The Effect of Insomnia on Neuropsychological Functioning in Patients with Comorbid Symptoms of Pain, Fatigue, and Mood Disorders

Julie Aasvik1,*, Tore C. Stiles2,3,4, Astrid Woodhouse2,3,5, Petter Borchgrevink1,2,3, Nils Inge Landrø1,3,6

1Department of Circulation and Medical Imaging, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway
2Hysnes Rehabilitation Center, St. Olav’s University Hospital, Trondheim, Norway
3National Competence Centre for Complex Disorders, St. Olav’s University Hospital, Trondheim, Norway
4Department of Psychology, Norwegian University of Science and Technology, Trondheim, Norway
5Department of Public Health and General Practice, Norwegian University of Science of Technology, Trondheim, Norway
6Clinical Neuroscience Group, Department of Psychology, University of Oslo, Oslo, Norway

*Corresponding author at: Department of Circulation and Medical Imaging, NTNU, Faculty of Medicine, P.O. Box 8905 MTFS, 7491 Trondheim, Norway. Tel.: +47 41035078.
E-mail address: Julie.K.Aasvik@ntnu.no (J. Aasvik).

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Abstract

Objectives: To examine if elevated symptoms of insomnia affects neuropsychological functioning in patients with concurrent symptoms of pain, fatigue, and mood disorders.

Methods and results: A total of seventy-six subjects participated in this (cross-sectional) study. Based on the cut-off score guidelines from The Insomnia Severity Index subjects were assigned to either a clinical insomnia group (N = 35) or a comparison group (N = 41). Factors such as age, general cognitive functioning, and symptoms of pain, fatigue, depression, and anxiety did not differ between the groups. Both groups completed a questionnaire which assessed subjective memory functioning. In addition they completed a set of neuropsychological tests measuring general cognitive functioning, spatial and verbal working memory, and inhibitory control. Although the subjects with clinical insomnia did not report more memory problems than the comparison group, they presented significant deficiencies on the tests assessing spatial and verbal working memory. There was no difference between the groups in inhibitory control.

Conclusions: This study shows that as the symptom severity of insomnia increases and become clinically significant, it has substantial effect on both spatial and verbal-numeric working memory functioning. By differentiating and testing different domains of working memory, this study provides a more detailed and nuanced characterization of working memory deficiencies than the previous studies within this field. The results need to be transferred to clinical practice so that neuropsychologists include assessments of sleep as part of their routine screenings.

Keywords: Sleep disorders; Spatial processing; Executive functions; Depression; Everyday functioning; Chronic pain

Introduction

Insomnia is defined as having difficulty in initiating and/or maintaining sleep (Morin, LeBlanc, Daley, Gregoire, & Merette, 2006). Approximately 10% of the general adult population meets the diagnostic criteria for clinical insomnia (Roth, 2007). Insomnia is a disorder of complex etiology, often involving multiple factors (i.e. physiological, circadian, emotional, cognitive, lifestyle factors, stress, etc.) that interact and interfere with sleep (Bootzin, Mauber, Perlis, Salvio, & Wyatt, 1993; Harvey, 2002).

The clinical presentation of insomnia goes beyond the nocturnal problems and complaints of inadequate sleep. It extends to include a sense of reduced quality of life (Leger et al., 2001) and patients often emphasize its negative effect on daytime performance. Insomnia is associated with both higher rates and risks of workplace injuries and accidents (Laugsand, Strand, Vatten, Janszky, & Bjørnegaard, 2014; Shahly et al., 2012). It is associated with increased absenteeism, and it is a strong predictor of future disability pension (Daley et al., 2009; Leger, Guillemaintault, Bader, Levy, & Paillard, 2002; Overland et al., 2008). Studies have shown that poor sleep is associated with increased medical morbidity (Bootzin, Mauber, Perlis, Salvio, & Wyatt, 2007), increased...
health care utilization (Bramoweth & Taylor, 2012; Wade, 2010), and patients consistently report problems with concentration and memory (Ancoli-Israel & Roth, 1999).

Symptoms of insomnia, mood disorders and pain often co-occur and the relationship is most likely bidirectional (Jansson-Frojmark & Lindblom, 2008; Mariman et al., 2012; Siverts et al., 2012; Sivertsen, Krokstad, Øverland & Myklebust, 2009; Smith & Haythornthwaite, 2004; Taylor, Lichstein, Durrence, Reidel, & Bush, 2005; Finan, Goodin & Smith, 2013). The frequent comorbidity relates to how the neurobiological (brain circuitry and neurotransmitters) and the psychosocial mechanisms involved in mood, pain and sleep disorders covary, aggravating existing symptoms, contributing to the development of multiple symptoms, including the cognitive impairments reported across these disorders (Chrousos, 2009; Finan & Smith, 2013; Harvey, 2002; Sapolsky, 2004; Waters and Bucks, 2011; Maletic & Raison, 2009).

There seems to be a tendency to trivialize sleep deficiencies, perceiving it as symptomatic of other disorders rather than recognizing it as a unique symptom dimension. There is no routine screening for the presence of sleep disorders and sleep deficiencies are probably underdiagnosed and untreated (Roth, 2001; Waters and Bucks, 2011). Furthermore, while the effect of depression, anxiety, pain and fatigue on cognitive functioning have been extensively studied (Cockshell & Mathias, 2014; Eysenck, Derakshan, Santos, & Calvo, 2007; Moriarty, McGuire, & Finn, 2011; Porter, Bourke, & Gallagher, 2007), and neuropsychologists are well aware of the need to include these symptom dimensions when conducting neuropsychological assessments, measurements of sleep are rarely included. This might be related to what has been a somewhat skewed focus within this field of research. A large body of research has documented how sleep facilitates memory by inhibiting interference and enhancing the stability of memory formation (Rasch, 2008; Rasch & Born, 2008; Stickgold, 2005; Born, Rasch & Gais, 2006). It is only in recent years that scientists have begun to examine how insufficient sleep affects neurocognitive functioning. In the context of comorbid symptoms there is a lack of knowledge when it comes to how symptoms of insomnia may contribute to the pattern of cognitive impairments found across these disorders.

Research examining the effect of insomnia on neuropsychological functioning has often used healthy control groups. The findings have been somewhat inconsistent (Drummond et al., 2013; Elvemo, Landrum, Borchgrevink, & Häberg, 2015; Fang, Huang, Yang, & Tsai, 2008; Fernandez-Mendoza et al., 2010; Fortier-Brochu & Morin, 2014; Fulda & Shulz, 2001; Goldman-Mellor et al., 2015; Orff, Drummond, Nowakowski, & Perlis, 2007; Shekleton et al., 2014; Shekleton, Rogers, & Rajaratnam, 2010; Vignola, Lamoureux, Bastien, & Morin, 2000), possibly due to methodological issues related to sample size, diagnostic criteria, the extent to which they have accounted for comorbidities and medications. A recent meta-analysis did, however, find evidence of significant impairments in working memory (WM) (Fortier-Brochu, Beaulieu-Bonneau, Ivers, & Morin, 2012). Working memory may be defined as a mental workspace that allows for the transient holding and manipulation of information while simultaneously inhibiting or preventing irrelevant information from entering the active state (Kane & Engle, 2000; Miyake, Friedman, Emerson, Witzki, & Howarter, 2000). Because WM and inhibitory control are so intertwined it makes sense to include measurements of both when examining this specific cognitive domain.

Examining how symptoms of insomnia affects neuropsychological functioning in the context of comorbid symptoms may provide key information aiding not only our understanding concerning the affect of sleep disturbances, but may also contribute to more targeted interventions.

The current study aims to examine the associations between different symptom levels of insomnia, subjective cognitive complaints, working memory, and inhibitory control.

1: It was hypothesized that the subjects with symptoms of clinical insomnia would report more memory problems than the subjects without clinical insomnia.

2: It was hypothesized that the subjects with clinical insomnia would show significant deficiencies on neuropsychological tests assessing visuospatial and verbal-numeric working memory, and inhibitory control.

Materials and Methods

The study was approved by the Regional Committee for Medical and Health Research Ethics and it adhered to the Helsinki Convention. All subjects were given a complete description of the study, and they gave written informed consent prior to their inclusion.

Study Design, Setting and Materials

This was a cross-sectional study, conducted during the period between September 2013 and April 2015. Subjects were consecutively recruited from an inpatient vocational rehabilitation center, connected to St. Olav’s University Hospital,
Trondheim. General practitioners referred patients who were on sick leave >8 weeks, to a 3.5 week intervention at a vocational rehabilitation center.

The exclusion criteria were diagnoses of severe mental disorders (acute psychosis, ongoing manic episode, or suicidal ideation), ongoing substance abuse, as well as any neurological traumas or illnesses.

**Participants**

A total of 80 subjects (67 females and 13 males) initially volunteered to take part in the study. Due to missing data on main outcome measures, four subjects were excluded from the study. The final cohort consisted of 76 subjects (64 females and 12 males). Mean age was 43.4 years ($SD = 10.5$).

The sample was broken down into two groups (clinical insomnia and comparison group) based on the cut-off score guidelines for the Insomnia Severity Index (ISI) (Bastien, Vallieres, & Morin, 2001). Subjects scoring ≥14 on ISI were included in the clinical insomnia group ($N = 35$). Subjects scoring ≤13 on ISI were included in the comparison group ($N = 41$). Further group characteristics are shown in Table 1. The subjects in the comparison group had been on sick leave for an average of 17.4 months ($SD = 14.7$), while the subjects in the insomnia group had been on sick leave for an average of 16.5 months ($SD = 17.4$). Five of the patients in the comparison group used sleep medication, while seven patients in the insomnia group used sleep medication. The types of medication used were Zopiclone, Imovane, and Circadin. According to a structured clinical interview for DSM-IV disorders (APA, 2013) six patients in the insomnia group were diagnosed with depressive, anxiety or an adjustment disorder, while seven patients in the comparison group were diagnosed with a depressive, anxiety or an adjustment disorder.

**Materials**

Upon referral, all subjects completed a web-based survey, which included socio-demographics, pain, insomnia, fatigue, depression, anxiety, and self-reported memory failures. The following questionnaires were included:

The ISI is a self-report questionnaire consisting of seven items designed to assess insomnia severity (Bastien et al., 2001). Each item has to be rated according to a 5-point scale, ranging from 0 (not at all) to 4 (very much). The items are: difficulty in falling asleep, night time awakenings, early morning awakenings, impairment of daytime functioning due to sleep disturbances, noticeability of problems, distress or worry caused by sleep disturbances, and dissatisfaction with sleep. The items are summed, giving a scale of 0–28. The ISI is a reliable, valid, and sensitive self-report questionnaire. It has been recommended as a screening device and an outcome measure in insomnia treatment and insomnia research. The psychometric properties of the instrument, in terms of detecting insomnia cases, are excellent. The internal consistency of the ISI was reported to be 0.74 (Bastien et al., 2001; Morin, Belleville, Belager, & Ivers, 2011).

**Memory complaints.** The Everyday Memory Questionnaire (EMQ) was originally developed by Sunderland, Harris, and Baddeley (1983), and later revised (EMQ-R) by Royle and Lincoln (2008). The EMQ-R consists of 13 items, where each item is rated on a 5-point scale ranging from A, scored as zero – “Once or less in the last month”, to E, scored as four – “Once or more in a day”. The items were summed, and given a scale within 0–52. Reliability tests on the EMQ-R have shown a strong internal reliability, with a Cronbach’s alpha score of 0.89 (Royle & Lincoln, 2008).

**Pain.** The SF8 health survey was used for measuring the intensity of pain (Ware, Kosinski, Dewey, & Gandek, 2001). The subjects were asked “How much bodily pain have you experienced during the last week?” (none, very mild, mild, moderate, severe, or very severe). The item has shown an intra-class correlation coefficient of 0.66 (95% CI 0.65–0.67) (Landmark, Romundstad, Dale, Borchgrevink, & Kaasa, 2012).

**Fatigue.** Fatigue was measured with The Chalder Fatigue Questionnaire, which consists of 11 questions, reflecting both physical and mental fatigue (Chalder et al., 1993). Each item has four response categories that are scored bimodally 0-0-1-1. Responses are summed up through a scale ranging between 0 and 11. The scale has been validated for a Norwegian population (Loge, Ekeberg, & Kaasa, 1998).

**Depression and anxiety.** The Hospital Anxiety and Depression Scale (HADS) was used to assess the symptoms of anxiety and depression (Zigmond & Snaith, 1983). The fourteen-item scale is divided into two sub-scales; one sub-scale scores depression and the other scores anxiety. Each item ranges from 0 to 3, and the items are summed, giving a score ranging from 0 to 21 in
each sub-scale. Higher scores indicate increased symptom severity. The psychometric properties of the scale have been validated in various populations, and also in the Norwegian general population, with Cronbach alpha of 0.80 and 0.76 for HADS anxiety and HADS depression, respectively (Bjelland, Dahl, & Neckelmann, 2001; Olsson, Mykletun, & Dahl, 2005).

Neuropsychological assessment. Neuropsychological testing was done at the outpatient clinic prior to the vocational rehabilitation program. All patients were tested between 09:30 and 17:00.

General cognitive functioning. General cognitive functioning was estimated from the scores on a subtest from the WAIS-III: picture completion (Wechsler, 1997). The test consists of 25 cards, where each card displays a picture where a part is missing. The subject is told to identify the missing part, within a time limit of 20 s. It has been found to give a reliable and valid indication of general cognitive functioning (Wechsler, 1997).

Working memory tests. The Paced Auditory Serial Addition Test (PASAT) is designed to assess auditory information processing, and is commonly used as a measure of sustained/divided attention and working memory (Gronwall & Wrightsman, 1974). Subjects listen to a series of single digit numbers presented in 2.0 s intervals, like 3-6-2-9, and as they listen, they are simultaneously required to add the two most recent digits and give the sum before the presentation of the next digit, 9-8-11, and so on. The subjects are given practice trials prior to the test in order to ensure they have understood the task requirements correctly. The chosen outcome measure was based on the number of correct responses. The PASAT has a high degree of internal consistency, around 0.76–0.95, and Cronbach alpha of 0.90 (Tombaugh, 2006).

Spatial Working Memory (SWM) from the CANTAB test battery measures the subject’s ability to retain, manipulate, and update spatial information in working memory (Owen, Downes, Sahakian, Polkey, & Robbins, 1990; Sahakian & Owen, 1992). The task also provides an assessment of heuristic strategy. The screen displays a number of colored boxes. The subjects are instructed to find a hidden token in each of the boxes, and use them to fill up an empty column on the side of the screen. Returning to a box where a token has already been found represents an error. The test starts with three boxes, then four, six, and finally eight boxes. The pattern and color of the boxes are changed in each trial. The outcomes of interest were strategy and total errors. An efficient strategy for managing the task is to follow a predetermined search sequence; beginning with a specific box and when a blue token has been found returning to that box to begin a new search. The strategy estimate is obtained by counting the number of times the subject start a new search with a different box (only for 6 and 8 box problems) A high score indicates a poor use of the strategy a low score indicates an effective use of the strategy, minimum score is 8, maximum score is 56. (Owen et al., 1990). Outcomes reflect the ability to adopt a heuristic and consistent strategy to complete the task, and the number of errors made during the test.

Inhibitory control. The Stop Signal Task (SST) from the CANTAB test battery provides a measure of response inhibition, which is the Stop Signal Reaction Time (Logan & Cowan, 1984; Logan, Cowan, & Davis, 1984). A white ring, containing a left or right pointing arrow, is shown on the screen. First, the subjects are instructed to press on the corresponding (left/right) button on a press pad, as soon as they see the direction of the arrow. They are given a trial to practice the instruction. In the second condition of the task, the subjects are told to press on the corresponding button like before, but they should avoid pressing the button whenever they hear a beep (the Stop Signal). By varying the timing of the Stop Signal Delay (SSD) throughout the test, the program regulates the probability of stopping, so that stopping occurs approximately 50% of the time for each subject. The Stop Signal Reaction Time is calculated by subtracting the SSD from the median GO Reaction Time (the reaction time on trials with no Stop Signal). The Stop Signal Reaction Time (SSRT) (last half) was chosen as the main outcome measure, and it reflects the ability to inhibit a dominant response.

Statistical Analyses

Data was analyzed using the Statistical Package for the Social Sciences (SPSS version 20.0; 185 IBM Corporation, Armonk, NY). Descriptive statistics are given as means and standard deviations. Comparisons between the clinical insomnia group versus the comparison group were initially done with the Student t-tests and included the following variables: age, general cognitive functioning, fatigue, depression, anxiety, and sleep variables. Regression analysis with the EMQ-R as the dependent variable was conducted to test the hypothesis that patients with clinical insomnia would report more memory problems than patients in the comparison group (hypothesis 1). Group (insomnia vs. comparison group) was added as a fixed factor and the model was adjusted for age and gender. In order to examine if patients with symptoms of clinical insomnia would show deficiencies in working memory and inhibitory control compared to the comparison group (hypothesis 2), we performed
similar regression models with PASAT (correct), SWM (strategy and total errors), and SST (SSRT-last half) as dependent variables. We did separate tests for each outcome variable, adjusting for age and gender. Natural log transformations were also performed for the SWM total errors and SWM strategy analyses in order to appropriately settle problems of increasing residuals with increasing predictive values in the original approach. This did not change the results and they are therefore presented as the non-transformed results. The significance level was set at $p < .05$.

**Results**

Descriptive data of age, general cognitive ability and self-reported levels of pain, fatigue, sleep variables, depression and anxiety are presented in Table 1, along with $t$-tests for group differences between these variables. The insomnia group consisted of 35 subjects (25 females and 6 males), while the comparison group consisted of 41 subjects (35 females and 6 males). Groups were similar in age, general cognitive ability, self-reported levels of pain, fatigue, depression, anxiety and average hours of sleep. The only variables that clearly differentiated the two groups were their symptom severity of insomnia ($p = .001$), and their self-reported level of sleep quality ($p = .002$). The comparison group scored within what is considered as sub-threshold insomnia (8–14), while the insomnia group showed symptoms of what is considered as clinical insomnia, with moderate severity (15–21) (Bastien et al., 2001; Morin et al., 2011).

Descriptive data (mean and SD) of the outcome measures are presented in Table 2. Both groups report quite substantial problems with regards to memory functioning. Neuropsychological tests of working memory show a difference between the two groups, in terms of poorer performance among the subjects in the clinical insomnia group.

### Table 1. Descriptive data along with $t$-tests for differences between these variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Comparison group</th>
<th>Insomnia group</th>
<th>$t$</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: number of females (%)</td>
<td>35 (85)</td>
<td>29 (93)</td>
<td>-</td>
<td>-0.254</td>
</tr>
<tr>
<td>Age (years)</td>
<td>41 43.1 10.8</td>
<td>35 43.7 10.3</td>
<td>-</td>
<td>-0.254</td>
</tr>
<tr>
<td>WAIS: picture completion</td>
<td>41 13.9 3.0</td>
<td>35 14.2 2.2</td>
<td>-</td>
<td>-0.490</td>
</tr>
<tr>
<td>Pain intensity (Score 0–6)</td>
<td>40 3.5 1.3</td>
<td>35 3.9 1.0</td>
<td>-</td>
<td>-1.267</td>
</tr>
<tr>
<td>CFQ fatigue (Score 0–11)</td>
<td>41 2.3 2.7</td>
<td>35 3.2 2.9</td>
<td>-</td>
<td>-1.321</td>
</tr>
<tr>
<td>ISI insomnia (Score 0–28)</td>
<td>41 8.8 3.5</td>
<td>35 17.7 3.2</td>
<td>-</td>
<td>-11.477</td>
</tr>
<tr>
<td>Hours of sleep</td>
<td>38 7.7 1.8</td>
<td>33 7.3 2.4</td>
<td>-</td>
<td>0.877</td>
</tr>
<tr>
<td>Sleep-quality (score 1–5)</td>
<td>38 2.9 0.8</td>
<td>33 3.6 0.8</td>
<td>-</td>
<td>-2.396</td>
</tr>
<tr>
<td>HADS Anxiety (Score 0–16)</td>
<td>40 7.8 3.3</td>
<td>35 9.2 3.5</td>
<td>-</td>
<td>-1.760</td>
</tr>
<tr>
<td>HADS Depression (Score 0–16)</td>
<td>40 6.9 3.5</td>
<td>35 7.2 3.3</td>
<td>-</td>
<td>-0.346</td>
</tr>
</tbody>
</table>

*Note: Pain intensity = SF-8 health survey item no. 4; CFQ = Chalder Fatigue Questionnaire; ISI = Insomnia Severity Index; HADS Anxiety and HADS Depression = The Hospital Anxiety and Depression Scale. Sleep quality (1 = very good, 2 = good, 3 = moderate, 4 = poor, 5 = very poor).*

Descriptive data (mean and SD) of the outcome measures are presented in Table 2. Both groups report quite substantial problems with regards to memory functioning. Neuropsychological tests of working memory show a difference between the two groups, in terms of poorer performance among the subjects in the clinical insomnia group.

### Table 2. Descriptive data of outcome measures

<table>
<thead>
<tr>
<th>Variables</th>
<th>Comparison group</th>
<th>Clinical insomnia</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMQ-R (Score 0–52)</td>
<td>41 20.5 12.3</td>
<td>35 21.8 9.6</td>
</tr>
<tr>
<td>PASAT correct (Score 0–60)</td>
<td>40 36.0 10.1</td>
<td>35 29.5 11.2</td>
</tr>
<tr>
<td>SWM strategy (lower score is better)</td>
<td>40 29.4 5.5</td>
<td>35 32.3 5.8</td>
</tr>
<tr>
<td>SWM (total errors)</td>
<td>39 19.7 14.3</td>
<td>35 28.4 17.8</td>
</tr>
<tr>
<td>Inhibition SSRT-last half (measured in milliseconds)</td>
<td>38 182.9 39.7</td>
<td>31 179.0 36.9</td>
</tr>
</tbody>
</table>

*Note: EMQ-R = Everyday Memory Questionnaire-Revised; PASAT = Paced Auditory Serial Addition Test; SWM = Spatial Working Memory; SSRT = Stop Signal Reaction Time.*

As presented in Table 3A, the linear regression showed no significant difference between the two groups with regards to self-reported memory problems. Women reported significantly more memory problems than men, and subjects reported less memory problems with increasing age. Analysis (Table 3B) showed a significant difference between the two groups on the PASAT. Subjects in the insomnia group had significantly fewer correct answers than the subjects in the comparison group. There was also a significant effect of gender, but not in effect of terms of age.
Subjects in the insomnia group used a poorer strategy as reflected by a lack of a systematic and efficient search strategy on the SWM test than the subjects in the comparison group (Tables 3C and 3D). There was also a significant effect of age, as demonstrated by poorer performance with increasing age, but no gender difference.

Table 3A. Linear regression with the average score from the Everyday Memory Questionnaire-Revised as the outcome variable (lower score is better)

<table>
<thead>
<tr>
<th>Variables</th>
<th>β-estimate</th>
<th>95% CI</th>
<th>F</th>
<th>Sign (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>−0.254</td>
<td>−0.486/−0.022</td>
<td>4.775</td>
<td>.032</td>
</tr>
<tr>
<td>Women versus men</td>
<td>7.617</td>
<td>0.950/14.283</td>
<td>5.187</td>
<td>.026</td>
</tr>
<tr>
<td>Clinical insomnia versus comparison group</td>
<td>1.617</td>
<td>6.496/3.263</td>
<td>0.436</td>
<td>.511</td>
</tr>
</tbody>
</table>

Note: Adjusted R squared 0.089.

Table 3B. Linear regression with the Paced Auditory Serial Addition Test

<table>
<thead>
<tr>
<th>Variables</th>
<th>β-estimate</th>
<th>95% CI</th>
<th>F</th>
<th>Sign (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.127</td>
<td>−0.099/0.353</td>
<td>1.260</td>
<td>.265</td>
</tr>
<tr>
<td>Women versus men</td>
<td>−7.789</td>
<td>−14.278/−1.300</td>
<td>5.728</td>
<td>.019</td>
</tr>
<tr>
<td>Clinical insomnia versus comparison group</td>
<td>−6.772</td>
<td>−2.002/−11.541</td>
<td>8.013</td>
<td>.006</td>
</tr>
</tbody>
</table>

Note: Adjusted R squared 0.134.

Subjects in the insomnia group used a poorer strategy as reflected by a lack of a systematic and efficient search strategy on the SWM test than the subjects in the comparison group (Tables 3C and 3D). There was also a significant effect of age, as demonstrated by poorer performance with increasing age, but no gender difference.

Table 3C. Linear regression with the average score from the Spatial Working Memory Test – strategy as the outcome variable (lower score is better)

<table>
<thead>
<tr>
<th>Variables</th>
<th>β-estimate</th>
<th>95% CI</th>
<th>F</th>
<th>Sign (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.181</td>
<td>0.063/0.299</td>
<td>9.420</td>
<td>.003</td>
</tr>
<tr>
<td>Women versus men</td>
<td>2.359</td>
<td>−1.125/5.844</td>
<td>1.821</td>
<td>.181</td>
</tr>
<tr>
<td>Clinical insomnia versus comparison group</td>
<td>2.840</td>
<td>5.313/0.367</td>
<td>5.242</td>
<td>.025</td>
</tr>
</tbody>
</table>

Note: Adjusted R squared 0.159.

Table 3D. Linear regression with the average score from the Spatial Working Memory Test – total errors as the outcome variable

<table>
<thead>
<tr>
<th>Variables</th>
<th>β-estimate</th>
<th>95% CI</th>
<th>F</th>
<th>Sign (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.524</td>
<td>0.180/0.867</td>
<td>9.234</td>
<td>.003</td>
</tr>
<tr>
<td>Women versus men</td>
<td>3.273</td>
<td>−6.727/13.273</td>
<td>0.426</td>
<td>.516</td>
</tr>
<tr>
<td>Clinical insomnia versus comparison group</td>
<td>8.597</td>
<td>15.719/1.475</td>
<td>5.796</td>
<td>.019</td>
</tr>
</tbody>
</table>

Note: Adjusted R squared 0.149.

Finally, as presented in Table 3E, there was no significant difference between the two groups, in terms of inhibitory control (SSRT). There was also no significant effect of gender or age.

Table 3E. Linear regression with Stop Signal Task – Stop Signal Reaction Time as the outcome variable (measured in milliseconds)

<table>
<thead>
<tr>
<th>Variables</th>
<th>β-estimate</th>
<th>95% CI</th>
<th>F</th>
<th>Sign (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>−0.180</td>
<td>−1.072/0.712</td>
<td>0.162</td>
<td>.689</td>
</tr>
<tr>
<td>Women versus men</td>
<td>7.180</td>
<td>−17.5/31.9</td>
<td>0.335</td>
<td>.565</td>
</tr>
<tr>
<td>Clinical insomnia versus comparison group</td>
<td>−3.483</td>
<td>−15.401/22.367</td>
<td>.136</td>
<td>.714</td>
</tr>
</tbody>
</table>

Note: Adjusted R squared 0.035.

**Discussion**

The aim of the current study was to examine if elevated symptoms of insomnia affects subjective memory complaints and neuropsychological functioning in patients currently on sick leave due to symptoms pain, fatigue and mood disorders. The sample was broken into two groups, based on the guidelines from the ISI. In contrast to our hypothesis we found no difference between the two groups with regards to subjective memory problems. In accordance with our hypothesis results showed
that patients with symptoms of clinical insomnia performed significantly worse on the neuropsychological tests assessing visuospatial and verbal-numeric working memory. There was no difference between the groups in inhibitory control.

The present study showed that it was the increased symptom level of insomnia and not the symptoms of depression, anxiety, pain and fatigue that affected working memory functioning. Although the synergistic effect of all symptom dimensions may have had some effect, it was the relative contribution of insomnia that was the determining factor in terms of the WM-deficiencies.

More women than men reported experiencing memory problems. The reason why women report more memory problems than men is essentially unknown. However, although somewhat speculative, it may be that women are more sensitive to changes in memory than men. Conversely, since there were no between-group differences in self-perceived memory functioning, our results indicate that assessments of cognitive functioning should be based on objective neuropsychological functioning.

The pattern of WM impairments indicates domain general working memory impairment. The findings are in line with other studies, which have also found mild to moderate working memory impairments among subjects with insomnia (Fortier-Brochu et al., 2012; Fortier-Brochu & Morin, 2014; Shekleton et al., 2014; Shekleton et al., 2010). Previous studies have shown that insomnia severity correlates with cognitive impairments (Szelenberger & Niemcewicz, 2000), and that cognitive impairments are not related to excessive sleepiness, per se (Bonnet & Arand, 1995; Shekleton et al., 2014).

Several studies have reported negative findings with regards to WM impairments (Goldman-Mellor et al., 2015; Orff et al., 2007). The somewhat inconsistent results within this field may at least partially stem from the fact that different tests may be more or less sensitive in terms of their ability to detect neuropsychological dysfunction (Chan, Shum, Touloupoulou, & Chen, 2008). Hence, establishing a set of neuropsychological tests, that are both sensitive enough and cognitively demanding enough to reliably identify WM deficiencies across studies is a process that takes time.

The working memory tests used in this study (SWM and PASAT) are known to be cognitively demanding and highly sensitive tests (Owen et al., 1990; Sahakian & Owen, 1992; Tombaugh, 2006). Their design allow for testing at different levels of difficulty either by increasing the number of items (SWM), or by reducing the time interval (PASAT). The tests have good psychometric properties in terms of internal consistency and test–retest reliability (Owen et al., 1990; Sahakian & Owen, 1992; Tombaugh, 2006).

Studies in this field of research are also characterized by small sample sizes (N ≤ 25) (Drummond et al., 2013; Elvemo et al., 2015; for a meta-analysis see Fortier-Brochu et al., 2012). This means that only very large effects would be statistical significant (Button et al., 2013). The studies that find impairments in working memory report subtle, mild, or moderate effects (Altena, Van Der Verf, Strijers, & Van Someren, 2008; Fortier-Brochu & Morin, 2014; Shekleton et al., 2010). Studies with small sample sizes may lack the statistical power to detect such mild effects and may have contributed to the negative findings.

Patients with symptoms of insomnia may not form a homogenous group. There might be subgroups that are more vulnerable, in terms of exhibiting cognitive impairments than others. Studies have found that objective short sleep time and treatment seeking is associated with cognitive deficiencies in patients with insomnia (Fernandez-Mendoza et al., 2010; Goldman-Mellor et al., 2015; Wilckens, Woo, Kirk, Erickson, & Wheeler, 2014).

Other authors have suggested that the lack of consistent and systematic data-collection may also have contributed to the contradicting results (Fortier-Brochu et al., 2012; Shekleton et al., 2010). Studies differ in which diagnostic criteria they use, this might cause heterogeneity in the samples making it difficult to compare results across studies (Shekleton et al., 2010). Factors, such as duration and/or severity of insomnia (Szelenberger & Niemcewicz, 2000), comorbidities (Christopher & MacDonald, 2005; Cockshell & Mathias, 2010; Hart, Wade, & Martelli, 2003; Moran, 2016; Moriarty et al., 2011) and age (Cricco, Simonsick, & Foley, 2001) and medication (Stein and Strickland, 1998) may affect cognitive functioning. There is extensive cross-study variability when it comes to whether or not such data have been collected and/or accounted for.

A recent study, using fMRI, found that although there were no differences in WM performance between the groups, insomniacs showed abnormalities in neural function, both in terms of reduced activation of task-related regions and the reduced ability to adjust activation with increasing task difficulty (Drummond et al., 2013). A similar pattern has also been found among chronic pain patients, where sleep disturbances had a stronger effect than both pain and depression on the modulation of neural activity (Elvemo et al., 2015). Such findings might suggest that cognitive deficiencies in insomnia are related to alterations in neural activity, rather than just being an epiphenomena of excessive sleepiness. If this is indeed the case, it has important implications for the understanding of how symptoms of insomnia affect cognitive functioning in comorbid symptom disorders.

The present study found no significant difference between groups in inhibitory control. In contrast a study by Schmidt, Gay and Ghisletta (2010) found that dysfunctional thought control characterized by impulsivity, urgency, lack of perseverance, aggressive suppression, and worry was positively correlated with insomnia severity. A previous study found that urgency is linked to deficiencies in the ability to suppress dominant responses, whereas lack of perseverance is linked to deficiencies in the ability to inhibit irrelevant thoughts and memories (Gay, Rochat, Billieux, d’Acremont, & Van der Linden, 2008). While the aforementioned studies used self-report questionnaires to assess thought control and inhibition the present
study used a neuropsychological test to assess actual performance. Self-report measures and objective measures of cognitive functioning sometimes show conflicting results (Grace, Nielson, Hopkins, & Berg, 1999; Goldman-Mellor et al., 2015), indicating that they may tap into different facets of information (Jacobsen, Aasvik, Borchgrevink, Landrø, & Stiles, 2016; Williams, Clauw, & Glass, 2011).

Even though the subjects (overall) scored quite high on the symptom measurements of insomnia, none of them were diagnosed with insomnia or referred to the vocational rehabilitation due to such symptoms. This might suggest a lack of awareness when it comes to insomnia as an important clinical condition in terms of health and sick leave. The present results emphasize the need to include assessments of sleep when conducting neuropsychological examinations of patients with symptoms of depression, anxiety, fatigue and pain as it may be a major contributor to the pattern of cognitive impairments found across these disorders. By failing to include such screenings one might ascribe impairments to the wrong symptom dimensions and thereby ultimately reduce the validity of neuropsychological findings (Waters & Bucks, 2011).

Limitations

Because we examined a selected group of subjects, our results may not generalize to population-based samples. Another limitation is the lack of objective sleep measures. Also, we did not gather information about the duration of insomnia symptoms, which may affect cognitive functioning.

Conclusion

Patients with symptoms of clinical insomnia exhibited significant deficiencies in working memory; deficiencies were related to both visuospatial and verbal-numeric processing. Our findings warrant attention, sleep difficulties need to be recognized as a major contributor to neuropsychological deficiencies.

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Conflict of interest

None declared.

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