Sleep Restriction Therapy for insomnia is associated with reduced total sleep time, increased daytime somnolence, and objectively-impaired vigilance: Implications for the clinical management of insomnia disorder

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Abstract

Aims: Adverse-effects of psychological therapies are rarely recorded or considered. Sleep Restriction Therapy (SRT), an effective component of cognitive-behavioral therapy for insomnia, limits time-in-bed and may result in reduced total sleep time. Clinical evidence suggests that daytime impairment may be experienced by patients in the acute treatment period, yet there has been little systematic study of this possibility. Here, we investigated whether SRT is associated with reduced total sleep time, increased daytime somnolence and impaired vigilance.

Design: Within-subjects, repeated measures treatment investigation with the addition of a matched good sleeper control group to permit between-group comparisons on performance measures.

Setting: Sleep Research Laboratory

Participants: Sixteen patients [10 female, Mean Age = 47.1 (10.8) yrs] with well-defined psychophysiological insomnia (PI) and an age and gender-matched control group of good sleepers [GS, n=15; 10 female, mean age = 47.1 (10.5) yrs].

Interventions: Patients were treated with single component SRT over a 4-week protocol, comprising one main session for treatment delivery and weekly sleep window titration (weeks 1-4). Patients slept in the laboratory for two nights prior to treatment initiation and for three nights (SRT night 1, 8, 22) during the acute interventional phase. In addition, those with PI completed the psychomotor vigilance task (PVT) at seven defined time-points [day 0 (baseline), day 1,7,8,21,22 (acute treatment) and day 84 (3 months)]. The Epworth Sleepiness Scale (ESS) was completed at baseline, weeks 1-4, and at three months. Matched good sleepers completed the PVT at one single time-point to permit baseline performance comparisons with patients.

Measurement and results: Subjective sleep outcomes and global insomnia severity significantly improved pre-to-post SRT. There was, however, a decrease in PSG-defined total sleep time during acute implementation of SRT, by an average of 91

minutes on night 1, 78 minutes on night 8, and 69 minutes on night 22, relative to baseline (*p's*<.001; effect size range=1.60-1.80). During SRT, PVT lapses were significantly increased from baseline (at 3/5 assessment points, all *p*<.05; effect size range=.69-.77), returning to baseline levels by three months (*p*=.43). A similar pattern was observed for RT, with RTs slowing during acute treatment (at 4/5 assessment points, all *p*<.05; effect size range=.57-.89) and returning to pre-treatment levels at three months (*p*=.88). While patients did not differ from good sleepers at baseline with respect to PVT performance (*p*'s<.20), between-group differences began to emerge during SRT, with patients showing relative impairment. Objective measures were paralleled by significant elevations in subjective daytime sleepiness at weeks 1, 2, and 3 (relative to baseline; all *p*<.05); by three months, sleepiness had returned to baseline (normative) levels (*p*=.65).

Conclusion: For the first time we show that acute SRT is associated with reduced total sleep time, increased daytime sleepiness and objective performance impairment. Our data have important implications for implementation guidelines around the safe and effective delivery of CBT-I.

Keywords: insomnia; CBT; sleep restriction therapy; vigilance; adverse effects; sleepiness

Introduction

Cognitive-Behavioral Therapy for insomnia (CBT-I) is commonly regarded as the treatment of first choice for persistent insomnia disorder.[1-3] CBT-I has been shown to be as effective as pharmacotherapy in the short-term but, in contrast to pharmacotherapy, leads to durable improvements in sleep (for up to 2 years post-intervention).[4] One of the frequently-cited advantages of CBT-I, and non-pharmacological approaches in general, is the absence of, or potential for treatment-related adverse effects.[5,6] This is in contrast to pharmacotherapy where, for example, negative short- and long-term effects of sedative hypnotics have been well-described.[7-10] Indeed, adverse effects are routinely assessed in randomised, placebo-controlled clinical trials of hypnotics and guide regulatory approval.[11] Somewhat surprisingly, adverse-effects are almost never systematically recorded and/or reported in trials of psychological/behavioral treatments.[5,12-14]

Sleep Restriction Therapy (SRT), a standard behavioral strategy used within multi-component CBT-I[2] and as a stand-alone intervention,[6,15,16] involves restricting a patient's time-in-bed (sleep window) to match their average (self-report) total sleep duration. The sleep window is then titrated, weekly, based on sleep efficiency (the proportion of time-in-bed spent asleep), in order to arrive at the patient's core sleep requirement. Decreasing the opportunity to sleep over successive nights, it is argued, builds homeostatic sleep pressure, stabilises circadian control of sleep and wakefulness, and dampens pre-sleep cognitive and physiological (hyper)arousal, leading to shorter sleep latencies and more consolidated, uninterrupted sleep.[6,17-20] CBT-I practitioners often advise patients that, because of the *reduced opportunity* for night-time sleep, coupled with 'prohibition' of daytime napping, increased sleepiness may emerge during the initial phases of SRT implementation, resulting in a transient worsening of daytime functioning.[18,21] Magnitude of time-in-bed restriction may also be affected by the well-established objective-subjective sleep discrepancies, known

to characterise some patients with insomnia.[22-24] That is, patients may be assigned time-in-bed prescriptions that are significantly lower than pre-treatment objective sleep, leading to marked sleep loss over several weeks.[6] Patients are, therefore, advised not to drive or operate heavy machinery if they feel excessively sleepy.[18,21]

Whilst these guidelines have evolved from clinical experience, there has been little systematic investigation of the nature or magnitude of CBT-I-induced daytime sleepiness and impairment. When investigating the utility of modafinil as an adjunct to CBT-I, Perlis and colleagues[25] showed that those receiving CBT+placebo (n=10) reported increased Epworth Sleepiness Scale (ESS) scores one week post-SRT delivery. In contrast, both the therapeutic arm (CBT+modafinil) and additional control group (modafinil+contact) did not exhibit such a marked increase in ESS scores. Kyle et al.[6] conducted the first in-depth examination of single-component SRT. A mixed-methods approach was applied; involving questionnaire-based measures, semi-structured interviews and real-time audio-diaries to probe the patient experience of treatment. During acute implementation of SRT, patients subjectively reported problems with excessive daytime sleepiness, which negatively affected daytime functioning beyond pre-treatment levels. Of note, over one-third of the audio-diary sub-sample complained, during real-time recordings, that driving was adversely affected [e.g.: *"Woke up bright and breezy, half six, Tuesday morning, raring to go, got into the car. . . and within twenty minutes I was absolutely exhausted, so bad that I swear I was nearly falling asleep all the way to work. It was torture, I was cross-eyed, eyes drooping, driving"; "driving was a nightmare, and I've never ever had an issue with driving before"; "I felt, really, I was a danger on the road"* (Kyle et al.[6]; p741-742)]. Despite these acute difficulties, patients responded well to treatment, evidencing robust improvements in sleep and daytime functioning at three months follow-up. Recently, Miller et al. (in press) complemented these qualitative findings using ecological momentary assessment. The authors reported that point-in-time

assessments of ‘sleepiness/fatigue’ increased during week 1 of SRT, while ‘positive mood’ and ‘alert cognition’ decreased, relative to baseline.

To date, no study has profiled whether subjective reports of treatment-related dysfunction are reflected in objective performance impairments. Moreover, it is unclear to what extent *sleep is actually restricted* during SRT and whether this is associated with elevated daytime sleepiness, measured with a validated instrument. Information on the magnitude and time-course of sleep loss, daytime sleepiness and performance impairment may have important implications for the future refinement, delivery and safe dissemination of CBT-I.

Method

In the present study, 16 patients with psychophysiological insomnia took part in brief SRT. In order to profile changes in sleep time and objective performance, patients slept in the lab on five occasions (2 x baseline, 3 x during acute treatment) and completed a psychomotor vigilance task (PVT) at 7 defined time-points. The Epworth Sleepiness Scale (ESS) was also completed on a weekly basis (baseline, weeks 1-4 and at 3 months) to index changes in daytime somnolence (see Figure 1 for schematic description of protocol). A control group of good sleepers (n=15) was recruited in order to examine baseline differences in PVT performance.

We hypothesised that acute implementation of SRT would lead to reduced total sleep time which would be accompanied by impairments in vigilance (lapses and RT) and increased daytime sleepiness.

Sample

Sixteen thoroughly-screened patients with psychophysiological insomnia were recruited to take part in sleep restriction therapy for insomnia disorder. Individuals initially responded to media adverts looking for poor sleepers to sleep for two nights in the sleep laboratory, as part of a study into sleep-related attentional bias (grant # R01MH077901). This was a non-interventional study, but on completion of the overnight protocol (see below for details), those without evidence of occult sleep disorder pathology were invited to take part in the present treatment study, using SRT. A group of healthy age- and gender-matched good sleepers (n=15) was recruited for comparative purposes.

Assessments

Sleep status: PI patients received a telephone interview by an expert in behavioral sleep medicine to assess the absence of co-morbidities and medication-use, as well

as the presence of insomnia, defined as satisfying the following criteria for subjective sleep impairment:

- report of sleep disturbance for at least 3 nights per week for at least 6 months
- sleep onset latency (SOL) and/or wake-time after sleep-onset (WASO) > 30 minutes
- total sleep time < 6 hrs
- sleep efficiency < 85%
- daytime impairment attributed to disturbed sleep
- Insomnia Severity Index score ≥ 15

The phone interview was based on Morin & Espie[21] and supplemented with a sleep disorders screening questionnaire.[26] Those deemed eligible were invited to attend a screening day, involving a thorough sleep and psychiatric interview (Mini-international Neuropsychiatric Interview; MINI[27]) with a licensed clinical psychologist trained in behavioral sleep medicine, and a medical assessment (ECG, blood chemistries, medical history, and drug screen) by a certified physician. Patients meeting Research Diagnostic Criteria for PI[28], and who met all other inclusion/exclusion criteria, subsequently slept for two consecutive nights at the University of Glasgow Sleep Centre where they underwent polysomnographic (PSG) assessment (see below).

Good sleepers received the same phone interview to assess inclusion/exclusion criteria, defined as the absence of sleep, psychiatric or (unstable) medical disorder, and the endorsement of good quality, restorative sleep, in addition to the following:

- sleep onset latency (SOL) and wake-time after sleep-onset (WASO) < 15 minutes
- number of night-time awakenings ≤ 2

- total sleep time > 6 hrs
- sleep efficiency > 85%
- stable sleep period between 22:00 and 08:00

All study participants completed a 7-day sleep diary (based on Morin & Espie[21]) to assess sleep continuity and quality and help rule out circadian phase disturbance. Patients completed sleep diaries for 6 weeks in total (baseline, treatment weeks 1-4 and at 3 months). Participants also completed the Hospital Anxiety and Depression Scale (HADS[30]), supplementing the psychiatric screening interview and helping to rule out clinical-level anxiety/affective disorders. Patients completed the Insomnia Severity Index (ISI[31]), a sensitive measure of insomnia severity, at baseline, 4 weeks (post-treatment) and 3 months. Finally, patients completed the Epworth Sleepiness Scale (ESS[32]) at six time-points (baseline, weeks 1-4, and 3 months). The standard ESS does not include a specified time-frame and thus for the purpose of the present study, modifications were made so that patients completed the ESS with reference to "in the last week…", permitting assessment of weekly sleepiness levels.

It should be noted that matching between patients and controls was initiated on a subject-by-subject basis, with each patient matched with a corresponding good sleeper in terms of gender and age ± 2 yrs. Successful one-to-one matching was achieved for 14/16 patients.

Polysomnography (PSG): A standard PSG montage was used, involving electroencephalographic [EEG: Fp1 (neutral), C3, P3 (reference), O1, Fpz, Fz, Cz, Pz, Oz, F4, C4], electrooculographic (EOG: horizontal and vertical) and electromyographic (submental) recordings. On night 1 of the baseline phase, all participants were screened for sleep-disordered breathing and periodic limb

movements through monitoring of abdominal and thoracic effort, nasal airflow, oximetry, and bilateral tibialis anterior EMG. Sleep was recorded on a lifelines trackit^{TM} ambulatory recorder and scored visually by two experienced scorers (> 90% inter-scorer reliability) according to criteria by Rechtschaffen and Kales.[29] For study inclusion, patients were required to have an Apnea Hypopnea Index (AHI) and Periodic Limb Movements of Sleep (PLMS) arousal index < 10. This initial night served as screening and adaptation to the sleep environment, while night 2 of the baseline phase was used as a comparator to index change during SRT. During baseline PSG assessment, patients implemented normal, 'at-home' bed and rise-times (guided by sleep diary records).

For the SRT intervention, patients slept in the sleep lab on three further nights (SRT nights 1, 8 and 22; see Figure 1) where sleep parameters were recorded (EEG, EMG, EOG) during implementation of a prescribed sleep window (based on sleep diary reports of total sleep time; see details of SRT intervention below). For the purpose of the present study, PSG-defined total sleep time (TST) was the only selected variable of interest, to index magnitude of sleep reduction between baseline and SRT nights. Future reports will focus on changes in objective sleep continuity parameters, as well as sleep macro and micro architecture, in relation to treatment response.

Psychomotor vigilance task (PVT): The PVT is a frequently-used task in sleep research to assess the impact of sleep restriction, total sleep deprivation or altered sleep timing on basic vigilant attention. Evidence also exists that PVT metrics relate to driving simulator performance during sleep deprivation[33] and that PVT performance is reliable across repeated administrations.[34] The version of the PVT used in the present study has been applied in studies of insomnia and sleep perturbation.[35,36] In the task, participants are asked to respond with a left mouse

click, as quickly as possible, to the presence of an asterisk located in the centre of the computer screen. Interval-onset for asterisks varied between 1 and 10 seconds in duration and there were 110 experimental trials. Participants completed five practice trials at the beginning of the session to aid task familiarity. The PVT was programmed in E-prime (http://www.pstnet.com/eprime.cfm) and completed on a Dell laptop, at a viewing distance of 40 cm. Task duration was approximately 13 minutes. Testing took place at 6pm. The following PVT metrics[37] were analysed: (1) attentional 'lapses' (defined as RTs > 500 msec); and (2) 1/mean RT (per trial).

Intervention

The SRT intervention involved one main session for delivery of treatment rationale and instructions, and four further brief, in-person or telephone interactions to titrate sleep efficiency (see Figure 1). Treatment was delivered by experts in behavioral sleep medicine via power-point slides to two patients at a time, and covered SRT rationale, sleep window calculation, and trouble-shooting around potential implementation difficulties. The sleep window was initially calculated based on one week of baseline sleep diaries, with time-in-bed prescriptions reflecting average total sleep time. The sleep window was subsequently titrated each week according to the following guidelines: sleep efficiency < 85%, decrease by 15 minutes; sleep efficiency ≥ 85-89%, no change; and sleep efficiency ≥ 90%, increase by 15 minutes.[17] The minimum sleep window was set at 5hrs. For those patients where the sleep window was deemed too difficult, restrictive or impossible to adhere to, a compromise was established between therapist and the patient. No other components of CBT-I were addressed during the intervention.

The study protocol was reviewed and approved by the West of Scotland NHS research ethics committee (protocol no. 10/SO701/85)

[Insert Figure 1]

Analysis

Group differences (patients versus good sleepers), with respect to demographic and sleep-related variables, were assessed using independent *t*-tests. Treatment-related change in subjective sleep-diary outcomes (sleep-onset latency [SOL], wake-time after sleep-onset [WASO], sleep efficiency [SE]) and insomnia severity (ISI) were assessed with repeated measures analysis of variance (ANOVA), across baseline, post-treatment (week 4) and three month follow-up. PSG-TST (mins), daytime sleepiness (ESS) and vigilance (lapses, RT) were similarly assessed with repeated measures ANOVA. Significant main effects were followed up using paired *t*-tests. PSG-TST was compared across four nights [baseline (night number 2), and treatment nights (1, 8, and 22)], vigilance across seven time-points [[day 0 (baseline), day 1,7,8,21,22 (acute treatment) and day 84 (3 months)] and sleepiness across six time-points [baseline, weeks 1-4, 3 month follow-up]; with comparisons focused on change from baseline assessments. Effect sizes (ES) for paired data were calculated as follows: [mean difference / standard deviation of difference]. All comparisons were two-sided, with $p<.05$ indicating statistical significance, but given the apriori nature of our directed hypotheses, *p* values and effect size data are also reported for *p*'s ≤.1.

While the primary analyses of interest focussed on assessment of within-subject change for vigilance, sleepiness and PSG-TST, recruitment of a group of good sleepers also permitted between-group comparisons. Thus, for PVT performance (lapses and RT), exploratory comparisons between healthy controls and PI patients were conducted at baseline and during treatment assessments, using independent *t*-tests (and effects quantified using Cohen's d: ($M1 - M2 / \delta_{pooled}$).[38]

Results

Sample

Sixteen patients [10 female, Mean Age = 47.1 (10.8) yrs] initially enrolled in the study and completed session 1. One patient dropped out in the first week due to concerns about the impact of SRT on work functioning. The fifteen remaining participants completed the full protocol (five lab nights and seven neurocognitive assessments), including 12-week follow-up. Mean age of the remaining 15 patients was 47.2 yrs (SD=10.4) and 10 (66.6%) were female. The control group of good sleepers were identical in both age (47.1, SD=10.5) and gender (10 female [66.6%]). As expected, PI patients demonstrated significant sleep disturbance at baseline relative to good sleepers (see Table 1), and reported greater levels of anxiety and depression. Of note, and consistent with the diagnosis of PI, anxiety and depression scores were in the mild range and approximate those found in large non-clinical samples.[39]

[Insert Table 1]

Subjective sleep: manipulation check of the SRT protocol

The average prescribed sleep window for the first week of therapy was 347.0 minutes (SD=32.0), which increased by 15 minutes over the four week acute SRT phase (week 4 = 362.0 minutes, SD=33.0; see Figure 2). Sleep diary records of time-in-bed decreased from a baseline of 483.2 minutes (SD=74.1) to 353.2 minutes (SD=36.1) during week 1, in line with prescribed sleep window times, indicating close adherence to the SRT protocol (see Figure 2).

[Insert Figure 2]

Insomnia severity (measured with the ISI) significantly reduced across assessment points [$F(2,24)=85.07$, $p<.001$), decreasing from 17.4 (SD=2.8) at baseline to 7.7

(SD=3.9) at four weeks (p<.001). Further reductions were observed between week 4 and 3 months (5.08, SD=4.1; p=.004, and p<.001 for comparison with baseline). Subjective reports of SOL similarly changed over assessment period [F(1.04,11.39)=16.24, p=.002], reducing from 32.2 (SD=21.8) minutes at baseline to 9.4 minutes (SD=5.4) at four weeks (p<.01) and remaining at this level (8.1, SD=5.2) at 3-months follow-up. Both WASO and sleep efficiency showed robust changes over time [WASO: F(1.04,11.41)=9.04, p=.011 and SE: F(1.07,11.75)=28.34, p<.001]. WASO significantly reduced from 66.8 (SD=60.7) minutes at baseline to 12.4 minutes (SD=10.1; p=.01) at post-treatment, remaining at this level at three months (16.2 minutes, SD=16.7). Changes in WASO and SOL were reflected in improved sleep efficiency, increasing from 68.0% (SD=13.7) at baseline, to 90.7% (SD=4.4; p<.001) at 4 weeks, which was maintained at three months (91.3%, SD=4.8). Finally, subjective TST estimates showed fluctuation over assessment points [F(2,22)=13.04, p=.001]. While there was no change in TST between baseline and post-treatment (326.8, SD=61.1 vs. 334.9, SD=37.1; p=.50), by three months TST had improved by approximately 1 hour, to 383.2 mins (SD=49.3; p<.01 for baseline comparison).

Psychomotor Vigilance Task (PVT) performance

PVT performance was first compared across good sleepers (n=15) and PI patients (n=15; pre-treatment). Independent t-tests did not reveal any significant baseline group differences for number of attentional lapses [PI = 7.4 (SD=7.2) vs. GS = 7.2 (SD=10.7); t=.49, p=.62] or 1/mean RT [PI = 2.87 (SD=.30) vs. GS = 3.03 (SD=.36); t=1.31, p=.20].

Changes in patient PVT performance across the treatment protocol [days 0,1,7,8,21,22,84] were next examined with repeated-measures ANOVA. A main effect of time was observed for attentional lapses [F(6,84)=4.45, p=.001] and a significant quadratic trend [F(1,39)=30.52, p<.001; see Figure 3]. Relative to baseline

(day 0), number of lapses increased (non-significantly) at day 1 (p=.10; ES=.45) and 7 (p=.075; ES=.50), and were significantly elevated at day 8 (p=.010; ES=.77), 21 (p=.009; ES=.78) and 22 (p=.018; ES=.69) of SRT. By day 84 (three months), lapses returned to baseline levels (baseline = 7.4 vs. 3 months = 7.0; p=.43). Exploratory comparisons between the PI group (during SRT) and good sleepers, revealed the emergence of group differences at day 8 (p=.046; Cohen's d=.76), and non-significant trends for day 21 (p=.075; Cohen's d=.68) and day 22 (p=.091; Cohen's d=.64), with patients evidencing relative impairment. Patient performance at follow-up (day 84) did not differ from good sleepers (p=.99).

Similar findings were observed for RT, reflected in a significant main effect of time [F(6,84)=3.11, p=.008], accompanied by a significant quadratic trend [F(1,14)=7.59, p=.015; see Figure 4]. Relative to baseline (day 0), patient RTs increased at day 1 (p=.042; ES=.58), day 8 (p=.045; ES=.57), day 21 (p=.034; ES=.61) and day 22 (p=.004; ES=.89). By day 84 (three months), RTs had returned to baseline levels (2.85, SD=.35 vs. 2.87, SD=.29; p=.78). Exploratory comparisons between the PI group (during SRT) and good sleepers, revealed the emergence of group differences at day 8 (p=.051; Cohen's d=.74), day 21 (p=.029; Cohen's d=.85) and day 22 (p=.009; Cohen's d=1.03), with patients evidencing relative impairment. Patient performance, at follow-up (day 84), did not differ from good sleepers (p=.20).

[Insert Figures 3 & 4]

Daytime Sleepiness

Sleepiness evidenced a significant main effect [F(5,60)=7.26, p<.001] and a significant quadratic trend [F(1,12)=11.58, p=.005; see Figure 5]. ESS scores significantly increased from baseline to week 1 [4.95, SD=3.02 vs. 8.69, SD=4.96; p=.004, ES=.98], week 2 [9.08, SD=5.84; p=.006, ES=.92], and week 3 [7.85,

SD=5.8; *p*=.035, ES=.66]. There were no significant differences between ESS scores at baseline and week 4 (6.85, SD=5.18; *p*=.112) or between baseline and week 12 (3.80, SD=4.96, *p*=.652).

[Insert Figure 5]

PSG-defined Total Sleep Time (TST)

We next assessed the magnitude of change in PSG-TST, from the baseline PSG night (pre-treatment) relative to SRT acute implementation, and the extent to which TST varied across the three SRT lab nights (nights 1, 8, and 22). There was a significant main effect of time [$F(3,39)=27.03$, $p<.001$; see Figure 6]. Baseline TST was 393.6 minutes (SD=43.0), which decreased by approximately 90 minutes on the first night of SRT (302.4, SD=53.0; *p*<.001, ES=1.62), remaining significantly reduced at night 8 (315.6, SD=26.7; *p*<.001, ES=1.80) and night 22 (324.6, SD=34.6; *p*<.001, ES=1.60). TST exhibited a trend towards improving between night 8 and 22 (by approximately 22 minutes; *p*=.052, ES=.57).

[Insert Figure 6]

Discussion

CBT-I is widely regarded as the most effective treatment option for chronic insomnia. Similar to psychological therapies in other fields, CBT-I is promoted as a safe and adverse-effect-free intervention. Our clinical and research experience suggests that CBT components, particularly SRT, may be associated with some negative effects, but examination and evidence is lacking.[6,21] Understanding possible treatment-related adverse effects has important implications for patient care. In the present study, we aimed to quantify the impact of SRT on objectively-defined vigilance, daytime sleepiness and objective total sleep time.

The first thing to say is that SRT effectively improved the core symptoms of insomnia. That is, by week 4, diary ratings of SOL, WASO and SE had all improved relative to baseline (with corresponding large effects). Changes in sleep diary parameters were also reflected in reduced ratings of overall insomnia severity. These findings were maintained (or enhanced) at three months follow-up. Of course, our aim was not to test the effectiveness of SRT per se, but results from our (uncontrolled) work support the growing literature that SRT is an effective, single-component intervention.[15,16] Furthermore, improvements in sleep, coupled with reductions in diary-reported TIB during SRT – almost overlapping with prescribed sleep window times – suggests that patients followed the protocol faithfully.

Despite these post-treatment improvements in sleep continuity and insomnia severity, PVT performance was found to deteriorate during *acute* SRT implementation, reflected in a greater number of attentional lapses and slowed RT. To our knowledge, this is the first evidence that SRT (or any component of CBT-I) is associated with *objective performance impairment*. Performance was impaired on 3/5 assessment points for attentional lapses and 4/5 assessment points for reaction time, relative to baseline (moderate-to-large effects). By 3 months, performance had

returned to baseline levels. Whilst patients did not differ from good sleepers at baseline, consistent with meta-analytic data,[40] between-group effects started to emerge when SRT was initiated; with patients showing slowed RTs and increased lapses. That is, in this study sample and protocol, insomnia per se was not associated with impaired vigilance, but acute treatment was.

Deterioration in PVT performance was paralleled by increased daytime sleepiness as reflected in ESS scores. Patients reported significantly elevated ESS scores during weeks 1-3 of treatment (moderate-to-large effects). By 3 months, however, and similar to PVT performance, ESS scores had returned to baseline levels. A reduction in total sleep time is the most intuitive explanation for degraded performance and increased sleepiness during treatment. Comparing PSG nights, we observed a large reduction in TST by approximately 91 minutes on SRT night 1, 78 minutes on night 8 and 69 minutes on SRT night 22. Chronic sleep restriction protocols in healthy subjects, even with sleep curtailment of just 1.5 hours, reveal cumulative impairments in PVT performance over a 14-day period.[41,42] Although we were not able to asses vigilance or objective sleep on a daily basis, it is interesting that performance appears to follow a relatively linear (cumulative) decline throughout the acute phase of SRT, with impairments tending to be most pronounced on days 8, 21 and 22. It is also clear that PSG-defined TST is relatively stable over the three assessment nights (increasing by 22 minutes from night 1 to night 22), and the prescribed sleep window was extended by just 15 minutes over the entire four week treatment protocol (see Figure 2).

Our findings are difficult to compare with published literature because few studies have investigated the acute phase of insomnia treatment; instead, tending to focus on pre-to-post treatment outcomes. Previous work by our group[6,20] and others[17,25,43,44] provide both systematic and clinical evidence of treatment-related difficulties,

including self-reported sleepiness, cognitive impairment and implementation challenges, but longitudinal tracking of sleep and functioning is lacking. Treatment studies that have used PSG to assess sleep outcomes, pre-to-post CBT-I, have not found convincing evidence of change in TST[4] and, to our knowledge, no published study has examined the magnitude of TST/TIB reduction during acute implementation. However, inspection of published CBT-I trial data, where both objective (PSG) and subjective (sleep diary) baseline data are reported, indicates that TST discrepancies often range between 50 and 60 minutes[45-47] (indeed, in one study, as high as 83 minutes)[47]; and it is well known that a general objective-subjective sleep discrepancy exists in some patients with insomnia.[23,24,48] This discrepancy has important implications for sleep window calculation and the degree to which patients may be sleep restricted during, and possibly after, CBT treatment monitoring.

On this point, Morin and colleagues[49] reported that PSG-defined TST was *significantly reduced* (moderate to large effect) in the CBT treatment arm at 6 weeks (post-treatment), and Buysse et al.[50] reported *significant reductions* in actigraphy-defined TST relative to an information-only control group after four weeks of brief behavioral therapy (SRT+Stimulus Control Therapy). Thus, it would appear that TST reduction during CBT-I is likely the norm, rather than the exception, but the field lacks consistent (week-by-week) process data to answer this question definitively. Crucially, TST appears to return to at least baseline levels during follow-up PSG assessments,[46,47,49,51] suggesting that CBT exerts its therapeutic effect, at least in part, through correction or restoration of sleep-wake perception.[45] Priming sleep pressure through TST reduction may also be necessary to overcome cognitive arousal and consolidate sleep,[6,19,20,52] but these putative mechanistic routes require further experimental attention. Importantly, there exists the possibility that some patients - perhaps treatment non-responders - continue to implement SRT for a

prolonged period of time which, if associated with chronic sleep restriction, could have detrimental health effects.[53]

Limitations

Our findings must be interpreted within the context of several limitations. Principally, our sample size was small and we did not include an untreated (patient) control group. This limitation is partially mitigated through triangulation of methodologies (PSG, performance impairment, self-reported sleepiness), coupled with *normalised trajectories* of sleepiness and vigilance, at follow-up; giving us some confidence in our conclusions. Nevertheless, we cannot conclude with certainty that SRT was responsible for the observed effects. Recruitment of a group of untreated insomnia patients, a group receiving another CBT-I component or an inactive intervention should be considered in future research studies. We also realise that SRT is often introduced within the context of a full CBT-I package and so our results may not generalise to all CBT-based interventions. An important point to bear in mind is that SRT is commonly introduced in the second or third session of CBT-I protocols[54-57] and as such the sleep window may not be calculated based on pre-treatment diary values, but instead from sleep parameters measured *during* the first 2 weeks of CBT-I. This would potentially lead to longer sleep window prescriptions, because sleep may already be improving, than if the sleep window were based on pre-treatment data. However, this remains an empirical question that could be addressed through re-analysis of existing datasets.

A related point is that in-lab SRT, due to increased monitoring and strict scheduling of the sleep window, may have led to greater adherence and possibly enhanced impairment. In practice, it is likely that patients tend to modify the duration and timing of the sleep window (in the home environment) based on individual preferences and ability to function. Nevertheless, it is important to understand the full impact of SRT

when patients adhere faithfully to the prescribed programme. Convergence of diary-recorded TIB and prescribed sleep window durations (see Figure 2), would support this conclusion.

In the present study our intention was to isolate SRT, since this intervention has been found to be very effective (when used in single-component interventions), yet difficult to implement[43] and our early work suggested the possibility of treatment-related impairment.[6,20] It is worth pointing out however, that stimulus control therapy may also be associated with acute sleep loss, and possible impairment. Future work should attempt to characterise the magnitude and time-course of stimulus-control-related impairment (in isolation) as well as in combination with SRT, since many programmes combine these two behavioral interventions.[50,54-58]

Finally, because we did not assess performance beyond three weeks (or sleepiness beyond 4 weeks) we cannot determine exactly when vigilance started to normalise. From ESS data it would appear that, by week 4, sleepiness was beginning to weaken, but future work should profile daytime performance (including objective measures of sleep debt e.g. multiple sleep latency test) for several weeks beyond active treatment/monitoring.

Clinical implications

We think it reasonable, even mandatory, to reflect on what might be the clinical impact of our results. Assuming there is a “necessary pain to achieve gain” with SRT, clinicians should emphasise that CBT-I may negatively affect vigilance levels, and those that are identified as excessively sleepy, pre-treatment, or appear to report gross subjective-objective sleep discrepancies, should be assigned a more liberal sleep window. There currently exists variation in the minimum TIB sleep window used in SRT, as well as variation in TIB calculation and titration method.[18] The field

should aim to reach a consensus on what is the recommended SRT protocol as well as any required modifications for specific populations (cancer, depression, bipolar disorder, co-morbid chronic pain).[56,59] Consensus should be guided by experimental manipulations, which are needed to reveal treatment mechanisms[6,20] and to provide empirical data on the 'dose' of sleep restriction required to bring about treatment response. Related to this, the suitability and feasibility of using objective measures to guide sleep-window generation and titration should also be considered.

Finally, we realise that some labs and therapists set a minimum TIB as low as 4.5 hours.[17,59] Indeed, had we set this as our minimum TIB three participants would have been assigned a 4.5hr sleep window and another patient, 4.75 hrs. It remains possible, indeed likely, that minimum TIB as low as 4.5hrs may lead to impairment greater than that observed in the present study. Going forward, the standardisation of SRT procedures, often regarded as the most effective ingredient of CBT-I interventions, should be considered a research and clinical priority for BSM specialists.

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Table 1: Demographic and sleep characteristics for PI patients and GS controls.

	GS (n=15)	PI (n=16)
Age (SD)	47.1 (10.5)	47.1 (10.8)
Gender % (F:M)	66.7/33.3	62.5/37.5
ISI	-	17.8 (2.8)
HADS-A	2.1 (2.3)	6.4** (4.0)
HADS-D	0.9 (1.6)	4.0** (2.2)
SOL (mins)	7.1 (7.9)	38.8** (32.4)
WASO (mins)	6.8 (11.2)	62.6** (58.8)
No. Awak	1.2 (1.4)	2.1# (1.3)
TST (mins)	449.9 (41.7)	338.7**(57.4)
TIB (mins)	503.1 (51.0)	490.6 (66.8)
SE (%)	89.9 (6.3)	69.3** (12.3)
SQ (0-4)	3.3 (0.4)	1.7** (0.6)

ISI=Insomnia Severity Index; HADS-A/D=Hospital Anxiety and Depression Scale; SOL=sleep-onset latency; WASO=wake-time after sleep-onset; TST=total sleep time; TIB=time-in-bed; SE=sleep efficiency; SQ=sleep quality

**p<.01, #p<.10 for group comparison

Figure 1: schematic presentation of study protocol.

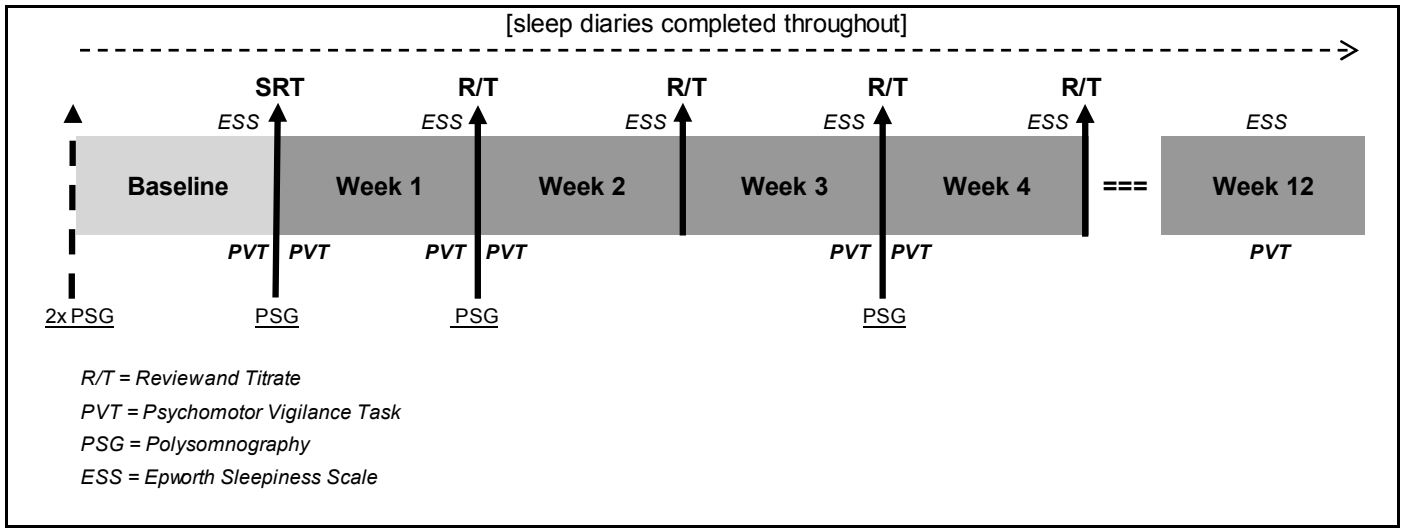


Figure 2: Descriptive profiles of mean (SE) time-in-bed sleep window prescriptions (weeks 1-4) and sleep-diary reported time-in-bed (TIB) over the course of SRT protocol.

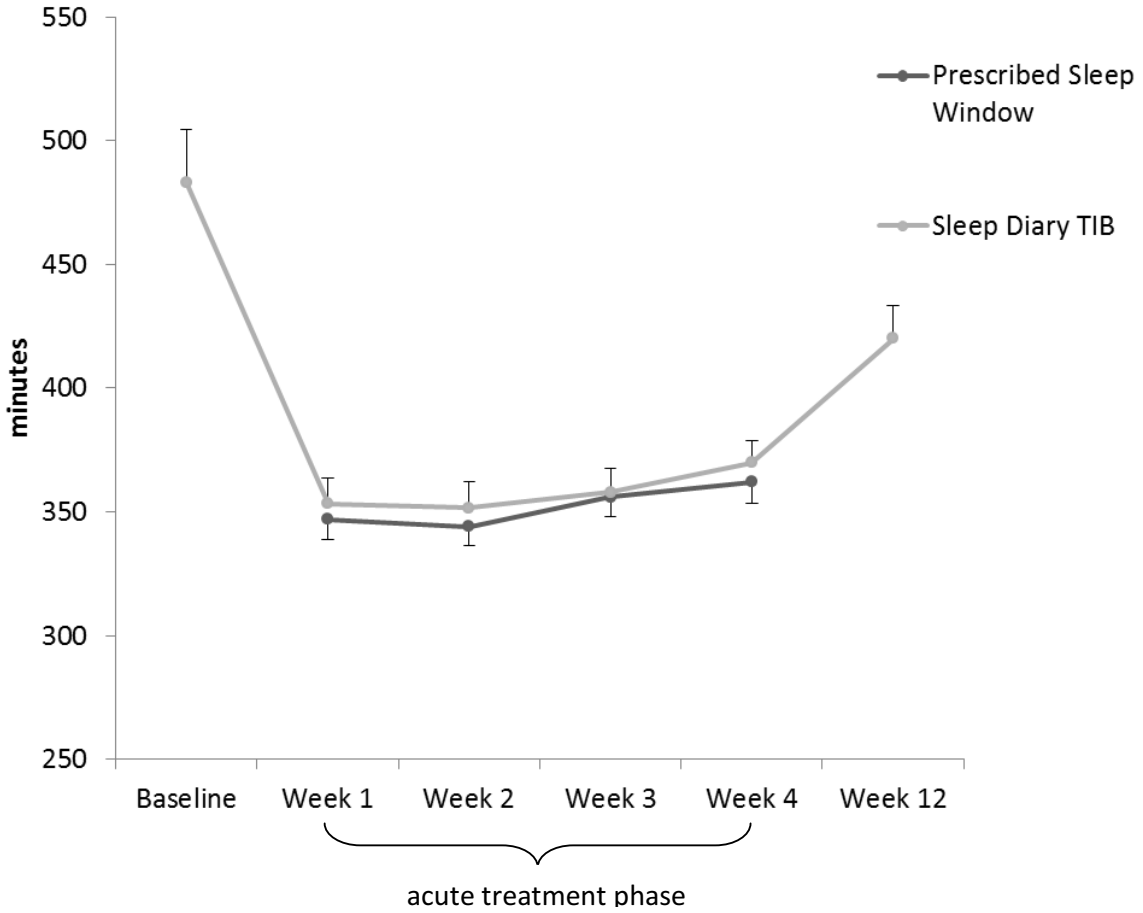


Figure 3: Mean (±SE) number of attentional lapses (RTs > 500 msec.) over the course of SRT treatment [**$p \leq .01$, *$p < .05$ for comparison with baseline].

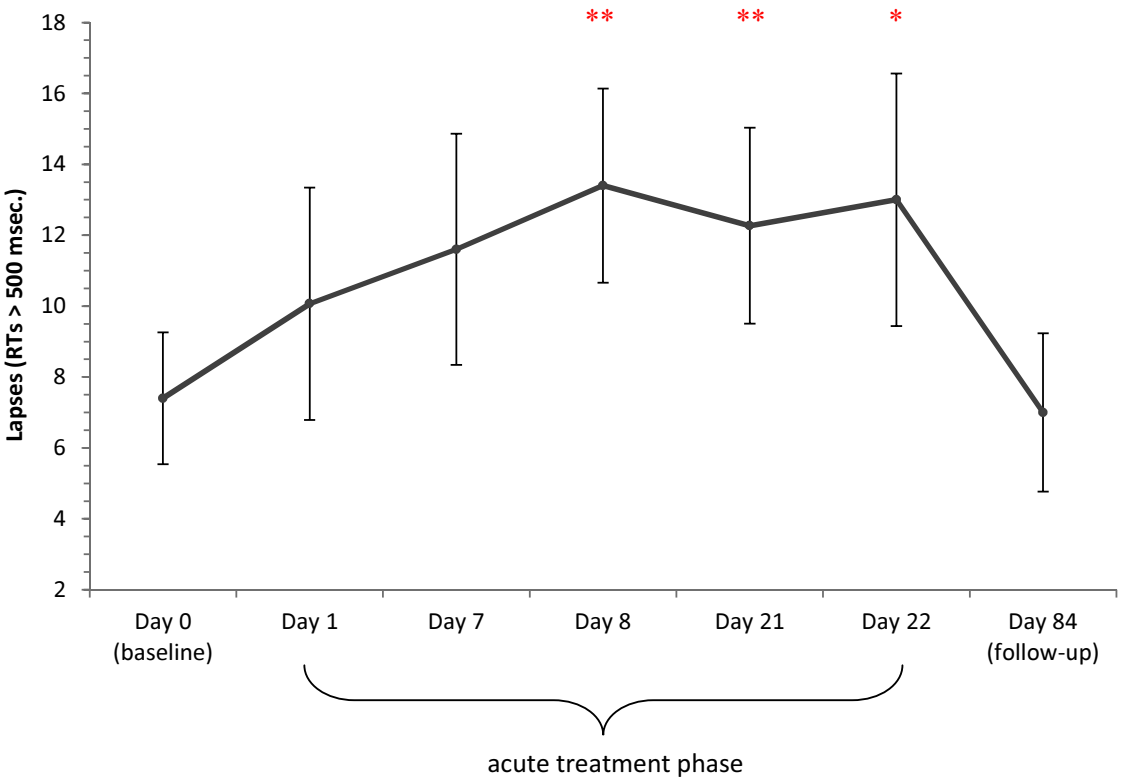


Figure 4: PVT RT (1/mean RT ± SE) over the course of SRT treatment. Note, lower scores indicate a slowing in RT. [**$p \leq .01$, *$p < .05$ for comparison with baseline]

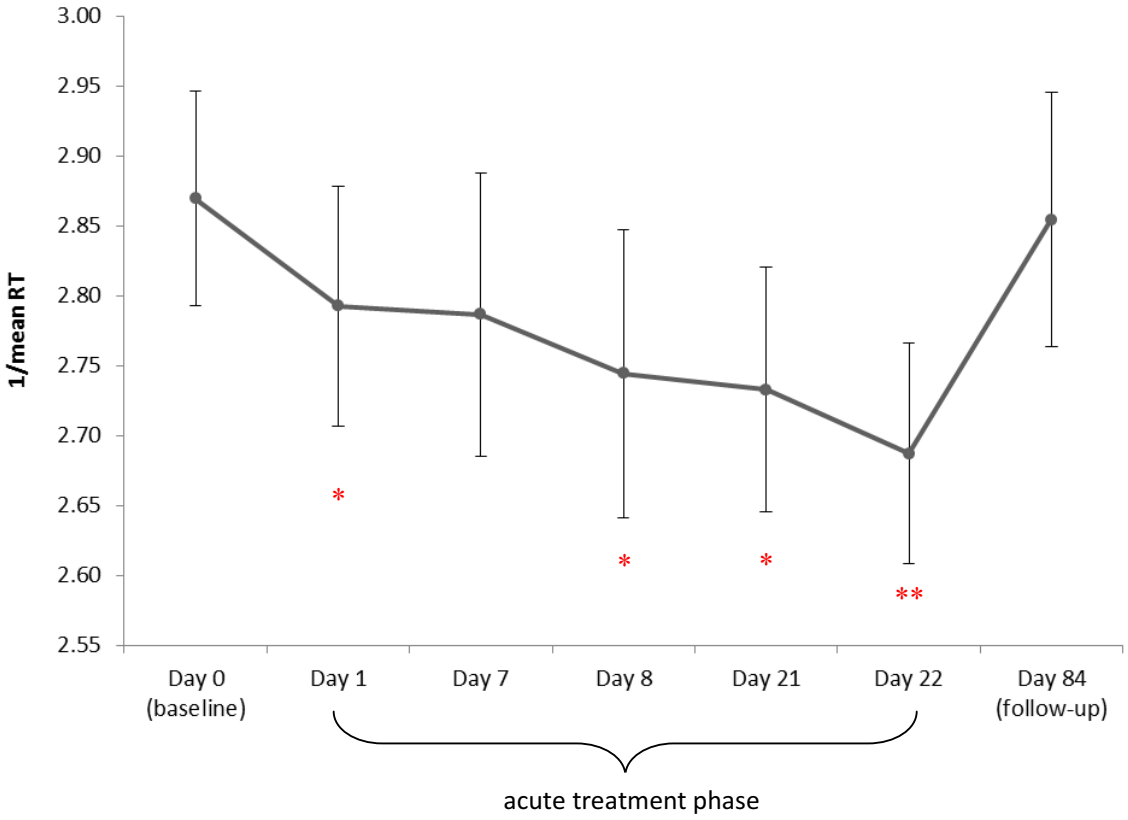


Figure 5: Mean (±SE) ESS scores throughout treatment weeks. [**p<.01, *p<.05 for comparison with baseline]

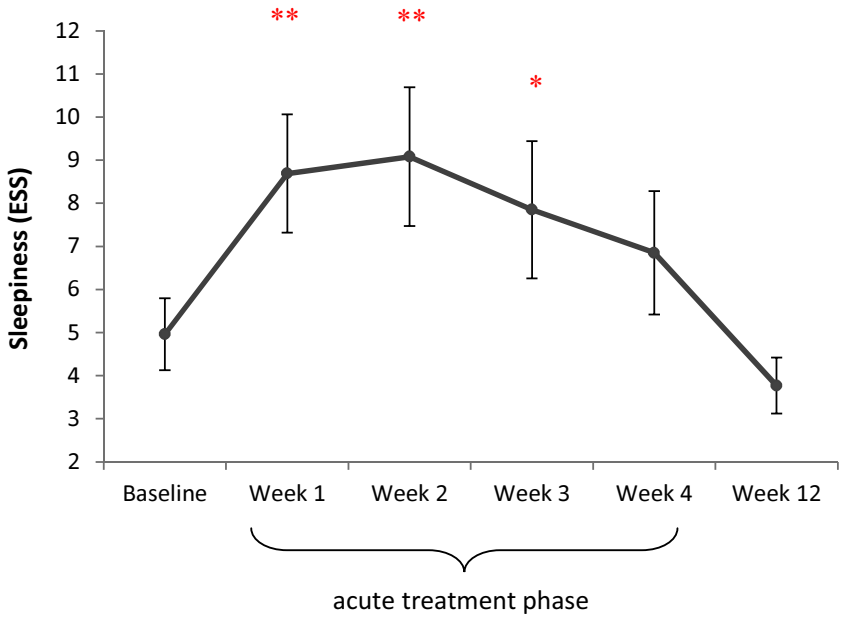
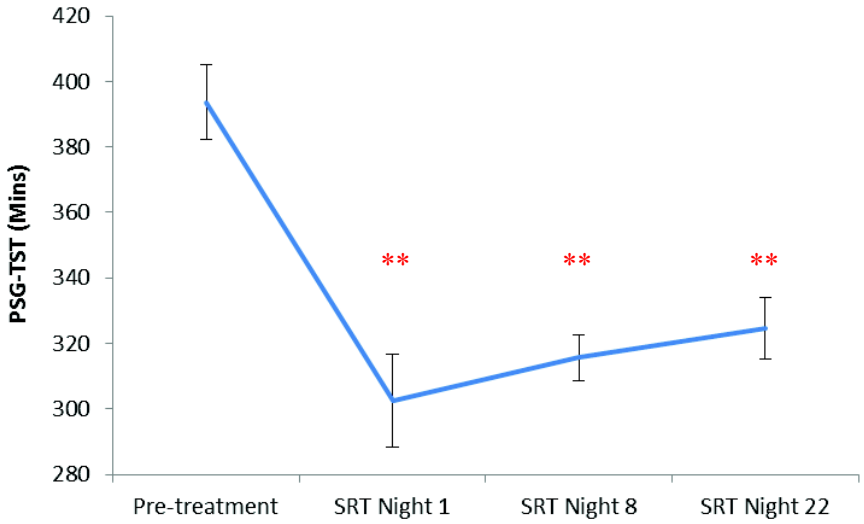


Figure 6: Mean (±SE) PSG-determined TST (mins) pre-treatment and during SRT. [**p<.001 for comparison with baseline]



References

1. Morin CM, Hauri PJ, Espie CA, Spielman AJ, Buysse DJ, Bootzin RR. Nonpharmacologic treatment of chronic insomnia. An American Academy of Sleep Medicine Review. SLEEP 1999;22(8):1134-56.
2. Morin CM, Bootzin RR, Buysse DJ, Edinger JD, Espie CA, Lichstein KL. Psychological and behavioral treatment of insomnia: update of the recent evidence (1998-2004). SLEEP 2006;29:1398-414.
3. Morin CM, Benca R. Chronic insomnia. Lancet 2012;379(9821):1129-41.
4. Riemann D, Perlis ML. The treatments of chronic insomnia: a review of benzodiazepine receptor agonists and psychological and behavioral therapies. Sleep Med Rev 2009;13(3):205-14.
5. Nutt DJ, Sharpe M. Uncritical positive regard? Issues in the efficacy and safety of psychotherapy. J Psychopharmacol 2008;22(1):3-6.
6. Kyle SD, Morgan K, Spiegelhalder K, Espie CA. No pain, no gain: an exploratory within-subjects mixed-methods evaluation of the patient experience of sleep restriction therapy (SRT) for insomnia. Sleep Med 2011;12(8):735-47.
7. Vermeeren A, Coenen A. Effects of the use of hypnotics on cognition. Prog Brain Res 2011;190:89.
8. Kripke DF. Chronic hypnotic use: deadly risks, doubtful benefit. Sleep Med Rev 2000;4(1):5-20.
9. Kripke DF, Langer RD, Kline LE. Hypnotics' association with mortality or cancer: a matched cohort study. BMJ Open 2012;2(1):e000850.
10. Glass J, Lanctot KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. BMJ 2005;331(7526):1169.

11. Krystal AD. A compendium of placebo-controlled trials of the risks/benefits of pharmacological treatment for insomnia: The empirical basis for U.S. clinical practice. Sleep Med Rev 2009;16:265-274.
12. Linden M. How to define, find and classify side effects in psychotherapy: from unwanted events to adverse treatment reactions. Clinical Psycho Psychother 2012; doi: 10.1002/cpp.1765.
13. Berk M, Parker G. The elephant on the couch: side-effects of psychotherapy. Aust N Z J Psychiatry 2009;43(9):787-94.
14. Lilienfeld SO. Psychological treatments that cause harm. Perspectives on Psychol Sci 2007; 2: 53-70.
15. Epstein DR, Sidani S, Bootzin RR, Belyea MJ. Dismantling multicomponent behavioral treatment for insomnia in older adults: a randomized controlled trial. SLEEP 2012;35(6):797-805.
16. Taylor DJ, Schmidt-Nowara W, Jessop CA, Ahearn J. Sleep Restriction Therapy and hypnotic withdrawal versus sleep hygiene education in hypnotic using patients with insomnia. J Clin Sleep Med 2010; 6(2):169-175.
17. Spielman AJ, Saskin P, Thorpy MJ. Treatment of chronic insomnia by restriction of time in bed. SLEEP 1987;10(1):45-56.
18. Spielman AJ, Yang C-M, Glovinsky PB. Sleep Restriction Therapy. In: Perlis ML, Aloia M, Kuhn B. (Eds.). Behavioral Treatments for Sleep Disorders: A Comprehensive Primer of Behavioral Sleep Medicine Interventions. Academic Press, 2010.
19. Pigeon WR, Perlis ML. Sleep homeostasis in primary insomnia. Sleep Med Rev 2006;10(4):247-54.
20. Miller CB, Kyle SD, Marshall NS, Espie CA. Ecological momentary assessment of daytime symptoms during sleep restriction therapy for insomnia. J Sleep Res 2013. DOI: 10.1111/jsr.12024

21. Morin CM, Espie CA. Insomnia: A clinician's guide to assessment and treatment: Springer, 2003.
22. Carskadon MA, Dement WC, Mitler MM, Guilleminault C, Zarcone VP, Spiegel R. Self-reports versus sleep laboratory findings in 122 drug-free subjects with complaints of chronic insomnia. Am J Psychiatry 1976;133(12):1382-8.
23. Manconi M, Ferri R, Sagrada C, et al. Measuring the error in sleep estimation in normal subjects and in patients with insomnia. J Sleep Res 2010;19(3):478-86.
24. Edinger JD, Krystal A. Subtyping primary insomnia: is sleep state misperception a distinct clinical entity? Sleep Med Rev 2003;7(3):203-214.
25. Perlis ML, Smith MT, Orff H, et al. The effects of modafinil and cognitive behavior therapy on sleep continuity in patients with primary insomnia. SLEEP 2004;27(4):715-25.
26. Wilson SJ, Nutt DJ, Alford C, et al. British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders. J Psychopharmacol 2010;24(11):1577-601.
27. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59: 22-33.
28. Edinger JD, Bonnet MH, Bootzin RR, et al. Derivation of research diagnostic criteria for insomnia: report of an American Academy of Sleep Medicine Work Group. SLEEP 2004;27(8):1567-96.
29. Rechtshaffen A, Kales A. A manual of standardized terminology. Techniques and Scoring System for Sleep Stages of Human Subjects. NIH, US Govt. Printing Office. Washington, DC. Publication, 1968.

30. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67(6):361-70.
31. Morin C. Insomnia: psychological assessment and management. Guilford Press. New York 1993.
32. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. SLEEP 1991;14(6):540-5.
33. Jackson ML, Croft RJ, Kennedy GA, Owens K, Howard ME. Cognitive components of simulated driving performance: sleep loss effects and predictors. Accid Anal Prev 2013; 50: 438-444.
34. Sunwoo BY, Jackson N, Maislin G, Gurubhagavatula I, George CF, Pack AI. Reliability of a single objective measure in assessing sleepiness. SLEEP 2012; 35: 149-158.
35. Altena E, Van Der Werf YD, Strijers RL, Van Someren EJ. Sleep loss affects vigilance: effects of chronic insomnia and sleep therapy. J Sleep Res 2008;17(3):335-43.
36. Van Der Werf Y, Altena E, Vis J, Koene T, Van Someren E. Reduction of nocturnal slow-wave activity affects daytime vigilance lapses and memory encoding but not reaction time or implicit learning. Prog Brain Res 2011;193:245.
37. Basner M, Dinges DF. Maximizing sensitivity of the psychomotor vigilance test (PVT) to sleep loss. SLEEP 2011;34(5):581-91.
38. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. 1988; Hillsdale, NJ: Erlbaum.
39. Crawford JR, Henry JD, Crombie C, Taylor EP. Normative data for the HADS from a large non-clinical sample. Br J Clin Psychol 2001; 40(4):429-434.

40. Fortier-Brochu E, Beaulieu-Bonneau S, Ivers H, Morin CM. Insomnia and daytime cognitive performance: A meta-analysis. Sleep Med Rev 2012;16: 83-94.
41. Van Dongen HP, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. SLEEP 2003;26(2):117-29.
42. Belenky G, Wesensten NJ, Thorne DR, et al. Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-response study. J Sleep Res 2003;12(1):1-12.
43. Vincent N, Lewycky S, Finnegan H. Barriers to engagement in sleep restriction and stimulus control in chronic insomnia. J Consult Clin Psychol 2008;76(5):820-8.
44. Hoelscher TJ, Edinger JD. Treatment of sleep-maintenance insomnia in older adults: Sleep period reduction, sleep education, and modified stimulus control. Psychol Aging 1988;3(3):258.
45. Lund HG, Rybarczyk BD, Perrin PB, Lesczsyn D, Stepanski E. The discrepancy between subjective and objective measures of sleep in older adults receiving CBT for comorbid insomnia. J Clin Psychol 2012 doi: 10.1002/jclp.21938
46. Morin CM, Colecchi C, Stone J, Sood R, Brink D. Behavioral and pharmacological therapies for late-life insomnia: a randomized controlled trial. JAMA 1999; 281(11):991-9.
47. Sivertsen B, Omvik S, Pallesen S, et al. Cognitive behavioural therapy vs zopiclone for treatment of chronic primary insomnia in older adults. JAMA 2006; 295:2851-2858.
48. McCall C, McCall WV. Comparison of actigraphy with polysomnography and sleep logs in depressed insomniacs. J Sleep Res 2012;21(1):122-7.

49. Morin CM, Vallières A, Guay B, et al. Cognitive behavioral therapy, singly and combined with medication, for persistent insomnia. JAMA 2009;301(19):2005-15.
50. Buysse DJ, Germain A, Moul DE, et al. Efficacy of brief behavioral treatment for chronic insomnia in older adults. Arch Intern Med 2011;171(10):887.
51. Edinger JD, Wohlgemuth WK, Radtke RA, Marsh GR, Quillian RE. Cognitive behavioural therapy for treatment of chronic primary insomnia: a randomized controlled trial. JAMA 2001; 258: 1856-64.
52. Krystal A D, Edinger JD. Sleep EEG predictors and correlates of the response to cognitive behavioral therapy for insomnia. SLEEP 2010; *33*(5): 669-677.
53. Reynolds CF, Serody L, Okun ML, et al. Protecting sleep, promoting health in later life: a randomized clinical trial. Psychosom Med 2010;72(2):178-86.
54. Espie CA, Inglis SJ, Tessier S, Harvey L. The clinical effectiveness of cognitive behaviour therapy for chronic insomnia: implementation and evaluation of a sleep clinic in general medical practice. Behav Res Ther 2001;39(1):45-60.
55. Espie CA, MacMahon KM, Kelly HL, et al. Randomized clinical effectiveness trial of nurse-administered small-group cognitive behaviour therapy for persistent insomnia in general practice. SLEEP 2007; 30: 574-584.
56. Espie CA, Fleming L, Cassidy J, et al. Randomized controlled clinical effectiveness trial of cognitive behavior therapy compared with treatment as usual for persistent insomnia in patients with cancer. J Clin Oncol 2008;26(28):4651-8.
57. Espie CA, Kyle SD, Williams C, et al. A randomized, placebo-controlled trial of online cognitive behavioral therapy for chronic insomnia disorder delivered via an automated media-rich web application. SLEEP 2012;35(6):769-81.
58. Troxel WM, Germain A, Buysse DJ. Clinical Management of Insomnia with Brief Behavioral Treatment (BBTI). Behav Sleep Med 2012;10(4):266-79.

59. Perlis ML, Jungquist C, Smith MT, Posner D. Cognitive behavioral treatment of insomnia: A session-by-session guide: Springer, 2005.