Differential effects of online insomnia treatment on executive functions in adolescents

de Bruin, E.J.; Dewald-Kaufmann, J.F.; Oort, F.J.; Bögels, S.M.; Meijer, A.M.

Published in:
Sleep Medicine

DOI:
10.1016/j.sleep.2014.12.009

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Differential effects of online insomnia treatment on executive functions in adolescents

Eduard J. de Bruin*, Julia F. Dewald-Kaufmann, Frans J. Oort, Susan M. Bögels, Anne Marie Meijer

Research Institute of Child Development and Education, University of Amsterdam, P.O. Box 94208, Amsterdam GE 1090, Netherlands

ARTICLE INFO

Article history:
Received 3 September 2014
Received in revised form 12 December 2014
Accepted 13 December 2014
Available online 21 January 2015

Objective: To examine the effects of online Cognitive Behavior Therapy for Insomnia (CBTI) on adolescents’ sleep and cognitive functioning.

Methods: 32 adolescents (13–19 years, M = 15.9, SD = 1.6) with DSM-5 insomnia disorder, were randomly assigned to a treatment group (n = 18) or a waiting list (n = 14). Treatment consisted of six guided self-help online CBTI sessions. Both groups were assessed at baseline and post-treatment. Sleep was measured with actigraphy, sleep logs, and questionnaires. Cognitive functioning was assessed with a battery of standard cognitive tests.

Results: After CBTI the treatment group showed significant improvements compared to the waiting list group in sleep efficiency from actigraphy and sleep logs. This finding was confirmed by improvements in other sleep variables from sleep logs, and in symptoms of chronic sleep reduction and insomnia. Most participants from the treatment group improved to sub clinical levels of insomnia. Cognitive functioning of the treatment group showed more improvement compared to the waiting list in visuospatial processing, selective attention and phonological working memory, and a trend of improvement in response inhibition and set shifting, letter fluency and sustained attention, but not in declarative memory, visuospatial working memory, category fluency, and general cognitive speed. Changes in sleep appeared to be related to changes in cognitive functioning.

Conclusions: These results indicate that CBTI can have positive effects on cognitive functions in adolescents, with notable improvements in visuospatial processing and phonological working memory but not in visuospatial working memory.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

Healthy sleep is important for many aspects of adolescents’ daily life, including mood, social behavior [1], school performance [2], cognitive performance [3] and adolescent development in general [4]. Insomnia (i.e., problems with initiating or maintaining sleep, or not feeling rested after waking up) is highly prevalent among adolescents with estimates ranging from 4–13% [5–8]. Adolescent insomnia can have serious consequences for physical and mental health, as well as social and cognitive functioning [1,9–11]. Considering the high prevalence and serious consequences of adolescent insomnia, it represents a severe problem in this age group.

A wide range of cognitive functions may be influenced by insufficient and/or poor sleep. Experimental studies with total or partial sleep loss in adults, modeling inadequate sleep as can be experienced due to insomnia, show that many areas of cognitive functioning can be affected, such as psychomotor performance, cognitive speed, working memory, attention, reaction time, vigilance, and higher executive functions (eg, [12–15]). Studies with younger children also show a broad range of cognitive domains that can be affected by inadequate or insufficient sleep (eg, [16–18]).

Studies on relations between sleep and cognitive functioning with adolescents, which are summarized below, show inconsistent results compared to results from studies with adults and children. In a study with a later school start time for a group of adolescents on Monday morning, and thus possibly extended sleep time for Sunday night, Vedaa et al. [19] found some indications of improved simple reaction
time. Dewald-Kaufmann et al. [20], however, found no beneficial effects of extended sleep on simple reaction time in adolescents with chronic sleep reduction. Two studies showed improvements in divided attention tasks after sleep extension in adolescents with chronic sleep reduction, daytime sleepiness or insufficient sleep [20,21]. Carskadon et al. [22] reported impaired performance on sustained attention tasks in adolescents after sleep deprivation, due to actual sleep according to EEG during the task, whereas Fallone et al. [23] and Randazzo et al. [24] found no deficits or relation between that cognitive domain and sleep. Gradisar et al. [25] demonstrated a worse working memory performance in adolescents reporting insufficient sleep. In accordance with this result Cousins Hasler [21] found improvements in working memory when comparing adolescents who successfully extended their sleep with non extenders. Carskadon et al. [22] found decrements in declarative memory after sleep deprivation and data from Kopasz et al. [16] indicated that sleep facilitates working memory and memory consolidation, but the study by Randazzo et al. [24] did not support such a relation, and Voderholzer et al. [26] did not find significant effects of sleep restriction on declarative memory consolidation. Andersons et al. [27] found worse executive functioning in adolescents with high levels of sleepiness or short sleep duration, and Randazzo et al. [24] reported that acute sleep restriction affects performance of executive functioning tasks containing abstract thinking and verbal creativity. However, Fallone et al. [23] did not find any deficits in tasks of cognitive inhibition after acute sleep restriction. In the general intelligence domain Carskadon et al. [22] showed relations between sleep and mathematical problem solving. Randazzo et al. [24], however, did not find a relation between sleep restriction and figural creativity.

In summary, these studies, all with adolescent samples, indicate possible relations of sleep, sleep restriction or daytime sleepiness with reaction times, attention processes, memory and working memory, executive functioning and general intelligence, although not all studies found corresponding results. Different study designs, different sleep parameters (eg, sleep deprivation versus extension, sleep quality, sleep fragmentation, excessive sleepiness etc.), subjective or objective sleep measures, use of different cognitive tests, and different inclusion criteria for participants (eg, sleep deprived or no sleep problem) may be responsible for the inconsistent results.

Despite the high prevalence of insomnia in adolescents and the relation of sleep with cognitive functions, to our knowledge only one study investigated the effects of a sleep intervention on adolescents’ cognitive functioning [20]. In that study Dewald-Kaufmann et al. [20] extended the sleep period (sleep extension) of 28 adolescents without sleep disorders but with symptoms of chronic sleep reduction, by gradually advancing the evening bedtimes 5 minutes each night over the course of two weeks, maintaining their usual rise times in the morning. Their sleep and cognitive functioning were compared to a control group of 27 adolescents with similar symptoms of chronic sleep reduction, who were instructed to sleep as usual. They found that after the two weeks of sleep extension the experimental group had earlier bedtimes and sleep onsets, and slept longer. Furthermore, they found improvements in divided attention and visuospatial processes. This indicates that improving sleep, even in a non-clinical sample, can have direct positive effects on cognitive functioning. The finding that cognitive functions can be improved by a sleep intervention is of special interest in the treatment of adolescents with symptoms of ADHD. Research has shown that ADHD is related to both disrupted sleep patterns and dysfunctions in executive processes, and primary sleep disorders may mimic ADHD-like symptoms or may exacerbate underlying ADHD [28,29]. Furthermore, studies show that excessive sleepiness has a negative impact on school functioning [11,30]. These findings underline the importance of developing and researching interventions which are aimed at improving sleep of adolescents and its effects on cognitive functioning.

A reason for the scarcity of studies on the effects of sleep improvement on cognitive functioning might be the lack of an evidence-based therapy for adolescents with chronic sleep problems like insomnia. Although Cognitive Behavior Therapy for insomnia (CBTI) has been shown to be effective in adults [31,32], only few studies have been conducted with adolescents. These studies, however, indicate that CBTI is also an effective treatment for adolescents suffering from insomnia [33,34]. Furthermore, similar effectiveness for internet delivered versus group CBTI has been shown in previous research [34].

Consequently, in the present study we aimed to investigate the effects of internet delivered CBTI treatment of adolescents with insomnia on their sleep and cognitive functioning. Based on the inconsistent findings from the literature as previously described we explored effects of improved sleep on many cognitive functions. We therefore administered a wide range of cognitive tests covering a broad range of cognitive domains and measuring simple reaction time, working memory, declarative memory, attention, cognitive inhibition, vigilance, cognitive speed, and more complex executive functions. To have a clear impression of sleep improvement we included both subjective and objective measures to assess sleep behavior. Furthermore, because individual sleep need may play a role with reference to sleep duration and daytime functioning, we also examined possible consequences of insomnia by measuring chronic sleep reduction [35]. Because of the importance of adequate sleep on school nights [11,30] we explored which aspects of improvements in sleep on school nights were related to improvements in cognitive functioning in the treated group.

2. Methods

2.1. Participants

Participants were recruited through electronic newsletters on websites for youth healthcare professionals and newspaper articles in the Netherlands. Inclusion criteria were (1) an age within the range of 12–19 years, (2) insomnia complaints according to the Diagnostic and Statistical Manual of Mental Disorders—Fifth Edition (DSM-5) [36] for at least three months and at least three days a week, based on self-report, the intake interview, and scores above cutoff on the insomnia scale of the Holland Sleep Disorder Questionnaire (HSDQ) [37]. Exclusion criteria were (1) suicidal intentions and drug abuse, investigated through clinical scores and item screening on the Youth Self Report (YSR) [38,39] and from the intake interview, (2) indication of other sleep disorders than insomnia indicated by scores above cutoff on the HSDQ and through information from the intake interview, (3) a diagnosis of other psychological disorders (eg, depression, ADHD), or presently being treated for psychological or sleep problems, (4) use of drugs or medication that interfere with sleep, or (5) a lack of chronicity or severity of the symptoms according to the DSM-5 criteria for insomnia disorder [36] as indicated in the one hour face to face diagnostic intake interview.

We included 18 participants in both groups. In the waiting list condition four participants dropped out during the baseline period of the study due to lack of time or motivation to fill out sleep logs or come to test sessions for cognitive functioning, and were excluded from the analyses. Consequently, 18 participants (4 boys, age = 15.4 years, SD = 1.4) remained in the treatment group and 14 participants (2 boys, age 16.6 years, SD = 1.7) in the waiting list group.

2.2. Procedure

This study is part of a larger study into effectiveness of CBTI for adolescents, which was approved by the medical ethical committee.
of the Academic Medical Center in Amsterdam and registered at the International Standard Randomised Controlled Trial Number Register with number ISRCTN33922163.

After registration through a website, participants and their parents received an information letter about the conditions of the study and the treatment, including an informed consent form. Personal login details were provided after the consent forms from participants and parents were returned, which enabled them to online complete the YSR, the HSDQ, the Chronic Sleep Reduction Questionnaire (CSRQ) [30,35], and questions on socio-economic status and school level. If participants met the inclusion criteria they were invited for an intake interview in which sleep complaints, bedtimes, sleep history, sleep circumstances, history of the complaints and medical history, family history of sleep, and secondary subjective complaints were explored in more detail. During the intake interview participants were also asked if they had appropriate internet access (as needed for online CBTI) and a mobile phone (for eventually receiving sms-reminders to fill out sleep logs).

Participants were matched in pairs of similar age and gender and from each pair one participant was randomly assigned to a treatment group (CBTIfor six weeks), and the other to a waiting list group (no treatment for six weeks). After the study was concluded, the participant was already asleep, we set the bedtime to the first peak before the drop off. If the reported time of getting up in the sleep log indicated a time at which it was obvious that the individual was still asleep, we corrected the data by changing the time of getting up to the first peak after the indicated time.

2.3. Measures

Both groups were measured two weeks before the treatment started (baseline) and directly after the treatment (post-treatment) (see Figure 1). All responses for sleep logs and questionnaires were collected online. Actigraphy was used at home, and cognitive testing occurred at the laboratory of the University of Amsterdam, the Netherlands.

2.3.1. Sleep

Sleep was measured objectively using wrist-actigraphy (Actiwatch type AW4; Cambridge Neurotechnology Ltd., Cambridge, UK) and subjectively by sleep logs for seven consecutive nights at baseline and post-treatment, and questionnaires at baseline and post-treatment.

2.3.2. Actigraphy

Activity during the night was recorded with one-minute epochs and analyzed with Actiwatch Sleep Analysis 7 software measuring sleep onset latency (SOL), wake after sleep onset (WASO), total sleep time (TST), time in bed (TIB), sleep efficiency (SE) and the fragmentation index (FI). TST equals TIB minus SOL, WASO and time between waking up and getting up. The fragmentation index is considered to be an indication of restlessness during the night and is calculated by summing the percentage of movement phases and the percentage of immobile phases. As recommended by the manufacturer, we used the medium sensitivity algorithm to score the actigraphy data which has best sensitivity (0.96), specificity (0.42), and accuracy (0.79) for insomnia based on estimates obtained from polysomnography [40].

Participants were instructed to wear the actiwatch on their non-dominant wrist when they went to bed and remove it in the morning after getting up. We examined all actigraphy data visually and corrected them where necessary as is recommended in other studies [41,42]. We applied the following general rule for data from the sleep logs or event-markers from the actiwatch that did not correspond with the visual inspection: If the sleep log indicated a bedtime at which it was obvious from the actigraphy data that the participant was already asleep, we set the bedtime to the first peak before the drop off. If the reported time of getting up in the sleep log indicated a time at which it was obvious that the individual was still asleep, we corrected the data by changing the time of getting up to the first peak after the indicated time.

2.3.3. Sleep logs

The sleep log consisted of eight questions registering bedtime, time of lights out, SOL, WASO, wake up time, and get up time, and one question on subjective sleep quality (SSQ) which was scored on a five-point Likert scale with higher scores indicating better sleep quality. From the bedtimes of the sleep logs we calculated TIB (time between time of lights out and get up time), TST (TIB minus SOL, WASO and time between waking up and getting up) and SE (percentage TST of TIB). Participants were instructed to fill out the sleep log every day within one hour after getting up. They received a reminder text message on their mobile phone if the sleep log was not completed before 4:00 pm. Sleep logs could be filled out at the latest up to midnight the following day as retrospective data with a larger time span were considered unreliable.

2.3.4. Questionnaires

The CSRQ consists of 20 items with three ordinal response categories (1 to 3) that measure symptoms of chronic sleep reduction in the previous two weeks. It has four subscales: ‘shortage of sleep’ (six items), ‘irritation’ (five items), ‘loss of energy’ (five items), and ‘sleepiness’ (four items). Higher scores indicate more chronic sleep reduction. Cronbach’s α in a pre-adolescent population was 0.84 [30], in a Dutch adolescent population 0.85, and in an Australian adolescent population 0.87 [34]. The questionnaire was also validated against actigraphy data [35].

The HSDQ [37] contains 40 items on a five-point rating scale, and screens for the six main categories of sleep disorders as described in the International Classification of Sleep Disorders—Second Edition [43]. It consists of the subscales insomnia, sleep-related breathing disorders, hypersomnia, circadian rhythm sleep disorders, parasomnia, and restless legs syndrome or periodic limb movement disorder. Cronbach’s alpha in a Dutch sample of 1,269 patients and 412 participants without sleep complaints was 0.90 and ranged from 0.73 to 0.81 for the six subscales. The overall accuracy was 88%, and a score above the cutoff of 3.68 on the Insomnia scale of the HSDQ (HSDQI) is an indication of insomnia.

<table>
<thead>
<tr>
<th>Intake</th>
<th>Day 1 - 7</th>
<th>Day 8 - 49</th>
<th>Day 50 - 57</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruitment, intake questionnaires, interview, selection, consent, and randomization of participants</td>
<td>Treatment condition</td>
<td>Baseline Tests</td>
<td>Treatment</td>
</tr>
<tr>
<td>Waiting list condition</td>
<td>Waiting list condition</td>
<td>No treatment</td>
<td>Post-treatment Tests</td>
</tr>
</tbody>
</table>

Fig. 1. Design of the study.
2.3.5. Cognitive functioning

To measure cognitive functioning we administered the five subtests Baseline Speed, Feature Identification, Memory Search Letters, Response Organization Arrows, and Spatial Temporal Span from the Amsterdam Neuropsychological Tasks (ANT) [44]. Furthermore we administered the Psychomotor Vigilance Task (PVT) [45], the Auditory Verbal Learning Test (AVLT) [46], and category and letter fluency [46].

The ANT is a computerized test-battery that consists of tests with stimuli presented on a computer screen. The participant is asked to respond to these stimuli with mouse-clicks, using the left and right mouse buttons in tasks where choice is required. The ANT subtest Baseline Speed measures simple reaction time. Participants are asked to press a mouse button as fast as possible after a fixation cross on the computer screen changes to a white square. After pressing the mouse button the square changes back to the fixation cross which changes to a square again with a random post-response interval of 500 to 2500 ms. The task consists of two parts of 32 trials each for each index finger.

The subtest Feature Identification from the ANT tests visuospatial processing. The participant is presented with a square that is divided in nine small compartments of which three are red and six are white. After 10 seconds the screen changes to four similar squares but with different patterns of red and white compartments and the participant has to decide as fast as possible whether or not the original square is present. From this subtest reaction time is measured, the number of correct responses, and the number of false positives and false negatives (ie, answering the original square is there when it is not, or answering the original square is not there when it is).

In the subtest Memory Search Letters from the ANT, which measures selective attention and working memory, the participant is shown a group of four letters and has to decide whether or not the original stimulus-letter is there. Also from this subtest reaction time is measured, as well as the number of correct responses, and the number of false positives and false negatives.

For the subtest Response Organization Arrows from the ANT, which measures response inhibition and set shifting, the participant has to respond to an arrow that is presented on screen by either pressing the mouse button that corresponds to the direction of the arrow (part one) or the mouse button in the reverse direction (part two). In part three the two different colored arrows are presented at random and the participant has to switch strategies and react as fast as possible. From this test also reaction times, and errors are measured.

In the subtest Spatial Temporal Span from the ANT, which measures visuospatial working memory, the participant is presented with a screen that shows nine squares that are highlighted in random order. The participant has to respond by clicking the squares in the same order (part one) or in the reverse order (part two). Each trial the number of squares being highlighted is increased. In this subtest the number of trials and reaction speed are measured.

The AVLT, which measures declarative memory, consists of five learning trials of 15 words that are verbally presented to the participants. The participant has to memorize and reproduce as many words as possible in one minute, that belong to a specific semantic category. Two trials were done with the categories animals and occupations. The score is the total number of words from the two trials.

The PVT measures sustained attention and consists of 30 reaction time stimuli presented with a random interval between 2–10 seconds on a handheld palm-device [47]. It measures two aspects of sustained attention: reaction time and lapses. The participant has to press a button as soon as the stimulus is displayed on the screen.

2.3.6. Data reduction

A speed composite score was calculated for all participants by the mean of z-transformed values of scores on tests in which cognitive speed is important (Response Organization Arrows and Baseline Speed from the ANT, and the inverse z-score of category fluency) [48] with a lower score indicating faster cognitive speed. Furthermore, all subtests of the ANT and the PVT contain outcome measures of reaction times and proportion of correct responses. Reaction times are subject to the speed-accuracy trade-off, meaning a participant can adopt a strategy that aims at shorter reaction times but with making more mistakes, or the other way around [49]. Therefore we calculated an efficiency measure of reaction time divided by proportion of correct responses (RT/p(Correct)), that takes this trade-off into account and is regarded to result in an objective measure that is not influenced by the adopted strategy of the participant [50]. A lower score indicates better efficiency.

2.4. Treatment

The protocol for the treatment of insomnia of the participants consisted of six weekly preprogrammed consults of CBTI [31,32,34] via an internet website. In addition, each week short personalized feedback from a certified sleep therapist was included, and one 15-minute chat-session with the sleep therapist in the week after the second session to promote therapy adherence and outcomes [51–53]. The CBTI contained psycho education, sleep hygiene, sleep restriction, stimulus control, cognitive therapy, and relaxation techniques (for more information on the treatment protocol see De Bruin et al. [34]).

Participants logged on to a personalized website where they received a consult at a fixed time and day of the week. Each consult consisted of several online pages in a fixed order with text, movies, pictures and short interactive questionnaires containing exercises and explanations based on the CBTI components. From the participants in the treatment condition 13 completed all six consults, two completed five consults, and three completed four consults.

2.5. Statistical analysis

All analyses were performed on an intention-to-treat sample. Data from actigraphy and sleep logs were analyzed using multilevel regression analysis in which repeated measures (ie, each day for one week at both baseline and post-treatment) were considered as nested within participants. With actigraphy and sleep log measures that were taken each day of the week, we distinguished between nights before school days, and nights before free days to account for associated differences in sleep behavior. Free days were weekends (Saturday and Sunday), public holidays, and dates where participants commented in their sleep log that they were free. Age showed no significant differences in effects on the sleep variables from actigraphy and sleep logs, so we analyzed the models without this variable. Multilevel regression analysis allows inclusion of participants with missing data at one or more measurement occasions [54] so all participants who provided baseline measurements were
3.2. Sleep

Multiple regression analyses of the sleep variables revealed a significant difference in SOL and SE between the groups at baseline with less SOL ($\beta = -0.60, p = 0.017$) and a higher SE ($\beta = 0.67, p = 0.006$) for the treatment condition. As expected there was also a significantly longer TST ($\beta = 0.48, p < 0.001$) and higher SE ($\beta = 0.21, p = 0.043$) on weekend nights compared to school nights.

After treatment the difference in SOL between the two groups did not change significantly, nor did SOL change significantly over time for either group. However, although SE was already higher in the treatment condition at baseline, the significant interaction between Condition (treatment versus waiting list) and Time showed that SE improved significantly more in this group after treatment than in the waiting list condition ($\beta = 0.35, p = 0.024$).

3.2.1. Actigraphy

Analyses of the sleep variables from actigraphy measurements revealed a significant difference in SOL and SE between the groups at baseline with less SOL ($\beta = -0.60, p = 0.017$) and a higher SE ($\beta = 0.67, p = 0.006$) for the treatment condition. As expected there was also a significantly longer TST ($\beta = 0.48, p < 0.001$) and higher SE ($\beta = 0.21, p = 0.043$) on weekend nights compared to school nights.

3.2.2. Sleep logs

From the sleep log measures no significant differences appeared between the two groups at baseline in any of the sleep variables. For weekend nights compared to school nights longer TST ($\beta = 0.40, p = 0.004$), longer TIB ($\beta = 0.45, p = 0.002$), shorter SOL ($\beta = -0.27, p = 0.019$), and better SSQ ($\beta = 0.61, p < 0.001$) was found.

For the whole group of participants together WASO increased significantly ($\beta = 0.30, p = 0.033$) and SE decreased significantly ($\beta = -0.30, p = 0.020$) after six weeks of either treatment or waiting list. However, the significant interactions between Condition and Time showed that SOL and WASO decreased more for the treatment group in comparison to the waiting list group ($\beta = -0.45, p = 0.001$ and $\beta = -0.67, p < 0.001$ respectively), while TST, SE and SSQ increased more ($\beta = 0.48, p = 0.010$, $\beta = 1.03, p < 0.001$ and $\beta = 0.44$, $p = 0.008$ respectively).

3.2.3. Questionnaires

Results from the ANOVA's with the CSRQ and the HSDQi showed a significant decrease on the total score of the CSRQ and the HSDQi for the whole group after six weeks of treatment or waiting list ($F(1,29) = 5.70, p = 0.023$, $\eta^2_p = 0.160$ and $F(1,29) = 4.73, p = 0.038$, $\eta^2_p = 0.136$ respectively). For the separate scales of the CSRQ there were no such significant decreases for the whole group over time. There were, however, significant interaction effects for Condition and Time for Shortness of sleep ($F(1,29) = 6.98, p = 0.013$, $\eta^2_p = 0.189$), Irritation ($F(1,29) = 14.73, p = 0.001$, $\eta^2_p = 0.329$), Loss of energy ($F(1,29) = 4.98, p = 0.033$, $\eta^2_p = 0.142$), the total scores of the CSRQ ($F(1,29) = 24.94, p < 0.001$, $\eta^2_p = 0.454$), and the HSDQi ($F(1,29) = 20.63, p < 0.001$, $\eta^2_p = 0.407$), indicating that in the treatment condition scores decreased significantly more in comparison to the waiting list condition (See Table 2). There was no significant interaction effect for Sleepiness.

3.3. Clinically significant insomnia

Analysis of the proportion of participants in both conditions still experiencing clinically significant insomnia showed that all 14 participants in the treatment waiting list condition still experienced clinically significant insomnia after six weeks. In the treatment condition, 11 of the 18 participants (61.1%) improved to sub-clinical levels of experienced insomnia after six weeks of treatment. These proportions were significantly different ($\chi^2(1) = 13.04, p < 0.001$).

3.4. Cognitive functioning

All means, standard deviations and results from the ANOVA’s of the outcome measures from the cognitive tests are presented in Table 3.

There were significant improvements for both groups after treatment or waiting list, of reaction times and efficiency of visuospatial processing, $F(1,30) = 23.40, p < 0.001$, $\eta^2_p = 0.438$ and $F(1,30) = 9.66, p = 0.004$, $\eta^2_p = 0.244$ respectively, selective attention and working memory, $F(1,30) = 58.05, p < 0.001$, $\eta^2_p = 0.659$ and $F(1,30) = 73.09, p < 0.001$, $\eta^2_p = 0.709$ respectively, and response inhibition and setting shifting, $F(1,30) = 29.48, p < 0.001$, $\eta^2_p = 0.496$ and $F(1,30) = 8.16, p = 0.008$, $\eta^2_p = 0.214$ respectively, which can be interpreted as
The significant interactions between time and condition however, showed that for visuospatial processing there was a larger decrease in reaction time, $F(1,30) = 7.09, p = 0.012, \eta^2_p = 0.191$, and due to more improvement of proportion of correct responses, $F(1,30) = 12.28, p = 0.001, \eta^2_p = 0.290$, also a greater improvement in efficiency, $F(1,30) = 17.35, p < 0.001, \eta^2_p = 0.366$, for the treatment condition in comparison to the waiting list. Furthermore, efficiency for selective attention and working memory improved more for the treatment condition, $F(1,30) = 6.28, p = 0.018, \eta^2_p = 0.173$. Reaction times for this domain also improved more for the treatment condition but this was not significant at the 0.05 level, $F(1,30) = 3.33, p = 0.078, \eta^2_p = 0.100$.

For response inhibition and set shifting there were also interactions between time and condition showing more improvements for proportion correct responses and efficiency in the treatment condition but these were not significant at the 0.05 level, $F(1,30) = 3.36, p = 0.066, \eta^2_p = 0.108$ and $F(1,30) = 3.17, p = 0.085, \eta^2_p = 0.096$ respectively.

The scores for declarative memory showed a significant improvement after treatment for both groups in total words and delayed recall, $F(1,30) = 4.66, p = 0.039, \eta^2_p = 0.134$ and $F(1,30) = 5.09, p = 0.032, \eta^2_p = 0.145$ respectively, but no significant interactions occurred between treatment and condition indicating no treatment effect.

On the fluency tests there was a significant increase of words on the letter fluency task for both groups, $F(1,30) = 5.09, p = 0.023, \eta^2_p = 0.165$, but the interaction for time and condition was not significant at the 0.05 level, $F(1,30) = 3.19, p = 0.084, \eta^2_p = 0.099$.

For sustained attention the reaction times and number of lapses showed a significant decrease over time for both groups, $F(1,30) = 4.50, p = 0.047, \eta^2_p = 0.184$ and $F(1,30) = 7.94, p = 0.011, \eta^2_p = 0.284$ respectively, and although there was an interaction for time and condition showing better reaction times and efficiency for the treatment condition after treatment, this was not significant at the 0.05 level, $F(1,30) = 3.33, p = 0.083, \eta^2_p = 0.143$ and $F(1,30) = 3.08, p = 0.095, \eta^2_p = 0.133$ respectively.

The scores for the cognitive tests for simple reaction times and visuospatial working memory, and the composite score for cognitive speed did not show any significant change over time for either group.
| Table 2 |
| Parameter Estimates from the Multilevel Regression Analyses of Sleep Variables from Actigraphy and Sleep Logs, for Time (Baseline versus Post Treatment or waiting list), Condition (Treatment versus waiting list), and Type of Night (Weekend/free versus School nights), and results from the Analyses of Variance for Questionnaires with condition (treatment versus waiting list) as between-subject factor, and time (baseline versus post treatment or waiting list) as the within-subject factor. |
|---|---|---|---|---|---|---|---|---|
| **Actigraphy** | **TST** | **TIB** | **SOL** | **WASO** | **SE** | **FI** |
| Condition (treatment vs waiting list) | 0.30 (0.19) | -0.26 (0.19) | 0.183 | -0.60 (0.24) | 0.17 | -0.48 (0.25) | 0.064 | 0.67 (0.23) | 0.006 | -0.09 (0.26) | 0.741 |
| Weekend (vs schoolday) | 0.48 (0.16) | 0.682 | -0.03 (0.16) | 0.847 | 0.03 (0.13) | 0.811 | 0.15 (0.25) | 0.252 | 0.09 (0.13) | 0.455 | -0.14 (0.13) | 0.287 |
| Time – Post treatment (vs baseline) | 0.07 (0.16) | 0.682 | -0.03 (0.16) | 0.847 | 0.03 (0.13) | 0.811 | 0.15 (0.25) | 0.252 | 0.09 (0.13) | 0.455 | -0.14 (0.13) | 0.287 |
| Condition × Time | 0.01 (0.19) | 0.955 | -0.23 (0.19) | 0.227 | -0.24 (0.16) | 0.140 | -0.18 (0.16) | 0.252 | 0.35 (0.15) | 0.024 | -0.23 (0.16) | 0.156 |
| Weekend × Time | -0.14 (0.20) | 0.482 | -0.03 (0.20) | 0.895 | 0.09 (0.17) | 0.604 | 0.10 (0.16) | 0.558 | -0.20 (0.16) | 0.208 | 0.20 (0.17) | 0.229 |

| **Sleep logs** | **TST** | **TIB** | **SOL** | **WASO** | **SE** | **SSQ** |
| Condition (treatment vs waiting list) | -0.14 (0.20) | 0.493 | -0.18 (0.18) | 0.343 | -0.19 (0.24) | 0.434 | -0.09 (0.21) | 0.683 | -0.01 (0.21) | 0.978 | 0.28 (0.22) | 0.210 |
| Weekend (vs schoolday) | 0.40 (0.14) | 0.004 | 0.45 (0.14) | 0.002 | -0.27 (0.11) | 0.019 | 0.07 (0.13) | 0.564 | 0.12 (0.12) | 0.312 | 0.61 (0.12) | -0.001 |
| Time – Post treatment (vs baseline) | -0.21 (0.15) | 0.161 | 0.07 (0.15) | 0.656 | -0.03 (0.13) | 0.831 | 0.30 (0.14) | 0.033 | 0.30 (0.13) | 0.020 | -0.02 (0.14) | 0.890 |
| Condition × Time | 0.48 (0.18) | 0.010 | -0.13 (0.19) | 0.499 | -0.45 (0.15) | 0.003 | 0.67 (0.17) | <0.001 | 1.03 (0.16) | <0.001 | 0.44 (0.17) | 0.008 |
| Weekend × Time | -0.17 (0.21) | 0.403 | -0.21 (0.21) | 0.316 | 0.12 (0.17) | 0.484 | 0.07 (0.19) | 0.723 | -0.03 (0.18) | 0.881 | -0.27 (0.18) | 0.151 |

| **Questionnaires** | **CSRQ Shortness of sleep** | **CSRQ Irritation** | **CSRQ Loss of energy** | **CSRQ Sleepiness** | **CSRQ Total score** | **HSDQi** |
| Condition (treatment vs waiting list) | .093 | 0.089 | 0.000 | 0.957 | 0.060 | 0.176 | 0.060 | 0.178 | 0.160 | 0.023 | 0.136 | 0.038 |
| Time – Post treatment (vs baseline) | .189 | 0.013 | 0.329 | 0.001 | 0.142 | 0.033 | 0.060 | 0.178 | 0.454 | <0.001 | 0.407 | <0.001 |

Note. All outcome variables for the multilevel regression analyses have been standardized so that β coefficients can be interpreted as Cohen’s d effect sizes with .20, .50, and .80 indicating small, medium, and large effect sizes [55]. SOL = sleep onset latency; WASO = wake after sleep onset; TST = total sleep time; TIB = time in bed; SE = sleep efficiency; HSDQi = insomnia scale Holland Sleep Disorder Questionnaire; CSRQ = Chronic Sleep Reduction Questionnaire. \(\eta^2\) = partial eta squared, effect size with .010, .050, and .140 indicating small, medium, and large effect sizes [55].
3.5. Correlations between improvements of cognitive functioning and improvements of sleep on school nights in the treatment group

From the results it appeared that visuospatial processing, selective attention and working memory, response inhibition and set shifting, letter fluency, and sustained attention either improved more after treatment than waiting list, or showed a trend in that direction. So for these cognitive outcome measures we calculated difference scores for efficiency between baseline and post treatment, and their correlations with the difference scores of the sleep variables in the treatment group from actigraphy and sleep logs on school nights, and scores on the questionnaires. Results are presented in Table 4.

Improvements in visuospatial processing were correlated with improvements of WASO and SSQ from the sleep logs, and with loss of energy, sleepiness, and the total score of the CRQ. Improvements in selective attention and working memory were correlated with WASO from sleep logs, and with shortness of sleep of the CRQ. There was also a relation of improvements in sustained attention with WASO, but contrary to expectation this was correlated with an increase (ie, deterioration) of WASO. No significant correlations were found of sleep variables from actigraphy with any of the cognitive measures.

4. Discussion

This study aimed to investigate the treatment effects of internet delivered CBTI on sleep and cognitive functioning of adolescents with insomnia. In addition, we aimed to explore whether changes in cognitive functioning were related to changes in sleep on school nights. The results showed that the experimental group, compared to waiting list, improved in objective SE and subjective SOL, WASO, SE, TST, and sleep quality. Symptoms of insomnia and chronic sleep reduction decreased. Furthermore, although improvements in sleep variables after treatment were relatively small with small to medium effect sizes, 11 out of 18 (61.1%) participants in the treatment condition improved to a sub-clinical level for subjective SOL, WASO, SE, TST, and sleep quality. Symptomsof insomnia and chronic sleep reduction decreased. Furthermore, although improvements in sleep variables after treatment were relatively small with small to medium effect sizes, 11 out of 18 (61.1%) participants in the treatment condition improved to a sub-clinical level for subjective SOL, WASO, SE, and TST.
Correlations between changes in sleep on school nights and changes in efficiency scores of cognitive functioning in the treatment group.

<table>
<thead>
<tr>
<th>Cognitive Functioning</th>
<th>Letter Fluency Total words</th>
<th>Sustained attention</th>
<th>Response inhibition and shifting</th>
<th>Selective attention and working memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTIGRAFHY</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TST</td>
<td>0.24</td>
<td>0.17</td>
<td>0.51</td>
<td>0.27</td>
</tr>
<tr>
<td>SE</td>
<td>-0.04</td>
<td>-0.08</td>
<td>0.05</td>
<td>0.04</td>
</tr>
<tr>
<td>SOL</td>
<td>-0.10</td>
<td>-0.12</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td>WASO</td>
<td>0.06</td>
<td>0.07</td>
<td>0.14</td>
<td>0.04</td>
</tr>
<tr>
<td>FI</td>
<td>0.06</td>
<td>0.08</td>
<td>0.08</td>
<td>0.06</td>
</tr>
<tr>
<td>SE</td>
<td>0.24</td>
<td>0.16</td>
<td>0.10</td>
<td>0.10</td>
</tr>
<tr>
<td>SOL</td>
<td>0.16</td>
<td>0.04</td>
<td>0.14</td>
<td>0.04</td>
</tr>
<tr>
<td>WASO</td>
<td>0.10</td>
<td>0.11</td>
<td>0.11</td>
<td>0.17</td>
</tr>
<tr>
<td>FI</td>
<td>0.02</td>
<td>0.05</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>HSDQi</td>
<td>0.28</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSRQ</td>
<td>0.35</td>
<td>0.15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Significant at a .05 level; ** significant at a .01 level; improve-ments in sleep variables are indicated by increases in total sleep time (TST), sleep efficiency (SE), and subjective sleep quality (SSQ), and decreases in sleep onset latency (SOL), wake after sleep onset (WASO), and fragmentation index (FI). Improvements of the sleep variables from the insomnia scale of the Holland Sleep Disorder Questionnaire (HSDQi) and the Chronic Sleep Reduction Questionnaire (CSRQ) are indicated by a decrease in scores. Improvements in cognitive functioning are indicated by an increase in total words for Letter Fluency, and lower (efficiency) scores for all other cognitive tasks. Therefore, relations between improvements in sleep and improvements in cognitive functioning are indicated by negative correlations of TST, SE and SSQ, and positive correlations of SOL, WASO and FI with all cognitive outcome measures, except Letter Fluency, for which inverse correlations indicate such a relation.

in the waiting list condition. This indicates that, as expected [34], CBTI was effective and that changes in cognitive functioning might be attributed to the treatment effect of CBTI. Improvements in cognitive functioning occurred in the cognitive domains of visuospatial processing, and selective attention and working memory, and trends of improvement in sustained attention. In executive functioning involving response inhibition and set shifting, and in verbal fluency. No significant effects were found in the domains of simple reaction time, visuospatial working memory, declarative memory, and category fluency, nor in overall cognitive speed. Finally, from the exploration of relations between improvements of cognitive functioning with improvements of sleep on school nights, WASO and SSQ from sleep logs, and some aspects of chronic sleep reduction appeared to be related to improvements in visuospatial processing, selective attention and working memory. However, WASO appeared inversely related to the sustained attention task as measured with the PVT, and no relations appeared for any of the actigraphy measures with cognitive functions.

The improvements in cognitive functioning were found despite only small improvements in most sleep measures, and a relatively small sample size. However, as noted before, most of the treated participants, who all started the treatment with a diagnosis of DSM-5 insomnia disorder, improved to a sub-clinical level of insomnia at post-treatment with self-reported SOL and WASO less than 30 minutes and SE higher than 90%, indicating that the subjective experience of insomnia may play an important role in this relation with cognitive functioning. Studies show that the subjective experience of insomnia seems to not always be adequately represented by objective sleep measures [61], and that patients put a strong emphasis on consequences of insomnia for daytime functioning [62], mostly showing a higher subjective suffering than indicated by objective sleep measures. Furthermore, in a previous study of CBTI for adolescent insomnia we found that TST, symptoms of insomnia, and chronic sleep reduction continued to improve in the two months after treatment. Consequently, some sleep variables will only improve after the treatment, or in other words: part of the treatment effect takes place after treatment, which means that the current study might not measure the eventual achievement in cognitive functioning after sleep improvement.

From the cognitive domains measured in this study, visuospatial processing showed the most prominent treatment effects, in which both reaction time and accuracy improved, resulting also in better efficiency. Dewald-Kaufmann et al. [20] found similar improvements in visuospatial processing in adolescents with chronic sleep reduction after completion of a program of gradual sleep extension over only two weeks. The present study and the study of Dewald-Kaufman et al. are thus far the only two studies known to the authors concerning the effect of sleep improvement on cognitive functioning in adolescents with sleep problems. Both these studies show effects on visuospatial processing, which could indicate that this is a sensitive cognitive domain for changes in sleep. In a study concerning sleep extension and cognitive functioning of pre-adolescents, Sadeh et al. [18] found improvements in simple reaction time, working memory and sustained attention. Although no explicit cognitive test measuring visuospatial processing was applied in that study, in a test that contains elements of visuospatial processing (Symbol-digit substitution) they reported no effects of sleep extension. Sadeh et al. [18] did find an improvement in working memory, and in a cross-sectional study Gradisar et al. [25] demonstrated relations between insufficient sleep and bad working memory performance in adolescents. Concurrent with these findings in working memory, we also found an improvement in a combined task of working memory and selective attention. These results support previous findings by Dewald-Kaufman et al. [20] who also found improvements in this same task after sleep extension in adolescents. In a study with children and young
Meijer AM, Reitz E, Dekovic M, et al. Longitudinal relations between sleep and cognitive functioning in adolescence. In this study the improvements of cognitive functions involving working memory, selective attention, and visuospatial processing showed relations with sleep parameters from subjective measures (sleep logs and questionnaires). These parameters included WASO, SSQ, and symptoms of chronic sleep reduction. This indicates that working memory, selective attention, and visuospatial processes are sensitive to changes in certain (subjective) aspects of sleep, such as fragmentation and restlessness. This was further confirmed by the strong relations of these cognitive functions with symptoms of chronic sleep reduction, such as shortness of sleep, loss of energy, and sleepiness— all symptoms that emerge after a longer period of insufficient sleep, which in turn has been shown to have a serious impact on school performance [11,30], and is related to symptoms of ADHD [28,29].

Limitations. There were several limitations in this study. First of all, the group sizes were small and power to detect changes in both sleep and cognitive functioning may have been limited. With the present sample size of 32 participants in total, the apriori power to detect large differential effects between groups [66] is 71% (assuming effect size $d = 0.8$, alpha = 5% one-sided), and the power to detect medium sized differential effects is only 40% (assuming effect size $d = 0.5$). However, the observed effect sizes in cognitive functioning were large and we did find statistically significant improvements after treatment. Apparently, improvements in cognitive functioning can be considerable. Another limitation was that despite randomization the waiting list group was significantly older than the treatment group. This may have influenced the findings for both sleep and cognitive outcomes. Although the main concern of this study was the change over time in sleep and cognitive functioning due to treatment or no treatment, this change may develop differently, or may react differently to treatment, in different ages. Our sample was too small to conduct analyses for different age groups. Finally, as mentioned before, the changes in sleep after treatment were limited to measurements directly after treatment, while a previous study [34] showed that some effects of CBTI in adolescents take place after conclusion of the treatment. Therefore we suggest further studies with larger groups with equal gender and age, including follow-up measurements.

In conclusion, this study indicated that CBTI for adolescents with insomnia can result in notable improvements in visuospatial processing and phonological working memory, but not in visual working memory. These findings have implications for research and interventions in the areas of adolescent sleep as related to school performance [9] and clinical areas like ADHD, which has been singled out as one of the main topics for research by a Consensus Working Group on sleep and ADHD [29].

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.12.009.

Acknowledgements

This study was supported by a grant from The Netherlands Organization for Health Research and Development ZonMw (number 15700.3008) to Anne Marie Meijer. The authors wish to thank Annette van Maanen for her assistance in cognitive testing.

References


[21] Meijer AM, Reitz E, Dekovic M, et al. Longitudinal relations between sleep and cognitive inhibition after acute sleep restriction, but we did find some indications of improved response inhibition and set shifting after treatment, and Cousins Hasler [21] found improvements in cognitive inhibition after sleep extension in adolescents. In our study, however, we found no relations between the improvements in response inhibition and set shifting with any of the sleep variables of school nights. These contradictory results could be due to the complexity of this executive function that depends on several lower level functions such as psychomotor functioning, reaction time, attention, visuospatial processing, working memory, and overall cognitive processing speed. This is known as the impurity problem [63], which purports that changes in any of these lower level functions could lead to changes in the higher order functions. Future studies on the effects of improvements of sleep in adolescents on these more complex and higher order cognitive functions need to disentangle these from lower level functions in order to differentiate between their respective changes.

As indicated in the introduction, several studies showed a relation of sleep and working memory in adolescents (eg, [21,25]) and children (eg, [16,18,64]). This indicates that working memory could be sensitive to changes in sleep. However, in the present study no significant improvement in visuospatial working memory occurred. According to the working memory model of Baddeley and Hitch [65], working memory consists of four distinct systems: the visuospatial sketchpad that processes and stores visuospatial information, the phonological loop that processes and stores written and spoken information, the episodic buffer with integrated information from different sources, and the central executive that controls these three. We found distinctly different results for tasks involving visuospatial working memory and phonological working memory (ie, the memory search letters task for selective attention and working memory), with no changes in visuospatial working memory and improvements in the phonological working memory. However, we also found improvements in visuospatial processing in which working memory is also involved. The difference between these two visual tasks is that in the visuospatial processing task the visual information has to be retained and manipulated to compare it to a target. In the task for visuospatial working memory the visual information has to be retained while gradually adding to the working memory load, and reproducing this visuospatial information in the same or the opposite order. There are distinct differences in amount and nature of the manipulation within the working memory needed for these tasks. Therefore it seems that the more complex working memory tasks, in which more complex manipulations take place and the central executive is engaged to a greater extent, are more sensitive to changes in sleep. Gradisar et al. [25] also concluded that more complex working memory tasks were related stronger to differences in sleep. However, although the stimuli in that study were presented on a computer screen giving it a visual component, the working memory tasks consisted mainly of phonological working memory, which concurs with our findings of improvements in phonological working memory as mentioned before. More research aimed at the relations between differentiated subcomponents of working memory and sleep is needed to gain insight on this matter.

In this study the improvements of cognitive functions involving working memory, selective attention, and visuospatial processing showed relations with sleep parameters from subjective measures (sleep logs and questionnaires). These parameters included WASO, SSQ, and symptoms of chronic sleep reduction. This indicates that working memory, selective attention, and visuospatial processes are sensitive to changes in certain (subjective) aspects of sleep, such as fragmentation and restlessness. This was further confirmed by the strong relations of these cognitive functions with symptoms of chronic sleep reduction, such as shortness of sleep, loss of energy, and sleepiness— all symptoms that emerge after a longer period of insufficient sleep, which in turn has been shown to have a serious impact on school performance [11,30], and is related to symptoms of ADHD [28,29].


