symptoms were also greater in the impulsive PD patients, $p < .05$. The results could not be explained by medications or disease severity.

Conclusions—Poor sleep efficiency, restless legs symptoms, and increased daytime sleepiness are associated with impulsivity in PD. Longitudinal studies are needed to determine whether sleep disturbances precede impulsivity in PD.

Keywords

Parkinson s disease; sleep; impulse control disorder; excessive daytime sleepiness

1. Introduction

Motor symptoms (i.e. tremor, rigidity, and slowness) are the defining features of Parkinson's disease (PD), however, non-motor symptoms may have a greater impact on patients' quality of life [1]. Of particular interest, PD is associated with an increased prevalence of impulse control disorders (ICDs) [2,3]. ICDs include compulsive shopping, compulsive eating, pathological gambling, dopamine dysregulation syndrome (impulsive dopaminergic medication use), and hypersexuality which involves exhibitionism, incestuous behavior, and

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even zoophilia [2,4]. Impulsivity can greatly impact the lives of patients and their families; for example, in one case, a PD patient with pathological gambling lost $100,000 [5].

Dopaminergic medication therapy—particularly the administration of dopamine receptor agonists—is associated with an increased risk for ICDs in PD patients by about three times that of those not treated with agonists [6–8]. With the exception of dopamine dysregulation, ICDs in PD patients have been hypothesized to also relate to non-pharmacological etiologies, including individual susceptibilities [5]. Risk of ICD in PD patients is associated with early age of disease onset, novelty seeking, family history of gambling or alcohol abuse, psychiatric symptoms (e.g., greater depression, anxiety, and obsessive-compulsive symptoms), and cognitive impairments [9,10].

A feature of ICDs that has received little attention is associated sleep fragmentation and daytime sleepiness. Sleep deprivation and fragmentation have been linked causally to a lack of control over impulsive behavior in healthy adults [11,12], presumably due to sleep-loss-related impairments in prefrontal cortex top-down inhibitory control [13,14]. Likewise, sleep fragmentation has been linked to impulsiveness in other clinical populations including attention-deficit/hyperactivity disorder (ADHD)[15] and restless legs syndrome (RLS)[16]. Three reports are suggestive of a similar relationship in PD. Nirenberg and Waters [17] reported two cases in which ICD development (compulsive eating) was associated with development of excessive daytime sleepiness. Pontone et al.[18] observed a nominal, but non- significant trend for increased PD patient endorsement of sleep disturbance with ICDs. O'Sullivan et al.[19] had ninety-two PD patients mail in responses to the PD sleep scale and observed worse overall sleep scores in impulsive compared to non-impulsive patients.

The above studies [17–19] are suggestive of a relationship between sleep and impulsivity in PD, but they are limited by being either underpowered or by not assessing specific sleep related symptoms. Our goal in the present study was to assess whether impulsivity is associated with sleep disturbances across specific domains: sleep efficiency, daytime sleepiness, nightmares/dreams, snoring, nocturia, and restless legs symptoms. The study included a relatively large sample of 143 PD patients who were administered a battery of validated measures in order to permit firmer conclusions about the presence of any associations.

2. Method

2.1. Patients

The study was approved by the Emory University Institutional Review Board. All participating subjects reviewed and signed an IRB approved consent document. Subject recruitment started February 9, 2009 and ended September 14, 2010. All subjects were recruited from the practices of two neurologists (SAF and AF) in the Emory University movement disorder center. The first 79 participants were also part of an initial cohort of 230 PD patients previously enrolled in a genetics study [20]. The last 73 were not part of that cohort and were recruited consecutively. All patients were evaluated by movement disorder neurologists (SAF and AF) and met standard clinical diagnostic criteria for PD (modified UK brain bank criteria)[21]. Patients were enrolled regardless of age at disease onset, family history of PD, or treatment status (treated or not, with any combination of antiparkinsonian medications). Exclusion criteria included late stage dementia where subjects were unable to complete the visit assessments, history of stroke, findings suggestive of atypical parkinsonism (extraocular movement abnormalities, pyramidal tract signs, ataxia, early dementia), past neuroleptic use, and past history of multiple head injuries with loss of consciousness. One neurologist (SAF) rated patients' motor symptoms in the "on" state using the Unified Parkinson's Disease Rating Scale (UPDRS) [22]. Cognitive status was

determined using the Mini-Mental State Examination (MMSE) [23]. Of the recruited sample (N = 152), 143 PD patients responded to both the sleep questionnaire and the Minnesota Impulse Disorder Interview (MIDI) [24]. Demographic information is provided in Table 1.

2.2. Assessments

The sleep questions are listed in Table 2 and were drawn from existing studies (e.g., restless legs epidemiology [25,26]). Patients also completed the Epworth Sleepiness Scale [27], in which they rated how likely they are to doze or to fall asleep in different situations. The MIDI [24] is a semistructured interview used to assess the degree of impulsivity relating to compulsive shopping, hypersexuality, and pathological gambling behaviors.

2.3. Statistical analyses

Presence of impulsivity was determined by a "yes" response to any of the MIDI questions about impulsive buying, gambling, or sexual behavior. For the sleep questionnaire (Table 2), after removing "don't know" responses, we compared sleep complaints between the impulsive PD group and the non-impulsive PD group by using t-tests (Levene's test corrections when necessary). In addition, we summed all "yes" MIDI responses to form a continuous measure of impulsivity and examined sleep—impulsivity associations using Spearman's rho.

Alpha was set to .05, unless otherwise specified. To protect against increases in Type I error, we combined responses on sleep questions to form composites of total sleep complaints (summation of questions 2–6, 9–12; see Table 2), frequency of dreams/nightmares (summation of questions 9–10), restless legs symptoms (summation of questions 11–12), and sleep efficiency (derived from questions 1–4, 7–8). For the sleep efficiency composite we first divided the number of hours sleeping at night (question 1) by the amount of time in bed (absolute difference between questions 7 and 8) and then standardized these values by converting them to z-scores using SPSS statistical software (i.e., the sample mean is subtracted from each individual score and the remainder is divided by the standard deviation). We also calculated the z-scores for questions 2–4 after transforming them with a sign reversal so that higher values represented better sleep efficiency (less fragmentation). The sleep efficiency composite was the average of these four z-score measures.

3. Results

3.1. Levels of impulsivity

One hundred and five PD patients were assigned to the non-impulsive group ($M_{\text{MIDI sum}}$ = 0.0) and 38 PD patients were assigned to the impulsive group ($M_{\text{MIDI sum}}$ = 2.74, SD = 2.89, range = 1–10). Most of these patients showed signs of only impulsive buying (n=21), though some showed only impulsive gambling (n=9), only hypersexuality (n=3), or some combination (n=5). The impulsive patients and non-impulsive patients did not differ significantly on any of the demographic or disease-related variables listed in Table 1.

3.2. Sleep and impulsivity

The sleep complaint results are listed in Table 3. The impulsive PD group reported significantly more sleep complaints than the non-impulsive PD group, and these sleep complaints were primarily attributable to poor sleep efficiency (i.e., increased fragmentation of sleep), excessive daytime sleepiness (higher Epworth scores), and increased incidence of restless legs symptoms. These significant effects replicated when considering impulsivity as a continuous variable (Spearman's rho ranged from .20–.25, all ps < .05). The association

with sleep efficiency related both to difficulty falling asleep, $t(141) = 2.13$, $p = .035$, as well as to more frequent nocturnal awakenings, $t(141) = 2.32$, $p = .022$.

3.3. Sleep and impulsivity by medication class

The relationship between sleep variables and impulsivity was similar when medication class was considered. When examining PD patients only taking levodopa ($n = 33$) there was a significant difference between the impulsive and non-impulsive groups for total sleep complaints, $t(31)=3.67$, $p<.001$, Epworth scores, $t(31)=4.01$, $p<.001$, and restless legs symptoms, $t(31)=3.91$, $p<.001$ (a trend was observed for sleep efficiency, $t(30)=1.79$, $p=.08$). Likewise, when examining PD patients only taking dopamine agonists (no levodopa; $n=28$), the impulsive group relative to the non-impulsive group demonstrated significantly more total sleep complaints, $t(26)=2.66$, $p=.013$, and greater restless legs symptoms, $t(25)=2.60$, $p=.015$ (Epworth scores and sleep efficiency scores were in the expected direction and of a similar magnitude but not statistically significant, ps > .10).

3.4. Sleep and impulsivity regression analyses

To rule out the impact of potential covariates we conducted a hierarchical linear regression on the continuous impulsiveness score. After co-varying for UPDRS, usage of any dopaminergic medication, MMSE, disease duration, age, years of education, and gender, we entered in step 2 the total sleep complaints score, which explained significant additional variance in impulsiveness, $\Delta R^2 = .062$, $\beta = .258$, $p = .003$. In a second hierarchical regression analysis, we replaced the total sleep complaints score with the sleep efficiency composite, restless legs symptoms, and Epworth scores (in step 2). These three measures collectively explained significant variance in impulsiveness, $\Delta R^2 = .076$, $p = .018$; of these three measures, only sleep efficiency explained significant unique variance, $\beta = -.226$, $p = .014$. We more closely examined the sleep efficiency effect by entering in step 2 the reported difficulty falling asleep and frequency of nocturnal awakenings. These two measures combined to explain significant variance in impulsiveness, $\Delta R^2 = .065$, $p = .010$, and nocturnal awakenings was a stronger contributor, $\beta = .215$, $p = .018$, than difficulty falling asleep, $\beta = .113$, $p = .196$.

4. Discussion

Sleep disruption has been linked causally to a lack of control over impulsive behavior in healthy individuals [11,12], and is associated with impulsivity in some neurologic disorders [15,16]. Previous research has provided suggestive data that impulsivity in PD patients is also associated with sleepiness and sleep disturbances [17–19]. The present findings confirm that impulsivity in PD is linked to sleep features, particularly excessive daytime sleepiness (Epworth scores) and sleep fragmentation (i.e., poor sleep efficiency). Disease-specific factors and/or individual susceptibility may explain these findings [5].

4.1. Disease and medication-specific factors

Impulsivity in PD first received attention over a decade ago due to its association with dopaminergic medication [2,7]. Impulsivity is linked more to dopamine agonists than levodopa [6], and may or may not be related to dosage [5,8]. In addition, greater daytime sleepiness has been linked to dopaminergic medications (particularly dopamine agonists), but such effects are not strongly related to nocturnal sleep [28]. In the present study, regression analyses demonstrated associations between sleep and impulsivity after controlling for usage of dopaminergic medication; the sleep—impulsivity link was also observed when isolating both levodopa and dopamine agonist drug classes.

A limitation of the present study was a lack of information on medication doses, therapy duration, and reliance on "on" state exams. Though limiting, available measures of disease progression did not explain the sleep—impulsivity association. There were no significant differences between the impulsive and non-impulsive PD groups in disease severity as measured by UPDRS motor score in the "on" state, disease duration, or cognitive ability (MMSE). Therefore, though dopamine dysregulation plays an important role in increasing risk of impulsivity in PD, it is not the only important variable [5], and the sleep—impulsivity relationship appears to go beyond medication effects.

4.2. Individual susceptibility

Another explanation of the sleep—impulsivity association in PD patients is that nocturnal sleep disturbances and daytime sleepiness increase susceptibility to developing an ICD. Sleep deprivation and sleepiness are known to increase impulsive behavior [11,12], either via disruption of the prefrontal cortex [13,14], which would otherwise provide top-down inhibitory control of impulsive behavior, or by amplifying the reactivity of brain reward networks [29]. Moreover, PD is associated with impairments to sleep including sleep fragmentation [30]. Case reports have suggested an association in PD patients between impulsivity and increased daytime sleepiness [17], and PD patients with impulsivity generally endorse more sleep complaints [18,19]. We confirmed and elucidated the nature of these associations with the Epworth sleepiness scale and a composite measure of sleep efficiency. It may be important to note that these effects occurred in the absence of a significant difference in total sleep time between impulsive and non-impulsive groups. Group differences in sleep fragmentation (and restless legs) are possible in the absence of differences in total sleep time (see Sleep Heart Health Study [31]). However, this null effect may have been due to insufficient statistical power (the groups differed by approximately 23 minutes) or participant confusion over the difference between total sleep time and total time in bed. We observed that sleep efficiency was the most potent of the sleep variables in explaining variance in impulsiveness, and the sleep efficiency effect was due more to frequency of nocturnal awakenings than to difficulty falling asleep. The latter pattern is more consistent with the idea of sleep deficiencies contributing to risk for ICDs than the hypothesis that ICDs cause difficulties with falling asleep at night. However, longitudinal studies that include caregiver reports are needed to determine whether sleep disturbances precede impulsive behaviors in PD patients.

4.3. PD, impulsivity, and restless legs

A final, unexpected result was that we observed an association between restless legs symptoms and impulsiveness in PD patients, which has not been previously reported. Though speculative, it is possible that the urge to move ones legs and the urge to compulsively gamble, shop, or have sex, constitutes a shared phenomenology of restless legs and PD plus impulsivity. The increased prevalence of restless legs symptoms in PD patients with impulsiveness warrants further attention.

4.4. Conclusions

We observed an association in PD patients between impulsivity and sleep disturbances including frequency of nocturnal awakenings, difficulty falling asleep, restless legs symptoms, and excessive daytime sleepiness. The association between impulsivity and sleep disturbances could not be attributed solely to disease- or medication-related factors. Longitudinal studies that investigate time of onset of sleep disturbances and impulsive behaviors will help determine whether impulsive behaviors cause nocturnal sleep disturbances or if sleepiness and disturbed nocturnal sleep increase vulnerability to developing ICDs.

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Table 1

Demographic information (standard deviations in parentheses) across the non-impulsive PD group and impulsive PD group. UPDRS (n=142), MMSE (n=141), and medication class (n=142) information was available for most patients. *P* values refers to the independent samples *t* test between the non-impulsive and impulsive PD groups.

	PD Total Group (n=143)	**Non-Impulsive PD Group (n=105)**	**Impulsive PD Group (n=38)**	***P value***
UPDRS Motor Scale	17.77(7.88)	17.46(7.81)	18.63 (8.11)	.44
MMSE (max=30 points)	28.21 (1.96)	28.29 (1.91)	27.97 (2.09)	.35
Disease Duration (years)	7.95(4.40)	7.87 (4.12)	8.18 (5.17)	.71
Age (years)	64.71(9.05)	64.50 (9.17)	65.26 (8.82)	.66
Education (years)	15.76(2.31)	15.76 (2.21)	15.76 (2.63)	.99
Gender (% Female)	35	32	42	.28
Levodopa (% on med)	52	49	62	.15
Dopamine agonist (% on med)	49	48	51	.69

PD=Parkinson's disease; UPDRS=Unified Parkinson's Disease Rating Scale; MMSE=Mini-Mental State Examination

Table 2

Sleep questionnaire, scale of individual sleep questions, and composite score subdivisions.

Sleep Question	Scale	Composite
1. How many hours do you usually get at night?		Sleep efficiency
2. How often do you have trouble falling asleep?	1 to 5	Sleep efficiency
3. How often do you have trouble waking up during the night?	1 to 5	Sleep efficiency
4. How often do you have trouble waking up too early and not being able to fall asleep again?	1 to 5	Sleep efficiency
5. When you awaken during the night, how often do you urinate?	1 to 4	Nocturia
6. How often do you snore in any way?	1 to 5	Snoring
7. What time do you typically go to bed at night?		Sleep efficiency
8. What time do you typically wake up in the morning?		Sleep efficiency
9. How often do you have a night full of intense, vivid dreams?	1 to 5	Dreams/Nightmares
10. How often do you have nightmares (frightening dreams)?	1 to 5	Dreams/Nightmares
11. At bedtime, how often does restlessness in your legs delay your falling asleep?	1 to 4	Restless Legs
12. When you wake up during the night, how often do you feel unpleasant sensations in the leg muscles that require you to move your legs or walk in order to be comfortable?	1 to 4	Restless Legs

Questions 2–4, 6, 9–10: 1 = never, 2=A few times, 3=Sometimes, 4=Quite often, 5=Usually, 6=Don’t know. Question 5: 1=Once, 2=Twice, 3=Three Times, 4=Four or more times. Questions 11–12: 1=Never, 2=Occasionally, 3=Often, 4=Very often

Table 3

Sleep questionnaire responses across non-impulsive and impulsive PD groups. Standard deviations are in parentheses.

	Non-Impulsive PD Group (n=105)	**Impulsive PD Group (n=38)**	***p* value**
Total Sleep Complaints Score	17.19 (4.06)	19.95 (4.96)	<.001***
Sleep Efficiency Z-Composite	.10 (.64)	−.26 (.77)	.008**
Restless Legs	2.96 (1.26)	3.55 (1.52)	.021*
Dreams/Nightmares†	3.23 (1.30)	3.83 (1.70)	.057
Nocturnal Sleeping Hours	6.96 (1.29)	6.58 (1.36)	.138
Bathroom trips	1.63 (.81)	1.92 (1.00)	.083
Snoring	2.75 (1.15)	3.06 (1.29)	.205
Epworth Score	9.00 (4.50)	11.58 (5.24)	.005**

Note:

†indicates that Levene's test for equality of variances was significant ($p < .05$) and the adjusted p value is reported. The sample sizes varied due to missing data or "don't know" responses. The available sample sizes were 137 for sleep efficiency, 141 for restless legs, 137 for dreams/nightmares, 140 for nocturnal sleeping hours, 142 for nocturia, 125 for snoring, and 141 for Epworth. PD=Parkinson's disease