Consequences of Comorbid Insomnia Symptoms and Sleep-Related Breathing Disorder in Elderly Subjects

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Background: The prevalence of sleep-related breathing disorder (SRBD) and insomnia symptoms increases considerably with advancing age, but little is known about their cooccurrence and their effects on daytime functioning when present together.

Methods: Older adults with (cases, n=99) and without (controls, n=100) symptoms of insomnia underwent 2 nights of in-laboratory polysomnography, daytime nap, and neurobehavioral testing and completed study questionnaires. Predictors of SRBD were identified (apnea-hypopnea index [indicating number of events per hour], ≥15). Participants were divided into 4 groups—with and without insomnia and with and without SRBD—and the groups were compared on measures of daytime functioning.

Results: Cases had a lower rate of SRBD (29.3%) than controls (38.0%). Body mass index (calculated as weight in kilograms divided by height in meters squared) of 30 or higher, neck circumference greater than 15.5 inches, and a history of “loud snoring” or “stops breathing, chokes, or struggles for breath” were independently predictive of SRBD in participants with insomnia symptoms. Having both insomnia symptoms and SRBD was associated with significantly lower daytime functioning and longer psychomotor reaction times compared with having neither condition.

Conclusion: Because insomnia comorbid with SRBD is associated with the greatest functional impairment, and SRBD is commonly found in the elderly population, health care providers should also consider SRBD in elderly patients with insomnia symptoms.

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With advancing age, many older adults are at increased risk of having a broad range of sleep problems, especially insomnia symptoms and sleep-related breathing disorder (SRBD). Twenty percent of adults older than 65 years have SRBD as defined by an apnea-hypopnea index (AHI) (measure of number of events per hour) of 15 or higher, \(^1\) while an even higher percentage report insomnia symptoms, such as frequent awakenings at night (59.5%). \(^2\) Given the high prevalence of insomnia symptoms and SRBD, it is likely that they will often co-occur with advanced age.

Despite the potentially high prevalence rate of this combined condition, its clinical significance is poorly understood. Most research studies in this area have asked the question, “How common are insomnia complaints in patients with SRBD?” \(^3\) In these studies, patients referred to a sleep clinic were screened for insomnia; nearly 40% to 50% of patients with SRBD were noted to have insomnia symptoms. Since these participants were drawn from a convenience sample, referral bias is a concern: patients with more sleep problems may be more likely to come to a sleep clinic, thus leading to artificially high rates of insomnia symptoms. In addition, most of the participants were middle-aged. For older adults, insomnia symptoms are more common than SRBD symptoms. \(^4\) Thus, it is more likely for physicians treating an elderly patient to face the inverse question, “How common is SRBD in patients with insomnia symptoms?” The data that address this question come from reports describing the screening process for randomized controlled trials to treat insomnia in older adults. One such study, for example, found that 29% of elderly participants screened were excluded because they had SRBD. \(^5\)

The interrelationship between SRBD and insomnia is also a matter of debate.

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While the excessive sleepiness often associated with SRBD might reduce the likelihood of insomnia, as suggested by studies that show an inverse relationship between insomnia severity and AHI, the frequent arousals that occur with SRBD might themselves lead to nocturnal awakenings, as implied by studies that show a positive correlation between insomnia severity and AHI. Furthermore, relatively few studies have examined the daytime consequences of having both of these conditions.

To determine the prevalence and consequences of coexistent insomnia symptoms and SRBD, we conducted a cross-sectional study in a sample of elderly community-dwelling residents using case-control methods. Older adults with frequent, long-lasting symptoms of insomnia were defined as cases (INS+), while controls (INS−) had no such difficulties. Our study included a battery of subjective and objective measures of both sleep and alertness. We hypothesized that coexistent insomnia symptoms and SRBD would be common in older adults and would be associated with higher degrees of daytime functional impairments relative to participants with either condition alone.

**STUDY POPULATION**

Research study participants were a cross-sectional sample of community-dwelling adults 65 years or older who resided in the greater Philadelphia metropolitan area. They were randomly selected from a database of 120,000 older adults who had received outpatient or inpatient care at the University of Pennsylvania Health System (60.1% of screened subjects) as well as recruited via radio and print media advertisements (39.9% of screened subjects). A total of 549 older adults were screened over the telephone. Of these, 145 (26.4%) were not interested. Other potential participants were excluded for the following reasons: 41 (7.5%) were interested but declined owing to active medical issues; 26 (4.7%) did not meet insomnia case or control status (eg, they currently had insomnia symptoms but for only the past week); 24 (4.4%) had medical exclusions (active use of sedatives or hypnotics, alcohol abuse, and/or anemia); 22 (4%) met depression criteria (defined herein); 11 (2.0%) met dementia criteria (defined herein); and 11 (2.0%) did not speak English. Sixty-nine (12.6%) dropped out after agreeing to participate, primarily owing to schedule conflicts. All participants completed and signed written informed consent forms, and the study protocol was approved by the University of Pennsylvania institutional review board.

Potential research participants were screened for depression using the Geriatric Depression Scale (score >11) and for dementia using the Short Blessed Examination Score (score >6). Individuals with depression or dementia were excluded because of the prominent changes in sleep that can occur in these conditions. The CAGE questionnaire was used to identify individuals with heavy alcohol use for exclusion. Individuals taking medications to promote sleep, either prescription or over-the-counter, were asked to refrain from use for the 4 weeks preceding their participation in the study. Participants were categorized as INS+ if they reported current trouble falling asleep or staying asleep or early morning awakenings at least 3 nights per week lasting for at least the last 3 weeks. The study was designed using a case-control framework with equal numbers of cases and controls.

**DATA COLLECTION**

Participants completed demographic questionnaires, underwent a detailed clinical history, and completed the SF-36 (Medical Outcomes Study 36-item short-form health survey) functional quality of life scale. Sleep-specific self-report measures included the Epworth Sleepiness Scale and the Functional Outcomes of Sleepiness Questionnaire (FOSQ). The Epworth Sleepiness Scale assesses the subjective likelihood of falling asleep in various settings and assigns higher scores for greater sleepiness. The FOSQ examines the impact of sleepiness on various domains of functioning. It yields a global score, with lower scores indicating worse functioning.

Participants spent 2 nights in the sleep laboratory during which they underwent a complete 24-channel polysomnography montage consisting of the following: electroencephalogram, electromyograph, electro-oculogram, measures of respiratory effort and flow, and monitoring of leg movements (Sandman system; Nellcor Puritan Bennett Inc, Pleasanton, Calif). The first night was used to adapt participants to the sleep laboratory. The next day, they completed the Psychomotor Vigilance Task (PVT) to assess behavioral alertness; the PVT has been shown to be a sensitive measure of the effects of daytime sleepiness. A total of four 10-minute PVT test bouts were administered after a PVT training bout. During each 10-minute PVT session, visual stimuli appeared at randomly variable intervals of 2 to 10 seconds. The PVT median reaction times and number of lapses of attention (defined as reaction times ≥500 milliseconds) were analyzed.

Following the second sleep study, participants underwent a Multiple Sleep Latency Test, which consisted of a series of four 20-minute nap opportunities every 2 hours. The time that it takes an individual to fall asleep, on average across the 4 naps, is used as a measure of daytime sleep propensity.

Sleep records were manually scored in 30-second epochs according to standard criteria. The average number of apneas and hypopneas per hour of sleep was computed as the AHI. Apneas were defined as a cessation of airflow for 10 seconds or longer, and hypopneas were defined as a 50% or greater reduction in airflow accompanied by either a 3% decrement in oxygen saturation or an arousal. Individuals with an AHI of 15 or higher were considered to have at least moderate SRBD (SRBD+), a widely used threshold for epidemiology studies. Four groups were thus created: INS+/SRBD+, INS+/SRBD−, INS−/SRBD+, and INS−/SRBD−.

**STATISTICAL ANALYSIS**

We examined the prevalence of SRBD in cases and controls, calculating odds ratios to estimate the relative odds of SRBD at various levels of severity with controls as the reference group. We next determined which aspects of a sleep clinical history (loud snoring, witnessed apneas, and other characteristics) could be used to identify SRBD in older adults by insomnia status. To derive an assessment of the utility of these history elements as a group, a multivariate logistic regression model was calculated using presence or absence of moderate SRBD (AHI, ≥15) in cases as the dependent variable.

To explore the functional outcomes of SRBD, the 4 groups were compared using analysis of variance (df=3) across a broad range of metrics, including subjective self-report (SF-36, Epworth Sleepiness Scale, and FOSQ), objective measures of sleepiness (Multiple Sleep Latency Test), and objective measures of performance (PVT). Pairwise comparisons by group, with INS−/SRBD− as the reference group, were then performed for each metric with a Bonferroni correction for multiple comparisons.
Table 1. Demographic Characteristics of Subjects With and Without Symptoms of Insomnia*  

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Participants</th>
<th>INS+ (n = 99)</th>
<th>INS− (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>71.9 ± 5.0</td>
<td>71.2 ± 4.5</td>
<td>72.6 ± 5.3†</td>
</tr>
<tr>
<td>BMI</td>
<td>28.5 ± 5.2</td>
<td>28.7 ± 5.8</td>
<td>28.3 ± 4.5</td>
</tr>
<tr>
<td>Neck circumference, in</td>
<td>14.9 ± 1.5</td>
<td>15.0 ± 1.6</td>
<td>14.9 ± 1.4</td>
</tr>
<tr>
<td>Women</td>
<td>65.5</td>
<td>68.0</td>
<td>63.6</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>53.5</td>
<td>52.8</td>
<td>54.3</td>
</tr>
<tr>
<td>Black</td>
<td>44.4</td>
<td>45.1</td>
<td>43.6</td>
</tr>
<tr>
<td>Other</td>
<td>2.1</td>
<td>2.1</td>
<td>2.1</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥Junior high</td>
<td>7.6</td>
<td>9.8</td>
<td>5.2</td>
</tr>
<tr>
<td>High school</td>
<td>41.9</td>
<td>45.1</td>
<td>39.0</td>
</tr>
<tr>
<td>College</td>
<td>31.7</td>
<td>25.3</td>
<td>37.9</td>
</tr>
<tr>
<td>Graduate school</td>
<td>18.8</td>
<td>19.8</td>
<td>17.9</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married with partner</td>
<td>40.0</td>
<td>39.8</td>
<td>40.4</td>
</tr>
<tr>
<td>Single</td>
<td>10.2</td>
<td>8.6</td>
<td>11.7</td>
</tr>
<tr>
<td>Separated or divorced</td>
<td>19.8</td>
<td>19.4</td>
<td>20.2</td>
</tr>
<tr>
<td>Widowed</td>
<td>30.0</td>
<td>32.2</td>
<td>27.7</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); INS−, subjects without INS (control subjects); INS+, subjects with INS (case subjects).
*All data are presented as mean ± SD values or percentage of subjects.
†P = .04 cases compared with controls.

All statistical analyses were 2-sided and conducted at the α = .05 level of significance using SAS software, version 9.1 (SAS Institute, Cary, NC).

RESULTS

A total of 200 older adults participated in the study (100 cases and 100 controls); complete data sets are available on 199 (the polysomnography of 1 case was lost owing to data collection difficulties). Cases and controls were similar in demographic characteristics (Table 1) except for age: cases were an average of 1.4 years younger than controls (P = .04).

We noted a lower prevalence of any SRBD (AHI ≥ 5) in cases (62.6%) than in controls (79.0%) (χ² = 6.46, P = .01). The odds ratio for having SRBD was thus 0.45 (95% confidence interval [CI], 0.24-0.84) for a case relative to a control. We next divided cases and controls into severity levels as a function of AHI, using an AHI lower than 5 as the reference range (Figure 1). The odds ratio for having mild SRBD (AHI ≥ 5 and < 15) for a case was 0.46 (95% CI, 0.23-0.92); for moderate SRBD (AHI ≥ 15 and < 30) was 0.46 (95% CI, 0.21-1.01); and for severe SRBD (AHI ≥ 30) was 0.36 (95% CI, 0.12-1.07).

Several history elements could be used to suggest the presence of SRBD in older adults with insomnia symptoms but in general were less useful in those without insomnia symptoms (Table 2 and Table 3). The history elements with marginally significant associations (P < .10) were used to derive a predictive model to identify SRBD in older adults who present with insomnia symptoms (Table 4). No evidence of interaction between these factors was noted when interaction terms were added to the model. The general symptom of excessive daytime sleepiness was not significantly different between groups. The adjusted R² statistic for the model was 0.46 (χ² = 37.8, P < .001), and the area under the curve of the model receiver-operating curve diagnostic was 0.84, suggesting moderate discriminant ability to identify SRBD in those with insomnia symptoms.

Our analysis then considered the daytime consequences of these sleep disorder categories. Figure 2 displays the Global score and the different subscale scores of the FOSQ. The presence of SRBD alone was associated with minor reductions in these measures, with more prominent functional deficits noted in the presence of insomnia and the largest impairment present in the group with both insomnia and SRBD. Deficits were most profound in 2 functional domains (P values for the pairwise comparisons are corrected with the Bonferroni multiple-comparisons adjustment): Activity Level (INS−/SRBD− vs INS−/SRBD−, P = .01; INS+/SRBD+ vs INS−/SRBD−, P < .001) and Intimacy (INS+/SRBD+ vs INS−/ SRBD−, P < .001) (the Intimacy subscale questions were optional: 58 INS+ and 61 INS− participants completed it). The General Productivity, Vigilance, and Social Outcome subscales did not show statistically significant differences in pairwise comparisons with the INS−/SRBD− reference group. For the Global FOSQ score, pairwise comparisons with the INS−/SRBD− group demonstrated increased Global impairment in the INS+/SRBD+ group (Bonferroni P = .001); the effect size of this difference was 0.9 (values ≥ 0.8 are considered large according to criteria established by Cohen). Other metrics analyzed included the Epworth Sleepiness Scale, which showed no pairwise differences between groups, and the SF-36 scale, which demonstrated differences between INS−/SRBD− and INS+/SRBD+ groups on the Mental Health Index (Bonferroni P = .03) but no pairwise differences on the Physical Health Index. To determine if subclinical depression, mild cogni-
tive impairment, or alcohol use was related to these differences, we compared our subgroups on these measures (Table 3): pairwise comparisons by insomnia groups showed no significant difference between those with SRBD and those without, thus suggesting that these factors did not mediate the additional functional impairments noted in older adults with SRBD and insomnia symptoms relative to those with insomnia symptoms and no SRBD.

In addition to these self-reported findings, we noted differences in PVT median reaction times: the INS+/SRBD+ group had the highest median reaction times (Bonferroni P = .04), indicating increased impairment. There were no differences in PVT lapses or the Multiple Sleep Latency Test scores (Table 5).

An intriguing relationship between SRBD and insomnia symptoms emerges from this study. On the one hand,
SRBD was less prevalent in participants with insomnia symptoms than in those without insomnia symptoms, even though these 2 groups were similar in other SRBD risk factors such as BMI and sex. However, SRBD was still quite common, affecting nearly 1 in 3 older adults with insomnia symptoms, as would be expected for this age group. Furthermore, the presence of coexisting insomnia symptoms and SRBD was associated with increased impairment in self-reported functional status relative to participants with neither or just 1 of the 2 conditions, thus suggesting an additive effect in functional impairment. The frequency of comorbid insomnia symptoms and SRBD and the functional consequences associated with their co-occurrence suggest that clinical consideration be given to sleep apnea screening as part of an insomnia evaluation in older adults, especially if the history reveals prominent functional deficits.

Our study is the first to our knowledge to focus on coexistent SRBD and insomnia symptoms in older adults and include an extensive outcome assessment. Furthermore, our study does not rely on a convenience sample of patients evaluated at a sleep clinic, thus reducing the risk of referral bias.

Several of our observations merit comment. The finding that SRBD was less common in participants with insomnia is of interest. One possible explanation is that sleepiness from SRBD produces sufficient drive for sleep to overcome insomnia symptoms. However, the perception that SRBD is protective against insomnia symptoms is not justified; it is, after all, an adverse effect of SRBD (ie, sleepiness) that may be mediating this effect. Whatever the mechanism, our study leads to the conclusion that the presence of insomnia symptoms does not indicate a higher likelihood of having sleep apnea but instead may be associated with a lower risk of sleep apnea in older adults.

There was a marked disparity between results of outcomes based on self-report and those from objective measures. While one of our objective outcome measures—PVT median response time—showed significantly greater slowing in psychomotor vigilance in those with both insomnia and SRBD, the Multiple Sleep Latency Test, a measure of daytime sleepiness, did not. The latter findings are consistent with several studies that have failed to find evidence of elevated Multiple Sleep Latency Test–derived sleep propensity in patients with insomnia despite subjective reports of sleepiness. Data on daytime neurobehavioral performance in patients with insomnia have been mixed, with some studies finding deficits relative to healthy sleepers but others failing to find these effects. Overall, our study shows marginal objective findings.

Among our subjective measures, the most robust differences were found in the FOSQ. Interestingly, the Intimacy and Sexual Relations subscale was affected, while the Social Outcomes subscale had no significant differences across the groups. Sleep-related breathing disorder, especially when severe, can lead to increased rates of impotence. However, the Intimacy and Sexual Relations subscale findings should be interpreted with caution because not all participants completed this section. Other questions, including those related to activity level, also showed significant differences in levels of impairment across groups, and the increased PVT median reaction time suggested a psychomotor deficit in the group with both insomnia and SRBD. Thus, although this group was not excessively sleepy by some objective measures (the Multiple Sleep Latency Test and PVT lapses), their sleep abnormality was associated with evidence of a psychomotor deficit (increased PVT median reaction time) and more marked decrements in functional quality of life.

One limitation of the study is that while participants were assessed for symptoms of insomnia, it was not determined if they met formal criteria for insomnia. According to current nosologic standards, insomnia con-

Table 4. Standardized Parameter Estimates for Significant History Predictors of SRBD in Older Adults With Insomnia Symptoms

<table>
<thead>
<tr>
<th>History Element</th>
<th>Parameter Estimate* (95% CI)</th>
<th>χ²</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI ≥ 30</td>
<td>2.0 (0.8-3.1)</td>
<td>11.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Stops breathing, chokes, or struggles for breath during sleep†</td>
<td>4.5 (1.9-7.1)</td>
<td>11.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Frequent tossing, turning or thrashing‡</td>
<td>2.1 (3.5-0.6)</td>
<td>8.2</td>
<td>.004</td>
</tr>
<tr>
<td>Morning headaches‡</td>
<td>3.0 (0.9-5.2)</td>
<td>7.5</td>
<td>.006</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; SRBD, sleep-related breathing disorder.

*These parameter estimates demonstrate the relative importance of each of these history elements in identifying SRBD in participants with insomnia as derived from a multivariate model.

†These sleep history items were divided into 2 response options: (1) less than once a week or (2) once a week or more.

‡These sleep history items were divided into 2 response options: (1) less than twice a week or (2) twice a week or more.
sists of difficulty sleeping at night plus associated daytime impairment.28,29 The rationale for not requiring that cases meet full diagnostic criteria was that we wanted to use a screening paradigm that reflects what most primary care clinicians encounter when patients report insomnia. Technically, none of our participants with coexisting insomnia symptoms and SRBD met the criteria for insomnia as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, because the presence of a coexisting sleep disorder excludes that diagnosis.29 Given our data that show the frequent coexistence of these sleep disorders in older adults, our study leads us to question current sleep nosologic standards.

Another limitation of our study is the slight difference in age between insomnia cases and controls; however, this 1.4-year difference is small and not likely to be clinically significant. Indeed, the prevalence of SRBD in people older than 65 years has been found to be fairly constant with increasing age, and hence this small age difference should not have affected the coexistence of these sleep disorders.1

A further limitation of our study is the wide confidence intervals noted for our odds ratio estimate for the history of “stops breathing, chokes, or struggles for breath.” This is because there were a small number of participants in the study who reported this symptom. However, the odds ratio is statistically significant and reflects the markedly increased prevalence of SRBD when this history element is present.

The finding that the most severe daytime functional impairments occur in participants with comorbid insomnia and SRBD suggests that we may need to reconsider our approach to evaluating older adults with insomnia. Traditionally, polysomnography has been reserved for patients with insomnia and coexisting symptoms of SRBD such as loud snoring.30 Yet, while we observed that several history elements had a high odds ratio for being associated with abnormal breathing during sleep, it is important to note that these symptoms were present in only a minority of the participants with SRBD. Furthermore, we observed that the general symptom of excessive daytime sleepiness did not differ significantly between INS+ subjects with SRBD and those without; thus, there is clearly a need to obtain a more detailed history of functional limitations in elderly populations. Limitations of daytime activities due to sleepiness that are out of proportion to insomnia symptoms, especially in domains related to activity level, may justify obtaining a polysomnography. In addition, patients with persistent symptoms of daytime dysfunction despite insomnia treatment may warrant evaluation by polysomnography.

The primary care physician is often the first and only physician with whom a patient may discuss insomnia symptoms. This study sheds light on the interaction between comorbid insomnia symptoms and SRBD in the population most vulnerable to both conditions, older adults. Our study shows that SRBD is less common in elderly subjects with insomnia; nevertheless, given its high prevalence, it is still common. Although in our study, SRBD was less frequent in elderly subjects with insomnia symptoms, having concomitant insomnia and SRBD was associated with more daytime dysfunction than having insomnia alone; therefore, there is a need to determine which patients with insomnia also have SRBD. While polysomnography is clearly not indicated in all older adults with insomnia symptoms, a polysomnogram may be warranted in patients whose functional deficits in activity level may seem pronounced. Future research is needed to explore the optimal method to adequately treat coexisting insomnia symptoms and SRBD.

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Table 5. Objective Alertness and Performance Measures*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>INS−/SRBD−</th>
<th>INS−/SRBD+</th>
<th>INS+/SRBD−</th>
<th>INS+/SRBD+</th>
<th>ANOVA P Value (df = 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSLT score, min</td>
<td>14.4 ± 4.4</td>
<td>13.6 ± 4.3</td>
<td>13.8 ± 4.2</td>
<td>13.7 ± 5.3</td>
<td>.04</td>
</tr>
<tr>
<td>PVT median reaction time, ms</td>
<td>275 ± 41</td>
<td>277 ± 43</td>
<td>283 ± 43</td>
<td>294 ± 50</td>
<td>.03</td>
</tr>
<tr>
<td>PVT transformed lapses†‡</td>
<td>3.30 ± 1.71</td>
<td>3.45 ± 1.94</td>
<td>3.60 ± 1.95</td>
<td>4.41 ± 2.43</td>
<td>.09</td>
</tr>
</tbody>
</table>

Abbreviations: ANOVA, analysis of variance; INS, symptoms of insomnia; INS−, subjects without INS (control subjects); INS+, subjects with INS (case subjects); MSLT, Multiple Sleep Latency Test, latency to stage 2 sleep27; PVT, Psychomotor Vigilance Test20,21; SRBD, sleep-related breathing disorder; SRBD−, subjects without SRBD; SRBD+, subjects with SRBD.

*Unless otherwise indicated, data are presented as mean ± SD.
†Relative to the INS−/SRBD− reference group, participants in the INS+ /SRBD+ group had significantly higher median response times (raw P = .004; Bonferroni P = .04).
‡Tukey transform (−X + .[X+1]) used to correct for heterogeneity of variance.
§Participants in the INS+ /SRBD+ group had a higher PVT transformed lapses value than the reference group, but this was not significant after multiple comparisons correction (raw P = .01; Bonferroni P = .12).
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REFERENCES