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RESEARCH ARTICLE

A blended eHealth intervention for insomnia following acquired brain injury: a randomised controlled trial

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Summary

The high prevalence and severe consequences of poor sleep following acquired brain injury emphasises the need for an effective treatment. However, treatment studies are scarce. The present study evaluates the efficacy of blended online cognitive behavioural therapy for insomnia (eCBT-I) developed specifically for people with acquired brain injury. In a multicentre prospective, open-label, blinded end-point randomised clinical trial, 52 participants with insomnia and a history of a stroke or traumatic brain injury were randomised to 6 weeks of guided eCBT-I or treatment as usual, with a 6-week follow-up. The primary outcome measure was the change in insomnia severity between baseline and after treatment, measured with the Insomnia Severity Index. Results showed that insomnia severity improved significantly more with eCBT-I than with treatment as usual compared to baseline, both at post-treatment (mean [SEM] 4.0 [1.3] insomnia severity index points stronger decrease, $d = 0.96$, $p < 0.003$) and at follow-up (mean [SEM] 3.2 [1.5] insomnia severity index points, $d = -0.78$, $p < 0.03$). In conclusion, our randomised clinical trial shows that blended CBT is an effective treatment for insomnia, and feasible for people with acquired brain injury, regardless of cognitive and psychiatric complaints. Online treatment has major advantages in terms of availability and cost and may contribute to the successful implementation of insomnia treatment for people with acquired brain injuries.

KEYWORDS
brain injuries, cognitive behavioural therapy, sleep, stroke, telemedicine, traumatic

Registration-URL: https://www.trialregister.nl.Unique identifier: NL6895.

INTRODUCTION

Insomnia following acquired brain injury is highly prevalent. Up to a third of all patients with a stroke (Leppavuori et al., 2002) or traumatic brain injury (TBI) (Ouellet et al., 2015) meet Diagnostic and Statistical Manual of Mental Disorders, fourth Edition (DSM-IV) criteria for insomnia disorder, including trouble falling asleep, staying asleep and waking up early. Insomnia is associated with health problems, mood problems, work absenteeism, and a reduced quality of life (Daley et al., 2009). In people with brain injury, insomnia is also associated with more severe physical disabilities, cognitive impairments, anxiety, depression, and pain (Bassetti & Hermann, 2011; Leppavuori et al., 2002; Ouellet et al., 2015). Moreover, insomnia may impede the recovery process (Duss et al., 2017). The high prevalence and severe consequences of insomnia following brain injury emphasises the need for an effective treatment.

Cognitive behavioural therapy for insomnia (CBT-I) is the first-choice treatment, and has impressive efficacy in populations with insomnia (Riemann et al., 2017; Trauer et al., 2015), whether or not insomnia occurs comorbid with another disorder (Johnson et al., 2016; Jungquist et al., 2010; Taylor & Pruiksma, 2014). Our review on non-pharmacological treatment for insomnia following acquired brain injury (Ford et al., 2020a) and a more recent randomised controlled trial (RCT) (Ymer et al., 2021) suggest that CBT-I is effective for people with brain injury as well. A main barrier for large-scale implementation is that CBT-I is not easily available (Baglioni et al., 2020). For example, Ouellet et al. found that almost 60% of the participants with insomnia out of a sample of 452 participants with TBI were untreated (Ouellet et al., 2006).

Online CBT-I (eCBT-I) could offer a more accessible, cheaper alternative and has demonstrated efficacy in adults with insomnia (Seyffert et al., 2016; Zachariae et al., 2016). Also, with better access to treatment, better utilisation of trained therapists, reduced time investment and cost (Espie, 2009), the eCBT-I has additional benefits. Online treatment for people with brain injury, and cognitive deficits in particular, gives the opportunity to reread the information and the freedom to follow the highly structured treatment at their own time and pace. However, adherence to treatment may be a problem. Studies in the general population showed an average drop-out rate of 24.7% for eCBT-I (Zachariae et al., 2016). Personal support and feedback are found to improve adherence and decrease the risk of drop-out (Andersson et al., 2009). As far as we know, only one study evaluated eCBT-I for insomnia following brain injury. Theadom et al. compared a completely online eCBT-I with an education only group in a RCT with 24 participants and found significant improvement in sleep quality after treatment with moderate effect size (Cohen's $d = 1.17$), no follow-up measurement was conducted (Theadom et al., 2017).

The present study compared a newly developed blended eCBT-I with treatment as usual (TAU) in patients with insomnia and TBI or stroke, to evaluate the added value to standard rehabilitation care. TAU does not address sleep. The eCBT-I was blended, including both online and face-to-face sessions, combining the strength of both treatment delivering methods. The primary aim was to evaluate the efficacy of eCBT-I in reducing insomnia severity post-treatment and at the 6-week follow-up in patients with insomnia comorbid to stroke or TBI, as compared to TAU. We hypothesised that eCBT-I would reduce insomnia after treatment more than TAU does, compared to baseline. The secondary hypothesis was that eCBT-I would also improve fatigue, cognitive functioning, emotional well-being, and societal participation.

METHODS

Study design

The RCT used a multicentre, prospective, randomised, open-label, blinded end-point study design (PROBE [Prospective Randomised Open, Blinded End-point]) (Hansson et al., 1992) to compare eCBT-I with TAU (Trial, NL6895; NTR7082). After informed consent, enrolled participants completed measurements at baseline and were randomised to the eCBT-I or TAU group. Randomisation was done by a research-randomiser program (www.randomizer.org) using permuted blocks to balance participants equal to both groups within centres. All participants received standard rehabilitation care for various complaints, which did not address insomnia. As complaints differed between persons, interventions differed as well. TAU included psychotherapy, therapy aimed at cognitive functioning, physiotherapy, fitness, occupational therapy, and social work (Table S1). The therapy dosage depended on the different needs and capacity of participants. The variation in rehabilitation care between participants is expected to be similar for both groups and will be registered at follow-up. The TAU group was offered eCBT-I after the follow-up measurement. All assessments were self-completed, administered online (sleep diary) or at home (questionnaires). Assessments were performed at baseline (week 1), post-treatment after the 6-week intervention period (week 7), and at a 6-week follow-up (week 14). See Table S2 for an overview of all measurements at all time-points. The relative anonymity of (online) self-completed assessments, instead of in-person, has been suggested to reduce social desirability (Richman et al., 1999). Data collectors were blinded to treatment allocation. The total duration of participation was 14 weeks. The study received ethics approval (Amsterdam University Medical Center, protocol 2017-223) and was conducted in accordance with the standards of the Declaration of Helsinki. A more detailed description of the study protocol was published elsewhere (Ford et al., 2020b).

Participants

In the Netherlands, patients can be referred to outpatient rehabilitation centres by their general practitioner and costs are covered by all healthcare insurance companies (Ribbers, 2007). Participants were recruited from January 2018 to December 2020 from four outpatient rehabilitation centres spread over the Netherlands. Participants were eligible if diagnosed with stroke or TBI (confirmed by data from computed tomography or magnetic resonance imaging in the medical record) and insomnia disorder according to DSM-5 criteria (confirmed by first author), Insomnia Severity Index

(ISI) score of ≥10, aged ≥18 years, and capable of using the internet. Capability to use the internet was sufficient if a participant was able to use an email program and a smartphone or could receive help of a close relative. Main exclusion criteria were a diagnosis of untreated sleep apnea, current or expected treatment with a main focus on fatigue or sleep during the study, and unstable medication regimens. Participants were excluded from the study if they had a psychiatric or medical condition that was unstable and required treatment first. Users of sleep medication were encouraged to finish medication before enrolment or to keep intake stable during the study period.

Intervention

The eCBT-I was based on standard CBT-I and adapted to brain injury, both with respect to content and the way of conveying information. The eCBT-I was available on the Mind district eHealth platform and included the following behavioural and cognitive techniques: sleep hygiene education, stimulus control, sleep restriction, cognitive restructuring, activation, relaxation, fatigue and stress management (Table S3). The eCBT-I comprised six guided weekly online sessions, combined with two face-to-face sessions, to optimise treatment adherence and to coach the patients to use the online tool, all guided by a registered healthcare psychologist trained in eCBT-I. Participants were asked to use a smartphone diary app for daily reports of sleep. Adherence was monitored by the online assignments done.

Outcomes

Sleep outcome measures

The primary outcome was the change in insomnia severity measured on the ISI after treatment as stated in our protocol paper (Ford et al., 2020b), which was a small adjustment to the trial registration (Trial, NL6895; NTR7082). The total score on the ISI ranges from 0 ("no insomnia") to 28 ("severe insomnia"). A cut-off of 10 indicates a clinical level of insomnia (Morin et al., 2011). The minimal clinically important difference, which indicates the minimal difference to be clinically significant, is a reduction of 6 points (Yang et al., 2009). Secondary sleep outcome measures included overall sleep quality assessed with the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) and subjective sleep features derived from the sleep diary app.

Other outcome measures

Fatigue was assessed with the Dutch Multifactor Fatigue Scale (DMFS) (Visser-Keizer et al., 2015); anxiety and depression with the 14-item Hospital Anxiety and Depression Scale (HADS) (Spinhoven et al., 1997); subjective cognitive functioning with the Cognitive Failure Questionnaire (CFQ) (Ponds et al., 2006); and societal participation after rehabilitation with the Utrecht Scale for Evaluation of Rehabilitation – Participation (USER-P) covering three aspects of societal participation: frequency of participation, restriction in participation, and satisfaction with participation (Van der Zee et al., 2010).

Sample size

Calculation of the required sample size using G*Power (Faul et al., 2007) with two repeated measures and an estimated intraclass correlation coefficient of 0.54, indicated that 48 completers would provide (2×24), at a significance of alpha $= 0.05$, sufficient power (1-beta $= 0.80$) for a minimal detectable time-by-group interaction effect of $f = 0.20$ (small to moderate).

Data analysis

Data analyses were performed with the Statistical Package for the Social Sciences (SPSS) version 26 (IBM; Armonk, NY, USA) and MLwiN 2.31(Rasbash et al., 2009). The demographic and injury-related variables and the clinical characteristics were compared with independent *t* tests, chi-square tests, and the Mann–Whitney *U* test, as appropriate. To accommodate likely occasional missing days or measures, the groups were compared on primary and secondary outcomes with mixed-effects models. This model enables the inclusion of participants with one measurement only, lends itself well for intention-to-treat (ITT) analysis, and properly accounts for correlation between repeated measurements on the same participant (Gueorguieva & Krystal, 2004).

Questionnaire measures were analysed using three-level random intercept mixed effect models with pre-, post- and follow-up observations nested within subjects nested within centre (e.g., $ISI_{ijk} = ß_{0ijk} + ß_1{}^*\text{CBT-I\_group}_{jk} + ß_2{}^*\text{Time}_{ijk} + ß_3{}^*\text{CBT-I\_group}_{jk}{}^*\text{Time}_{ijk}$, where subscripts indicated *i*th time point in the *j*th participant in centre *k*). Diary measures were analysed using four-level random intercept mixed-effect models with individual nights nested within pre-, post- and follow-up observations nested within subjects nested within centre (e.g., $SE_{ijkl} = ß_{0ijk} + ß_1{}^*\text{CBT-I\_group}_{kl} + ß_2{}^*\text{Time}_{jkl} + ß_3{}^*\text{CBT-I\_group}_{kl}{}^*\text{Time}_{jkl}$, where subscripts indicate *i*th night within the *j*th time point in the *k*th participant in centre *l*). A log transformation was used for sleep onset latency and time since injury, as these variables were not normally distributed. In all analyses, the effect of interest was the group by time effect, where separate models were run for changes from baseline (week 1) to post-treatment (week 7) and for changes from baseline to follow-up (week 14). Significance was evaluated using the Wald test *z* statistic that results from the ratio of the estimated effect size and its standard error. Cohen's *d* treatment effect sizes were estimated using the pooled pre-test standard deviations (SDs) according to Morris (Morris, 2008) Cohen's *d* of 0.2–0.5 is considered a "small" effect size, 0.5–0.8 represents a "medium" effect size, and ≥0.8 a "large" effect size (Sawilowsky, 2009). Ancillary mixed-effect models explored whether treatment efficacy, that is, the time-by-treatment effect, is modified by time since brain injury and by diagnosis (stroke

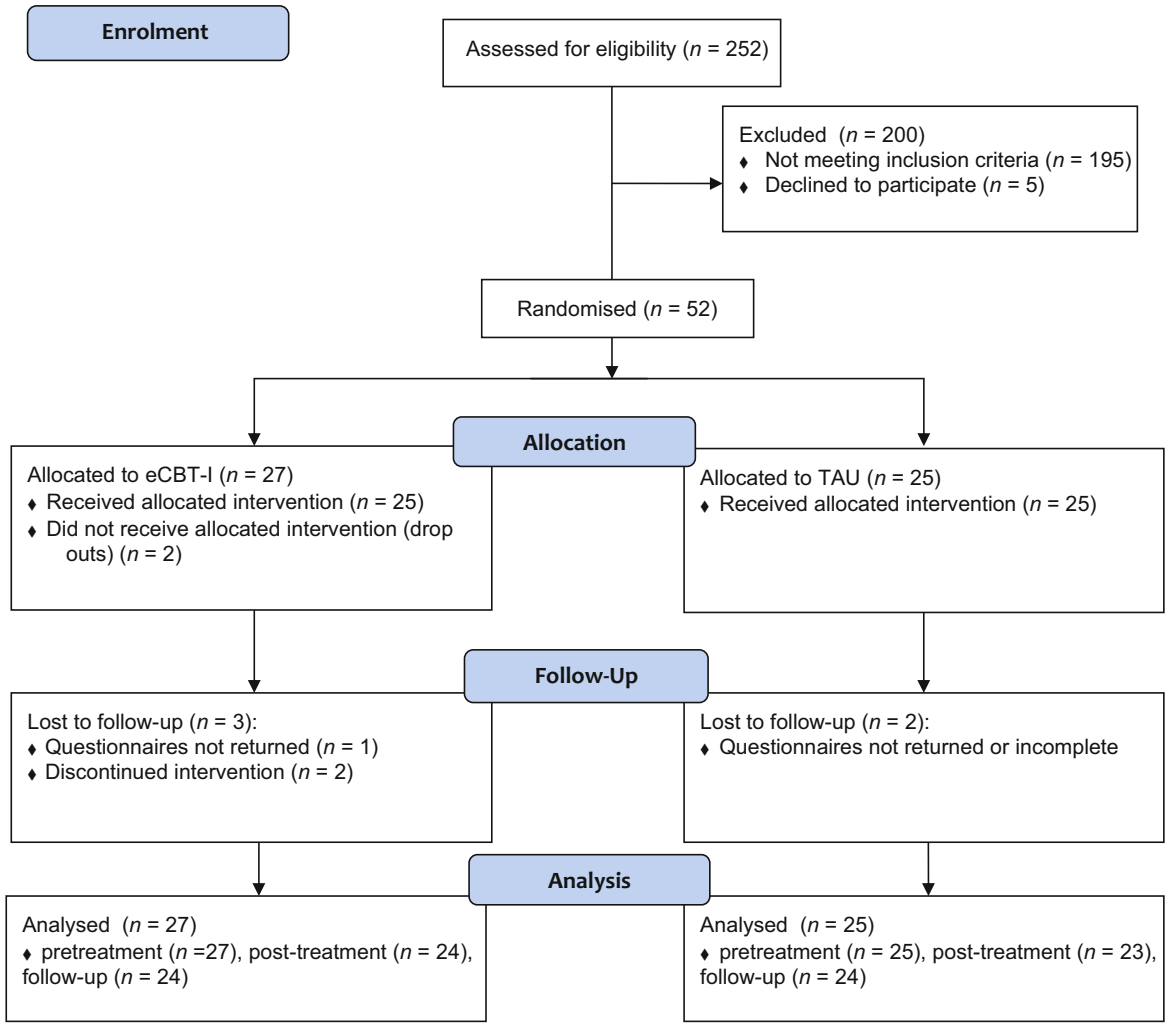

FIGURE 1 Flow of participants through enrolment, randomisation and follow-up in the study (CONSORT [CONsolidated Standards of Reporting Trials] 2010). eCBT-I, blended online cognitive behavioural therapy for insomnia; TAU, treatment as usual

versus TBI). The first model added terms for time since brain injury and its interactions with group, with time and with group-by-time, where the latter term is the treatment effect modification of interest. Likewise, the second model added terms for the dummy-coded diagnosis and its interactions.

As clinical improvement and remission is an important outcome of treatment, the number and percentage of participants that have improved (reduction of ≥6 points on the ISI) (Yang et al., 2009) and recovered (ISI score of <10) were compared between groups at post-treatment and at the follow-up with chi-square tests. For all statistical tests, significance was set at $p \leq 0.05$.

RESULTS

Recruitment

Of 252 patients screened for eligibility, 52 were randomised, with 27 allocated to the eCBT-I group and 25 to the TAU group (Figure 1). Of the 27 participants in the eCBT-I group, 25 completed all sessions and online assignments. Two participants of the eCBT-I group withdrew prior to completing the study as daily sleep diary measurements were too much of a burden (one) or referral to psychiatry for comorbidity was necessary (one). Data of five participants were missing or incomplete at post-treatment and/or follow-up (eCBT-I, three; TAU, two), ITT analyses were performed using available data.

Participants

There were no statistically significant group differences on demographic and clinical characteristics of participants at baseline (Table 1). The median (range) age of participants was 54 (22–79) years, 18 were diagnosed with TBI and 34 with stroke (see Supplementary Table S4 for more specified injury characteristics). The median time since injury was 17 months (range between 2 months and 49 years), and the median self-reported insomnia duration was 20 months (range between 3 months and 49 years). Formal diagnostics of sleep apnea

TABLE 1 Demographic characteristics and relevant clinical features

Characteristic	eCBT-I ($n = 27$)	TAU ($n = 25$)	Total ($n = 52$)	p
Demographic				
Age, years mean (SD)*	53 (14)	56 (16)	54 (14)	0.49
Gender (female), *n* (%)	15 (56)	17 (68)	32 (61.5)	0.36
Education score, median (range)†	6 (2–7)	5 (3–7)	6 (2–7)	0.30
Working, *n* (%)	15 (56)	10 (40)	25 (48)	0.26
Clinical				
Type of injury, *n* (%)				0.43
Stroke	19 (70)	15 (60)	34 (65)	
TBI	8 (30)	10 (40)	18 (35)	
TBI, mild	4 (15)	4 (16)	8 (15)	
TBI, moderate and severe	4 (15)	6 (24)	10 (19)	
Time since injury, months, mean (SD)*	15 (20)	20 (29)	17 (28)	0.38
Insomnia duration, months, mean (SD)*	12.7 (23.7)	22 (55.2)	20.2 (35.3)	0.35
z Sleep apnea (formal diagnosed), *n* (%)	2 (7)	2 (8)	4 (8)	0.94
Medication with (side)-effects on sleep, *n* (%)	4 (15)	4 (16)	8 (15)	0.91
Insomnia severity, ISI score, mean (SD)	17.33 (3.79)	17.84 (4.34)	17.59 (4.03)	0.66
Emotional well-being, HADS score, mean (SD)	16.09 (6.97)	17.17 (7.04)	16.60 (6.96)	0.59
Cognitive complaints, CFQ score, mean (SD)	42.60 (15.22)	45.02 (15.17)	43.76 (15.09)	0.58
Pain (yes), *n* (%)	6 (22)	9 (36)	15 (29)	0.27

Note: CFQ, Cognitive Failure Questionnaire; eCBT-I, blended online cognitive behavioural therapy for insomnia; HADS, Hospital Anxiety and Depression Scale; ISI, Insomnia Severity Index; TAU, treatment as usual; TBI, traumatic brain injury.
Note: Mean (SD) and Student's *t* test for normally distributed continuous data; median (range) and Mann–Whitney *U* test for not normally distributed or ordinal data (*); number, percentage, and chi-square for categorical data.
†Education is based on Verhage Education scores: low = 1–4, middle = 5, high = 6–7 (Verhage, 1964). Significance at $p < 0.05$, two-tailed.

with home oximetry and/or polysomnography was performed for clinical purposes in 20 of the 52 participants, four of them had sleep apnea (with adequate treatment). At baseline, 38.5% reported clinically significant symptoms of anxiety and depression (HADS score of ≥19), 50% scored high on cognitive failures (CFQ score of >43) and 29% reported pain.

Treatment effects on primary outcome

Insomnia severity

The eCBT-I group had a significantly larger decrease compared to the TAU group on the ISI (mean [SEM] 4.0 [1.3] points, $z = -3.017$, $p < 0.003$, $d = -0.96$). At follow-up, the decrease in the ISI relative to baseline was still significantly larger in the eCBT-I group (mean [SEM] 3.2 [1.5] points, $z = -2.184$, $p < 0.03$, $d = -0.78$). An ancillary time-by-treatment analysis integrating all three time-points showed on average a − mean (SEM) 3.4 (1.1) ISI points stronger decrease across post-treatment and follow-up in the eCBT-I group than in the control group (mean [SEM] 3.2 [1.5] points, $z = -3.032$, $p < 0.003$). See Figure 2 for the ISI scores at all time-points for the eCBT-I and TAU groups.

Effect of diagnosis and time since injury on insomnia severity

Although the third order diagnosis-by-time-by-treatment group interaction effect did not reach significance, a trend ($z = 1.753$, $p = 0.08$) suggested that the intervention could be differentially effective depending on diagnosis. Separate analyses within diagnostic groups indicated significant effectiveness of eCBT-I in the 34 participants with stroke but not the in the 18 participants with TBI. Relative to stroke participants from the TAU group, stroke participants from the eCBT-I group showed a significant decrease in insomnia severity from baseline to post-treatment (mean [SEM] 5.4 [1.6] points, $z = -3.317$, $p = 0.000$, $d = -1.30$) and from baseline to follow-up (mean [SEM] 3–9 [1.9] points, $z = -2.071$, $p = 0.04$, $d = -0.93$). Relative to TBI participants from the TAU group, TBI participants from the eCBT-I group on average showed a reduction of insomnia severity of about 1 point on the ISI, which was not significant either at post-treatment or follow-up (all $p > 0.45$). Analysis of demographic and clinical variables showed significantly more participants in the TBI (four) than in the stroke group (none) diagnosed with sleep apnea ($\chi^2[1] = 8.19$; $p = 0.004$). Sleep apnea was adequately treated in all four participants. TBI participants were also slightly more likely to have work and to suffer from comorbidity as pain, but these group differences were

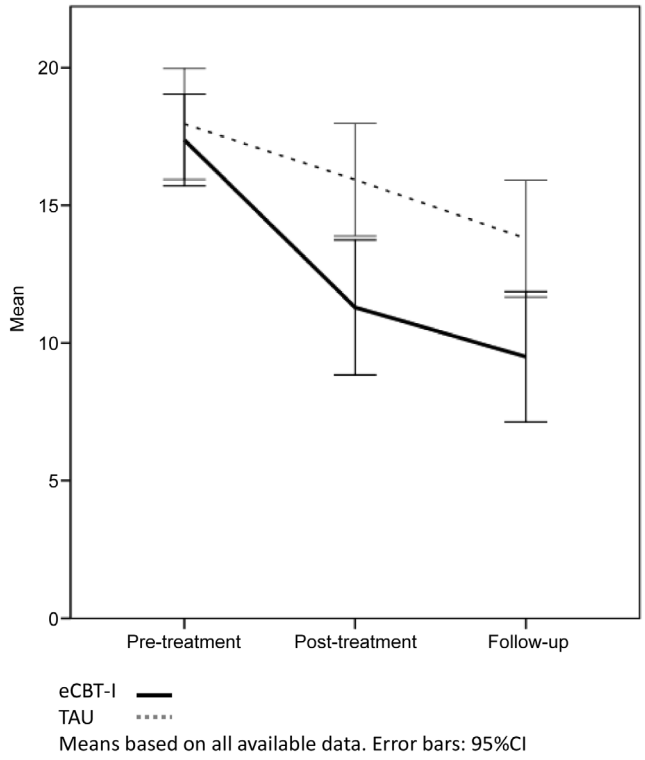

FIGURE 2 Insomnia Severity Index scores. CI, confidence interval; eCBT-I, blended online cognitive behavioural therapy for insomnia; TAU, treatment as usual

not significant. The injury or insomnia duration did not modify the treatment effect.

Clinically relevant changes of insomnia

At post-treatment, clinical remission (ISI score of <10) was attained by more participants in the eCBT-I group (11/24, 45.8%) compared to the TAU group (one of 24, 4.2%) ($\chi^2[1] = 10.63$; $p = 0.001$). This difference was maintained at follow-up (eCBT-I: 14/24, 58%; TAU: five of 24, 20.8%; $\chi^2[1] = 7.06$; $p = 0.008$). At post-treatment relative to baseline, a clinical meaningful improvement (reduction of >6 points on the ISI) was attained by more participants in the eCBT-I group (12/24, 50%) compared to TAU group (five of 24, 21%) ($\chi^2[1] = 4.06$; $p = 0.04$). At follow-up, this difference in improvement diminished (eCBT-I: 15/24, 62.5%; TAU: 11/24, 45.8%, $\chi^2[1] = 1.34$; $p = 0.25$). See Table S5 for all sleep outcomes.

Treatment effects on secondary outcomes

Pittsburgh Sleep Quality Index

At post-treatment, the PSQI decreased significantly more in the eCBT-I than in the TAU group (mean [SEM] 2.0 [0.7] points, $z = -3.017$, $p < 0.003$, $d = -0.71$), and at follow-up this decrease was 2.1 (0.8) points more ($z = -2.618$, $p = 0.007$, $d = -0.76$). Separate analyses within diagnostic groups again indicated significant effectiveness of eCBT-I in the participants with stroke (all $p < 0.01$) but not in the participants with TBI (all $p > 0.50$).

Sleep diary

Mixed-effect analyses found no significant group differences in the change from baseline to either post-treatment or follow-up for the sleep diary measures total sleep time, sleep onset latency, wake after sleep onset, sleep efficiency, or subjective sleep quality. Only trends for eCBT-I benefits for sleep efficiency and wake after sleep onset were seen at follow-up relative to baseline ($p \leq 0.08$).

Fatigue, mood, anxiety, cognition, and societal participation

Mixed-effect regression showed no significant benefits of eCBT-I over TAU for fatigue, emotional well-being, or subjective cognitive functioning either at post-treatment or follow-up versus baseline (Table S6). Only the "satisfaction with societal participation" subscale of the USER-P showed a significant effect of eCBT-I over TAU, both at post-treatment versus baseline (mean [SEM] 7.8 [2.9] points, $z = 2.705$, $p < 0.007$, $d = 0.38$) and at follow-up versus baseline (mean [SEM] 12.9 [3.4] points, $z = 3.754$, $p < 0.0002$, $d = 0.67$).

DISCUSSION

This study demonstrated eCBT-I to be effective in reducing insomnia severity at post-treatment compared to TAU in people with acquired brain injury, with large effect size (Cohen's $d = -0.96$). The superiority of eCGT-I was also observed with regard to sleep quality, and the proportion of participants who had clinical remission of insomnia, but not for the outcomes of sleep diary data. Improvements in insomnia severity and sleep quality were maintained at the 6-week follow-up. The positive findings on insomnia severity and sleep quality are promising and in line with the small group studies on the efficacy of face-to-face CBT-I for people with a stroke or TBI (Nguyen et al., 2017a, 2017b; Theadom et al., 2017; Ymer et al., 2021).

Contrary to our expectation, separate explorative analyses within diagnostic groups indicated significant effectiveness of eCBT-I in the 34 participants with stroke (eCBT-I, 19; TAU, 15) but not in the in 18 participants with TBI (eCBT-I, eight; TAU, 10). However, within this small sample of TBI participants, caution must be applied, as the risk is high that observations will be due to chance.

The effects of eCBT-I on secondary outcomes were less pronounced. There were no clear benefits of eCBT-I over TAU on fatigue, emotional well-being, cognitive functioning, and societal participation. Only on the "satisfaction with societal participation" subscale of the

USER-P questionnaire, significant benefits were found. Larger group studies in the general population show that eCBT-I improves not only insomnia, but also emotional well-being, fatigue, and cognitive functioning with small effect sizes (Espie et al., 2018). However, prior CBT-I studies in populations with acquired brain injury show mixed results on secondary outcomes (Nguyen et al., 2017a, 2017b; Ouellet & Morin, 2004, 2007; Theadom et al., 2017; Ymer et al., 2021). This might be attributable to the lack of power or the need of longer adjustment periods in people with acquired brain injury to experience the benefits of improved sleep on secondary outcomes. However, other studies emphasised that fatigue and insomnia are separate consequences of brain injury and should both be addressed in treatment (Nguyen et al., 2017a, 2017b; Ymer et al., 2021), this might apply to other secondary outcomes as well.

Strengths and limitations

This study has several strengths; insomnia is assessed according to DSM-5 criteria, comorbidity affecting sleep is well documented, and treatment adherence was good with 92% of participants completing the blended eCBT-I. In comparison, an average drop-out rate of 24.7% was found for completely online delivery formats of eCBT-I in the general population (Zachariae et al., 2016), and 17% in a population with TBI (Theadom et al., 2017). Study participants adhered to the eCBT-I, despite cognitive complaints, pain or other comorbidities.

However, some limitations should be noted. A possible limitation is the low inclusion rate, 20% of screened patients were included. Almost 14% were excluded by their therapist as their medical or psychiatric condition was unstable and required attention first. Results may be influenced by a selection bias. However, a percentage of participants in the study sample that had clinically significant symptoms of anxiety and depression (38.5%), cognitive complaints (50%) and pain (29%) at baseline is comparable or more severe compared to other CBT-I intervention studies (Nguyen et al., 2017a, 2017b; Theadom et al., 2017; Ymer et al., 2021) or acquired brain injury studies (Appelros, 2006; Medeiros et al., 2020; Rafsten et al., 2018; Whelan-Goodinson et al., 2009). The second limitation is the heterogeneity of the population studied. We hypothesised that eCBT-I would be effective for both TBI and stroke participants, as it is for other populations. However, post hoc explorative analysis revealed differential effects between type of brain injury. Also, no time frame was added to the eligibility criteria for time after injury, as a result of this participants were included with a range of 2 months to 49 years after injury. Third, an effect of undiagnosed and thus untreated sleep apnea on outcome cannot be completely excluded, as 32 of the 52 participants were not formally diagnosed. Fourth, sleep is assessed by subjective sleep measures only, as insomnia was our primary focus of interest. Adding actigraphy as an objective measure of sleep is recommended in the standard research assessment of insomnia (Buysse et al., 2006). However, we expected this to be an additional burden for the participants and chose not to do this. The last limitation concerns the control group, as TAU is not defined and all participants were allowed to continue usual rehabilitation care, which resulted in heterogeneity in the therapies and in the number of therapy sessions received. TAU seems to improve sleep, as commonly observed in comparable studies (Nguyen et al., 2017a, 2017b), making it more difficult to distinguish between both groups, although eCBT-I improved significantly more. Also, a favourable effect of eCBT-I alone on fatigue, emotional well-being, cognition, and societal participation could be missed as both groups were allowed to continue standard rehabilitation care, which addresses all these factors in contrast to a waitlist-control group or an active control group such as online information. However, the TAU group is ecologically valid as a real-world comparison and enhances generalisability of the results for translation into rehabilitation.

CONCLUSIONS

This study demonstrates that blended eCBT-I is a feasible and effective treatment to accelerate clinical meaningful recovery from insomnia following acquired brain injury. Exploring predictors of treatment response, including type of brain injury, will be a valuable next step, as would comparing the intervention to a completely eCBT-I to find out to what extent the face-to-face sessions are necessary. Future research should also include an evaluation of the acceptability of the blended eCBT-I for participants and therapists, to optimise further dissemination.

AUTHOR CONTRIBUTIONS

Marthe E. Ford, Erny Groet, Gert J. Geurtsen and Coen A.M. Van Bennekom conceived and designed the study. Marthe E. Ford, Erny Groet, Coen A.M. Van Bennekom and Radha D. Rambaran Mishre acquired subjects and collected data. Marthe E. Ford and Eus J.W. Van Someren conducted the statistical analysis. Gert J. Geurtsen, Coen A.M. Van Bennekom and Eus J.W. Van Someren supervised the study, and Marthe E. Ford prepared the initial draft with input from all the authors. All authors provided critical reviews of the manuscript.

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CONFLICT OF INTEREST

No potential conflict of interest is reported by the authors.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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