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RESEARCH ARTICLE



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Cognitive strategies to improve symptoms of restless legs syndrome

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Summary

Symptoms of restless legs syndrome are relieved by movement. Whether a cognitive task decreases sensory discomfort remains understudied. We aimed to assess the frequency of patients with restless legs syndrome who report decreased sensory discomfort during cognitive activities, and quantify this decrease during a cognitive task. Three-hundred and fifty-eight consecutive adults with restless legs syndrome (age 55.17 ± 14.62 years; 55.87% women; 27.65% treated) answered the question: "Does the intensity of your restless legs syndrome symptoms decrease when you perform activities other than moving your legs?" rated on a nine-point Likert scale (from fullyagree to totally-disagree). A subgroup of 65 consecutive drug-free patients underwent an 80-min suggested immobilisation test at 20:00 hours to quantify legs discomfort on a visual analogue scale before polysomnography, including 40 patients performing a cognitive task (balloon analogue risk task) from the 60 to 80 min. A total of 130 (36.3%) patients reported a decrease, 158 (44.1%) no decrease, and 70 (19.5%) uncertain changes in severity of restless legs syndrome symptoms during cognitive activities, with a similar proportion whether treated or not. Patients experiencing a decrease had less severe restless legs syndrome symptoms. In the suggested immobilisation test, mixed-effect regression models showed that legs discomfort decreased in patients performing the cognitive task while it continued to increase in those without task, with a larger difference in patients reporting a selfreported decrease in restless legs syndrome during cognitive activities. In conclusion, one-third of patients reported a self-reported decrease of restless legs syndrome symptoms during cognitive activities, this improvement in restless legs syndrome was confirmed during a sustained cognitive task. Cognitive strategies could be implemented for the management of restless legs syndrome.

KEYWORDS

balloon analogue risk test, cognitive activities, restless legs syndrome, sensory discomfort, suggested immobilisation test

1 | INTRODUCTION

Restless legs syndrome (RLS) is a frequent chronic sensorimotor disorder defined by an urge to move the legs in the evening/night when at

rest, which improves with movement (Allen et al., 2014). RLS symptoms vary considerably in frequency and severity, with symptoms fluctuating significantly over 24 hr, and from day to day, and with severe forms having a significant impact on sleep, quality of life and

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mood (Allen et al., 2005; Chenini et al., 2022; Fuhs et al., 2014). By definition, symptoms begin or worsen during periods of inactivity, and are partially or totally relieved by movement (Allen et al., 2014). Although each patient has his own strategy to relieve symptoms, the most frequently reported are walking, stretching, massages or other actions such as cold shower on the legs. Many patients also report that RLS symptoms decrease when engaging in a cognitive task such as writing, surfing the web, watching exciting movies, playing video games, doing crossword puzzles and even driving, so without necessarily having to move their legs. However, little is known about these strategies that decrease RLS symptoms, with few studies performed in this area. Moreover, to our best knowledge, no study has quantified the effect of a cognitive task on sensory discomfort in a controlled condition in RLS.

Here, we aimed: (1) to assess the frequency of patients who report a decrease in RLS sensory discomfort during cognitive activities; (2) to identify their clinical, biological and polysomnographic (PSG) characteristics; and (3) to quantify in a subgroup of consecutive patients whether their sensory RLS discomfort changes during a sustained cognitive task.

METHODS

2.1 **Participants**

A total of 358 consecutive adult patients (age 55.17 ± 14.62 years old; 55.87% women; 72.35% untreated) with primary RLS diagnosed at the sleep unit (Gui de Chauliac Hospital Montpellier, France) were included in this study. All patients had a clinical interview with a sleep specialist to confirm RLS diagnosis and exclude mimic conditions, according to the International RLS Study Group (IRLSSG) criteria (Allen et al., 2014). Inclusion criteria were diagnosis of primary RLS and an IRLSSG Severity Scale ≥ 15/40 (moderate to severe) for untreated patients (Walters et al., 2003). A total of 99 patients were treated for RLS at time of study. Exclusion criteria were: iron overload disorders, pregnancy, chronic kidney and liver diseases, inflammatory and neurological comorbidities (Parkinson's disease, multiple sclerosis, polyneuropathy, dementia, myelitis and spinal cerebellar ataxia).

This study was approved by the Montpellier University review board, France. The study was performed in accordance with the Declaration of Helsinki and the French Good Clinical Practices.

Assessment of RLS symptoms during 2.2 cognitive activities

After a face-to-face clinical interview to confirm RLS, all patients answered a written question specifically created for this study: "Does the intensity of your RLS symptoms decrease when you perform activities other than moving your legs (with some proposed examples of intellectual, emotional and motor [only upper limbs] activities: computer use, crosswords, puzzles, games, reading, writing, drawing,

painting, ...)?" Responses were reported on a visual analogue scale (VAS) that ranged from 1 to 9 (1: fully agree; 3: somewhat agree; 5: neither agree nor disagree; 7: somewhat disagree; 9: totally disagree). Patients were then asked to precise the cognitive activities associated with RLS symptoms decrease and the most significant relief time slot.

Sociodemographic, clinical and biological 2.3 assessment

Age at RLS onset, family history of RLS, comorbidities, body mass index (BMI) and educational level (categorised as < 12 years: high school/college; ≥ 12 years: university level of education) were recorded. All patients completed the IRLSSG questionnaire (≥ 15 moderate to severe symptoms), the Epworth Sleepiness Scale (ESS) with a total score ≥ 11/24 indicating excessive daytime sleepiness (EDS; Johns, 1991), the Insomnia Severity Index (ISI; cut-off score > 14: significant insomnia and > 21: severe insomnia symptoms: Bastien et al., 2001) the Beck Depression Inventory-II (BDI-II; cut-off: 0-13 = no or minimal; 14-19 = mild; 20-28 = moderate; and 29-63 = severe depressive symptoms; Beck et al., 1996), the State-Trait Anxiety Inventory (STAI; scores range from 20 to 80, with higher scores reflecting greater anxiety; Spielberger, 1983) They also completed the Urgency, Premeditation, Perseverance, Sensation seeking (UPPS) impulsive behaviour scale that provides scores for each of the four dimensions of impulsivity, with higher scores reflecting higher levels of impulsivity (Whiteside & Lynam, 2001).

Venous blood samples were collected between 07:00 hours and 08:00 hours after overnight fasting with quantification of serum ferritin levels.

Polysomnography

Untreated patients (n = 228) underwent 1-night PSG recording in the sleep laboratory monitoring electroencephalogram (EEG) leads (C3/A2, C4/A1, O2/A1), electrooculography, chin electromyography (EMG) and electrocardiogram. Respiration was monitored with a nasal cannula/pressure transducer system, mouth thermistor, chest and abdominal bands, and pulse oximeter. Leg movements were evaluated with surface EMG electrodes placed on the right and left anterior tibialis muscles. Sleep stages (N1, N2, N3 and rapid eye movement [REM] sleep) were scored manually, as well as micro-arousals, periodic leg movements during sleep (PLMS) and apnea-hypopnea index (AHI) according to standard criteria (Iber, 2007; Zucconi et al., 2006).

Assessment of RLS sensory discomfort during the suggested immobilisation test (SIT)

Prior to PSG, a subgroup of 65 consecutive patients underwent an 80-min SIT at 20:00 hours to quantify RLS sensory discomfort under standardised conditions. These 65 patients were selected on a



voluntary basis and agreed to perform the modified 80-min SIT. The SIT was initially developed to quantify RLS sensory discomfort and leg movements during 60 min in standardised conditions (De Cock et al., 2012; Michaud et al., 2002; Rassu et al., 2020). In this study, we performed the sensory SIT only, without recording legs movements and EEG. Patients were instructed to stay, legs outstretched in a bed reclined at 45° for 80 min. Talking, reading or other cognitive activities were forbidden. Patients were asked to rate their sensory discomfort using a VAS ranging from 0 to 10 (no discomfort to extreme discomfort) at the start and every 10 min (nine values).

2.6 Balloon analogue risk task (BART)

At the 60th minute, 40 patients were consecutively selected to perform a sustained cognitive task (i.e. BART) during 20 min, and 25 patients to continue the SIT unchanged until the 80th minute, thus constituting a control group. Patients were not aware in advance (before the 60th minute) in which group they were assigned.

The BART is a validated computer-based tool that assesses the risk-taking propensity (Lejuez et al., 2002). We used the BART as a distractive task by placing a computer in front of the patient at the 60th minute of the SIT. The computer's screen shows a deflated balloon, a button to pump the balloon, another one to collect the money, and two boxes that show the played money and the collected money in the bank. The patient begins to pump up the balloon that increase the played money. After each pump, the participant had two options: collect the accumulated played money, or pump up the balloon again to increase the played money. If the balloon pops, the trial ends and the patient loses all the played money. If the money is collected, the trial ends and the patient keeps the money safe in the bank. The balloons have a different number of inflations before explosion distributed randomly. Patients are instructed to pump up the balloon without exploding it, and earn the greatest amount of money in 30 trials, for a period of 20 min. The average number of pumps, the adjusted average number of pumps (number of pumps minus number of explosions) and the number of explosions were quantified. Higher scores indicate higher risk-taking propensity (Lejuez et al., 2003).

2.7 Statistical analysis

Categorical variables were presented as numbers and percentages, and quantitative variables as means and standard deviation. Sociodemographic, clinical and PSG features were compared between the three groups (e.g. agree, RLS symptoms decreased with cognitive activities [score 1-3]; neither-agree-nor-disagree [score 4-6]; disagree, RLS symptoms did not decrease with cognitive activities [score 7–9]) using multinomial regression logistic models. When comparisons were statistically significant between groups, two-by-two comparisons were carried out, using a correction for multiple comparisons with the Bonferroni method. Binary regression logistic models were also used to analyse the association between exposures and two

groups (e.g. patients who performed the SIT with the BART versus the SIT alone). Mixed-effect regression models were used to examine the RLS sensory discomfort during the SIT changes during 80 min, by taking into account the repeated measures (nine \times 10-min time periods) and the two groups (with or without the BART). Patients were considered as random effects. Time periods, groups and their interaction with the time periods were considered as fixed effects. Changes of RLS discomfort between two time points were compared using dependent t-tests for continuous variables. Statistical significance was set at p < 0.05. Statistical analyses were performed with SAS, version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Among the 358 consecutive patients, 191 (56.01%) had educational level above 12 years. The mean BMI was $25.62 \pm 4.65 \text{ kg} \text{ m}^{-2}$, and 53 (15.14%) were obese. The mean age at RLS onset was 38.67 ± 16.54 years, and 133 (38.89%) reported a positive family history of RLS. The mean IRLSSG score for untreated patients was 24.94 ± 5.56 , with 69 (26.64%) having moderate, 142 (54.83%) severe and 48 (18.53%) very-severe RLS symptoms. At time of evaluation, 99 (27.65%) patients were treated for their RLS and related insomnia (86 took at least one DA alone or combined with alpha-2-delta ligands, opioids or clonazepam, and 13 took at least an alpha-2-delta ligand alone or combined with opiate and clonazepam). The mean IRLSSG score for the treated group was 24.45 ± 6.59, with two patients (2.02%) having mild, 25 (25.25%) moderate, 55 (55.56%) severe and 17 (17.17%) very-severe RLS symptoms.

Compared with untreated patients, those treated were older $(61.40 \pm 12.11 \text{ years } \text{ versus } 52.78 \pm 14.81 \text{ years, } p < 0.0001)$, with older age at RLS onset (43.25 ± 14.98 years versus 36.88 \pm 16.80 years, p = 0.001). They had less EDS (41.05% versus 53.33% with ESS > 10, p = 0.04), less insomnia symptoms (12.37% versus 20.80% with ISI > 21; 45.36% versus 50.80% with ISI = 15-21, p = 0.03), less sensation seeking (22.59 ± 7.59 versus 25.45 ± 8.28, p=0.01) and lack of premeditation (19.49 ± 4.88 versus 20.97 ± 5.37, p = 0.04) on UPPS subscores.

RLS symptoms decreased during cognitive 3.1 activities

Based on the questionnaire, 130 (36.31%) patients experienced a decrease, 158 (44.13%) no decrease and 70 (19.55%) uncertain changes in severity of RLS symptoms when performing a cognitive activity during symptomatic periods. The most frequent intellectual, emotional and motor (only upper limbs) activities reported by participants with decreased RLS symptoms were computer use (39.23%), reading (38.46%), tinkering/knitting (16.15%), writing/drawing/painting (11.53%), watching films/series (9.23%) and crosswords/Sudoku (7.69%). The greatest time range of RLS symptoms relief was between 18:00 hours and 00:00 hours.

 TABLE 1
 Socio-demographic, clinical, biological and PSG characteristics of patients with RLS based on the self-reported changes in severity
 of RLS symptoms during cognitive activities

	A—Decrease in RLS symptoms during cognitive activities N = 130		B—Uncertain N = 70		C-No decrease in RLS symptoms during cognitive activities N = 158			
								Post hoc
Variable	n	%	n	%	n	%	Global p	comparisons
Sex, male	62	47.69	31	44.29	65	41.14	0.54	
Age (years) ^a	130; 56.11 (±1	4.60)	70; 56.21 (±14.28)	158; 53.93	(±14.77)	0.36	
Educational level, ≥12 years	69	55.20	35	51.47	87	58.78	0.59	
BMI (kg m^{-2}) ^a	126; 25.03 (±3	.87)	70; 26.18 (±5.16)	154; 25.85	(±4.96)	0.18	
BMI (kg m ⁻²), ≥30	13	10.32	15	21.43	25	16.23	0.11	
Treatment status, treated	41	31.54	16	22.86	42	26.58	0.39	
Age at RLS symptom at onset (in years) ^a	126; 39.27 (±1	6.39)	68; 40.93 (±16.12)	158; 37.23	(±16.80)	0.27	
Duration of RLS (in years) ^a	126; 16.85 (±1	3.56)	68; 15.13 (±13.08)	158; 16.70	(±13.68)	0.67	
RLS family history, yes	50	40.32	24	37.50	59	38.31	0.91	
RLS severity scale ^a	130; 24.08 (±6	.08)	70; 23.99 (±5.34)	158; 25.76	(±5.78)	0.02	-
RLS severity scale, >20	88	67.69	47	67.14	127	80.38	0.03	A < C
Ferritin (μg L ⁻¹) ^a	113; 146.15 (±	127.93)	63; 156.73	(±104.22)	141; 149.0	9 (±139.23)	0.87	
Cardiovascular comorbidities ^b , yes	41	33.61	16	23.88	36	25.17	0.22	
ESS score ^a	126; 9.62 (±5.8	39)	69; 10.14 (±4.83)	155; 11.19	(±5.40)	0.05	-
ESS score, >10	52	41.27	37	53.62	86	55.48	0.05	A < C
ISI score ^a	126; 16.09 (±5	.78)	69; 17.19 (±5.02)	152; 16.81	(±5.27)	0.34	
ISI score								
≤14	49	38.89	20	28.99	43	28.29	0.40	
15-21	56	44.44	35	50.72	80	52.63		
>21	21	16.67	14	20.29	29	19.08		
BDI-II total score ^a	120; 16.52 (±9	.66)	65; 15.11 (±8.65)	152; 15.39	(±10.42)	0.55	
BDI-II total score, ≥20	48	40.00	21	32.31	47	30.92	0.27	
UPPS – Urgency ^a	116; 29.53 (±6	.44)	57; 27.19 (±6.11)	129; 29.37	(±7.07)	0.07	
UPPS - Urgency, ≥32	48	41.38	10	17.54	52	40.31	0.007	A, C >B
UPPS - Lack of premeditation ^a	116; 20.50 (±5	.23)	56; 20.43 (±4.95)	128; 20.88	(±5.51)	0.82	
UPPS – Lack of premeditation, ≥22 ^c	48	41.38	24	42.86	58	45.31	0.82	
UPPS - Lack of perseverance ^a	117; 19.41 (±5	.18)	57; 18.93 (±4.25)	128; 18.98	(±4.41)	0.72	
UPPS – Lack of perseverance, ≥21 ^c	46	39.32	18	31.58	41	32.03	0.42	
UPPS - Sensation seeking ^a	116; 24.96 (±8	.00)	56; 23.46 (±8.36)	129; 25.26	(±8.32)	0.38	
UPPS - Sensation seeking, ≥28 ^c	39	33.62	16	28.57	50	38.76	0.39	
STAI - State anxiety ^a	41; 40.41 (±13	.84)	18; 36.89 (±14.14)	52; 39.17 (±11.86)	0.63	
STAI - Trait anxiety ^a	42; 44.64 (±12	.54)	17; 39.65 (±11.22)	49; 44.65 (±11.70)	0.29	
PSG characteristics ^d								
Total sleep time (min) ^a	75; 336.05 (±8	7.93)	45; 311.44	(±127.55)	108; 352.8	1 (±88.98)	0.06	
Total sleep time, < 6 hr	45	60.00	27	60.00	47	43.52	0.05	-
Sleep efficiency (%) ^a	75; 71.02 (±17	.36)	44; 65.42 (±24.79)	107; 74.86	(±17.08)	0.03	B < C
Sleep efficiency, ≥85%	15	20.00	9	20.45	37	34.58	0.05	
WASO (min) ^a	75; 97.99 (±73	.68)	45; 98.78 (±92.88)	108; 81.59	(±65.22)	0.24	
		.59)	45; 39.89 (45.40\	108; 30.64		0.50	

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TABLE 1 (Continued)

	A—Decrease in RLS symptoms during cognitive activities N = 130		B—Uncertain N = 70		C-No decrease in RLS symptoms during cognitive activities $N = 158$			
Variable	n	%	n	%	n	%	Global p	Post hoc comparisons
N1 (%) ^a	75; 9.19 (±6.28)		45; 12.44 (±15.78)		108; 7.98 (±8.24)		0.06	
N2 (%) ^a	75; 51.43 (±10.07)		45; 49.77 (±12.81)		108; 50.95 (±10.55)		0.71	
N3 (%) ^a	75; 21.03 (±9.43)		44; 20.13 (±11.63)		107; 21.25 (±9.22)		0.81	
REM sleep (%) ^a	75; 18.33 (±6.6)		44; 18.51 (±8.7)		106; 20.37 (±6.44)		0.11	
PLMS index (per hr) ^a	75; 31.96 (±41.82)		45; 47.59 (±57.99)		108; 32.98 (±45.16)		0.17	
PLMS index (per hr) ^a , ≥15	40	53.33	24	53.33	58	53.70	0.99	
AHI (per hr) ^a	75; 9.97 (±11.18)		45; 9.68 (±15.23)		107; 8.96 (±12.76)		0.86	
SaO ₂ , % ^a	75; 94.79 (±	1.63)	45; 94.18 ((±4.75)	107; 95.2	2 (±1.9)	0.12	

Abbreviations: AHI, apnea-hypopnea index; BDI-II, Beck Depression Inventory-II; BMI, body mass index; ESS, Epworth Sleepiness Scale; ISI, Insomnia Severity Index; PLMS, periodic leg movements during sleep; REM sleep, rapid eye movement sleep; RLS, restless legs syndrome; SaO₂, average oxygen saturation; STAI, State-Trait Anxiety Inventory; UPPS, urgency, premeditation, perseverance, and sensation seeking; WASO, wake time after sleep onset.

^aContinuous variables are expressed as number; means (± standard deviation).

Compared with patients without a self-reported decrease, patients with decreased RLS symptoms during a cognitive activity (n = 130) had less severe RLS symptoms based on the IRLSSG score, with a similar trend for EDS (Table 1). Unexpectedly, the urgency dimension on UPPS was higher in patients with or without a self-reported decrease in RLS symptoms during a cognitive activity compared with those with uncertain changes. In contrast, we found no age, gender, disease duration, insomnia and depressive symptoms, and treatment effect. In a sensitivity analysis including only untreated patients with RLS, 89 (34.36%) patients reported a decrease in RLS symptoms during a cognitive activity, 116 (44.79%) no decrease, and 54 (20.85%) uncertain changes. We also found that untreated patients with a self-reported decrease of RLS symptoms during a cognitive activity had less RLS symptoms than those with no RLS decrease, and higher urgency dimension than those with uncertain changes. In the untreated subgroup with PSG (n = 228), sleep efficiency was lower in the group with uncertain changes compared with the group without a self-reported decrease in RLS symptoms, with a similar trend for total sleep time being higher in the group with no RLS decrease (Table 1).

3.2 | RLS symptoms during the SIT based on the presence of the BART

No differences between the groups performing or not the BART were found for demographic and clinical characteristics (Table 2). Among

the 40 patients who underwent the BART, 14 (35.00%) experienced a decrease, 20 (50.00%) no decrease, and six (15.00%) uncertain self-reported changes in severity of RLS symptoms during cognitive activities, with no differences between these percentage distributions with the group that did not perform the BART.

Mixed-effect regression models showed that over the SIT, the mean sensory RLS discomfort differed in the two groups (with or without the BART; Figure 1). Interactions between groups and the SIT periods were found for sensory RLS discomfort ($p_{TestxGroup} < 0.0001$), showing differences in the response profiles. Specifically, we observed a significant decrease in legs discomfort assessed by the VAS score from 5.33 ± 2.80 to 3.68 ± 2.90 between the 60th and 80th minute in the BART group, while the sensory discomfort continued to increase from 4.28 ± 2.51 to 5.08 ± 2.72 between the 60th and 80th minute in the group without the BART. Moreover, patients with a self-reported decrease in RLS symptoms during cognitive activities who underwent the SIT-BART (n = 14) showed greater differences in mean legs discomfort between the 60th and 80th minute compared with other groups $(-3.43 \pm 3.18 \text{ versus } -0.69 \pm 1.49, p = 0.007)$. During the BART, the mean unadjusted number of pumps was 22.05 ± 11.41, the mean adjusted number of pumps 23.92 ± 13.10, and the mean number of explosions 5.97 ± 3.27. The 22 patients with decreased legs discomfort between 60 and 80 min during the SIT-BART had a lower number of explosions than the 18 patients with stable or increased legs discomfort (4.86 \pm 2.24 versus 7.28 \pm 3.83, p = 0.03), without differences for unadjusted and adjusted number of pumps. Finally, we found a positive correlation between the sensation seeking subscore on the UPPS scale

^bAt least one of the following comorbidities: diabetes, hypertension, hypercholesterolaemia or cardiovascular diseases (coronary artery disease, chronic heart failure, arrhythmia and stroke).

^cLast tertile of the distribution.

^dPSG for untreated RLS patients.

TABLE 2 Comparison of socio-demographic and clinical characteristics between patients with RLS performing the BART (n = 40) or not (n = 25) during the SIT

	Patients with	nout BART N = 25	Patients wit	Patients with BART N = 40	
Variables	n	%	n	%	р
Age (years) ^a	25; 57.12 (±1	12.99)	40; 53.80 (±	15.02)	0.36
Sex, male	11	44.00	21	52.50	0.51
Educational level, ≥12 years	16	66.67	18	46.15	0.12
BMI (kg m ⁻²) ^a	25; 24.86 (±2	2.66)	39; 25.40 (±	3.26)	0.48
BMI (kg m ⁻²), ≥30	1	4.00	3	7.69	0.56
Age at RLS symptom onset (years) ^a	25; 38.72 (±1	17.51)	40; 36.68 (±	15.14)	0.61
Duration of RLS (years) ^a	25; 18.40 (±1	17.35)	40; 17.13 (±	12.09)	0.72
RLS family history, yes	9	37.50	19	47.50	0.44
RLS severity scale ^a	25; 24.08 (±6	5.03)	40; 24.60 (±	5.34)	0.71
RLS severity scale ^a					
[11-20]	9	36.00	10	25.00	0.51
[21-30]	12	48.00	25	62.50	
[31-40]	4	16.00	5	12.50	
Self-reported changes on the severity of	RLS symptoms dur	ing cognitive activities			
Decrease	11	44.00	14	35.00	0.72
Uncertain	4	16.00	6	15.00	
No decrease	10	40.00	20	50.00	

Abbreviations: BART, balloon analogue risk task; BMI, body mass index; RLS, restless legs syndrome.

^aContinuous variables are expressed as number; means (±standard deviation).

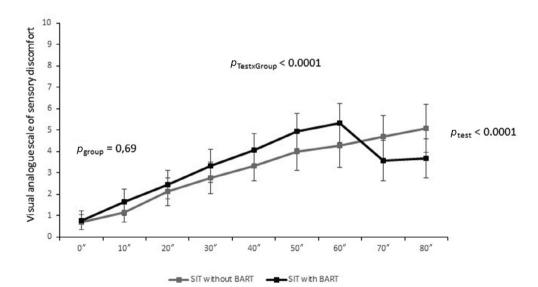


FIGURE 1 Sensory restless legs syndrome (RLS) discomfort during the suggested immobilisation test (SIT) in patients with RLS performing the balloon analogue risk task (BART; n = 40) or not (n = 25)

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and the number of explosions on the BART (r = 0.40; p = 0.02), with no significant association with other subscores.

4 **DISCUSSION**

This study found that one-third of patients with primary RLS reported a decrease in RLS symptoms during cognitive activities, with a similar proportion in patients treated or untreated for RLS. In a 80-min SIT,

we highlighted that legs discomfort decreased in patients performing a sustained cognitive task, while it continued to increase in those without a cognitive task.

There are important inter- and intra-individual differences in RLS symptoms, and those symptoms are not always present every day and at the same time for a single patient (Fuhs et al., 2014). Although RLS symptoms are partially or totally relieved by movement, some patients also reported that RLS symptoms decrease when engaging in a distractive cognitive task. Using a self-reported questionnaire, we found

that one-third of patients with primary RLS reported a decrease in RLS symptoms during cognitive activities, especially those that require more attention (e.g. computer use, reading, ...). However, these activities are less effective to reduce severe RLS symptoms, but with similar effectiveness in untreated and drug-treated RLS patients. Patients with a self-reported decrease in RLS symptoms during cognitive activities tend to be less sleepy, which may help them engage in a cognitive task. We also reported impulsive behaviour characterised by a higher urgency dimension on UPPS in these subjects, a symptom previously reported in RLS (Chenini et al., 2022), which may in this context help them engage in another activity despite RLS symptoms. Here, we found no other key differences in the clinical RLS phenotype (age at RLS onset, family history of RLS), insomnia and depressive symptoms, nor for the characteristics of PSG to individualise this population reporting a decrease of RLS symptoms during cognitive activities.

In a 80-min SIT, we highlighted that legs discomfort decreased in patients performing a sustained cognitive task, while it continued to increase in those without a cognitive task. The SIT is a reliable tool to induce RLS symptoms by intentional immobilisation in standardised conditions to avoid the confounding effect caused by changing degrees of physical activity (De Cock et al., 2012; Michaud et al., 2002; Rassu et al., 2020). We administered the 80-min SIT at a fixed time (starting at 20:00 hours) during the symptomatic period for the 65 consecutive participants to assess in a controlled condition the evolution of the sensory discomfort during the test. The mean leg discomfort improvement was greater in patients with a self-reported decrease in RLS symptoms during cognitive activity. The BART is a validated tool that assesses the risk-taking propensity, which involves the brain mesolimbic-frontal pathway (Rao et al., 2008), but used primarily in this study as a distractive task. However, patients with decreased legs discomfort during the SIT-BART had a lower number of balloon explosions, which may suggest less severe risk-taking propensity. The number of explosions is a good marker of risk-taking, and positively correlates with self-reported risky behaviours, sensation seeking and impulsivity (Bornovalova et al., 2009; Canning et al., 2022; Hunt et al., 2005; Lejuez et al., 2002, 2003, 2004). Here, we found that more balloon explosions on the BART were associated with higher sensation seeking, further supporting the link between the impulsive dimension and RLS symptoms during the uncomfortable SIT.

Restless legs syndrome is not strictly speaking a chronic pain disorder; however, the word "pain" is not infrequently used by patients (Karroum et al., 2012). The pain experience can be influenced by emotional and attentional processes (Bushnell et al., 2013). Clinical and experimental studies showed that a distraction can have a powerful effect on our perception of pain (Villemure & Bushnell, 2002; Wiech, 2016). Our emotional state also has an influence on pain; a negative emotional state increases pain, whereas a positive state lowers pain (Villemure & Bushnell, 2009). The neural mechanisms underlying the modulation of pain by cognitive and emotional states are not yet fully understood, but certainly involved anterior cingulate cortex, insula, prefrontal cortex, somatosensory and periaqueductal grey/midbrain areas. In RLS, functional imaging studies also found an

involvement of the nociceptive network (von Spiczak et al., 2005). Our current results highlighted the positive impact of cognitive activities on sensory symptoms in RLS that may share similar pathways with pain disorder modulating sensory perception and activating endogenous opioid circuits. Based on our data, non-pharmacological management such as engagement in mental activities (e.g. card games and computer work) should be recommended for mild to moderate cases to better control the symptoms (Garcia-Borreguero et al., 2016; Sharon, 2015), and may be effective individually or in combination in at least one-third of patients with RLS.

This study has several limitations. This is a single-centre study. The population might not be representative of the general RLS population, with a lower percentage of women than generally seen in practice. The question on performing activities other than leg movements may be too general, although some examples of intellectual, emotional and motor (only upper limbs) activities have been proposed. We performed the BART task during the SIT in a subgroup of patients only. The persistence of improvement in leg discomfort after the cognitive task was not assessed. We also assessed the sensory SIT only, without the motor component or EEG record. The absence of EEG failed to control for the arousal effect of the cognitive task that may participate in the mechanism that improves RLS symptoms during the last 20 min of the BART. These changes in CNS arousal can modulate the severity of RLS symptoms, with worsening frequently associated with drowsiness, and improvement with motor and cognitive activities that may compromise the applicability of these cognitive strategies at bedtime.

To conclude, in a large sample of patients with primary moderate to severe RLS, we found that one-third of patients reported a self-reported decrease of RLS symptoms during cognitive activities with its confirmation in a controlled setting. Further studies are needed to confirm the usefulness of such non-pharmacological strategies, under controlled conditions, but distractive activities could be easily implemented in the management of RLS symptoms and effective individually or in combination in at least one-third of patients.

AUTHOR CONTRIBUTIONS

Sofiene Chenini: study concept and design, data acquisition, result interpretation, preliminary draft writing. Lucie Barateau: data acquisition, manuscript revision. Lily Guiraud: data acquisition, manuscript revision. Marie Lou Rollin: data acquisition, manuscript revision. Régis Lopez: data acquisition, manuscript revision. Isabelle Jaussent: statistical analysis and interpretation. Séverine Béziat: statistical analysis and interpretation. Yves Dauvilliers: study concept and design, data acquisition, result interpretation, manuscript revision and drafting.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this article. YD received speaking honoraria and board engagements with UCB Pharma, JAZZ; Orexia, Bioprojet, Avadel, Idorsia and Takeda. LB received speaking honoraria from UCB Pharma, JAZZ and Bioprojet; board engagements from Jazz, Bioprojet and Takeda; travel to congress from UCB Pharma and Bioprojet. RL received funds for speaking by UCB Pharma and Shire. LG, MLR, SB, SC and IJ report no disclosure.

DATA AVAILABILITY STATEMENT

The data that support this study findings are available from the corresponding authors, upon reasonable request.

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