Working memory impairment and cardiovascular hyperarousal in young primary insomniacs

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Abstract

We investigated memory performance and cardiovascular activity in 13 primary insomniacs (PI) compared to 13 good sleepers (GS). Cardiovascular and hemodynamic measures, including heart rate, pre-ejection period, and blood pressure, were continuously recorded at rest and during two memory tasks. PI showed working memory impairment under high cognitive load, but performed as well as GS in an easy memory task. In addition, PI exhibited markers of hyperarousal both at rest and during the execution of the two tasks. However, we failed to find a clear-cut relationship between cardiovascular hyperarousal and cognitive performance in insomniacs. Our data provide further evidence of both cognitive impairment and cardiovascular hyperarousal in primary insomnia, while not supporting the hypothesis of hyperarousal as a compensatory mechanism to overcome cognitive challenges.

Descriptors: Autonomic activity, Heart rate variability, Hyperarousal, Impedance cardiography, Insomnia, Working memory

Insomnia is the most common sleep disorder characterized by difficulty initiating and/or maintaining sleep, as well as waking up too early and nonrestorative sleep (American Academy of Sleep Medicine, 2005). Insomnia is a widespread sleep problem, affecting between 6–10% of the general adult population (Morin, LeBlanc, Daley, Gregoire, & Merette, 2006; Ohayon, 2002) with estimates for primary insomnia (i.e., insomnia that is not secondary to another sleep or psychiatric disorder, and is not due to substance use or a general medical condition) ranging from 3–5% (Ohayon, 2002). For a diagnosis of primary insomnia, nocturnal symptoms should impact upon daytime functioning resulting in daytime sleepiness, fatigue, mood disturbance, or cognitive impairment. The latter dysfunction affects several domains such as attention, problem solving, and working and episodic memory (for a review, see Fortier-Brochu, Beaulieu-Bonneau, Ivers, & Morin, 2011). However, since some studies have failed to find any cognitive deficit in this population (see Riedel & Lichstein, 2000), it has been hypothesized that insomniacs could suffer from a “daytime performance misperception,” which has been defined as “a discrepancy between a patient’s self-perception of daytime impairment and objective measures of such impairment” (Orff, Drummond, Nowakowski, & Perlis, 2007, pp. 1209–1210). In opposition to this view, it has been suggested that cognitive impairments are elusive and relatively subtle in insomnia and that these reports are the result of tasks not sensitive enough to detect these deficits (Espie & Kyle, 2008; Fortier-Brochu et al., 2011). Another hypothesis refers to the hyperarousal theory of insomnia (Perlis, Giles, Mendelson, Bootzin, & Wyatt, 1997; Perlis, Merica, Smith, & Giles, 2001): According to this concept, insomnia is a disorder characterized by a condition of elevated physiological activation that affects somatic, cortical, and cognitive functioning throughout the day as well as at night, leading to nocturnal and diurnal symptoms (see also Bonnet & Arand, 2010; Riemann et al., 2010). Within this framework, a recent study by Lovato and colleagues (Lovato, Lack, Wright, Cant, & Humphreys, 2013) reported similar performances between older adults with insomnia and age-matched good sleepers in a double span memory test. The authors explained this lack of difference referring to the hyperarousal concept as a compensatory mechanism (i.e., a mobilization of extra effort such as increased heart rate, blood pressure, and/or brain activation, which assists insomniacs in compensating for sleep-related performance impairment), which could allow insomniacs to perform as well as good sleepers in cognitive tasks. However, they did not collect any physiological index to support this hypothesis. Given that, Lovato and colleagues (2013) suggested that future research examining cognitive performance in insomnia should include objective assessment of hyperarousal in order to evaluate whether the physiological arousal could act as a compensatory mechanism to overcome cognitive challenges in this population. Indeed, to date the few studies assessing the relationship between hyperarousal, resources mobilization, and cognitive performance have yielded unclear results. For instance, Schmidt and coauthors (Schmidt, Richter, Gendolla, & Van Der Linden, 2010) found that self-rated insomnia severity covaried with performance on an easy memory task in a nonclinical population (i.e., university students without insomnia diagnosis),
and this severity was positively associated with the rise in systolic blood pressure during the task. Conversely, Covassin and colleagues (2011), by assessing inhibition control efficiency using a stop-signal task in a group of primary insomniacs, reported no significant differences in cardiovascular reactivity (i.e., heart rate, pre-ejection period, cardiac output) during the task in spite of reduced motor inhibition control.

Therefore, in this study we aimed to investigate the relationship between memory performance, task difficulty, and arousal activity (measured as hemodynamic and autonomic indices) in a group of primary insomniacs relative to a group of good sleepers. Firstly, we sought to compare the performance between insomniacs and good sleepers in two different tasks involving different cognitive loads. Since it has been suggested that complex or highly demanding tasks should be employed with insomniacs in order to unmask cognitive impairment (Espie & Kyle, 2008; Shekleton, Rogers, & Rajaratnam, 2010), we hypothesized that insomniacs will perform worse than good sleepers in a complex and resource-demanding task such as the N-back task (Owen, McMillan, Laird, & Bullmore, 2005) but not in an easy memory task (Schmidt et al., 2010). Secondly, assuming the hyperarousal as a potential compensatory mechanism that enables adequate cognitive functioning in spite of poor sleep (Orff et al., 2007; see above), we evaluated the role of the arousal in modulating cognitive performance by exploring the cardiovascular profile during task execution.

Method

Participants

Twenty-six nonsmoking young adults between the ages of 20 and 28 years (mean 23.81 years, SD 2.12 years) participated in the study: 13 healthy good sleepers (GS; 6 women) and 13 drug-free primary insomniacs (PI; 8 women). All participants were enrolled by way of advertisements posted at the University of Padua, and they underwent an intense screening to ensure they met the eligibility criteria for the study. Eligibility criteria for the PI group followed the Recommendations for a Standard Research Assessment of Insomnia (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006). PI participants had to report insomnia symptoms lasting at least 6 months and meet the Research Diagnostic Criteria for Primary Insomnia (Edinger et al., 2004) as determined from a screening semistructured interview (administered at least 1 week prior to the main experiment). They also had to score ≥5 on the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) and ≥11 on the Insomnia Severity Index (ISI; Morin, 1993). Conversely, GS had to report lower scores than these cut-offs and had to satisfy the Research Diagnostic Criteria for Normal Sleepers (Edinger et al., 2004).

Exclusion criteria for all participants were body mass index (BMI; kg m⁻²) ≥ 30, extreme chronotype (≤30 or ≥70, assessed using the Morningness-Eveningness Questionnaire, MEQ; Horne & Ostberg, 1976), use of any medications, psychiatric or somatic diseases as evaluated by the screening interview, and shift work or time-zone travels in the 6 months prior to the study.

Participants gave written informed consent to participate in the experiment, which complied with the 1975 Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Department of Psychology, University of Padua. Participants received €100 for their participation.

Cognitive Tasks

Easy letter memory task. In this task, participants have to memorize four meaningless strings of letters, each consisting of four letters (e.g., RFZS). One string at a time appeared for 75 s on a computer screen. At the end of the 5-min learning phase, participants had to write down the four-letter strings on a response sheet (immediate recall test). After about 6 min, during which participants had to fill out a demographic information form, they were required to write down again the four strings (surprise delayed recall test). The number of letters correctly reported (ranging from 1 to 16) was used to compute the immediate recall (number of items) and delayed recall (number of items) performance indices. Each letter was considered as a correct response only if it was reported in its exact serial position and string. The task was the same as that used by Schmidt and colleagues (2010) and has been evaluated as relatively easy by college students (Brinkmann & Gendolla, 2008; Gendolla & Richter, 2006; Schmidt et al., 2010).

N-back task. The N-back task is a widely used task involving great cognitive load on working memory processes (see Owen et al., 2005). A stream of white alphabetical letters was presented on a black background at the center of a computer screen. Participants were required to press as quickly as possible the L key on the keyboard whenever the letter presented on the screen matched the one presented two trials previously (target), and the A key in all the other cases (nontarget). Response keys were covered by a green (L) and a red (A) disk in order to avoid any alphabetical influence. Each letter was presented for 250 ms, followed by a response interval of 1,550 ms. The task consisted of three 5-min blocks; each block was structured as follows: 1 min of baseline with a fixation cross on a blank screen, 3 min of testing on 100 letters (30 targets and 70 nontargets) and 1 min of recovery with a fixation cross on a blank screen. During the baseline and recovery intervals, the subject was instructed to stay still and fixate on the cross presented in the center of the screen. The order of presentation of the letters was counterbalanced across the blocks. Stimulus presentation and data collection were controlled using E-Prime 1.1 (Psychology Software Tools, Inc., Pittsburgh, PA). Total accuracy (AccTot; %), target accuracy (AccTarg; %), nontarget accuracy (AccNTarg; %), errors (Err; number of errors), and reaction times (RTs; ms) were calculated.

Cardiovascular Recording

Beat-to-beat systolic (SBP; mmHg) and diastolic (DBP; mmHg) blood pressure was continuously recorded using the Ohmeda 2300 device (Finapres, Englewood, CO). The cuff was positioned at the second phalanx of the middle finger of the participant’s left hand. The position of the hand was kept at heart level during the recording.

Electrocardiogram (ECG) data were acquired at 512 Hz sampling rate using a modified Lead II Einthoven configuration. R-wave peaks were detected automatically through dedicated software, visually examined, and incorrectly detected R-peaks were manually edited. Missing and ectopic beats were corrected via cubic spline interpolation. Interbeat intervals were computed, and a third-order polynomial filter was applied on the time series in order to remove trend components. A fast Fourier transformation was employed to quantify the spectral power in the high frequency (HF; 0.15–0.4 Hz; ms²) band, which is thought to be a specific index of
vagal modulation (Berntson et al., 1997). This analysis was conducted by means of the Kubios HRV Analysis Software 2.0 (MATLAB, Kuopio, Finland).

A tetrapolar band electrode configuration was employed to acquire the impedance signal (Z0) and the derivative of the impedance signal (dZ/dt). In accordance with guidelines (Sherwood et al., 1990), the four bands were placed as follows: around the upper (1) and lower (2) part of the neck, around the thoracic xiphisternal process (3), and at the abdominal level (4). By means of a Minnesota Impedance Cardiograph Model 304B (IFM Inc., Greenwich, CT), a 4 mA, 100 KHz alternating current was transmitted through the outer electrodes (1 and 4) and the voltage reflecting the rate of change in the impedance waveform on a given beat (dZ/dt; Ω) was estimated by the inner electrodes (2 and 3). Impedance signals were acquired at 500 Hz sampling rate and processed by the COP-WIN software system (BIT Inc., Chapel Hill, NC), which uses an ensemble averaging procedure to generate 30-s epochs after filtering out movement and respiratory artifacts. The positions of the B (i.e., the beginning of the left ventricular ejection) and the X (i.e., the closure of the aortic valve) points on the dZ/dt waveform and on the Q-wave onset of the QRS complex (Q-point; indicating the onset of the ventricular depolarization) on the ECG were automatically marked. Each cardiac cycle was visually checked and edited when the algorithm failed to detect these points (i.e., the B-point was positioned at the start of the upstroke or positive inflection on the rising dZ/dt waveform). Heart rate (HR; bpm) was defined as the number of heart beats per minute. Pre-ejection period (PEP; ms), a noninvasive index inversely related to the sympathetic beta-adrenergic activity on myocardium (Sherwood et al., 1990), was computed as the time interval between the onset of ventricular depolarization (Q-onset in the ECG signal) and the onset of left ventricular ejection (B-point in the dZ/dt signal).

Rate pressure product (RPP; bpm × mmHg/100), an index of the overall cardiac workload (Campbell & Langston, 1995), was calculated as follows: HR × SBP/100 (Kitamura, Jorgensen, Gobel, Taylor, & Wang, 1972).

Polysomnography

A standard overnight polysomnography (PSG) recording was run (Siesta 802, Compumedics, Abbotsford, Australia), including six electroencephalogram leads (EEG: C3-A2, C4-A1, F3-A2, F4-A1, O1-A2, O2-A1), a bilateral electrooculography (EOG: right EOG-A1, left EOG-A2), and a submental bipolar electromyography (EMG). Each signal was amplified, band-pass filtered (EEG and EOG: 0.3–35 Hz; EMG: 10–100 Hz), and digitized at 500 Hz. Sleep stages (Wake, N1, N2, N3, REM) were manually scored at consecutive 30-s epochs to obtain the following parameters: Total sleep time (TST; min), sleep efficiency (SE; %), sleep onset latency (SOL; min), wake after sleep onset (WASO), and duration of each sleep stage (N1, N2, N3, REM; min). PSG montage and sleep scoring followed the American Academy of Sleep Medicine guidelines (Iber, Ancoli-Israel, Chesson, & Quan, 2007).

Procedure

Participants spent two consecutive nights at the sleep laboratory of the University of Padua for PSG recordings (adaptation and experimental nights). Participants had to refrain from naps, alcohol, and caffeine consumption for 24 h prior to the recording sessions. They arrived at the laboratory at 8 pm and the electrodes were attached. Then, they relaxed quietly for 10 min to allow physiological parameters to stabilize. A 3-min resting period (rest) preceded the easy letter memory task. Then, after a 15-min break, participants performed the N-back task. Cardiovascular monitoring was continuous throughout the resting period and the tasks execution. At the end of the tasks, participants were allowed to read, talk, listen to music, or watch TV until 11:30 pm. Time available for sleep was fixed from 12 pm (lights out) to 8 am (lights on). After awakening, PSG equipment was removed and the subject debriefed. In order to avoid any sleep-related bias due to spending a night in the lab (i.e., first-night effect), cognitive tasks were only performed in the adaptation evening. The adaptation night, used in order to becoming familiar with the lab environment, confirmed no further sleep disorders (e.g., obstructive sleep apnea or periodic limb movement syndrome) while only sleep data from the experimental night were analyzed.

Data Reduction

Due to skewed distribution, PEP, RPP, and HF variables were log-transformed prior to the analysis. To assess the cardionic autonomic profile during the rest condition, cardiovascular absolute values (HR, PEPsa, RPPsa, SBP, DBP, HFsa) were averaged within the 3-min resting period prior to the tasks (baseline).

For the easy letter memory task, cardiovascular and autonomic absolute values were averaged within the 5-min recording of the task. For the N-back task, the absolute values of the same parameters were averaged for each 3-min block.

Statistical Analysis

Between-group differences in demographic, subjective screening measures, PSG variables, and absolute cardiovascular values during the resting period were evaluated through unpaired t tests. Due to nonnormal distributions (determined by Shapiro–Wilk W tests), we used the Mann–Whitney U test to compare performance variables both for the easy letter memory task and the N-back task.

In order to assess the cardiovascular response patterns to the easy letter memory task, we ran separate repeated measure analyses of variance (ANOVA) with group (GS, PI) as between-subjects factor and time (baseline, task) as within-subjects factor for each cardiovascular measure.

The cardiovascular response pattern to the N-back was analyzed by applying to each cardiovascular measure a repeated measures ANOVA with group (GS, PI) as between-subjects factor and time (baseline, block 1, block 2, block 3) as within-subjects factor, using the Greenhouse-Geisser correction where appropriate, but original degrees of freedom are reported. Tukey’s HSD test was used for post hoc comparisons, and partial eta squared (ηp2) is reported as estimate of effect.

Lastly, explorative Spearman correlations were performed to assess the relationship between cognitive performance and interindividual differences in the resting cardiovascular measures.

For all analyses, the probability level was set at p < .05 for significance.

Results

Demographic, Subjective Screening Measures and PSG Data

As reported in Table 1, groups did not differ in age, body mass index, and circadian typology. As expected by selection criterion,
PI reported higher PSQI and ISI scores, indicating poorer sleep quality compared to GS. This poor sleep quality was confirmed by the PSG data. Insomniacs slept significantly less, had lower sleep efficiency, showed longer sleep onset latency, and spent more time awake after sleep onset than did normal sleepers (see Table 1).

Resting Period
Cardiovascular absolute values are summarized in Table 2. Results from unpaired t tests revealed a significant shorter PEPlog (enhanced sympathetic tone), higher RPPlog (increased cardiac metabolic demand), and lower HFlog (reduced vagal tone) in PI compared to GS. Insomniacs also exhibited a higher HR, although this difference did not reach statistical significance (p = .06).

Table 1. Demographic, Subjective Screening Measures and PSG Data

<table>
<thead>
<tr>
<th></th>
<th>Good sleepers</th>
<th>Insomniacs</th>
<th>n(24)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Demographic data</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>24.31 ± 1.60</td>
<td>23.31 ± 2.50</td>
<td>1.22</td>
<td>.236</td>
</tr>
<tr>
<td>BMI (kg m⁻²)</td>
<td>22.91 ± 1.88</td>
<td>22.82 ± 2.81</td>
<td>0.09</td>
<td>.926</td>
</tr>
<tr>
<td>Screening measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSQI</td>
<td>2.00 ± 0.91</td>
<td>10.00 ± 2.00</td>
<td>−13.12</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>ISI</td>
<td>1.00 ± 1.29</td>
<td>15.77 ± 3.27</td>
<td>−15.15</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>MEQ</td>
<td>49.42 ± 6.83</td>
<td>45.08 ± 8.22</td>
<td>1.43</td>
<td>.166</td>
</tr>
<tr>
<td>Sleep parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TST (min)</td>
<td>454.77 ± 13.92</td>
<td>417.92 ± 40.39</td>
<td>3.11</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>SE (%)</td>
<td>0.95 ± 0.03</td>
<td>0.87 ± 0.08</td>
<td>3.10</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>SOL (min)</td>
<td>6.50 ± 4.82</td>
<td>16.19 ± 16.42</td>
<td>−2.04</td>
<td>.052</td>
</tr>
<tr>
<td>WASO (min)</td>
<td>18.73 ± 12.20</td>
<td>45.88 ± 30.17</td>
<td>−3.01</td>
<td>.006</td>
</tr>
<tr>
<td>N1 (min)</td>
<td>29.77 ± 17.54</td>
<td>27.23 ± 12.94</td>
<td>0.42</td>
<td>.678</td>
</tr>
<tr>
<td>N2 (min)</td>
<td>208.92 ± 23.10</td>
<td>189.81 ± 36.69</td>
<td>1.59</td>
<td>.125</td>
</tr>
<tr>
<td>N3 (min)</td>
<td>115.23 ± 30.66</td>
<td>113.12 ± 35.52</td>
<td>0.16</td>
<td>.872</td>
</tr>
<tr>
<td>REM (min)</td>
<td>100.65 ± 18.87</td>
<td>85.46 ± 26.24</td>
<td>1.69</td>
<td>.103</td>
</tr>
</tbody>
</table>

Note. BMI = body mass index; ISI = Insomnia Severity Index; MEQ = Morningness-Eveningness Questionnaire; PSQI = Pittsburgh Sleep Quality Index; REM = rapid eye movement; SE = sleep efficiency; SOL = sleep onset latency; TST = total sleep time; WASO = wake after sleep onset.

N-Back Task
Performance in this task was significantly poorer for insomniacs compared to good sleepers. PI reported lower total and nontarget accuracy and higher number of errors, whereas target accuracy and RTs were similar between groups (Table 3).

Exploratory Analysis
Exploratory correlations performed between the easy letter memory task performance and cardiovascular resting values failed to find significant relationships.

In the current study, we aimed to investigate the performance of primary insomniacs in two different memory tasks involving

Discussion
In the current study, we aimed to investigate the performance of primary insomniacs in two different memory tasks involving F(1,22) = 4.23, p = .061, η² = .15. As illustrated in Figure 1, the significant interaction Group × Time for HFlog, F(1,22) = 5.18, p = .033, η² = .19, suggested vagal activation in PI and vagal withdrawal in GS during the task (although these changes were not statistically significant at the post hoc tests).

Table 2. Mean and Standard Deviation (SD) of Cardiovascular Measures at Rest

<table>
<thead>
<tr>
<th></th>
<th>Good sleepers</th>
<th>Insomniacs</th>
<th>n(24)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>65.68 ± 7.45</td>
<td>74.38 ± 13.97</td>
<td>−1.98</td>
<td>.059</td>
</tr>
<tr>
<td>PEPlog (log ms)</td>
<td>2.10 ± 0.03</td>
<td>2.05 ± 0.07</td>
<td>2.14</td>
<td>.043</td>
</tr>
<tr>
<td>RPPlog (log bpm × mmHg/100)</td>
<td>1.88 ± 0.05</td>
<td>1.96 ± 0.11</td>
<td>−2.12</td>
<td>.047</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>118.68 ± 9.84</td>
<td>125.66 ± 14.73</td>
<td>−1.42</td>
<td>.168</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>73.45 ± 10.12</td>
<td>75.47 ± 11.39</td>
<td>−0.48</td>
<td>.638</td>
</tr>
<tr>
<td>HFlog (log ms⁻²)</td>
<td>2.99 ± 0.36</td>
<td>2.51 ± 0.69</td>
<td>2.21</td>
<td>.037</td>
</tr>
</tbody>
</table>

Note. DBP = diastolic blood pressure; HR = heart rate; HFlog = high frequency; PEPlog = pre-ejection period; RPPlog = rate pressure product; SBP = systolic blood pressure.
different cognitive loads. In order to achieve this goal, we compared a group of young PI and a group of young GS undergoing an easy memory task (easy letter memory task) and a highly demanding task (N-back). In the easy task, PI exhibited a performance comparable to GS, whereas on the N-back, PI showed a poorer performance. Recently, Schmidt and colleagues (2010), testing the easy letter memory task with a group of university students, found a relationship between self-rated insomnia severity (assessed by the ISI, Morin, 1993) and delayed recall performance. On the contrary, we found no differences between groups both in the immediate and in the delay recall tests. The main difference between the two studies lies in the sample tested: Schmidt and co-authors investigated a nonclinical population whereas our sample was composed of young adults who met the criteria of primary insomnia as defined by the Research Diagnostic Criteria for Primary Insomnia.

**Table 3. Mean and Standard Deviation (SD) of N-Back Performance Indices**

<table>
<thead>
<tr>
<th></th>
<th>Good sleepers</th>
<th>Insomniacs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 13)</td>
<td>(n = 13)</td>
</tr>
<tr>
<td>Mean</td>
<td>94.00</td>
<td>89.31</td>
</tr>
<tr>
<td>SD</td>
<td>4.84</td>
<td>7.97</td>
</tr>
<tr>
<td>Z(24)</td>
<td>2.00</td>
<td>.045</td>
</tr>
<tr>
<td>AccTot (%)</td>
<td>88.03</td>
<td>81.79</td>
</tr>
<tr>
<td>AccTarg (%)</td>
<td>10.51</td>
<td>16.22</td>
</tr>
<tr>
<td>AccNTarg (%)</td>
<td>96.56</td>
<td>92.53</td>
</tr>
<tr>
<td>Err (n°)</td>
<td>16.92</td>
<td>27.69</td>
</tr>
<tr>
<td>RTs (ms)</td>
<td>597.95</td>
<td>597.58</td>
</tr>
</tbody>
</table>

*Note.* AccTot = total accuracy; AccTarg = target accuracy; AccNTarg = nontarget accuracy; Err = errors; RTs = reaction times.
(Edinger et al., 2004), criteria which were also compatible with both the International Classification of Sleep Disorders (ICSD-2; American Academy of Sleep Medicine, 2005) and the DSM-IV (American Psychiatric Association, 1994) diagnostic criteria for primary insomnia. PSG data further confirmed the diagnosis, showing an objective sleep difference between the groups.

Our small sample, which may have decreased our statistical power, could also account for the lack of significant differences between groups and the different results between these studies. Nevertheless, it is also possible that the easy letter memory task is not demanding enough to disclose the subtle deficits that characterize chronic insomnia (Espie & Kyle, 2008; Fortier-Brochu et al., 2011; Shekleton et al., 2010). Furthermore, considering that neural systems underpinning executive functions are particularly sensitive to sleep loss and sleep deprivation (Durmer & Dinges, 2005), it is possible that sleep problems other than chronic insomnia (e.g., circadian rhythm disorders, lifestyle choices) could explain the inconsistency between these studies. This suggests that chronic insomniacs could use different strategies to respond to mental challenges compared to other poor sleeper populations. Further studies comparing cognitive performance across different sleep disorders and under sleep deprivation are warranted.

On the other hand, in the N-back task, PI performed significantly poorer than GS, reporting lower total and nontarget accuracy and higher number of errors, with no differences in RTs between the groups. Thus, the N-back task was sensitive enough to disclose working memory difficulties in PI. Our results also confirm data from Varkevisser, Van Dongen, and Kerkhof (2005). These authors, using a controlled 24-h constant routine protocol, reported a worse performance in insomniacs than in age-matched good sleepers in a similar N-back paradigm. It should be noted that the authors reported no effect of circadian phase either on performance or in

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**Figure 2.** Mean values and standard errors of cardiovascular indices at baseline and over the three N-back blocks. BL = baseline; DBP = diastolic blood pressure; HR = heart rate; HF\(_{log}\) = high frequency; PEP\(_{log}\) = pre-ejection period; RPP\(_{log}\) = rate pressure product; SBP = systolic blood pressure.
body temperature in the insomniacs relative to good sleepers, thus suggesting independence of the cognitive performance from the time of day. It is worth noting that the mean age of the sample in our study participants was relatively younger (age range 20–28) than in the constant routine study (age range 31–54). These results indicate that working memory impairment is not merely a misperception, but could be highlighted by increasing the level of cognitive demand of a task. Taken together, these results suggest that (a) working memory is objectively impaired even in young PI, and (b) insomniacs can perform adequately on an easy memory task, but show difficulties with challenges that place great cognitive load on working memory processes.

As the hyperarousal model claims, insomniacs are characterized by an elevated state of cognitive (e.g., excessive worry and rumination), somatic (e.g., high autonomic drive), and cortical (e.g., increased beta EEG frequencies) hyperactivity (Perlis et al., 1997, 2001). Compared to GS, our PI group exhibited cardiac (elevated HR and RPPlog) and autonomic (lower PEPlog and HFlog) hyperarousal at rest. Although the HR difference between groups only approached the significance level (p = .06), the mean difference was 8.7 bpm, meaning that the HR showed by PI was 13% higher than that recorded in GS. Since resting HR is assumed to be a relatively stable measure and could be considered as an indicator of an individual’s traitlike baseline arousal (see Schmidt, Mussel, & Hewig, 2013), our results suggest a state of hyperarousal in the insomnia group.

The RPP is a metric highly correlated with the myocardial oxygen consumption associated with mental or physical challenge (see Capuana, Dywan, Tays, & Segalowitz, 2012). Insomniacs displayed a higher resting RPPlog, suggesting that their heart was experiencing a relatively greater workload even without performing any task (Fredericks, Choi, Hart, Butt, & Mital, 2005).

Regarding the autonomic pattern in insomniacs, reports have shown a decrease in HF power in PI compared to GS during overnight sleep (Bonnet & Arand, 1998; Spiegelhalder et al., 2011) whereas other studies found no autonomic dysregulation during sleep (de Zambotti et al., 2012; Jurysta et al., 2009; Varkevisser et al., 2005). Our data are in line with a recent study reporting lower HF at rest in insomniacs (Fang, Huang, Yang, & Tsai, 2008), indicating a reduction of the vagal tone in PI compared to GS. We also found a reduced PEPlog at rest in insomniacs, suggesting an increase in the sympathetic drive in this population. Taken together, these results indicate an autonomic dysregulation in PI at rest, with a reduction of the vagal tone coupled with an enhanced cardiac sympathetic drive.

During the execution of the two tasks, both groups displayed an elevated cardiovascular response relative to the resting period. Compared to the GS, insomniacs also showed a tendency to exhibit higher cardiovascular activation during both tasks, but the differences between groups achieved significance only for the PEPlog during the easy letter memory task. An interesting pattern was observed for the HFlog. Whereas GS seems to show a vagal withdrawal in response to the tasks, a modest parasympathetic modulation occurred in PI. This latter conclusion is drawn by the evidence of unchanged vagal tone in PI during the execution of the easy letter memory task, while a nonsignificant increase from baseline was seen during the N-back task. However, the absence of any other significant interaction in the ANOVAs indicates a similar cardiovascular response to the tasks in the two groups. Thus, our data showed no clear mobilization of extra cardiovascular effort in PI relative to GS. This result is in contrast to Stepanski and co-authors (Stepanski, Glinn, Zorick, Roehrs, & Roth, 1994), who reported in insomnia an increased HR during a reaction time task (with no baseline differences) and partially differs from Schmidt et al.’s (2010) results, who observed a positive relation between subjective insomnia severity and rise of SBP during an easy memory task. In fact, our data revealed a similar SBP and DBP pattern for PI and GS in the easy letter memory task. In addition, our results are consistent with other works reporting no cardiovascular differences during a stop-signal task (Covassin et al., 2011) and a mathematical task (Haynes, Adams, & Franzen, 1981) in PI compared to GS.

Since it has been suggested that the hyperarousal is not just a task-related state but rather a trait in insomniacs (for a review, see Riemann et al., 2010), and given that resting cardiovascular indices such as heart rate and blood pressure have been associated with performance efficacy (Capuana et al., 2012; Hansen, Johnsen, & Thayer, 2003; Park, Vasey, Van Bavel, & Thayer, 2013; Wharton et al., 2006), we performed explorative correlations to assess the association between interindividual differences in the cardiovascular-autonomic variables at rest and cognitive performance.

We found a positive relationship between HR and RPPlog at rest and all performance indices (with the exception of nontarget accuracy) in the GS group and only a significant positive relationship between RPPlog and total accuracy in the PI group for the N-back. These results suggest that a higher resting cardiac state is optimal for GS to better perform a highly demanding task such as the N-back. Conversely, PI, who exhibited a pattern of higher cardiovascular activity at rest than GS, showed a slight association between resting values and performance. We also found no significant correlations between resting values and performance indices in the easy letter memory task. This is likely attributable to a ceiling effect on the performance due to the low cognitive demand of the task. We might speculate that these results can be accounted for by an “inverted U-shaped” relationship between arousal (i.e., cardiac activity) and cognitive performance (see Duschek, Werner, & Reyes del Paso, 2013). This idea suggests that the best performance is achieved at an optimal level of arousal (e.g., the normotensive range for BP), and a progressive reduction occurs when moving away from this level (see Duschek, Muckenthaler, Werner, & Reyes del Paso, 2009; Fischer, Langner, Birbaumer, & Brocke, 2008; Vazemousavi, Barry, & Clarke, 2009). According to this hypothesis, within the GS group, participants with the higher level of HR and RPP fell into the “optimal range,” whereas the cardiovascular resting pattern of PI was hyperactivated, thus being inadequate for successful performance in the N-back. In this framework, it has also been hypothesized that the “optimal arousal range” depends on the difficulty of a task (Diamond, Campbell, Park, Halonen, & Zoladz, 2007), which could explain the absence of correlations between the easy letter memory task and baseline cardiovascular measures.

Another explanation is that the cognitive impairments in PI are not associated with the somatic (i.e., cardiovascular) hyperarousal, but lie in possible alterations in brain structure, such as a reduction in orbitofrontal gray matter volume (Altela, Vrenken, Van Der Werf, van den Heuvel, & Van Someren, 2010), or in hypoactivation of the prefrontal circuits (Altela et al., 2008; Nofzinger et al., 2004) in insomniacs. Indeed, alterations or dysfunctions in these brain regions have been associated with impairment of working memory (Baier et al., 2010) and severity of ruminations (Zuo et al., 2012), suggesting a shared variance between these problems in insomnia, which could also explain the observed association between cognitive impairment, autonomic dysfunctions, and worry, anxiety, and rumination (see Harvey, 2002).

Future studies should address the contribution of these variables in the modulation of both somatic activation and cognitive...
performance in insomnia. Overall, our cardiovascular results complement previous findings showing that young primary insomniacs display markers of cardiovascular hyperarousal during task performance (Covassin et al., 2011), presleep onset period (de Zambotti, Covassin, De Min Tona, Sarlo, & Stegagno, 2011; Haynes et al., 1981), and nighttime sleep (Bonnet & Arand, 1998; de Zambotti et al., 2012).

A number of weaknesses of the current study must be acknowledged. The main limitation of the current work is the small sample size, which, as discussed above, may have reduced our statistical power leading to a type II error. This limitation should be taken into account when comparing our results to studies involving larger samples. Another important issue is related to the different tasks administered in the present study. The different performance exhibited by PI relative to GS in the easy task and in the N-back could be due to differences in cognitive load or to any other factor that differed between the tasks (e.g., length of the task, type of response required, presentation rate of stimuli). Further studies should address this limitation by employing the same task manipulating the level of resource (e.g., 1-back, 2-back, 3-back).

According to the current criteria (American Academy of Sleep Medicine, 2005), the diagnosis of insomnia requires, along with sleep symptoms, the complaint of daytime impairment related to the nighttime sleep difficulty, such as excessive sleepiness, mood disturbance, fatigue and attention, concentration, or memory deficit. Although these cognitive impairments have been shown to be subtle and elusive, we demonstrated that they are not a mere “misperception” but they are objectively measurable using sensitive tests. Results from the current study suggest that young primary insomniacs suffer from a working memory impairment while performing a high-demanding memory task, but they can perform as well as GS on an easy memory challenge. In addition, we reported that PI present markers of somatic (i.e., hemodynamic and autonomic) hyperarousal at a relatively young age. However, we failed to find a clear-cut relationship between cardiovascular hyperarousal and cognitive performance in insomniacs. Therefore, our findings do not support the idea of hyperarousal as a compensatory mechanism to respond to cognitive challenges in this population. Future studies should address the relationship between other hyperarousal components (e.g., cortical, cerebral hemodynamic, anxiety, worry) and cognitive performance in insomnia.

References


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