Insomnia with Objective Short Sleep Duration is Associated with Deficits in Neuropsychological Performance: A General Population Study

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Study Objectives: To examine the joint effect of insomnia and objective short sleep duration on neuropsychological performance.
Design: Representative cross-sectional study.
Setting: Sleep laboratory.
Participants: 1,741 men and women randomly selected from central Pennsylvania.
Interventions: None.
Measurements: Insomnia (n = 116) was defined by a complaint of insomnia with a duration ≥ 1 year and the absence of sleep disordered breathing (SDB), while normal sleep (n = 562) was defined as the absence of insomnia, excessive daytime sleepiness, and SDB. Both groups were split according to polysomnographic sleep duration into 2 categories: ≥ 6 h of sleep ("normal sleep duration") and < 6 h of sleep ("short sleep duration"). We compared the groups' performance on a comprehensive neuropsychological battery that measured processing speed, attention, visual memory, and verbal fluency, while controlling for age, race, gender, education, body mass index, and physical and mental health.
Results: No significant differences were detected between insomniacs and controls. However, the insomnia with short sleep duration group compared to the control with normal or short sleep duration groups showed poorer neuropsychological performance in variables such as processing speed, set-switching attention, and number of visual memory errors and omissions. In contrast, the insomnia with normal sleep duration group showed no significant deficits.
Conclusions: Insomnia with objective short sleep duration is associated with deficits in set-switching attentional abilities, a key component of the "executive control of attention." These findings suggest that objective sleep duration may predict the severity of chronic insomnia, including its effect on neurocognitive function.
Keywords: Insomnia, short sleep duration, cognitive performance, neuropsychology
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INSOMNIA IS THE MOST COMMON SLEEP DISORDER, YET LITTLE IS KNOWN ABOUT THE MECHANISMS, CAUSES, CLINICAL COURSE, AND CONSEQUENCES of this highly prevalent chronic condition.[1] Many studies have established that insomnia is highly comorbid with psychiatric disorders and is a risk factor for the development of depression, anxiety, and suicide.[2] However, the evidence on the association of insomnia with medical morbidity is very limited.[1,2]

Although insomniacs commonly complain of cognitive deficits, mainly of attention and concentration, there is a surprising lack of evidence to suggest a link between chronic insomnia and cognitive dysfunction in objective testing.[3-5] In fact, published reviews demonstrated poorer performance among patients with insomnia in only a small number of studies (approximately 10% to 25%), according to the 2006 Standards in Insomnia Committee. Thus they concluded that no specific psychomotor or cognitive-performance measure can be recommended for routine use in insomnia studies.[6] In the 3 most recent studies,[7-9] using polysomnography and performance data to compare insomniacs to normal sleepers, results were mixed. Two of 3 studies included only small sample sizes, whereas the third included a relatively large group of research volunteer primary insomniacs and used a rather narrowly focused battery. To date, our sample is the largest population-based study using full polysomnography and a comprehensive neuropsychological battery that has been conducted in adults to investigate the association of insomnia and performance.

We have previously reported that objective short sleep duration in insomnia may be an index of the biological severity of the disorder. Specifically, insomnia with short sleep duration has been shown to be associated with a high risk for hypertension[10] and type 2 diabetes[11] as well as with activation of the hypothalamic-pituitary-adrenal (HPA) axis.[12-14] The latter finding is particularly relevant to neuropsychological performance because hyperactivity of the HPA axis has been shown to be associated with neurocognitive deficits.[15-18]

Based on these observations, we speculate that insomniacs with short sleep duration may be at high risk for deficits in neuropsychological performance. In order to test this hypothesis, we examined the joint effects of the complaint of chronic insomnia and objective sleep duration on the neuropsychological

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performance of a large cross-sectional population-based sample from The Penn State Cohort.

METHODS

Population

The data presented here were collected as part of a 2-phase protocol whose primary purpose was to establish the age distribution of sleep disordered breathing.[19,20] In the first phase of the study, a sample of adult men and women (age ≥ 20 y) was randomly selected from local telephone households in 2 counties of Central Pennsylvania (Dauphin and Lebanon) using the Mitofsky-Waksberg 2-stage random digit dialing procedure.[21] A within-household selection procedure described by Kish was used to select the specific man or woman to be interviewed.[22] Telephone interviews were conducted with 4,364 age-eligible men and 12,219 age-eligible women residing in the sample households for a total sample of 16,583, with a response rate of 73.5% and 74.1%, respectively. The questionnaire employed in this interview included basic demographic and sleep information.

In the second phase of this study, a subsample of 741 men and 1,000 women selected from those subjects previously interviewed by telephone were studied in our sleep laboratory. The response rate for this phase was 67.8% and 65.8% for men and women, respectively. We contrasted those subjects who were recorded in the laboratory with those who were selected but not recorded in terms of age, BMI, and prevalence of sleep disorders. There were no significant differences between these 2 groups on any of these variables. After complete description of the study to the subjects, written informed consent was obtained.

Each subject selected for laboratory evaluation completed a comprehensive sleep history and physical examination. All subjects were evaluated for one night in the sleep laboratory in sound-attenuated, light- and temperature-controlled rooms. During this evaluation, each subject was continuously monitored for 8 h using 16-channel polygraphs including electroencephalogram, electrooculogram, and electromyogram. Bedtimes were adjusted to conform to subjects' usual bedtimes, and subjects were recorded between 22:00–23:00 and 06:00–07:00. In this random general sample of Central Pennsylvania the vast majority of individuals went to bed between 22:00 and 23:00, whereas only a small minority went to sleep outside of this time window and none for more than an hour. Thus, the maximum adjustment we had to do was of 1 hour. The sleep records were subsequently scored independently according to standardized criteria.[23] Percent sleep time is total sleep time (duration of sleep) divided by recorded time in bed and multiplied by 100. Respiration was monitored throughout the night by use of thermocouples at the nose and mouth and thoracic strain gauges. All-night recordings of hemoglobin oxygen saturation (SpO_2) were obtained with an oximeter attached to the finger.

Key Measurements

As part of this protocol we also assessed for the presence of all sleep disorders, based on a standardized questionnaire completed by the subjects on the evening of their sleep laboratory visit. The characteristics and content of this questionnaire have been extensively presented elsewhere.[10,11,19,20] To control for possible confounding variables influencing the relationship between insomnia and neuropsychological performance, we ascertained whether the respondent was currently treated for physical health (i.e., hypertension, diabetes, thyroid, allergies/asthma, anemia, birth defect, cancer/tumor, colitis, encephalitis, epilepsy, heart trouble, kidney/bladder, migraine, Parkinson, rheumatism, stroke, and ulcer) or mental health (i.e., depression, suicide thoughts and attempts, alcohol, drug, and marital) problems at the time of the interview. Depression as a stand-alone variable was considered to be present if the individual was currently treated for depression or had a history of suicidal thoughts or attempts.[10,11,19,20,24] A composite summary variable for each general category (physical health or mental health) was calculated by indicating a positive response when at least one variable within that category was present, as described elsewhere.[24] Additional information obtained during the polysomnographic evaluation included sleep apnea and periodic limb movement assessment. For the purpose of this study, sleep apnea was defined as an obstructive apnea or hypopnea index ≥ 5 (AHI ≥ 5). The condition of periodic limb movements was considered present when there were ≥ 5 movements per hour of sleep. A leg movement was scored when it lasted more than 0.5 sec, less than 5.0 sec, and in intervals of < 90 sec between movements.[25] Body mass index was based on measured height (cm) and weight (kg) during the subjects' sleep laboratory visit, and data are presented in terms of mean within each category.

Sample and Subgroups

From the 1,741 individuals, a total of 1,405 completed all tasks of a neuropsychological battery and were classified as chronic insomniacs or controls. The inclusion criteria for the "insomnia" group were: 1) a complaint of insomnia with a duration ≥ 1 year, and 2) an AHI < 5 in the sleep lab. A total of 116 subjects met the criteria for chronic insomnia. The inclusion criteria for the control group were: 1) absence of "insomnia," as defined above; 2) absence of "poor sleep" (defined as a moderate to severe complaint, based on a mild to severe scale, of difficulty falling asleep, difficulty staying asleep, early final awakening, or unrefreshing sleep); 3) absence of "excessive daytime sleepiness," ascertained by moderate to severe responses to 2 questions: "*do you feel drowsy or sleepy most of the day but manage to stay awake?*" and "*do you have any irresistible sleep attacks during the day?*"; and 4) an AHI < 5. The total number of normal sleepers in the control group was 562. The remaining 727 subjects did not fulfill the criteria stated for each group. The majority of them (n = 415) were excluded because they reported "poor sleep" as defined above. From the objectively recorded sleep time data, we split the groups into two categories (based on the median sleep duration of the entire sample, which is 6 h): the "normal sleep duration group" consisted of those who slept ≥ 6 h, and the "short sleep duration group" of those who slept < 6 h. Thus, we created the following 4 groups: the "controls with normal sleep duration group" consisted of those controls who slept ≥ 6 h (n = 343), the "controls with short sleep duration group" of those controls who slept < 6 h (n = 219), the "insomniacs with normal sleep duration group" of those chronic insomniacs who slept ≥ 6 h (n = 65), and the "insomniacs with short sleep duration group" of those chronic insomniacs who slept < 6 h (n = 51).

Neuropsychological Assessment

On the evening before the sleep recording, each participant completed a battery of neuropsychological standardized tests[26,27] consisting of measures commonly used in clinical practice to assess a range of cognitive domains that included information processing speed, attention, visual memory, and verbal fluency. All testing sessions occurred between 19:00 and 20:00. During the 1-h testing session, 5 neuropsychological tests were administered. The *Mini-Mental State Examination* (MMSE) is a global measure of dementia and assesses global cognitive status[26,27]; subjects with a total score < 26 were excluded from the analyses. The *Symbol Digit Modalities Test* (SDMT) primarily assesses psychomotor processing speed and the visual scanning and tracking aspects of complex attention.[26,27] The *Trail Making Test* (TMT) is a 2-part test that assesses different aspects of attention. Part A (TMT-A) assesses visual conceptual tracking, psychomotor processing speed, and attention.[26-28] Part B (TMT-B) also assesses visual conceptual tracking, psychomotor processing speed, and, in addition, it requires set-switching attention.[26-28] The TMT B–A is a derived score that removes the speed element from the test evaluation by subtracting part A from part B; it is considered to be a purer measure of the set-switching task required in Part B.[26,27] The *Benton Visual Retention Test* (BVRT; administration A, immediate recall) assesses short-term visual memory, visual perception, and visual-constructive abilities.[26,27] The *Thurstone Word Fluency Test* (TWFT) assesses the spontaneous oral and written production of words under restricted search conditions and the ability to inhibit previous responses.[26,27]

Statistical Analyses

The design of this study included oversampling of those at higher risk for sleep disordered breathing (SDB) and women with markedly higher levels of BMI to increase the precision of the risk estimates. Because of this sampling strategy, numeric sampling weights were developed for the analysis so that the estimates could be inferred to the original target population. A comprehensive presentation of this sampling strategy has been presented elsewhere,[10,11,19,20,24] including the use of the NHANES III laboratory data as the standard[29] to adjust both the men and women in terms of sociodemographics to be representative of the national population. Two by 2 (*insomnia × short sleep duration*) multivariate analyses of variance (MANOVA) were used to assess the effects of chronic insomnia, objective short sleep duration and their interaction on sociodemographic, health-related, and polysomnographic variables. A 2 by 2 (*insomnia × short sleep duration*) MANOVA was used to assess the effects of chronic insomnia, objective short sleep duration, and their interaction on all neuropsychological measures, while controlling for major confounding factors expected to influence these effects (i.e., age, race, gender, education, BMI, physical health, mental health, and sampling weight). Post hoc Dunnett tests were applied to control for type I errors, performing multiple comparisons against the control with normal sleep duration group, while controlling for all confounding factors. In addition, to compare controls with short sleep duration *vs.* insomniacs with short sleep duration, the least square difference post hoc test was used. Partial correlations, controlling for all confounders, between neuropsychological measures were also conducted. The critical statistical confidence level for all analyses was $P = 0.05$. Analyses were performed using SPSS 15.0 (Chicago, IL, USA).

RESULTS

The demographic, clinical, and sleep characteristics of the control and the insomnia subgroups, based on objective sleep duration, are presented in Table 1. There were no significant interactions between insomnia and short sleep duration on any PSG variables.

We first tested the effects of insomnia, short sleep duration, and their interaction on all neuropsychological performance measures in a 2 by 2 MANOVA while controlling for gender, age, race, education, BMI, physical health, mental health, and sampling weight. The *insomnia × short sleep duration* interaction (Wilk's $\lambda = 0.963$; $F = 2.104$; $P < 0.05$) was significant on SDMT ($P < 0.05$), TMT-B ($P < 0.01$), TMT B–A ($P < 0.01$), and number of omissions ($P < 0.05$) on the BVRT. These significant interactions are suggestive of synergistic effects of insomnia and short sleep duration on these four neuropsychological measures. Consistently, a significant multivariate effect was revealed for short sleep duration (Wilk's $\lambda = 0.956$; $F = 2.534$; $P < 0.01$), whereas insomnia alone failed to show multivariate significance (Wilk's $\lambda = 0.981$; $F = 1.034$; $P > 0.1$). Table 2 presents the adjusted mean scores and the F-values for the interaction effects, the insomnia main effects, and the short sleep duration main effects.

Because of the observed significant interaction between insomnia and short sleep duration, we examined mean differences in neuropsychological performance between the control with normal sleep duration (≥ 6 h) group and the insomnia with normal sleep duration (≥ 6 h) group, the insomnia with short sleep duration (< 6 h) group and the control with short sleep duration (< 6 h) group. Dunnett multiple comparisons were used to test mean differences between the controls with normal sleep duration and the other groups, while controlling for potential confounders.

Dunnett post hoc tests revealed significant differences between the insomnia with short sleep duration group and the control with normal sleep duration group in SDMT ($P < 0.01$), TMT-B ($P < 0.05$), TMT B–A ($P < 0.05$), and total number of errors ($P < 0.05$) and number of omissions ($P < 0.05$) on the BVRT, with the former performing worse than the latter (Table 2). In addition, post-hoc analyses showed that the insomnia with normal sleep duration group was not significantly different from the control with normal sleep duration group in terms of neuropsychological performance. Furthermore, the control with short sleep duration group showed significant difference in SDMT ($P < 0.05$) when compared with the control with normal sleep duration group. Finally, the insomnia with short sleep duration group showed differences in TMT-B ($P < 0.05$), TMT B–A ($P < 0.08$), and number of omissions ($P < 0.01$) on the BVRT when compared to the control with short sleep duration group. No differences were found between groups in the oral or written sections of the TWFT. These results remained significant, and the mean scores very similar to those reported in Table 2 even after adjusting for the number of wakes, number of sleep stage changes, percent stage 1 sleep, and periodic limb movements (Wilk's $\lambda = 0.890$;

Table 1—Sociodemographic, polysomnographic and health-related characteristics of control and insomnia subgroups

Sociodemographics	Controls ≥ 6h (*n* = 343)	Insomniacs ≥ 6h (*n* = 65)	Controls < 6h (*n* = 219)	Insomniacs < 6h (*n* = 51)	*F* Interaction	*F* Insomnia	*F* Short sleep duration
Female[a]	199 (58)	51 (78.5)	121 (55.3)	38 (74.5)	0.01	15.79**	0.45
Age, years[b]	47.43 ± 11.61	44.51 ± 10.07	55.59 ± 11.29	55.92 ± 12.88	1.89	1.20	68.53**
Caucasian[a]	292 (85.1)	41 (63.1)	197 (90)	38 (74.5)	0.79	25.35**	4.76*
BMI, kg/m^2 [b]	29.43 ± 5.66	31.84 ± 8.85	31.10 ± 6.89	29.80 ± 7.22	7.51**	0.68	0.08
Education, years[b]	13.40 ± 2.28	13.41 ± 2.26	13.41 ± 2.39	12.35 ± 2.22	5.06*	4.71*	4.87*
PSG measures							
SOL, minutes[b]	19.00 ± 13.57	22.73 ± 20.13	46.40 ± 38.80	48.53 ± 38.70	2.59	0.10	51.09**
WASO, minutes[b]	55.78 ± 24.09	50.39 ± 23.34	133.60 ± 47.27	141.31 ± 44.28	2.51	1.74	439.05**
Total sleep time, minutes[b]	400.21 ± 28.14	400.64 ± 39.26	292.40 ± 55.10	282.11 ± 57.13	0.70	3.37	399.74**
Total wake time, minutes[b]	74.73 ± 26.47	73.12 ± 27.75	180.19 ± 48.25	189.85 ± 57.74	1.38	1.33	458.44**
Sleep efficiency, %[b]	84.28 ± 5.54	84.58 ± 5.67	62.07 ± 9.83	59.82 ± 11.53	1.36	1.74	512.83**
Stage 1, %[b]	7.12 ± 4.60	6.53 ± 4.83	13.14 ± 9.04	12.65 ± 9.34	0.85	0.23	42.54**
Stage 2, %[b]	70.88 ± 7.98	71.23 ± 8.50	70.69 ± 9.41	69.58 ± 10.41	1.29	0.38	1.98
Stage 3, %[b]	3.21 ± 4.88	3.12 ± 4.78	2.68 ± 5.40	3.35 ± 5.36	0.33	0.22	1.74
Stage 4, %[b]	0.28 ± 1.22	0.44 ± 1.72	0.18 ± 1.03	0.16 ± 0.72	0.01	0.10	0.06
SWS (3+4), %[b]	3.49 ± 5.43	3.56 ± 5.52	2.87 ± 5.72	3.51 ± 5.43	0.26	0.13	1.65
Stage REM, %[b]	18.51 ± 5.97	18.68 ± 6.03	13.30 ± 6.90	14.26 ± 8.66	0.13	0.65	18.34**
REM latency, minutes[b]	95.95 ± 50.64	111.43 ± 73.00	150.16 ± 95.36	122.73 ± 62.04	2.80	0.60	3.35
AHI[b]	0.57 ± 1.15	0.60 ± 1.26	0.73 ± 1.39	0.63 ± 1.24	0.11	1.02	0.03
Health and cognitive status							
Physical health problems[a]	252 (73.5)	56 (86.2)	162 (74.0)	46 (90.2)	0.16	10.93**	0.27
Mental health problems[a]	56 (16.3)	32 (49.2)	35 (16)	18 (35.3)	2.81	41.54**	3.11
MMSE, score[b]	29.22 ± 1.04	29.00 ± 1.29	29.16 ± 1.05	29.08 ± 1.11	0.51	2.09	0.02

[a] values are in n(%); [b] values are in mean ± SD; BMI, body mass index; MMSE, Mini Mental Status Examination; AHI, obstructive apnea/hypopnea index; SOL, sleep onset latency; SWS, slow wave sleep; WASO, wake time after sleep onset; *P < 0.05; **P < 0.01

Table 2—Neuropsychological mean scores of control and insomnia subgroups

Symbol Digit Modalities Test	Controls ≥ 6h (*n* = 343)	Insomniacs ≥ 6h (*n* = 65)	Controls < 6h (*n* = 219)	Insomniacs < 6h (*n* = 51)	*F* Interaction	*F* Insomnia	*F* Short sleep duration
Number Correct[a]	50.64 ± 8.90	52.39 ± 9.19	48.58 ± 9.03	46.26 ± 8.93	5.00*	0.07	16.69**
Trail Making Test							
TMT-A, seconds[a]	31.53 ± 10.93	32.02 ± 11.37	31.12 ± 11.25	33.21 ± 11.00	0.52	1.19	0.11
TMT-B, seconds[a]	75.18 ± 33.52	68.03 ± 34.59	77.48 ± 34.04	87.83 ± 33.49	6.59**	0.12	8.08**
TMT B–A, seconds[a]	43.65 ± 29.45	36.01 ± 30.47	46.36 ± 30.04	54.61 ± 29.42	7.03**	0.00	9.67**
Benton Visual Retention Test							
Number Correct[a]	6.79 ± 1.67	6.85 ± 1.69	6.64 ± 1.63	6.27 ± 1.64	0.01	1.88	3.07
Number of Errors[a]	4.76 ± 2.78	5.20 ± 2.82	5.13 ± 2.81	5.72 ± 2.71	3.39	0.85	4.45*
Omissions[a]	0.40 ± 0.93	0.44 ± 0.97	0.38 ± 0.89	0.75 ± 0.93	4.33*	1.77	4.22*
Distortions[a]	2.14 ± 1.67	2.27 ± 1.77	2.41 ± 1.78	2.28 ± 1.71	0.91	0.04	0.26
Perseverations[a]	0.69 ± 0.93	0.72 ± 1.05	0.75 ± 0.89	0.81 ± 0.93	0.41	0.35	0.02
Rotations[a]	0.76 ± 0.93	0.84 ± 0.97	0.70 ± 0.89	1.00 ± 0.86	0.99	1.25	0.13
Misplacements[a]	0.68 ± 0.93	0.69 ± 0.97	0.78 ± 1.04	0.86 ± 1.00	0.01	0.17	1.40
Size error[a]	0.10 ± 0.37	0.14 ± 0.48	0.12 ± 0.44	0.10 ± 0.43	0.34	0.08	0.21
Thurstone Word Fluency Test							
Oral, number of words[a]	11.65 ± 4.26	12.19 ± 4.35	11.67 ± 4.29	12.15 ± 4.21	0.00	1.34	0.01
Written, number of words[a]	11.56 ± 3.70	12.09 ± 3.87	11.75 ± 3.85	11.31 ± 3.71	1.91	0.02	0.54

[a] values are mean ± SD adjusted for age, education, gender, race, BMI, physical health, mental health, and sampling weight; *P < 0.05, **P < 0.01

F = 2.151; P < 0.01). Furthermore, when the analyses were repeated by removing the subjects with PLMS or by controlling for depression as a stand-alone variable the results did not change significantly.

In order to help explain the neuropsychological profiles found, partial correlation analyses (controlling for all confounders) were conducted between all neuropsychological tests separately for the control and insomnia subgroups. Within the insomnia with short sleep duration group, omissions on the BVRT showed a significant correlation with TMT B–A (r = 0.54; P < 0.01). Perseverations on the BVRT within the insomnia with short sleep duration group significantly correlated with TMT B–A (r = 0.33; P < 0.05), but not with SDMT (r = −0.21; P > 0.1). Within the control with short sleep duration group, TMT B–A did not significantly correlate with omissions (r = -0.04; P > 0.1) or perseverations (r = −0.06; P > 0.1) on the BVRT.

DISCUSSION

This large, population-based study demonstrates that chronic insomnia with objectively measured short sleep duration is significantly associated with deficits in neuropsychological performance. This poorer performance is independent of other factors frequently associated with insomnia or with deficits in neuropsychological performance, such as age, education, race, gender, obesity, sleep disordered breathing, or depression. Specifically, impairment on measures of processing speed, set-switching attention, and short-term visual memory clearly emerged, suggesting deficits in the "executive control of attention," a high-order cognitive function that involves the prefrontal and the anterior cingulate cortices.[30-32] Furthermore, our findings, together with those of previous studies,[10,11] suggest that objective measures of sleep duration in insomnia may be a useful marker of the biological severity and medical impact of this very prevalent disorder.

In the past, most studies found no clear evidence of neuropsychological performance deficits between insomniacs and normal sleepers.[4,5] This has led to the conclusion by the 2006 Standard Committee for Insomnia that these measures were not diagnostically useful.[6] More recently, 3 studies[7-9] that also presented objective sleep data assessed neuropsychological performance in insomnia patients. Two of them included small samples and reported opposite results. The difference between the insomniacs of these 2 studies is that in the positive study, insomniacs slept objectively worse than the controls,[7] whereas in the negative study the insomniacs slept as well as the controls.[8] The third one included a large group of research volunteers with primary insomnia and found a significantly longer response latency on psychomotor tasks.[9] Interestingly, in this study, there was a modest but significant correlation between objective wake time after sleep onset and psychomotor performance. Our study confirms and expands on previous findings on the association between objective measures of sleep and neuropsychological impairment.[7,9] In our study, we found no difference when we compared the entire group of insomniacs to controls, as well as when we compared the group of insomniacs with normal objective sleep duration and normal controls. These findings can explain why most of the previous studies failed to document differences between insomniacs and controls.

In the present study, the insomnia with short sleep duration group showed poorer neuropsychological performance in measures of processing speed (SDMT), set-switching attention (TMT-B and TMT B–A), and short-term visual memory (BVRT). However, deficits in the short-term visual memory domain, as assessed by increased number of errors and omissions on the BVRT, could be better explained by the above mentioned set-switching attentional deficits, as the BVRT is very sensitive to attentional problems, typically revealed as omissions.[26,27] Indeed, executive processes play an important role in memory tasks.[33] In the present study, omissions and perseverations on the BVRT were strongly correlated with TMT B–A scores within the insomnia with short sleep duration group. Taking these findings together, the neuropsychological profile of insomniacs with short sleep duration suggests deficits in the "executive control of attention," as especially revealed by significantly poorer performance in TMT B–A, which is considered a purer measure of the ability to flexibly switch attention.[27,28]

The present data on poorer performance on the SDMT in insomniacs with short sleep duration partially support the view of a pure "slowed processing" deficit, consistent with the findings of sleep fragmentation and sleep deprivation studies.[34-36] However, the present results also suggest that in addition to slowness, the degree of controlled processing required to flexibly perform a set-switching task once the effect of psychomotor processing speed is eliminated (TMT B–A) is also an important factor affecting the insomniacs with short sleep duration. A recent study has revealed that insomniacs may have faster processing speed on a simple reaction time task, yet suffer more when the complexity of the task is slightly increased.[37] Thus, insomniacs with short sleep duration show specific impairment on tasks with high set-switching/cognitive flexibility[28] demands.

Task switching, interference control, allocation of attentional resources, and working memory have been all linked in functional neuroimaging studies to the "executive network," which is supposed to be located in the anterior areas of the brain.[30,31] Tasks of executive attention, such as TMT-B, have been shown to be mediated by activation of the prefrontal and the anterior cingulate cortices.[32,38] Considering the findings from the neuroimaging and factor analytic reports on the tests used in the present study,[38,39] a broader neuropsychological battery of tests would be necessary to assess the different components of the attentional and executive network, such as working memory and interference control, in chronic insomniacs. Nevertheless, the findings of the present study are in agreement with a recent functional neuroimaging study[40] that revealed hypoactivation of the prefrontal cortex during task performance in insomniacs.

Furthermore, our findings on the additive or synergistic effect of chronic insomnia and objective sleep duration on neuropsychological performance are consistent with previous reports that insomnia with short sleep duration is associated with hypercortisolemia,[12-14] increased catecholaminergic activity,[41] and sympathetic activity,[42-45] all of which may lead to neurocognitive deficits. Indeed, diminished sleep-related memory consolidation in chronic insomniacs has been shown to be associated with increased cortisol levels during nighttime sleep.[46] Given the association between objective short sleep duration and hypercortisolemia, it is plausible that cortisol is the mediating pathway of neuropsychological performance deficits.

In the present population-based study, controls with short sleep duration showed a significant slowed information processing speed as assessed by SDMT scores, but no other differences with the control with normal sleep duration group in terms of neuropsychological measures were revealed. Studies exploring the psychomotor effects of sleep loss have consistently shown decreased vigilance and reaction-time performance and increased objective and subjective sleepiness.[35] Although our group of controls with short sleep duration was free of subjective EDS, we could not ascertain their degree of objective daytime sleepiness. However, our findings corroborate the known effects of sleep loss on neurocognitive performance, i.e., slowing in information processing speed.[35,36] Furthermore, the presence of this normal, short sleep duration group allow us to demonstrate that neuropsychological deficits are associated to underlying physiologic hyperarousal, a characteristic of chronic insomnia, rather than to short sleep per se.

The association of depression with insomnia[1,2] and with neurocognitive deficits[15,16] is well established. In our study, controlling for depression did not significantly diminish the association between insomnia and neurocognitive deficits. This suggests that the two disorders, despite the overlap, have distinct pathophysiologic mechanisms; their delineation will lead to more specific treatments.[2]

The objective sleep duration in this study was based on one night of polysomnography, which may not be representative of the subjects' habitual sleep duration. However, in our previous studies, the association between objective sleep duration and hypercortisolemia was based on a 4 consecutive night sleep laboratory protocol, which should represent better the typical sleep profile of the subjects.[12,13] Future studies should explore the association between insomnia, sleep duration, and neuropsychological performance using multiple night recordings.

The field of sleep disorders medicine has attempted to define subgroups within insomnia based on etiology, e.g., primary vs. secondary, age of onset, childhood vs. adult, and discrepancy between subjective and objective findings.[25] The data on the association of insomnia with neurocognitive deficits, hypertension,[10] and diabetes,[11] as well as previous reports on insomnia and the stress system[12-14,41] and the autonomic system,[42-45] provide the basis for a meaningful subtyping of chronic insomnia based on objective duration of sleep. One subtype is associated with physiologic hyperarousal, i.e., short sleep duration, activation of the stress system, and significant medical sequelae (neurocognitive deficits, hypertension, diabetes). The other subtype is not associated with physiologic hyperarousal, i.e., normal sleep duration, normal activity of the stress system, and lack of significant medical sequelae. These 2 subtypes may respond differentially to treatment approaches; the first subtype may respond better to medication or other biological treatment, whereas the second subtype may respond better to psychological treatment, such as cognitive-behavioral therapy. The diagnostic validity and utility of this subtyping should be tested in future studies.

In conclusion, chronic insomnia based solely on clinical criteria did not impact performance on objective neuropsychological measures, but chronic insomnia in combination with objective short sleep duration was associated with significant deficits in neuropsychological performance. Specifically, poorer processing speed and set-switching attention/cognitive flexibility clearly emerged, that suggest deficits in the "executive control of attention," a higher-order cognitive function that involves the lateral prefrontal and the anterior cingulate cortices. Objective measures of sleep duration may serve as clinically useful predictors of the biological severity of chronic insomnia; thus, there is a need for validation of practical, easy to use, inexpensive methods to measure sleep duration outside of the sleep laboratory. Finally, insomnia with objective short sleep duration may represent a phenotype within chronic insomnia that may respond differentially to treatment.

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DISCLOSURE STATEMENT

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