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Cognitive Behavioural Therapy for Insomnia

How, for Whom and What about Acceptance?

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Abstract

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Sleep is essential for survival but a significant minority of the adult population are dissatisfied with their sleep, and 6-10% meet the criteria for insomnia disorder, characterised by difficulties falling asleep at bedtime, waking up in the middle of the night or too early in the morning, and daytime symptoms. Cognitive behavioural therapy for insomnia (CBT-I), an evidence-based sleep-focused intervention, has been suggested as the treatment of choice for chronic insomnia. However, access to specialised sleep therapists is sparse, and a service delivery model based on the principles of 'stepped care' has been proposed. Even though CBT-I is shown to be effective, there is a need to continue the development of cognitive behavioural treatments for insomnia. As a complement to traditional interventions, the potential value of acceptance, that is, to make an active choice of openness towards psychological experiences, has been recognized. However, it has not yet been systematically investigated, and specific instruments for studying acceptance in insomnia are lacking.

The present thesis is based on three studies: Study I showed that manual-guided CBT for insomnia delivered by ordinary primary care personnel has a significant effect on perceived insomnia severity, sleep onset latency and wake time after sleep onset. Study II demonstrated that non-responders in Study I reported shorter sleep time at baseline than did responders, a notion that may help select patients for this type of low-end intervention in a stepped care treatment approach. Study III aimed to develop a new assessment instrument for studying acceptance of insomnia, the Sleep Problem Acceptance Questionnaire (SPAQ), resulting in an eight-item questionnaire with two factors; the first being Activity Engagement, persisting with normal activities even when sleep is unsatisfactory, and the second involving Willingness, avoiding fighting and trying to control sleep problems.

In conclusion, the present thesis demonstrates that it is feasible to treat patients with insomnia using CBT-I administrated by ordinary primary care personnel in general practice, and that those with relatively longer initial sleep duration benefit most from treatment, enabling allocation to relevant treatment intensity. In addition, acceptance of sleep difficulties may be quantified using the SPAQ.

Keywords: Insomnia, cognitive behavioural therapy, sleep, primary care, stepped care, questionnaire, acceptance

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To My Beloved Family

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals:

1. Bothelius, K., Kyhle, K., Espie, C.A., & Broman, J-E. Manual-Guided Cognitive-Behavioural Therapy for Insomnia Delivered by Ordinary Primary Care Personnel in General Medical Practice: A Randomized Controlled Effectiveness Trial. *Journal of Sleep Research*. 2013 Dec; 22(6), 688-696.
2. Bothelius, K., Kyhle, K., Broman, J-E., Gordh, T., & Fredrikson, M. Initial Sleep Time Predicts Success in Manual-Guided Cognitive Behavioral Therapy for Insomnia. *Behavioral Sleep Medicine*. Forthcoming 2015.
3. Bothelius, K., Jernelöv, S., Fredrikson, M., McCracken, L.M. & Kaldo, V. Measuring Acceptance of Sleep Difficulties: The Development of the Sleep Problem Acceptance Questionnaire. *Sleep*. Forthcoming 2015.

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Abbreviations

AAQ-II	Acceptance and Action Questionnaire-II
ANOVA	Analysis of Variance
BzRAs	Benzodiazepine Receptor Agonists
BS	Best Scenario
CBT-I	Cognitive Behavioural Therapy for Insomnia
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CI	Confidence Interval
CT	Cognitive Therapy
DBAS	Dysfunctional Beliefs and Attitudes about Sleep Scale
DF	Degrees of Freedom
DSM	Diagnostic and Statistical Manual of Mental Disorders
ESS	Epworth Sleepiness Scale
FSS	Fatigue Severity Scale
HADS	Hospital Anxiety and Depression Scale
ICSD	International Classification of Sleep Disorders
ISI	Insomnia Severity Index
ITT	Intention to Treat
LOCF	Last Observation Carried Forward
NWAK	Number of Awakenings
PCA	Principal Component Analysis
PI	Paradoxical Intention
PSG	Polysomnography
REM	Rapid Eye Movement
RMSEA	Root Mean Square Error of Approximation
RT	Relaxation Training
SCT	Stimulus Control Therapy
SE	Sleep Efficiency
SEM	Structural Equation Modelling
SF-36	MOS 36-Item Short-Form Health Survey
SH	Sleep Hygiene
SOL	Sleep Onset Latency
SPAQ	Sleep Problem Acceptance Questionnaire
SQ	Sleep Quality
SRBQ	Sleep-Related Behaviours Questionnaire
SRMR	Standardised Root Mean Square Residual
SRT	Sleep Restriction Therapy

TST	Total Sleep Time
WASO	Wake Time after Sleep Onset
WL	Waiting List
WS	Worst Scenario
χ^2	Chi-Square

Introduction

All animals seem to sleep, from miniscule roundworms to unihemispheric sleeping dolphins, suggesting that sleep serves some essential functions.[1] 'If sleep does not serve an absolutely vital function, then it is the biggest mistake the evolutionary process has ever made', as pioneer sleep researcher Allan Rechtschaffen stated.[2] Sleep seems to be critical for brain homeostatis,[3] memory consolidation,[4] emotion regulation,[5] metabolism,[6] and the removal of potentially neurotoxic waste products from the central nervous system.[7] Neuroimaging evidence has shown the prefrontal cortex to be particularly vulnerable to insufficient sleep.[8] Prolonged sleep loss is associated with metabolic[9] and cardiovascular diseases,[10] with death as the ultimate consequence of extended total sleep deprivation in rodents.[11] Circadian disruption resulting from rotating shift work has been associated with increased risk for metabolic syndrome, diabetes, cardiovascular disease and cancer.[12] Extended sleep, on the other hand, leads to substantial improvements in daytime alertness, reaction time, and mood,[13] although a total sleep length of more than eight hours on average per night is associated with increased all-cause mortality (e.g. cardiovascular-related mortality, and cancer-related mortality) not explained by comorbid conditions, lifestyle or socio-economic factors.[14] Possible mechanisms mediating the effect of short duration of sleep as a cause of disorders and mortality include changes in levels of leptin and ghrelin, and an activation of low-grade inflammation.[15] Sleeping more than eight hours on a typical night is related to systemic inflammation.[16]

Given that it is essential for survival, sleep is regulated multifactorially, and no specific neuroanatomical location regulates sleep on its own, even though the brain stem and the hypothalamus may be particularly important in the regulation of sleep and wakefulness.[17] A number of signalling molecules have been related to the regulation of sleep and wakefulness: adenosine is a significant homeostatic sleep factor,[18] and gamma-aminobutyric acid, cytokines, growth hormone-releasing hormone and prolactin are all involved in sleep promotion,[19] while acetylcholine, monoamines, glutamate, histamine, and hypocretin/orexin are important for wakefulness.[20] Both normal sleep and several types of sleep disturbances have been found to have significant genetic influences,[21] and in humans heredity impacts for example sleep length; *Clock* mutant mice sleep two hours less than wild-type

mice,[22] and a mutation in the *Dec2* gene has been found in a family characterised by short sleep.[23]

More than 25% of the adult population are dissatisfied with their sleep, and 6-10% meet the criteria for insomnia disorder.[24, 25] Insomnia is characterised by non-restorative sleep (i.e. the subjective feeling that sleep is not refreshing enough), difficulties falling asleep at bedtime, waking up in the middle of the night or too early in the morning, and daytime symptoms (fatigue, mood disturbances and impaired attention, concentration, and memory).[26] Insomnia is diagnosed anamnestically in a clinical interview, covering specific insomnia complaints, sleep-related symptoms as well as daytime impairment. In-home sleep diaries and self-administered questionnaires may provide useful data. Physical and psychological assessments give information about differential diagnosis and possible comorbidities.[27] Objective sleep impairments, like increased wakefulness after sleep onset and reduced overall sleep efficiency, have been detected in polysomnographic (PSG) assessments but results are inconsistent.[28] Furthermore, objectively verified sleep impairment does not often accord very well with the subjective complaints, and PSG is not indicated in most routine evaluations.[29]

Historically, diagnostic manuals have tended to differentiate between 'subjective' and 'objective' insomnia. The second edition of the International Classification of Sleep Disorders (ICSD-2), for example, differentiated between psychophysiological insomnia and sleep state misperception. Learned sleep-preventing associations and a somatised tension characterised 'psychophysiological insomnia', with PSG data showing relatively longer sleep onset latency (SOL) and wake time after sleep onset (WASO), and lower sleep efficiency (SE). Sleep efficiency refers to the percentage of time in bed spent asleep. 'Sleep state misperception', on the other hand, was a disorder of insomnia-related complaints when sleep duration and quality is normal (i.e. SOL less then 15-20 minutes and total sleep exceeding 6.5 hours).[30] However, reviews of existing studies have failed to support this form of division, suggesting that sleep state misperception is ubiquitous among all individuals with insomnia.[31, 32] It has been shown that high frequency beta and gamma activity are enhanced in insomnia patients, indicating maintained information and memory processing, which leads to sleep being perceived as wakefulness.[33] Alpha-delta sleep, that is alpha waves (indicating relaxed wakefulness) superimposed on deep sleep delta waves, has been correlated with a subjective experience of shallow sleep and underestimations of total sleep time.[34] Even though not apparent in standard PSG examinations, contemporary research on sleep microstructure indicates heightened sensitivity to sensory stimuli, both during wake time and at sleep onset,[35] and

increased instability of both rapid eye movement (REM) sleep and non-REM sleep.[36] In the light of the commonness of sleep state misperception, the third revision of ICSD replaced 'sleep state misperception' with 'paradoxical insomnia', a subtype rather than an independently occurring type of insomnia.[37] In the fifth edition of The Diagnostic and Statistical Manual of Mental Disorders (DSM-5), only one diagnosis is used, 'insomnia disorder' (i.e. a combination of dissatisfaction with sleep and a significant negative impact on daytime functioning),[38] thus abandoning the subdivision into 'primary' and 'secondary' (comorbid) insomnia from earlier versions of the manual.

Chronic insomnia is highly stable over time,[39] and it is a major health problem causing a substantial burden for those affected and their families.[40] More than 80% of the individuals with insomnia report at least one comorbid physical or psychiatric disorder,[41] and insomnia is associated with significant health-care utilisation, work absenteeism and reduced productivity.[42] The yearly direct and indirect cost for younger adults with untreated insomnia has been calculated to CAD 5,010 per person in Canada,[43] while a workplace cost of USD 2,280 has been reported in the United States,[44] with total direct and indirect costs exceeding USD 100 billion annually.[45] Presenteeism, attending work while sick, with decreased productivity, has been observed in individuals at-risk for insomnia symptoms,[46] while there after adjustment for insomnia medications seems to be low risk for longer periods (i.e. more than 14 days) of all-cause sickness absence in relation to insomnia.[47]

The diathesis-stress model (the '3-P'-model) proposed by the American psychologist Arthur J. Spielman and colleagues, outlines elements relevant to insomnia development and maintenance: (1) *Predisposing factors* include physiological and psychological differences that increase the vulnerability for insomnia; (2) *Precipitating factors* concern stressors (e.g. environmental, psychological or physiological) that give acute insomnia; (3) *Perpetuating factors* include behavioural, psychological, environmental, and physiological factors that prevent the insomnia from wearing off with time.[48] Additional theories emphasise the role of classical conditioning principles (i.e. the stimulus control model),[49] and how thoughts and beliefs can interfere with sleep (i.e. the cognitive model).[50]

Sleep reactivity (i.e. the degree of sleep disruption in response to stressful events) has been suggested to be a predisposing factor for insomnia, and seems to have a substantial genetic component.[51] Stressful experiences early in life may contribute to persistent changes in stress reactivity, and it has been hypothesised that epigenetic mechanisms are involved.[52] Insomnia may be the result of a relative over activity in corticolimbic areas that interferes with sleep initiation and maintenance.[53] Neuroimaging studies have showed

increased cerebral glucose metabolism, both during sleep and while awake, which correlates with the amount of wake time after sleep onset.[54] Insomnia is in fact hypothesised to reflect a 24-hour state of hyperarousal, but this seems however only to be true in some people with insomnia, and in a stable 'trait-like' way.[28]

Negative health consequences associated with insomnia seem to relate to sleep length rather than insomnia per se. Insomnia with objective short sleep duration is associated with secondary diseases such as hypertension,[55] diabetes,[56] neurocognitive deficits,[57] and increased mortality.[58] This is perhaps due to its association with physiological hyperarousal, including hyperactivity of the hypothalamic-pituitary-adrenal axis.[20] Insomnia with normal sleep duration seems on the other hand to be related to cortical arousal but normal activity of the stress system, and a lack of significant medical impact.[59] Sleep length seems to be associated not only with health consequences, but also with productivity. Physiological hyperarousal in insomnia is related to increased error rates on tasks requiring attention,[60] and both insomnia and short sleep duration correlate with reduced work capacity, and the highest risk of poor work ability has been shown in insomnia patients with short sleep duration.[61] The optimal average sleep duration, regarding risk of sickness absence, has been shown to be 7.6 hours for women and 7.8 hours for men.[62] With the possible exception of depression,[63, 64] negative health consequences seem thus to be related to short sleep length in insomnia, not the insomnia as such.

Cognitive and behavioural processes (i.e. worry, dysfunctional beliefs, somatic arousal, selective attention and monitoring, and safety behaviours) are associated with both continuity and remission of insomnia.[65, 66] Cognitive behavioural therapy for insomnia (CBT-I), a sleep-focused intervention comprising the following cognitive and behavioural procedures,[67, 68] has consequently been suggested as the treatment of choice for chronic insomnia:[69]

Stimulus control therapy (SCT). An intervention originally developed by Richard R. Bootzin, an American psychologist and a founder of behavioural therapy for insomnia. SCT is designed to decrease a maladaptive association between the bed/bedroom and anxiety, worry and other sleep incompatible behaviours, and to reinforce the association between the bed/bedroom and sleep.[49] The rationale is as follows: (a) avoid day-time napping, (b) the bed is for sleep only, (c) only go to bed when sleepy, (d) get out of bed if not sleeping after 15-20 minutes, (e) keep a regular morning rise time.[68]

Sleep restriction therapy (SRT). Sleep restriction or, more accurately, bed restriction, is based on the assumption that excessive time in bed perpetuates insomnia, and that sleep deprivation will increase the drive to sleep and to remain asleep. The method, developed by Spielman, involves producing a mild sleep deprivation by initially curtailing time spent in bed to the actual sleep time, followed by a gradual elongation of time in bed in order to arrive at the individual's core sleep requirement.[70] SRT may, in spite of its proven efficacy,[71] cause adherence challenges since reported side-effects are common, along with expected events such as fatigue and sleepiness, also reduced energy and headache/migraine.[72]

Relaxation training (RT). Techniques for monitoring and controlling somatic tension, for example progressive muscle relaxation developed by the Chicago physician Edmund Jacobson in the 1920s,[73] or sleep interfering intrusive thoughts,[74] for example imagery distraction.[75]

Cognitive therapy (CT). A psychotherapeutic method first expounded in the 1960s by the American psychiatrist Aaron T. Beck,[76] consisting of behavioural and verbal techniques to change unhelpful cognitions and error in logic in the patient's thinking.[77] CT for insomnia seeks to reverse unhelpful sleep beliefs, attributions, expectations, perception and attention.[78]

Sleep hygiene (SH). The term was first used by the Swiss-born psychologist Peter J. Hauri, implying behavioural and environmental recommendations developed to promote healthy sleep, for example to avoid stimulants (caffeine and nicotine) for several hours before bedtime, and to keep the sleeping environment dark and quiet.[79] To date, there are no empirical data showing that good SH alone improves sleep in individuals with insomnia.[80]

Paradoxical intention (PI). PI is a well validated therapy,[81] based on the notion that 'performance anxiety' seems to emerge as a response to the patient's fears of being unable to fall asleep.[82] The rationale is to expose the patient to these fears through the paradoxical intention to remain awake for as long as possible rather than continuing the effort to fall asleep. This reduces performance anxiety and may help sleep come more easily.[83]

All of the interventions above, with the exception for CT and SH, are evidence-based treatments of their own,[81] but recent evidence has shown full CBT-I (i.e. a combination of the interventions) to be the treatment of choice.[84] CBT-I has been shown to be effective for primary insomnia,[81, 85] insomnia comorbid with medical or psychiatric disorders,[86, 87] insomnia among long-term hypnotic users, [88] and insomnia in older adults.[89] This is, according to the 2005 US National Institutes of Health state-of-the-science conference on insomnia, the only evidence-based treatment modality in the

management of chronic insomnia aside from benzodiazepine receptor agonists (BzRAs).[40] CBT-I and pharmacological treatment are equally effective in the short-term, with a mean effect size greater than 0.80, indicating a large treatment effect.[90] While relapse is common after drug discontinuation, CBT-I produces sleep improvements that generally are sustained over time.[81] Meta-analyses have shown CBT-I to yield moderate to large effect sizes on subjective measures for SOL and sleep quality (SQ), and small to moderate effect sizes for WASO, number of awakenings (NWAK), and TST.[26] Primary care providers have been recommended to consider CBT-I as the first treatment option.[91] However, in routine practice, the majority of insomnia patients receive drug treatment rather than CBT-I,[92] because access to specialised sleep therapists is sparse.[93]

For society to meet the costs and demands of chronic insomnia, denoted 'a public health crisis', an increased availability of behavioural sleep medicine approaches has been requested.[94] Due to the lack of readily available CBT-I, a service delivery model based on the principles of 'stepped care' has been proposed.[92] Not all patients may require individual and tailored treatment delivered by clinical psychologists or sleep behavioural specialists (i.e. the top of a stepped care 'pyramid'). The entry level could, for example, be self-administered treatment via the internet or self-help booklets, two efficacious and acceptable forms of low-intensity treatment.[95, 96] Progressively smaller volumes of patients could then move up to more costly and specialised treatments. As middle steps, manualised brief CBT-I in small group settings has gained scientific support, either conducted by trained therapists (lower middle step) or graduate psychologists (higher middle step).[92, 97]

Even though CBT-I is shown to be effective, effect sizes are moderate, and there is a need to continue the development of cognitive behavioural treatments for insomnia.[98] In other behavioural medicine disciplines there is accumulating evidence that acceptance-based components might be a successful alternative or supplement to traditional treatment approaches in the face of chronic diseases.[99] Acceptance, or 'psychological flexibility' (as the central theoretical concept in acceptance-based therapies is named), reflects an active choice to experience the present moment without trying to change it, and to engage in personally important activities even when encountering unwanted thoughts, feelings or symtoms.[100] Psychological flexibility has been shown to be an important mediator in the treatment of chronic pain and tinnitus.[101-103] Recent meta-analyses have shown acceptance-based treatments to be equally effective and acceptable as cognitive behavioural treatments for anxiety,[104, 105] depression,[106] and chronic pain,[107] although more high-quality studies are warranted. The development of paradoxical intention during the 1970s was in fact based on the notion that conventional treatment programmes for insomnia (e.g. deep muscle

relaxation) may exacerbate the problems by focusing on gaining voluntary control over the sleep onset process.[82] During the last decade, the potential value of acceptance-based approaches in insomnia has been recognised, but has not yet been systematically investigated.[108-111]Acceptance techniques could increase awareness of a possibly problematic change agenda (i.e. trying to eliminate sleeplessness and other unwanted experiences), as well as lost non-sleep personal life values.[110]

Psychological flexibility includes conscious contact with thoughts and feelings.[100] To train one's ability to mindfully observe, without trying to control, spontaneously occurring physical and psychological events has been proposed to develop a more accepting approach to these events, and thus to have a beneficial effect on sleep.[112] Mindfulness stems from a meditation practice that develops present moment awareness, and has received increased research interest in recent years. With roots in the Buddhist practices *zen* (literally 'meditation') and *vipassana* ('inward vision'),[113] mindfulness involves 'attending to relevant aspects of experience in a nonjudgmental manner'.[114] The link with meditation practices has caused some confusion; acceptance-based treatment processes like mindfulness are not necessarily coupled with meditation, and an open and non-evaluating connection with reality may emerge from a variety of methods.[115] Mindfulness may target multiple factors associated with insomnia: efforts to sleep, avoidance strategies, and rumination and worrying,[116] with the goal of increased ability to respond to sleep disturbances in a deliberate way in line with one's personal life values, rather than to react automatically with efforts to rest or to avoid endeavours.[117]

Aim of the thesis

The origin of the current thesis was a wish to find alternative and effective ways of delivering CBT for insomnia, based on a stepped care approach.[92] At this time there was a burgeoning interest in letting non-specialists mediate the treatment,[93] and a few studies of nurse-administered CBT-I received a lot of attention.[118, 119] To increase knowledge about this form of treatment, through investigating the clinical effectiveness of manual-guided CBT-I, a randomised controlled trial (RCT) with CBT-I delivered by ordinary primary care personnel in general medical practice was implemented. It was hypothesised that CBT-I would reduce the level of sleep disturbances significantly compared to waiting-list controls. Study I reports the main results from this study. Study II then aimed to analyse for whom this form of treatment could be effective through studying individually linked predictors for treatment success, that is individual differences in sleep related measures as related to treatment outcome. Studies I and II showed that a relatively large portion of the participants did not show clinically relevant treatment effect, and since acceptance-based interventions may be appropriate in some cases,[109] Study III aimed to develop a new assessment instrument for studying acceptance in insomnia. The measure was intended to be able to examine the role of acceptance in relation to sleep quality-related variables, and thus for example to determine if acceptance could be considered a relevant treatment process variable.

Methods

Participants and procedures

Participants

Paper I: Seventy-eight subjects were initially included in the study. Twelve subjects (15.4%) did not complete pre-treatment assessment, and thus 66 subjects entered the study, see participant flow diagram in Figure 1. 60.3% had a concurrent medical illness, and 35.3% were using sleep medication. For an overview of the participants in Studies I-III, see Table 1.

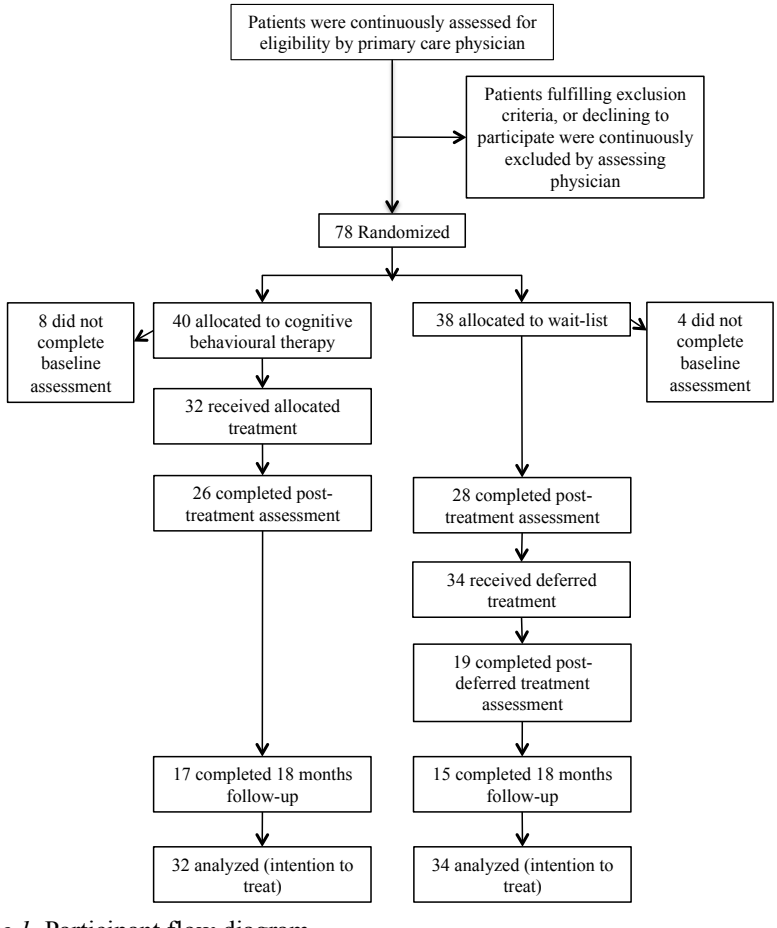

Figure 1. Participant flow diagram.

Table 1. Overview of the participant characteristics and measures used.

	Studies I and II	Study III	
Disorder	Insomnia	Insomnia	
Sample		A[2]	B[1, 2]
Participants	57 females 9 males	268 females 104 males	161 females 54 males
Age	50.7 (SD = 11.6)	42.0 (SD = 15.0)	50.8 (SD = 11.8)
Education level (compulsory school, upper secondary school, college/university)	23.7% 55.5% 23.8%	5.5% 26.6% 67.9%	10.7% 35.8% 53.5%
Screening	Clinical interview Medical examination	Telephone interview	
Outcome measures	The Insomnia Severity Index Total sleep time[3] Sleep onset latency[3] Wake time after sleep onset[3] Sleep efficiency[3] The Epworth Sleepiness Scale The Fatigue Severity Scale The MOS 36-item short-form health survey The Hospital Anxiety and Depression Scale	The Insomnia Severity Index Total sleep time[3] Sleep onset latency[3] Wake time after sleep onset[3] Sleep efficiency[3] The Acceptance and Action Questionnaire-II The Dysfunctional Beliefs and Attitudes about Sleep Scale The Sleep-Related Behaviours Questionnaire	

1) The participants from Studies I and II were included in sample B in Study III
2) Sample C (n = 820) was formed by merging sample A and an additional 233 subjects who were screened after the principal component analysis had been performed with sample B
3) Data derived from sleep diaries

Paper II: 26 responders and 40 non-responders from paper I were analysed. Due to missing baseline data for 10 individuals, 56 of these subjects were included in the analysis.

Paper III: Sample A consisted of screening assessments of 372 subjects applying for two studies of internet-delivered cognitive behavioural therapy for insomnia.[120, 121] In sample B (total n=215) subjects from two trials were merged: (I) Pre-treatment assessments of 156 media-recruited subjects with primary or comorbid insomnia participating in a bibliotherapy study,[122] (II) pre-treatment assessment of 59 subjects from paper I.[123] Construct validity was tested on a combined sample C, comprising sample A+ (sample A with another 233 participants added) and sample B, resulting in a total of 820 subjects.

Statistical approaches

In Study I, 32 subjects in a treatment condition (CBT-I) were compared with the 34 untreated subjects in a waiting list (WL). Data were analysed using

mixed between-within subjects design analyses of variance (ANOVAs) to test the null hypothesis, with an intention to treat (ITT) approach. Contrast analyses was used to draw more precise conclusions. The last observation carried forward (LOCF) technique was used to impute missing values in the post-treatment and follow-up assessments. Since LOCF imputation may result in non-conservative estimations when used at follow-up, both a best scenario (BS) where post-treatment results were maintained, and a worst scenario (WS) where the figures had returned to baseline level, were calculated.

In Study II a logistic regression (forced entry) with a responder vs. non-responder dichotomisation as outcome variable was used to find predictors for being a treatment responder. Missing values in the post-treatment assessment were estimated based on pre-treatment data (LOCF). Ten tentative predictors, based on earlier studies, were included in the initial analysis. Because of the risk of overfitting, i.e. using many predictors on a small sample, related covariables were combined into a single composite score. A separate regression including four predictors based on behavioural measures was then performed to confirm the results.

In Study III, aiming to establish a short form of acceptance questionnaire, item reduction was performed stepwise using an initial principal component analysis (PCA) with oblique rotation, starting with all 34 items. Since a two-factor solution was expected, the number of factors was restricted to two. Structural equation modelling (SEM) was used to perform a confirmatory factor analysis (CFA) of the factors suggested by the PCA. Construct validity was assessed by examining the relations with theoretically linked variables, using correlations and a multiple regression.

Measures

The Insomnia Severity Index, ISI, is a seven-item self-report measure for insomnia, evaluating subjective symptoms and consequences of insomnia.[124] (Studies I, II, III)

Sleep diaries are self-reported records of individual sleeping and waking times and yield reliable quantification of sleep parameters: Total sleep time (TST), sleep onset latency (SOL), wake time after sleep onset (WASO), sleep efficiency (SE), number of awakenings (NWAK), and sleep quality (SQ).[125] (Studies I, II, III)

The Acceptance and Action Questionnaire-II, AAQ-II, is a seven-item scale focused on psychological acceptance of general private events.[126] (Study III)

The Dysfunctional Beliefs and Attitudes about Sleep Scale, DBAS, is a 30-item self-report questionnaire assessing sleep-disruptive cognitions.[67] (Study III)

The Sleep-Related Behaviours Questionnaire, SRBQ, is a 32-item measure of safety behaviours in insomnia.[127] (Study III)

The Epworth Sleepiness Scale, ESS, is an eight-item questionnaire assessing daytime sleepiness.[128] (Study I)

The Fatigue Severity Scale, FSS, is a nine-item instrument designed to assess fatigue as a symptom in a variety of different disorders.[129] (Study I)

The MOS 36-item short-form health survey, SF-36, is a measure of physical and mental health constructs.[130] (Study I)

The Hospital Anxiety and Depression Scale, HADS, is divided into an anxiety and a depression subscale, both containing seven intermingled items.[131] (Studies I, II)

Study I

Background and aims

Insomnia is one of the most prevalent health concerns in the population,[132] and a common reason to seek primary care.[133, 134] Even though evidence-based guidelines support the use of cognitive behavioural therapy,[135] most health care centres are unable to provide this form of treatment.[136] To enhance treatment availability in general medical practice a stepped care approach has been suggested,[92] and nurse-administered cognitive behavioural therapy for insomnia delivered by ordinary primary care personnel has been evaluated.[118, 119] The aim of this randomised controlled study was to investigate the clinical effectiveness of manual-guided CBT-I delivered in small groups by ordinary primary care personnel (four nurses and one social worker) in Swedish health care centres. The study design was a randomised controlled parallel group design with a CBT-I arm and a WL arm.

Results

There were statistical significant main effects for the Group by Time interaction for ISI, SOL and WASO (Table 2).

Table 2. Untransformed means, standard deviations and interference statistics for the Insomnia Severity Index (ISI), sleep onset latency (SOL) and wake time after sleep onset WASO across assessment points ($\bar{x}$ (SD)). Follow-up $_{WORST}$ = worst scenario, with baseline data imputations.

Measure	CBT	WL	Statistics for the main effect of Group
ISI (score)			
Baseline	19.0 (5.5)	18.1 (4.5)	$F(1.82, 107.4) = 7.83$, $p = .001$
Post-treatment	13.4 (6.3)	17.1 (3.9)	
Follow-up $_{WORST}$	16.5 (6.8)	-	
SOL (minutes)			
Baseline	68.8 (41.8)	75.4 (50.8)	$F(2, 114) = 3.71$, $p = .027$
Post-treatment	59.6 (71.9)	71.5 (43.4)	
Follow-up $_{WORST}$	62.5 (56.6)	-	
WASO (minutes)			
Baseline	76.0 (63.6)	103.1 (67.9)	$F(2, 114) = 5.33$, $p = .006$
Post-treatment	54.2 (76.6)	96.3 (67.9)	
Follow-up $_{WORST}$	63.0 (63.5)	-	

Contrasts showed that, at post-treatment assessment, the treatment group had improved significantly more than the untreated control group on the primary outcome measure, the ISI, $F_{(1, 59)} = 16.57$, $p < 0.001$, with a high within-group effect size, $d = 0.90$ (Figure 2). Sleep diary data showed at the same time statistically significant medium-sized treatment effects on SOL, $F_{(1, 57)} = 6.35$, $p = .015$, $d = 0.57$, and WASO, $F_{(1, 57)} = 6.52$, $p = .013$, $d = 0.55$. However, the treatment did not significantly affect NWAK, SE, TST, SQ, or any daytime symptoms. The treatment effect was somewhat lower compared to studies where the treatment has been delivered in more traditional ways.

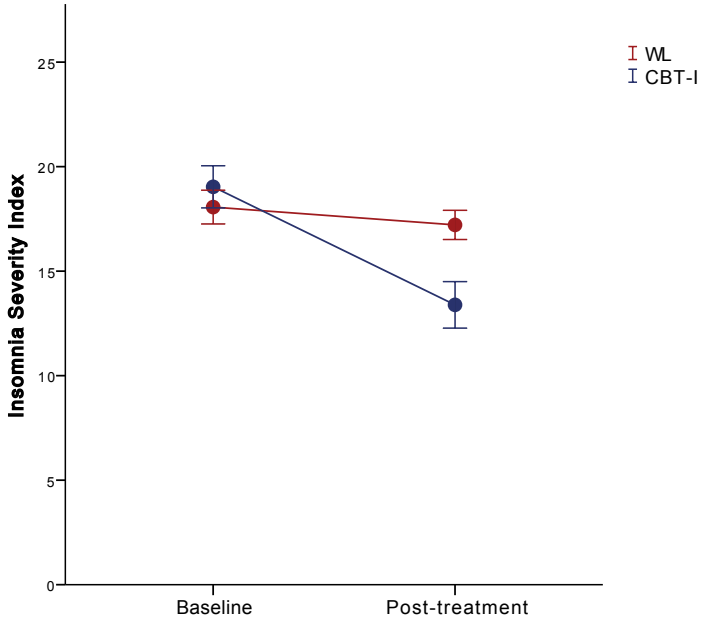

Figure 2. The Insomnia Severity Index score at baseline versus post-treatment for cognitive behavioural therapy (CBT-I) and waiting list (WL) groups. Error bars indicate 1 standard error of the mean.

Almost half the treated subjects (47%) had a clinically relevant effect: 'in remission' or 'improved, but not recovered'. Since insomnia can be perceived in different ways, this was defined using the ISI parallel with SOL and WASO. For *the ISI* 'in remission' was defined as scoring 2 standard deviations below the mean for the population,[137] which corresponds to below 11.5 points,[124] while 'improved, but not recovered' was defined as a reduction of more than 8.4 points, which corresponds to a 'moderate improvement'.[138] For *SOL and WASO* 'in remission' was defined as less than 30 minutes,[139] and 'improved, but not recovered' was defined as a reduction of more than 50% (arbitrary but widely used).[140] The number needed to treat was 2.4. At the 18-month follow-up assessment comparisons between the CBT-I and WL conditions could no longer be done since the WL had received deferred treatment. Within-group effect sizes for the treatment group (anywhere from small in the WS to large (BS) for the ISI, and small (WS) to medium (BS) for SOL and WASO) reveal slight decreases in effect over time.

Conclusion

Manual-guided CBT for insomnia delivered by ordinary primary care personnel seems effective for a substantial minority of insomnia patients in

primary care, although the effect may not be as powerful or stable over time as that associated with more traditional methods.

Study II

Background and aims

Study I explored a lower step on a treatment ladder, in line with 'stepped care'. Stepped care is often conceptualised as a pyramid, where low intensity treatments (e.g. internet-delivered and manual-guided treatment) manage high patient volumes at the base.[92] Individuals not responding at this step should be offered a higher step where treatment is administered in a more individually tailored fashion. In line with previous data,[141] only half the treated subjects demonstrated a clinically relevant effect in Study I, suggesting that treatment response may be modulated by individual differences. This raises the question if there are clinically useful treatment predictors. Finding separate predictors for low and high-end treatment modalities could help us refer patients to the optimal intervention level already from the start. Although several predictors have been suggested, data are inconsistent.[142-149] Study II thus aimed at identifying individually linked predictors for treatment success in a low-end treatment.

Results

In Study I, subjects where classified as treatment responders or non-responders if they were considered 'in remission' or had improved substantially (but not recovered) at post-treatment assessments. In Study II, a logistic regression with ten tentative predictors (SOL, WASO, SE, TST, SQ, the ISI, HADS depression and anxiety subscale, age and education level) was performed, using this responder vs. non-responder dichotomisation as an outcome. This analysis revealed that TST (i.e. sleep diary reported total sleep time) at baseline was the only statistically significant predictor of treatment response, B = .016, p = .027, 95% CI [1.002, 1.030]. Because of the risk of overfitting reported above, a separate logistic regression with only four predictors was performed, reproducing these results, B = .011, p = .034, 95% CI [1.001, 1.022]. The responders slept on average three quarters of an hour longer at baseline, and a cut-off just below 6 hours (350 minutes) of sleep correctly identified the majority of the responders (72.0%) and non-responders (72.2%), see Figure 3.

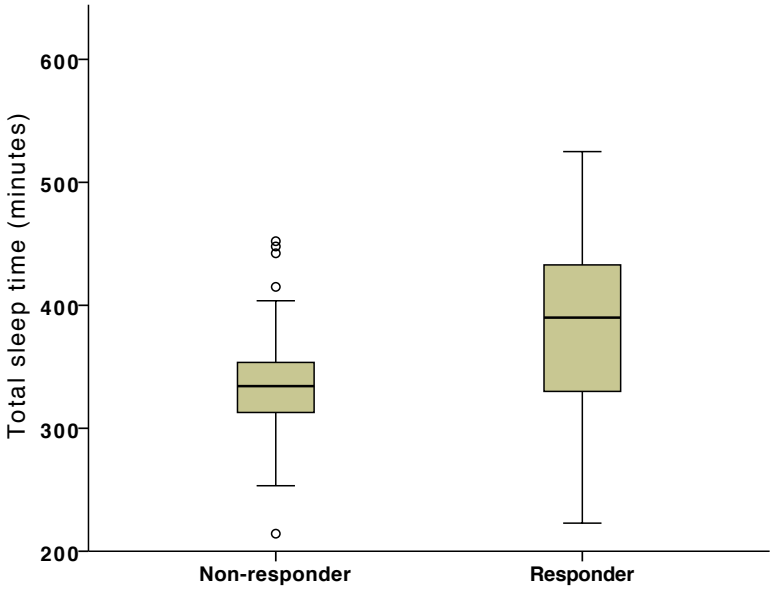

Figure 3. Total sleep time (minutes) at baseline for responders ($\bar{x}$ = 378 minutes, *SD* = 75.1), and non-responders ($\bar{x}$ = 334 minutes, *SD* = 55.3).

Furthermore, complementary analyses showed that responders attended more sessions, 4.65 (*SD* = 0.63) out of five, than non-responders, 3.38 (*SD* = 1.83), $t(50.26) = 3.99$, $p < .001$.

Conclusion

Non-responders reported less sleep at baseline than did responders, a notion that may help select patients for this type of low-end intervention. However, sleep data were assessed with self-reported sleep-diaries. In the absence of objective data, this result could depend either on difference in actual sleep length or in misperception of sleep. Either way, both of these populations may require different treatment approaches: (a) improving the accuracy of the sleep perceptions as proposed by Edinger & Krystal in case of severe sleep state misperceptions,[150] and (b) pharmacological treatments as suggested by Vgontzas and colleagues when it comes to insomnia with objective short sleep duration.[151]

Study III

Background and aims

The objective of CBT-I is to change behavioural, cognitive, and physiological factors that perpetuate insomnia,[26] with the aim to decrease SOL and WASO, for example. That, in a way, represents a 'symptom- and syndrome-focused change agenda that has come to characterise much of mainstream CBT'.[152] As an alternative to this agenda, the concept of acceptance (i.e. to make an active choice of openness towards psychological experiences),[100] has gained scientific support within the field of behavioural medicine.[99] In Study II it was concluded that the insomnia treatment evaluated in Study I may not be very helpful for patients with short reported total sleep time. Insomnia is a heterogenic disorder and some subgroups have been resistant to treatment.[153] This has led to the suggestion that an acceptance-based therapy may be appropriate for some cases.[109] There are tools for measuring general acceptance of personal events,[126] but since specific instruments often are more responsive,[154] we aimed to develop a new assessment instrument for studying acceptance of insomnia, the Sleep Problem Acceptance Questionnaire (SPAQ).

Results

A principal component analysis was performed on a first sample and a final eight-item solution with two factors was presented, supported by the scree plot and an eigenvalue above one, see Table 3. The sub-scales were labelled 'Activity Engagement' and 'Willingness'. This solution explained 65.9% of the total variance among all eight items. Structural equation modelling was used to test this initial model on a second sample. This confirmatory factor analysis supported the model (SRMR = 0.063, CFI = 0.96, χ^2/df = 2.4, RMSEA = 0.081).

Table 3. Rotated factor loadings for the two-factor solution

Item	Content summary	Factor 1	Factor 2
1	Although things have changed, I am living a normal life despite my sleeping problems.	.88	-.056
2	I lead a full life even though I have sleeping problems.	.87	-.003
3	My life is going well, even though I have sleeping problems.	.84	-.076
4	Despite the sleeping problems, I am now sticking to a certain course in my life.	.84	-.003
5	Keeping my sleeping problems under control takes first priority.	-.16	.78
6	I need to concentrate on getting rid of my sleeping problems.	-.061	.79
7	It's important to keep on fighting these sleeping problems.	.17	.77
8	My thoughts and feelings about my sleeping problems must change before I can take important steps in my life.	-.18	.61

N = 372.

An analysis of construct validity showed a moderate negative correlation between the SPAQ and the ISI, r = -.563, $p < .001$, demonstrating that accepting insomnia is related to relatively less subjective problems, while low acceptance characterises subjects with a higher degree of problems. There were only weak negative correlations with SOL, r = -.149, $p < .01$, and WASO, r = -.223, $p < .01$, suggesting that level of acceptance is less clearly associated with diary description of sleep. A multiple regression in two steps showed that the SRBQ and the DBAS predicted 17% of the variance in ISI score in the first step. In the second step, where the SPAQ was added, the predicted variance increased by another 15%, $p < .001$, with the SPAQ as the only significant predictor, B = -0.22, $p < .001$.

Conclusion

The process of developing and validating a brief insomnia-specific measure of acceptance resulted in an eight-item questionnaire with two factors: (1) Activity Engagement, persisting with normal activities even when sleep is unsatisfactory, and (2) Willingness, avoiding fighting and trying to control sleep problems. Together these two factors reflect the two sides of the central theoretical construct in acceptance-based therapies, 'psychological flexibility',[115] that is the ability to experience the present moment without

trying to change it, and to engage in personally important activities despite resistance. Aspects of psychological flexibility can perhaps help us to better select, target, and optimise methods for the subpopulations with insomnia that do not gain from CBT-I.

General Discussion

The present thesis demonstrates that it is feasible to treat patients with insomnia using CBT-I administered by ordinary primary care personnel in general practice, and that those with a relatively longer initial sleep duration benefit more from treatment than those with shorter sleep times, also enabling allocation to relevant treatment intensity. In addition, accepting sleep difficulties seems beneficial and may be quantified using the SPAQ.

Chronic insomnia is a burdensome and costly disorder affecting a substantial minority of the population. While an effective non-pharmacological treatment exists (CBT-I), access is limited, and even when patients receive empirically validated treatment, recovery is not guaranteed. As noted by Harvey and Tang, patients cannot yet be offered a maximally effective psychological treatment.[98] The present thesis aimed to further validate a possible way to increase availability of CBT-I, following the stepped care model:[95] manual-guided treatment in primary care. While Study I supports the notion that the treatment effect is statistically significant, the effect seems to be somewhat less stable over time compared to traditional ways of delivering treatment. In line with earlier research on CBT-I, the clinical effectiveness is somewhat unsatisfactory. It is perhaps naïve to believe that one single way of delivering treatment, or even one single treatment regime, will suit everyone with this inherently heterogenic diagnosis. Study II reveals that individuals with relatively short reported total sleep time at baseline gain little from this form of treatment. Sleep time was derived from in-home sleep logs and, in the absence of objective sleep data, this could stem from either a high degree of sleep state misperception or an objective short sleep length.

It is possible that a short experienced sleep length may affect the motivation to follow the treatment regime. Number of sessions attained did not correlate with initial sleep time, but one could speculate whether other aspects of treatment adherence might have been affected. SRT is, for example, connected to unwanted adverse effects (e.g. headache),[72] and compliance is known to be varied.[155] When sleep is considered to be very short, restricting time in bed may seem unnecessary or counterproductive. If the therapist is not perceived as a sleep medicine authority, patients may be unwilling to fully undergo this procedure, and it may be wise to allocate the individual to

a higher treatment step from the beginning. It may also be the fact that when sleep is objectively short, a manualised bed time restriction format may not result in sufficient sleep deprivation, and a more individualised form of therapy would be advisable. The present trend is toward abandoning different insomnia diagnoses, maintaining only one diagnosis of 'insomnia disorder'. However, objective sleep duration has recently been recognised as a possible analysis for discriminating distinctive insomnia subtypes, with pharmacological treatments proposed for those with objectively short total sleep time (of possible genetic origin), and behavioural interventions for those with normal sleep duration.[156] This is in line with the results from Study II in this thesis. Furthermore, individuals with objective normal sleep duration but with a high degree of sleep state misperception may constitute a separate insomnia subgroup,[157] with treatment needs that differ from those with objective normal sleep length but less misperception. Treatments designed to improve the accuracy of the sleep perceptions rather than conventional CBT-I techniques have been proposed.[150, 158] Yet it has been noted that the clinical value of sleep misperception is not well recognised.[159]

In the search for new treatment approaches, whether for insomnia with high sleep state misperception or objective short sleep length, acceptance of personal events (as opposed to experiential avoidance) may be one construct worth examining. Although fighting or avoiding unwanted private events might result in temporary relief from symptoms, it may result in increased interference with life in the long run; with regard to both chronic pain and chronic fatigue, low acceptance seems to be correlated with high psychological distress and low physical functioning.[160-164] A therapy focusing on acceptance in insomnia would, however, not have acceptance as a long-term treatment goal in itself, increased acceptance would rather be a way of living more closely according to one's life values.[100] Generic instruments for studying acceptance exist already,[126] but specific measures are often more sensitive.[154] There are, for example, a number of questionnaires measuring acceptance in relation to chronic pain.[165] For studying acceptance in insomnia, Study III aimed to develop a new assessment tool, the Sleep Problem Acceptance Questionnaire (SPAQ), revealing two independent factors: Activity Engagement (persistence with normal activities, even when sleep is perceived as not being satisfying), and Willingness (refraining from attempts to fight or control sleep problems).

In the development of the questionnaire, the Willingness factor showed a somewhat different form of control compared to tinnitus and chronic pain; the unwillingness to experience unwanted symptoms was characterised by fight rather than avoidance. Thus, an acceptance-based treatment, where abandoning a fighting style of avoidance is likely to be a treatment target, may have a beneficial impact on the dysregulated stress systems and states

of physiological hyperarousal found in individuals with insomnia with objective short sleep duration.

One approach to encouraging acceptance of the present moment is mindfulness,[166] a common component of acceptance-based treatments. Mindfulness has been shown to be a viable treatment option for chronic insomnia and might provide a complement or an alternative to traditional CBT-I.[167] The instability of REM sleep in insomnia, with increased frequency of micro-arousal, may render wake-like cognitions more accessible to conscious perception, resulting in a subjective overestimation of nocturnal waking time, which constitutes sleep-state misperception.[36] There is a strong activation of limbic regions during REM sleep (suggesting a role in regulation of emotion). Sleep disruption interferes with the normal restorative functions of REM sleep, resulting in changes in emotional reactivity (i.e. negative thinking and emotional patterns activated by a mild state of distress or stress).[168] The effect of mindfulness seems partly mediated by a change in cognitive and emotional reactivity,[169] and participation in mindfulness-based interventions is associated with changes in grey matter concentration in brain regions involved in emotion regulation.[170] Besides self and emotion regulation, structural changes in brain regions important for meta-awareness and interoceptive body awareness have been associated with mindfulness,[171] and enhanced cerebral activity has been showed in areas related to interoception and attention,[172] of potential importance in the perception of sleep. This opens up for speculations that mindfulness could potentially influence sleep-state misperception, or help prevent negative impact of sleep disruption on emotional reactivity.

This thesis started off with a wish to find alternative and effective ways of delivering CBT for insomnia. Following a stepped care model, a lower step in the treatment pyramid was evaluated in Study I. From studying predictors for treatment success, initial reported total sleep time emerged as an important factor in Study II. The reported sleep time could stem from either objective short sleep time or high levels of misperception. It was then discussed whether the non-responders could gain from treatments focusing on acceptance rather than change, where level of acceptance could be assessed with the questionnaire developed in Study III. Future psychologically-based insomnia treatment studies may gain from assessing both objective and subjective total sleep time at baseline, examining acceptance as a possible mediator, and incorporating physiological outcome measures such as the microstructure of sleep.

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