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SCIENTIFIC INVESTIGATIONS

Presleep Cognitive Arousal and Insomnia Comorbid to Parkinson Disease: Evidence for a Serial Mediation Model of Sleep-Related Safety Behaviors and Dysfunctional Beliefs About Sleep

Cindy Lebrun, MS[1]; Marie-Christine Gély-Nargeot, PhD[1]; Khaalid Hassan Maudarbocus, MS[1]; Alexia Rossignol, MS[2]; Christian Geny, MD[2]; Sophie Bayard, PhD[1]

[1]Univ Paul Valéry Montpellier 3, Univ Montpellier, Montpellier, France; [2]Centre Expert Maladie de Parkinson, Service de Neurologie, Hôpital Gui de Chauliac, Montpellier, France

Study Objectives: Insomnia disorder (ID) is highly associated with Parkinson disease (PD) with great negative effect on health-related quality of life. Nonetheless, the relevance of psychological processes involved in the maintenance of insomnia is yet to be established in the context of this neurological condition. Our aim was to examine a serial meditation model of sleep-related safety behaviors and dysfunctional beliefs about sleep in association with presleep cognitive arousal and ID in patients with PD.

Methods: A total of 68 patients with PD completed self-report measures including the Sleep-Related Behaviors Questionnaire (SRBQ-20), Dysfunctional Beliefs and Attitudes about Sleep (DBAS-16), and the cognitive subscale of the Presleep Arousal Scale (PSAS-C). ID was assessed according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria. Bootstrapped serial mediation analyses were conducted to test indirect effects.

Results: Overall, 55.6% of patients with PD met diagnostic criteria for ID. The association between presleep cognitive arousal (PSAS-C) and ID was serially mediated by sleep-related safety behaviors (SRBQ-20) and strong endorsement of dysfunctional beliefs about sleep (DBAS-16) (bias-corrected 95% confidence interval for the indirect effect = 0.013, 0.093). An alternate serial mediation model in which dysfunctional beliefs about sleep precede sleep-related safety behaviors was not statistically significant (bias-corrected 95% confidence interval for the indirect effect = −0.001, 0.046).

Conclusions: ID comorbid to PD is associated with the classic psychological factors perpetuating ID in neurological disease-free individuals with insomnia. Target-oriented interventions for instance cognitive behavioral therapy for chronic insomnia should be considered as a treatment approach for ID comorbid to PD.

Keywords: dysfunctional beliefs, insomnia, Parkinson disease, presleep cognitive arousal, sleep-related safety behaviors

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BRIEF SUMMARY

Current Knowledge/study Rationale: Insomnia is common among individuals with Parkinson disease (PD). In individuals free of neurological disease who are affected by insomnia disorder, cognitive and behavioral processes play a central role in both the maintenance and treatment of insomnia.

Study Impact: This study documents the high relevance of these psychological processes in the specific context of insomnia comorbid to PD. Target-oriented interventions such as cognitive behavioral therapy should be considered as a treatment approach for insomnia disorder comorbid to PD.

INTRODUCTION

Insomnia is a common complaint in Parkinson disease (PD). The definitions and assessment methods of insomnia symptoms in PD in the different studies result in prevalence estimates ranging from 27% to 80%.[1–8] A thorough search of the relevant literature yielded only one study that has estimated the prevalence of insomnia disorder (ID) according to the International Classification of Sleep Disorders, Third Edition (ICSD-3)[9] and the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).[10] Indeed, when these standardized criteria are used, it is estimated that 55.7% of patients with PD meet the criteria for ID.[5] This rate is three to four times as high as in the general population, which indubitably makes ID one of the most prevalent sleep disorders in PD[11] with a substantial negative effect on health-related quality of life.

As in the general population, female sex,[3] increasing age,[12] symptoms of depression,[2–4,7] anxiety,[2,4] fatigue, and daytime sleepiness[2,13] have been associated with insomnia complaint severity in PD. In contrast, clinical features of the disease were very slightly related to insomnia with small effect sizes. These features include motor fluctuations,[8] autonomic problems,[2] cardiovascular and thermoregulatory dysfunctions[13] and doses of dopaminergic medications.[2–4,7,8,13]

Clinical and research evidence have highlighted that both cognitive and behavioral processes play an important mediating role in perpetuating or even exacerbating insomnia.[14,15] These processes and their causal relationships are synthesized in a largely accepted comprehensive model proposed by Harvey in 2002.[15] On the whole, this model acknowledges the central role of excessive presleep cognitive activity (also called presleep cognitive arousal) in the maintenance of insomnia. In its relationship with insomnia, presleep cognitive activity mainly

composed of intrusive negative-toned thoughts is reinforced by both sleep-related safety behaviors and dysfunctional beliefs about sleep.[15] Furthermore, it has also been documented that safety behaviors exacerbate dysfunctional beliefs about sleep, worsening sleep disturbance.[14,15] Safety behaviors are defined as overt or covert behaviors that are adopted to avoid a feared situation. In the case of insomnia, sleep-related safety behaviors are used at night because of the fear of not sleeping, or during the day as coping mechanisms to prevent the consequences of a night of disturbed sleep. For example, individuals with insomnia may go to bed early, or catch up on sleep by napping, thus attempting to avoid fatigue during the day. Safety behaviors may also manifest as more subtle coping strategies, such as use of cognitive distraction and thought suppression strategies, with the aim to suppress presleep cognitive activity. Dysfunctional beliefs about sleep refer to sleep-related cognitions including erroneous beliefs and appraisals, worry, unrealistic expectations, and perceptual and attention bias.

To the best of our knowledge, no study has yet validated the cognitive model of insomnia in PD. Consequently, our study seeks to determine, in a serial mediation model, the interrelationships between presleep cognitive arousal, sleep-related safety behaviors, and dysfunctional beliefs about sleep in their association with ID in PD. More specifically, we hypothesized that presleep cognitive arousal should indirectly influence ID through sleep-related safety behaviors and dysfunctional beliefs about sleep, standing as causally related mediators.

METHODS

Participants

Sixty-eight nonconsecutive nondemented patients with idiopathic PD were recruited during their neurological routine clinic visit with their attending neurologist. Inclusion criteria included PD based on the United Kingdom Parkinson's Disease Society Brain Bank criteria. Patients with a history of psychotic disorder, substance abuse, head injury, and an active, progressive or unstable physical illness (eg, cancer or acute pain) were excluded. There were no other criteria of selection. Written informed consent was obtained from all patients and the study has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and was approved by the local ethics committee. No compensation was provided to study patients.

Data Collection and Assessment

Demographic data, information on disease characteristics, and medication details (with particular attention to dopaminergic agents and psychoactive drugs) were collected during a face-to-face interview. The levodopa equivalent daily dose was calculated. Motor experiences of daily living and motor disability were assessed using, respectively, Part II of the Movement Disorder Society of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS)[16] and the modified Hoehn and Yahr staging.[17]

All patients individually underwent a face-to-face clinical interview to assess ID, sleep history, and medical and psychological states. Current insomnia, mood, and anxiety disorders were diagnosed as per DSM-5 criteria, using a local translation of the clinical version of the structured interview for DSM-5 (SCID-5-CV). ID was diagnosed in patients with PD[9,10] if they (1) self-reported difficulty in initiating and/or maintaining sleep and/or early morning awakening despite having adequate opportunity to sleep, (2) were undergoing significant distress and/or impairment in daytime functioning, and (3) were at least 3 months and at least 3 nights a week on the SCID-5-CV.

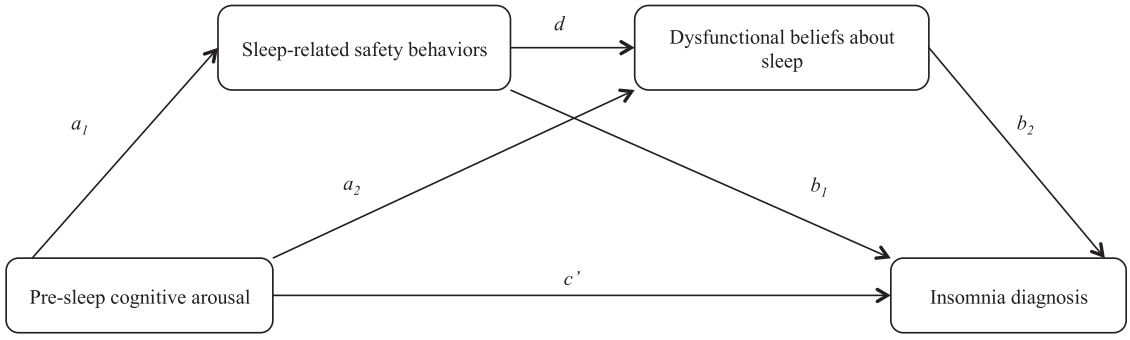
All patients were screened for restless legs syndrome/Willis-Ekbom disease (RLS/WED) and rapid eye movement sleep behavior disorder (RBD). RLS/WED was assessed based on the International Restless Legs Syndrome Study Group criteria.[18] RBD Single-Question Screen was applied to screen possible RBD.[19]

Self-reported insomnia symptoms were scored using the French version of the Sleep Condition Indicator,[20] with lower scores indicating worse sleep. Self-reported depression and anxiety severity was assessed with the 21-item Beck Depression Inventory-II (BDI-II)[21] and Parkinson's Anxiety Scale (PAS).[22] The cognitive processes associated with insomnia were evaluated with the Sleep-Related Behaviors Questionnaire (SRBQ-20),[23] the short version of the Dysfunctional Beliefs and Attitudes about Sleep (DBAS-16),[24] and the cognitive subscale of the Presleep Arousal Scale (PSAS-C).[25] Higher scores on these scales respectively indicated a more frequent use of counterproductive behavioral strategies to cope with fatigue or to improve sleep, a stronger endorsement of dysfunctional beliefs about sleep and a higher level of presleep cognitive activity.

Statistical Analysis

The data were analyzed using IBM SPSS Statistics for Macintosh, Version 24.0 (IBM Corp., Armonk, New York, United States). The continuous variables were expressed as mean ± standard deviation and categorical variables as frequency and percentage. The *t* test was used to assess group differences for continuous variables, and the chi-square test was performed for categorical variables. In addition, we calculated the Cohen *d* as measure of the effect size. The effect size was considered small ($d = 0.2$), medium ($d = 0.5$), or large ($d = 0.8$). Values of *P* were corrected for multiple testing with Benjamini and Hochberg false- discovery rate approach (1995).[26] Prior to conducting the mediation analyses, zero-order correlations were performed for the entire sample to examine associations among the variables of interest. Next, we conducted a serial mediation analysis[27] in which we assessed the indirect effect of presleep cognitive arousal on insomnia diagnosis through both sleep-related safety behaviors and dysfunctional beliefs about sleep (ie, the a_1 - d - b_2 path; **Figure 1**). We chose a bootstrapping procedure with 10000 repetitions using Hayes and Preacher PROCESS Macro for SPSS. The indirect effect is deemed significant if the confidence interval does not cover zero. The aim of the serial mediation model is to test a specific theoretical sequence among the variables. Thus, to clarify the direction of the indirect effect, we also tested an alternate model in which dysfunctional beliefs about sleep preceded sleep-related safety behaviors. A value of $P < .05$ was considered as statistically significant.

Figure 1—Serial mediation model.



RESULTS

Descriptive Statistics

PD Clinical Characteristics

Of the total number of patients (n = 68), 54.4% were males; ages varied between 47 and 78 years with a mean of 64.02 ± 7.65. The average years of schooling were 13.32 ± 3.87. Most patients (67.6%) were retired and 14.7% were employed. Sixty-six patients were undergoing treatment with the following antiparkinsonian medications: dopamine agonist monotherapy (n = 5), levodopa monotherapy (n = 21), or combined levodopa-agonist therapy (n = 40). The mean levodopa equivalent daily dose was 742.56 ± 499.60 mg. The mean MDS-UPDRS II score was 14.20 ± 8.15. The Hoehn and Yahr staging varied between 1 and 4 with a mean staging of 2.14 ± 0.97. Mean duration of disease was 9.88 ± 6.86 years. Among the 68 patients enrolled in the study, 55.8% met the clinical criteria for insomnia disorder. Most patients with PD with a diagnosis of ID had mixed insomnia (58%). The mean insomnia duration was 97.08 ± 94.3 months.

PD-ID and PD-NID Group Comparisons

Group comparisons are shown in **Table 1**. The demographic characteristics of PD were comparable in both groups; however, female sex was more frequently associated with ID ($P = .02$). Regarding PD characteristics, no group effect was observed as for age at onset ($P = .74$), duration of the disease ($P = .32$), Hoehn and Yahr scale ($P = .76$), and UPDRS-II ($P = .44$). The proportion of individuals with RLS/WED and possible RBD did not differ between the two groups ($P = .64$, $P = .43$, respectively). The benzodiazepines intake was comparable in both groups ($P = .05$). Patients with PD-ID reported higher levels of depressive and anxiety symptoms compared to patients with PD-NID ($P < .006$, $d' = -0.81$; $P < .04$, $d' = -0.61$, respectively). These effects were medium to large.

Significant group effects were observed for DBAS-16, SRBQ-20, and PSAS-C questionnaires. Patients with PD-ID reported higher endorsement of dysfunctional beliefs about sleep ($P < .001$, $d' = -1.32$), higher engagement in safety behaviors ($P = .001$, $d' = -1.17$) and higher cognitive manifestations of arousal at bedtime ($P = .005$, $d' = -1$) compared to patients with PD-NID. These effects were large.

Serial Mediation Analysis

Power Analysis

Based on preexisting established relations, a large magnitude effect size was predicted between presleep cognitive arousal and sleep-related safety behaviors (β = 0.74),[28] sleep-related safety behaviors and dysfunctional beliefs about sleep ($r = .58$),[29] whereas a moderate effect size was predicted between dysfunctional beliefs about sleep and insomnia ($r = .45$).[24] Based on these predictions, mediation analysis using bias-corrected bootstrapping requires 54 total participants to achieve .80 power[30] and 68 patients participated in the current study.

Preliminary Analysis and Zero-Order Correlations

As mentioned previously, sex was associated with the dependent variable insomnia diagnosis ($P = .02$), but was not associated with independent (PSAS-C, $P = .4$) and mediating variables (SRBQ-20, $P = .14$; DBAS-16, $P = .25$).

Depressive (BDI-II) and anxiety (PAS) symptoms were correlated to all independent (PSAS-C, respectively, $r = .50$; $r = .50$), dependent (insomnia diagnosis, respectively, $t_{66} = -3.31$; $t_{66} = -2.5$), and SRBQ-20 mediating variables (SRBQ-20, respectively, $r = .40$; $r = .30$). Only depressive symptoms were associated with the DBAS-16 mediating variable ($r = .25$) (**Table 2**). Given this pattern of results, the BDI-II was considered as a covariate in the mediation analysis. PAS was not analyzed as a covariate because it shared highly significant variance with the BDI-II ($r = .66$). In a mediation model, mediators have to be significantly correlated with both the predictors and outcome variables. All correlations showed the expected links (**Table 2**), such as presleep cognitive arousal, and insomnia diagnosis were significantly associated with the mediating variables sleep-related safety behaviors (SRBQ-20, respectively, $r = .47$; $r = .50$) and dysfunctional beliefs about sleep (DBAS-16, respectively, $r = .35$; $r = .55$). Therefore, the proposed mediators were submitted for serial mediation analysis.

Test of the Serial Mediation Models

After controlling for depressive symptoms, the overall regression model predicting insomnia diagnosis from presleep cognitive arousal, sleep-related safety behaviors, and dysfunctional beliefs about sleep was significant, explaining

Table 1—Demographic, clinical, and insomnia characteristics and cognitive processes of insomnia in patients with PD with insomnia disorder and without insomnia disorder.

	PD-ID (n = 38)	PD-NID (n = 30)	Statistics (degree of freedom)	*P*
Demographic data				
Age, years	62.6 ± 8.0	65.8 ± 6.8	t_{66} = 1.75	.19
Sex (%female/%male)	61/39	27/73	χ^2_1 = 7.74	**.02**
Education, years	13.4 ± 3.5	13.2 ± 4.3	t_{66} = −0.23	.81
Clinical characteristics				
Age at onset, years	53.7 ± 8.7	54.7 ± 10.9	t_{66} = 0.41	.74
Duration of disease, years	8.9 ± 6.5	11.1 ± 7.1	t_{66} = 1.34	.32
UPDRS-II score	12.9 ± 7.7	15.1 ± 8.4	t_{66} = −1.11	.44
Hoehn and Yahr score	2.1 ± 1.0	2.1 ± 0.9	t_{66} = −0.35	.76
MoCA score	26.6 ± 3.1	25.2 ± 3.2	t_{66} = −1.85	.17
Levodopa equivalent dose (mg/d)	831.0 ± 541.0	629.0 ± 422.0	t_{66} = −1.67	.20
Dopamine agonists (n)	26	18	χ^2_2 = 0.90	.70
Antidepressants (n)	8	4	χ^2_1 = 0.86	.93
Benzodiazepines (n)	11	2	χ^2_1 = 5.90	.05
Melatonin (n)	6	1	χ^2_1 = 2.80	.24
Restless legs syndrome (n)	2	0	χ^2_1 = 1.70	.64
Probable REM sleep behavior disorder (n)	10	12	χ^2_1 = 1.10	.43
Mood and anxiety assessment				
Beck Depression Inventory score	16.5 ± 9.7	10.0 ± 6.7	t_{66} = −3.30	**.006**
Current mood disorder (n)	14	8	χ^2_1 = 0.79	.50
Parkinson Anxiety Scale score	20.3 ± 8.0	15.6 ± 8.8	t_{66} = −2.5	**.04**
Current anxiety disorder (n)	4	6	$\chi^2(1)$ = 1.2	.42
Insomnia disorder				
Type of insomnia (%)				
Sleep onset insomnia	8.7	–	–	–
Sleep maintenance insomnia	18.5	–	–	–
Terminal insomnia	15.0	–	–	–
Mixed insomnia	57.8	–	–	–
Insomnia duration, months	97.1 ± 94.3	–	–	–
Frequency of sleep difficulties, d/wk	5.4 ± 1.8	–	–	–
Sleep Condition Indicator score	24.9 ± 6.0	11.8 ± 4.6	t_{66} = 10	**< .001**
Questionnaires of cognitive processes related to insomnia				
Dysfunctional Beliefs About Sleep score	89.4 ± 22.2	58.1 ± 25.4	t_{66} = −5.3	**< .001**
Sleep-Related Behaviors Questionnaire score	36.1 ± 12.8	21.8 ± 11.8	t_{66} = −4.6	**.001**
Presleep cognitive arousal score	18.5 ± 7.6	12.1 ± 3.7	t_{66} = −4.1	**.005**

Data presented as mean ± standard deviation unless otherwise indicated. Values of *P* are corrected for multiple testing with Benjamini and Hochberg false discovery rate approach. Bold values indicates a significant correlation ($P < .05$ after correction from multiple comparisons). MoCA = Montreal Cognitive Assessment, PD = Parkinson disease, PD-ID = Parkinson disease and insomnia disorder diagnosis, PD-NID = Parkinson disease without insomnia disorder diagnosis, UPDRS-II = Unified Parkinson's Disease Rating Scale.

53% of the variance in insomnia diagnosis (**Figure 2**). Path coefficient from the bootstrapped regression showed that presleep cognitive arousal was positively and significantly associated with higher use of sleep-related safety behaviors (β = 0.725, standard error [SE] = 0.252, $P = .005$), which was positively associated with higher endorsement of dysfunctional beliefs about sleep (β = .590, SE = 0.257, $P = .02$), being in turn positively and significantly associated with insomnia diagnosis (β = 0.054, SE = 0.017, $P = .002$) (**Figure 2**).

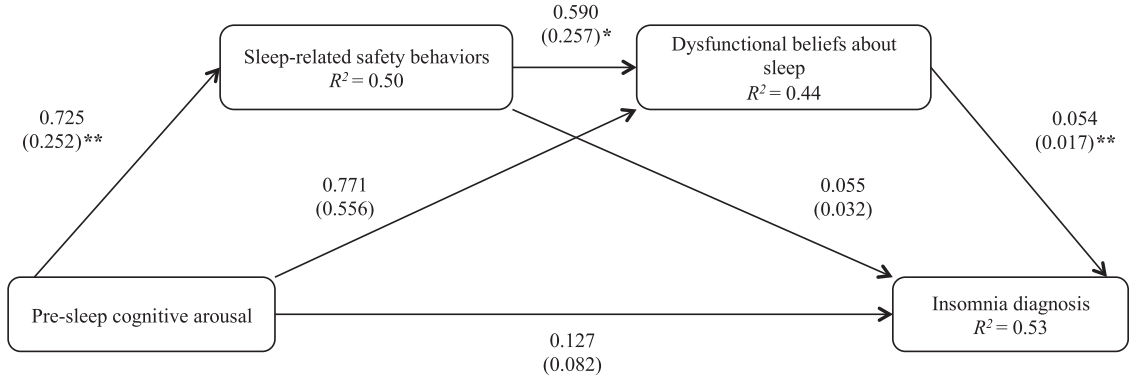
As predicted, mediation analyses showed that the serial indirect effect from presleep cognitive arousal to insomnia diagnosis through both sleep-related safety behaviors and dysfunctional beliefs about sleep was statistically significant (β = 0.023, SE = 0.024, bootstrapped 95% confidence interval

Table 2—Zero-order correlations between variables of interest and potential confounding variables.

		1	2	3	4	5
1	Beck Depression Inventory	1.00				
2	Parkinson Anxiety Scale	.66 * (.50 to .79)	1.00			
3	Dysfunctional Beliefs About Sleep	.26 * (.17 to .46)	.24 (−.04 to .50)	1.00		
4	Sleep-Related Behaviors Questionnaire	.40 * (.20 to .58)	.30 * (.10 to .48)	.40 * (.19 to .58)	1.00	
5	Presleep cognitive arousal	.50 * (.25 to .69)	.50 * (.28 to .66)	.35 * (.15 to .52)	.47 * (.29 to .62)	1.00
6	Insomnia diagnosis	.38 * (.17 to .55)	.30 * (.06 to .51)	.55 * (.38 to .59)	.50 * (.31 to .66)	.45 * (.29 to .59)

Correlations reflect bias corrected, bootstrapped Pearson correlation coefficients with 10,000 samples derived from the original sample. 95% confidence intervals are presented in parentheses below the corresponding correlation coefficient. * Correlation is significant based on confidence intervals that do not include 0.

Figure 2—Regression coefficients and standard errors for the serial mediation model.



Controlling for depressive symptoms, the serial indirect effects of sleep-related safety behaviors and dysfunctional beliefs about sleep on the relationship between presleep cognitive arousal and insomnia diagnosis is statistically significant (β = 0.023, standard error = 0.024, bootstrapped 95% confidence interval = 0.013, 0.093) * $P < .05$, ** $P < .01$.

[CI] = 0.013, 0.093), whereas the direct effect of presleep cognitive arousal on insomnia diagnosis was not statistically significant (β = 0.127, SE = 0.082, $P = .12$) (**Figure 2**). This model indicates that the relationship between presleep cognitive arousal and insomnia diagnosis is fully mediated by sleep-related safety behaviors and dysfunctional beliefs about sleep.

When substituting the order of the mediators so that dysfunctional beliefs about sleep preceded sleep-related safety behaviors in the model, the indirect path was no longer significant (β = 0.008, SE = 0.010, 95% CI = −0.001, 0.046).

Note that there was no significant path from presleep cognitive arousal to dysfunctional beliefs about sleep (β = 0.771, SE = 0.556, $P = .17$) and also from sleep-related safety behaviors to insomnia diagnosis (β = 0.055, SE = 0.032, $P = .08$). Therefore, there was no significant indirect path from presleep cognitive arousal to insomnia diagnosis through either safety behaviors (β = 0.040, SE = 0.040, bootstrapped 95% CI = −0.018, 0.136) or dysfunctional beliefs about sleep (β = 0.041, SE = 0.044, bootstrapped 95% CI = −0.019, 0.136).

DISCUSSION

To the extent of our knowledge, this is the first study designed to identify the interrelationships between behavioral and cognitive factors in their contribution to ID comorbid to PD after controlling for potential confounders. We confirmed our hypothesis by showing that, among a clinical sample of patients with PD, higher presleep cognitive activity predicted higher frequency of engagement in sleep-related safety behaviors, which in turn predicted stronger endorsement of dysfunctional / erroneous beliefs about sleep and insomnia diagnosis.

In the current study, 55.6% of patients with PD had a diagnosis of ID based on DSM-5/ICSD-3 criteria. This rate is in accordance with a recent Brazilian study that has assessed ID in PD based on international standard diagnostic criteria.[5] Furthermore, we found that female sex and higher scores of depressive and anxious symptoms were significantly associated with ID comorbid to PD. These results are consistent with previous studies conducted in PD showing a robust association between insomnia complaint and female sex[3,4] and severity of both depressive[2–4,7,31] and anxious symptoms.[2,4,31] Interestingly, female sex, anxiety, and depression have also been systematically related to chronic insomnia in the general population.[32] Finally, in accordance with the large cross-sectional French CoPark cohort study (n = 636),[4] we reported no association between insomnia and PD-related features. In view of these results, one may presume that ID comorbid to PD is not the direct consequence of the disease itself, but rather an independent sleep condition underpinned

by the same maintaining factors identified in the absence of a neurological disease.

In support of this assertion, we found that ID comorbid to PD was strongly associated with increased level of presleep cognitive arousal, higher frequency of engagement in sleep-related safety behaviors, and higher endorsement of dysfunctional beliefs about sleep. For decades, it has been largely documented that presleep cognitive hyperarousal,[33] dysfunctional sleep-related cognitions,[34] and safety behaviors[35] are important maintaining factors of insomnia in the absence of any neurological condition. For the first time, we documented the specific contribution of these factors in ID comorbid to PD. We therefore highlighted the relevance of the cognitive model of insomnia proposed by Harvey in this neurodegenerative condition.[15] Note that our results are also in line with a very recent study performed by our group showing that ID comorbid to multiple sclerosis was associated with the classic psychological factors perpetuating ID in neurological disease-free individuals afflicted with insomnia.[36]

As previously reported in the absence of neurological disease,[29] analyses from our serial mediation model revealed a direct and positive association between erroneous beliefs about sleep and sleep-related safety behaviors considered as mediators. In addition, we observed that the direct effect between presleep cognitive arousal and insomnia diagnosis was fully mediated by these two variables. In fact, when controlling for these two proposed mediators, the effect of presleep cognitive arousal on insomnia diagnosis was no longer significant. Past research has suggested that the association between cognitive arousal and insomnia in older adults could be explained in part by the effect of mediating psychological maladjustment, (ie worry, anxious state, neuroticism trait, negative thoughts, beliefs about the ability to sleep),[37] and maladaptive sleep-related behaviors.[38] Our findings confirm and extend this perspective by demonstrating that excessive presleep cognitive activity was related to insomnia in PD via a sequential mediation pathway of safety behaviors and maladaptive beliefs about sleep. Interestingly, our serial mediation analyses indicated that sleep-related safety behaviors precede dysfunctional beliefs about sleep in the link between cognitive arousal and insomnia diagnosis. This result can be integrated into models of insomnia by both Espie et al[14] and Harvey.[15] These models postulate that because safety behaviors are derived from dysfunctional beliefs about sleep and triggered by worries about sleeplessness, their influence on insomnia might have been accounted for by their interaction with erroneous beliefs and by the influence of the level of cognitive arousal.

Finally, our results are in line with recently published studies that have shown the efficacy of cognitive behavioral therapy for insomnia in patients with PD on sleep diary parameters only.[39,40] Unfortunately, these pioneering studies did not assess the effect of the intervention on dysfunctional beliefs about sleep, sleep-related safety behaviors, and presleep cognitive arousal. These results pinpoint the need to consider ID comorbid to PD as a full-fledged clinical entity, underpinned by psychological factors and requiring a specific care/attention. With this perspective, DSM-5 and ICSD-3 nosological systems no longer consider the notion of "primary" and "secondary" insomnia.[9,10]

Some limitations of this study should be considered. First, although we applied a serial mediation model using a gold standard approach,[27] our results did not allow for causal inferences. Second, we did not extensively assess physical symptoms related to PD (eg, nocturia, pain, spasticity, muscle twitching) that may negatively affect sleep and lead to sleep disturbances. In this context, the Parkinson's Disease Sleep Scale would have been a suitable tool to address these issues,[41] even though it is not validated in the French language. Also, we cannot rule out, in our sample, the nocturnal/early morning off-state contribution to insomnia. In addition, it would have been interesting to assess excessive daytime sleepiness, which is a common symptom associated with insomnia in PD.[2] Finally, no polysomnography was performed to assess sleep parameters (eg, sleep fragmentation and sleep efficiency), and comorbid sleep disorders, in particular, sleep apnea syndrome, RBD and sleep-related movement disorders such as periodic limb movement disorder or RLS/WED. In this context, it is widely acknowledged that in its asymptomatic and early stages PD is associated with lesions through abnormal accumulation of α-synuclein in subcortical and brainstem nuclei involved in paradoxical and slow-wave sleep regulation.[42] As a consequence, the neuropathophysiology associated with PD needs to be considered in the development of insomnia. Nevertheless, no clear association has been established between sleep apnea syndrome,[2,43] RBD,[44] or sleep-related movement disorders[45,46] and insomnia symptoms in PD. The unique study having directly explored the links between objective sleep parameters and sleep perception in PD found no relationship between polysomnographic parameters (including total sleep time, sleep efficiency, apnea-hypopnea index, and periodic limb movement index) and insomnia severity (Insomnia Severity Index ≥ 8 versus < 8).[2] In addition, dysfunctional psychological processes, particularly sleep/insomnia-related cognition, have been identified in individuals affected by insomnia with comorbid sleep apnea syndrome.[47] This observation indicates that these "organic" sleep disorders deserve more diagnostic attention regarding possible insomnia-specific symptoms.

In conclusion, even if the neuropathophysiology of PD is doubtlessly a vulnerability factor contributing to the development of insomnia, our study emphasizes that sleep-related emotional, behavioral, and cognitive processes and their interrelationships are also involved in ID comorbid to PD. These processes and their interrelationships are similar to those identified in individuals with no neurological disease and who have insomnia. Furthermore, very recent literature provided evidence toward cognitive behavioral therapy for insomnia as an effective treatment for ID comorbid to PD. Primary care providers and neurologists should consider target-oriented interventions such as cognitive behavioral therapy for chronic insomnia as a treatment approach for ID comorbid to PD.

ABBREVIATIONS

BDI, Beck Depression Inventory
CI, confidence interval
DBAS, Dysfunctional Beliefs and Attitudes About Sleep

DSM, Diagnostic and Statistical Manual of Mental Disorders
ICSD, International Classification of Sleep Disorders
ID, insomnia disorder
MDS-UPDRS, Movement Disorder Society of the Unified Parkinson's Disease Rating Scale
PAS, Parkinson's Anxiety Scale
PD, Parkinson disease
PD-ID, Parkinson disease and insomnia disorder diagnosis
PD-NID, Parkinson disease without insomnia disorder diagnosis
PSAS-C, Cognitive subscale of the Presleep Arousal Scale
RBD, rapid eye movement sleep behavior disorder
RLS/WED, restless legs syndrome/Willis-Ekbom disease
SCID-5-CV, clinical version of the structured interview for DSM-5
SE, standard error
SRBQ, Sleep-Related Behaviors Questionnaire

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Address correspondence to: Cindy Lebrun, MS, Laboratoire Epsylon, EA 4556, Université Montpellier 3, Rue du Pr. Henri Serre, 34000 Montpellier, France, Tel: (33) 6 24 05 04 50; Email: cindylebrun@yahoo.com

DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. The authors report no conflicts of interest.