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Implications of psychological factors for diagnosis and treatment

Merijn van de Laar

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PROEFSCHRIFT

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Contents

Chapter 1

General introduction

General introduction

Almost everyone has an occasional night of bad sleep. For most people, this complaint lasts a few days and disappears without treatment. However, factors such as stress can cause more severe sleep problems and after a while these symptoms can become chronic. Even after the disappearance of a possible precipitating event or stressful period, the sleep problems continue to occur and affect daytime functioning. When these symptoms persist for more than three months for at least three nights a week, they can be classified as chronic insomnia. Insomnia is defined as a repeated difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity and circumstances for sleep, and results in some form of daytime impairment (AASM, 2014). A sleep/wake diary is often used to chart the subjective severity of the sleep problems (Figure 1.1). From this diary, different variables can be extracted as described in Box 1.1.

1.1 Pathophysiology of chronic insomnia

The development of chronic insomnia is described in a model by Spielman and Glovinsky (1991), generally known as the "3P-model". It describes how predisposing, precipitating and perpetuating factors play a pivotal role in the persistence of insomnia (Figure 1.2). According to this model, personality is an example of an important predisposing factor. Stress, mental disorders and medical disease can precipitate insomnia. And finally, maladaptive coping strategies (e.g. extending time spent in bed to try to sleep more; fear of sleeplessness, excessive worries about daytime consequences) can lead to the perpetuation of insomnia.
Another model by Morin et al. (1993) specifically focuses on factors that lead to this vicious circle of chronic insomnia (Figure 1.3). In this model, cognitions, behavioral aspects, arousal and consequences lead to the perpetuation of insomnia.

Chronic insomnia is accompanied with daytime symptoms such as fatigue, concentration problems and decreased mood. It is a highly prevalent sleep disorder, affecting 9-10% of the general population in the United States (Ancoli-Israel & Roth, 1999). Chronic insomnia has a significant negative impact on psychological wellbeing and quality of life, and may predispose to other disorders. For example, untreated persistent insomnia is believed to be a risk factor to develop a major depression (Ford & Kamerow, 1989).

Box 1.1 The sleep/wake diary

The sleep/ wake diary is a self-report of individual sleep and wake times, usually over a period of one to two weeks (Figure 1.1). Several sleep measures can be derived from this method including total bed time (TBT), total sleep time (TST), wake after sleep onset (WASO) and number of awakenings (NOA). These sleep measures give a good indication of different aspects of sleep that are subjectively disturbed.

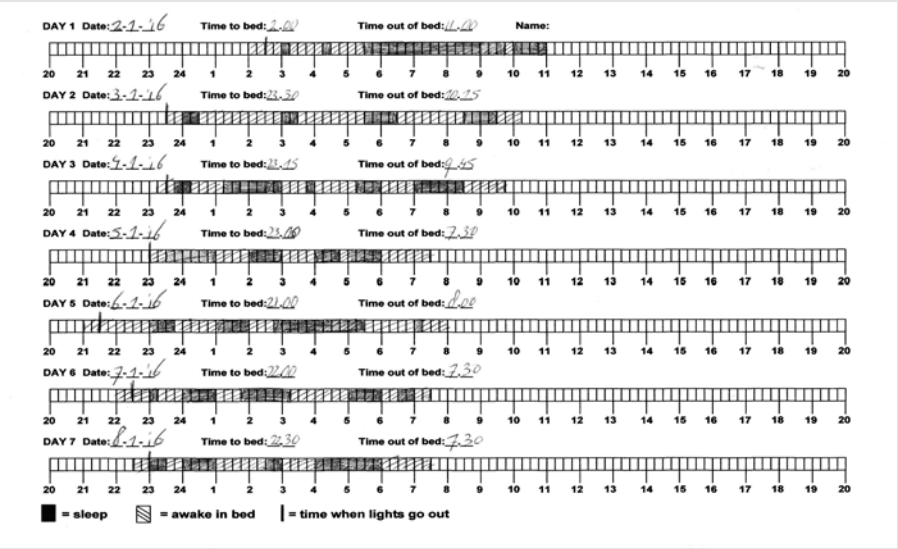

Figure 1.1 Example of a sleep/wake diary.

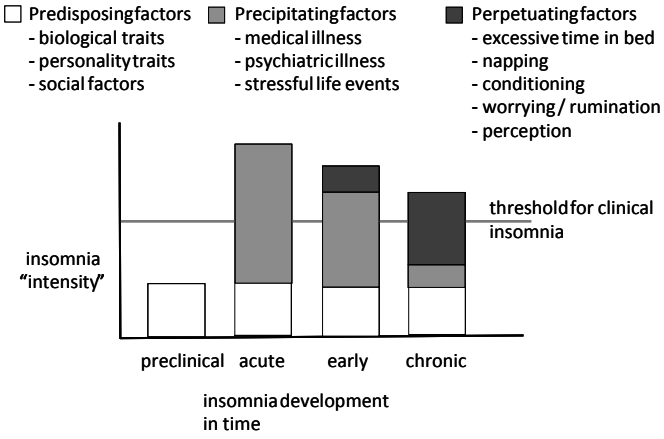

Figure 1.2 The 3P-model of chronic insomnia according to Spielman and Glovinsky (1991).

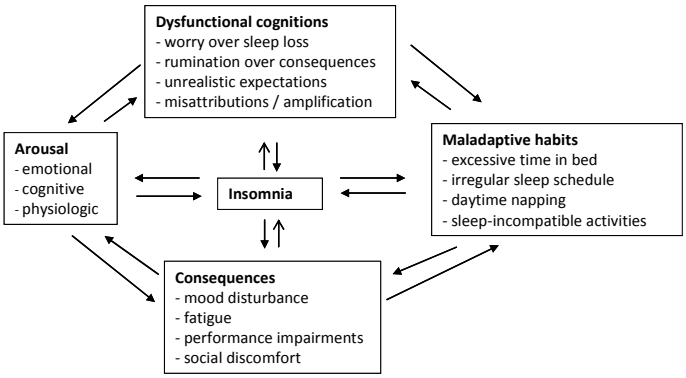

Figure 1.3 A model of chronic insomnia by Morin (1993).

Espie et al. (2006) described another model that is often used in clinical practice. In this so-called intention-attention-effort pathway model, normal sleep is a relatively automatic process that may be inhibited by focused attention and direct attempts to control its expression. Focusing on sleep too much and trying too hard to sleep has a negative effect on sleep itself in this model.

1.2 Nosological classification of insomnia

There are different nosological systems that are used to classify insomnia and insomnia subtypes. In the DSM-IV a clear distinction is made between primary insomnia and secondary insomnia (APA, 2000). In primary insomnia, symptoms do not occur exclusively during the course of another sleep disorder, mental disorder, medical disorder or result from use of substances or medications. In secondary insomnia symptoms are believed to be directly related to a coexisting mental disorder or medical disorder or to the effects of substances or medications. In the previous International Classification of Sleep Disorders (ICSD-2), 11 subtypes of insomnia were described (AASM, 2005). One of these subtypes is insomnia due to mental disorder, characterized by the accompanying diagnosis of a mental disorder and insomnia starting around the same time or a few days or weeks prior to the mental disorder. In the DSM-V and current ICSD-3 however, the more general term “chronic insomnia disorder” is used and –perhaps unfortunately- there is no distinction made anymore according to underlying causes for the insomnia (APA, 2013; AASM, 2014).

1.3 Psychiatric disorders and insomnia

In the 3P-model, mental disorders are described as possible precipitating factors for insomnia. However, it has been shown that untreated persistent insomnia is also a risk

factor for developing a major depression (Ford & Kamerow, 1989), showing a reciprocal relationship between insomnia and psychological/psychiatric factors. Therefore, in the clinical field, insomnia accompanied with a mental disorder is often referred to as "comorbid insomnia" instead of "insomnia due to a mental disorder".
Insomniacs often suffer from comorbid psychiatric disorders, such as depression or anxiety disorders. In fact, according to earlier research, around 50 percent of insomniac patients suffer from one or more comorbid mental disorders (Mahendran, Subramaniam & Chan, 2007).

In the past, the relationship between insomnia and depression has been studied extensively (Baglioni et al, 2011). In an early stage, primary insomnia is often accompanied by affective symptoms, while a depressive disorder cannot (yet) be formally diagnosed. Research suggests that certain individuals are more prone to the negative consequences of sleep problems. Personality might play an important role in this vulnerability to negative consequences. For example, baseline neuroticism was found to predict the effect of experimentally induced insomnia on mood (Blagrove & Akehurst, 2001).

1.4 Personality traits in insomnia

The 3P-model describes personality as one of the possible predisposing factors for insomnia (Spielman & Glovinsky, 1991). The degree to which people exhibit a specific personality trait varies strongly. When traits are implied in psychological distress and life coping problems, they may become predominant and even contribute to the development of a personality disorder. In this case, the pervasive and inflexible nature of the cognitions, motivations and behavior results in maladaptation of the individual to the environment.
The first personality study in insomnia by Coursey et al. dates from the mid 1970's (Coursey, 1975). Although the personality traits of 'good' and 'poor' sleepers had already been investigated before this time, Coursey described that insomniacs showed general dissatisfaction and sensitivity to anxiety, obsessive worrying and hypochondriacal concerns. After this publication, several studies have focused on this matter, using different groups of insomniacs and studying different aspects of personality. Although psychiatric disorders are among the most common diagnosis in insomnia patients visiting a sleep disorder center and the fact that there is a strong link between psychiatric disorders and personality traits, personality research is scarce in well-defined comorbid insomnia (Buysse et al., 1994).

1.5 CBT-I treatment for insomnia

Cognitive behavioral therapy (also known as CBT-I) is the gold standard non-pharmacological method to treat chronic insomnia (Edinger et al., 2009; Morin & Espie, 2003; Sanchez-Ortuno & Edinger, 2012). It entails a stepwise combination of sleep

hygiene advice, relaxation therapy, sleep restriction, stimulus control, and cognitive therapy. The treatment usually consists of six weekly individual or group treatment sessions and two follow-up sessions, after one and 3 months. The content of the different sessions is described in Box 1.2.

Box 1.2 Content of CBT-I sessions
Session 1:Information on normal sleep and sleep hygiene is provided. Homework instructions concerning basic sleep hygiene rules are given by the sleep therapist.
Session 2: Homework on sleep hygiene is evaluated. Sleep restriction/stimulus control and basic relaxation techniques are discussed. In sleep restriction a temporary mild state of sleep deprivation is induced to stimulate sleep. In stimulus control therapy a patient is advised to get up and move to another room when sleep-onset does not occur within fifteen minutes. This method aims to associate the bed with sleeping and limit its association with being awake.
Session 3: Sleep restriction and/or stimulus control techniques are evaluated. The patient receives instructions on progressive relaxation techniques and is asked to plan these exercises during the day. An introduction is given on the basics of cognitive therapy and how negative thoughts can interfere with sleep. They keep a thought log for registration of negative sleep interfering thoughts.
Session 4: Patients learn to challenge their automatic thoughts and create alternative thoughts that are less sleep-interfering.
Session 5: Cognitive therapy is further discussed and evaluated. Patients practice more with cognitive techniques.
Session 6: All cognitive behavioral techniques are evaluated
Session 7 + 8: Follow-up evaluations

Morin, Culbert and Schwartz (1994) performed a meta-analysis studying the effect of cognitive behavioral therapy in insomnia and found that patients with insomnia were better off after treatment than 81% and 74% of untreated control subjects, in terms of sleep induction and sleep maintenance, respectively. Clinical improvements seen at treatment completion were well maintained at follow-ups averaging 6 months in duration. A more recent meta-analysis by Riemann and Perlis (2009) showed that benzodiazepine receptor agonists and cognitive behavioral techniques are both effective to treat insomnia in the short term. However, they also concluded that cognitive behavioral techniques have more durable effects when active treatment is discontinued.

1.6 Background and scope of this thesis

The main goal of this thesis is to identify individual differences in patients with insomnia, based on psychological factors. The current nosological classification as described above seems to lead to an "overgeneralization" of insomnia categories. The problem with this "overgeneralization" is that the role of possible mental disorders in the onset or perpetuation of insomnia is not given any attention anymore, while research suggests that mental disorders and insomnia are strongly linked (Riemann, 2007). Moreover, patients with comorbid psychiatric disorders might form a separate diagnostic entity, showing different psychological and sleep related characteristics and requiring different types of treatment.

Personality traits may be one of the important distinguishing features in patients with and without psychiatric comorbidity. The study of personality in insomnia is complicated by the fact that there might be reciprocal interactions between insomnia and personality. Certain personality traits might be predisposing for insomnia. However, personality tests are also variably influenced by different disorders, and results are therefore more or less 'state-dependent'. 'State-dependency' refers to instability of personality measurements over time, in contrast to 'trait-dependency' which implies stable personality factors. With this in mind, a more dynamic approach towards personality traits and insomnia might be more adequate. In theory, these characteristics might not only be predisposing or perpetuating for insomnia but might also be influenced by the presence of insomnia and might play a role in the vicious circle of chronic insomnia.

Next to individual psychological differences between insomnia subgroups, possible differences in treatment effect are important to explore. Most of the research on cognitive behavioral therapy in insomnia has focused on primary insomniacs. Edinger et al. (2008) compared the effectiveness of CBT-I between primary insomniacs and insomniacs with comorbid psychiatric disorders. This study mainly focused on nighttime symptoms of insomnia, with the main conclusion that CBT-I produced similar benefits for both groups across most sleep diary and actigraphy measures. Although CBT-I effect studies in insomniacs generally show positive results, there is still a group of patients who do not benefit from this type of treatment. Research on characteristics that define this group of non-responders might guide the choice for type of treatment and help to develop and implement new treatment strategies for CBT-I treatment non-responders in the future.

Different psychosocial factors may play a role in the treatment effect in the insomniacs. Personality research has shown that insomniacs reporting less 'guardedness' and who have a higher score on the MMPI 'hypomania'-scale show less improvement through psychological treatment (Shealy, Lowe & Ritzler, 1980; Edinger, Stout & Hoelscher, 1988). Cognitive factors have also been identified as possible predictors of treatment

effect. For example, patients with relatively high levels of unhelpful sleep-related beliefs showed better clinically significant improvement (Edinger, Carney & Wolgemuth, 2008). Two studies on patients with persistent insomnia showed that reductions in negative sleep-related beliefs were associated with positive CBT-I treatment response (Morin, Blais & Savard 2002; Edinger et al., 2001). A related psychological construct that seems important to examine is cognitive coping. Cognitive coping refers to what someone thinks after experiencing a negative event (Garnefski & Kraaij, 2007). Patients who tend to ruminate or catastrophize might be more prone to have negative sleep-related beliefs after experiencing several nights of bad sleep. Because patients with high levels of negative sleep-related beliefs are known to show better improvement after sleep therapy, high scores on cognitive coping factors such as 'rumination' and 'catastrophizing' might be subject characteristics that might be related to a better treatment effect (Edinger et al., 2008).

1.7 Content

The main goal of this thesis is to investigate the role of psychological aspects in insomnia. Group differences depending on these aspects might help in the development of more tailored nonpharmacological treatments enhancing the effect of cognitive behavioral therapy in insomnia. Specific personality traits of insomnia and differences in subjective sleep variables depending on the presence and type of psychiatric disorders as well as psychosocial predictors of quality of life and CBT-I treatment effect will be discussed.

Chapter 2 contains a detailed review of the current knowledge on the role of personality traits in insomnia, with an emphasis on "typical insomniac personality traits" and associations between personality traits and CBT-I treatment effects. Also, limitations in previous research and recommendations for future investigations are highlighted.

In **Chapter 3** it is assessed whether differences exist in subjective sleep-wake variables between patients with primary insomnia and insomnia with comorbid depressive and anxiety disorders. Differences in these variables might give insight in more tailored treatment strategies that can be used in these different clinical groups.

In **Chapter 4** sleep and psychosocial predictors of quality of life are assessed and compared in primary versus comorbid insomnia. Based on the findings, treatment suggestions are given to improve QOL in patients with primary insomnia.

Chapter 5 focuses on predictors of treatment success in insomniacs following cognitive behavioral therapy for insomnia. Psychiatric comorbidity, personality features, social factors and coping strategies are examined.

In **Chapter 6** phenotypes of insomnia are explored. Personality traits, the presence of psychiatric comorbidity and sleep variables are assessed in a large cohort of insomniacs. Subgroups are described using a cluster analysis approach.

In **Chapter 7** the findings of the thesis are discussed together and remaining unsolved issues are identified.

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Chapter 2

The role of personality traits in insomnia

van de Laar, M., Verbeek, I., Pevernagie, D., Aldenkamp, A. & Overeem, S. (2010). The role of personality traits in insomnia. Sleep Medicine Reviews, 14, 61-68.

Summary

Insomnia is a highly prevalent sleep disorder, known to affect psychological well-being and quality of life. While perpetuating factors have received much attention, the role of predisposing factors has not been studied in much detail. The susceptibility to develop insomnia may be linked to the presence of certain personality features. Here, we review studies that assessed this particular aspect of insomnia. Due to various methodological issues, definitive conclusions cannot be drawn as of yet, and several conflicting findings remain. However, there is a common trend indicating that insomniacs display more signs of 'neuroticism', 'internalization', anxious concerns and traits associated with perfectionism. These factors may play varying roles depending on the specific subdiagnosis of insomnia. In addition, certain personality traits may be related to the response to (cognitive) behavioral treatment. For instance, insomniacs reporting less 'guardedness' and have a higher score on the MMPI 'hypomania' scale show less improvement through psychological treatment. The specific role of personality traits in the etiology of insomnia is not yet clear, because of a lack of longitudinal data. Personality factors may play a causal role in the development of insomnia, but may also be a consequence of the sleep problem and the associated daytime dysfunction. Future longitudinal studies should not view personality as a single predisposing factor, but assess it as a part of a larger group of interacting psychological and physiological factors involved in the predisposition to and perpetuation of chronic insomnia.

Introduction

Insomnia is one of the most common sleep disorders, affecting 9–10% of the general population in the United States (Ancoli-Israel & Roth, 1999). Chronic insomnia has a significant negative impact on psychological wellbeing and quality of life (Zammit Weiner, Damato, Sillup & McMillan, 1999; Idzikowski, 1996), and may predispose to other disorders. For example, untreated persistent insomnia is believed to be a risk factor to develop a major depression (Ford & Kamerow, 1989).
According to the second edition of the International Classification of Sleep Disorders (ICSD-2), insomnia can be divided into several subdiagnoses, including psycho-physiological insomnia, paradoxical insomnia, idiopathic insomnia and insomnia due to mental disorder (ICSO, 2005). Although this distinction has clinical relevance, the pathophysiology of many forms of insomnia is explained by the three-factor model of Spielman and Glovinsky (1991). This model describes how (relatively stable) predispositions, varying precipitants and varying perpetuating factors interact to induce and maintain insomnia (Figure 2.1).

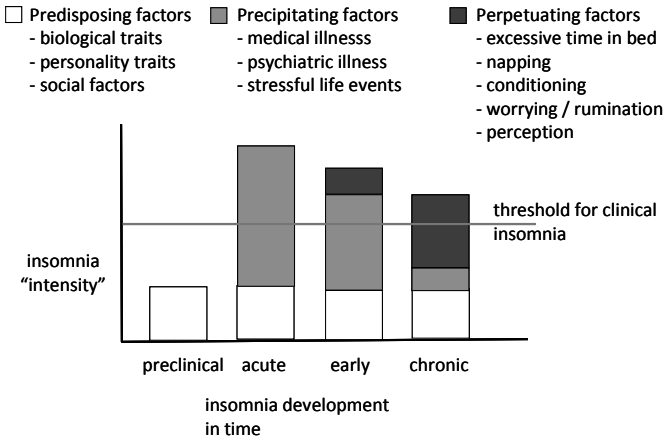

Figure 2.1 A model of chronic insomnia based on a model by Spielman and Glovinsky (1991). This model describes predisposing, precipitating and perpetuating factors for chronic insomnia.

Perpetuating factors have been the main topic of insomnia research, putting an emphasis on inadequate sleep hygiene and classical conditioning. However, both predisposing and precipitating factors may be a relevant focus for diagnostic and therapeutic studies as well. Hypothetically, certain personality traits may constitute important predisposing as well as perpetuating factors for insomnia. For example, a high level of 'neuroticism' (Table 2.1) has been shown to increase the mood depressing effect of experimentally induced insomnia (Blagrove & Akehurst, 2001). In return, the

negative impact on mood can be a perpetuating factor for chronic insomnia (Figure 2.2) (Morin, 1993).

Table 2.1 Glossary of relevant personality traits and terms

Conventionality	Conformity with conventional thought and behavior
Depression (MMPI-scale)	Scale measuring symptomatic depression, which is a general attitude characterized by poor morale, lack of hope in the future, and general dissatisfaction with one's own status
Extraversion	Tendency to enjoy human interactions and to be enthusiastic, talkative, assertive, and gregarious
Histrionic	Pattern of excessive emotionalism and attention seeking
Hysteria (MMPI-scale)	Scale consisting of two general types of items: items reflecting specific somatic complaints and items that show that the patient consides himself or herself well socialized and adjusted. These two items are closely associated in persons whose personality revolves around histrionic dynamics
Hypochondriacal	Neurotic concern over bodily functioning
Hypochondriasis (MMPI-scale)	Scale designed to assess a neurotic concern over bodily functioning
Hypomania (MMPI-scale)	MMPI-scale assessing the milder degrees of manic excitement, characterized by an elated but unstable mood, psychomotor excitement, and flight of ideas
Internalization	Overcontrolled negative affect, such as depression and fear
Introverted	Tendency to be low-key, deliberate, and relatively passive in social situations
Neuroticism	Enduring tendency to experience negative emotional states
Perfectionism	setting excessively high standards of performance
Psychasthenia (MMPI-scale)	Scale assessing the person's inability to resist specific actions or thoughts regardless of their maladaptive nature
Psychopathic Deviation (MMPI-scale)	Scale assessing general social maladjustment and the absence of strongly pleasant experiences
Repressive	Tendency to show less vulnerability and more guardedness
Schizophrenia (MMPI-scale)	Scale assessing a wide variety of content areas, including bizarre thought processes and peculiar perceptions, social alienation, poor familial relationships, difficulties in concentration and impulse control, lack of deep interests, disturbing questions of self-worth and self-identity, and sexual difficulties
Somatization	Tendency to experience and communicate somatic distress in response to psychosocial stress and to seek medical help for it

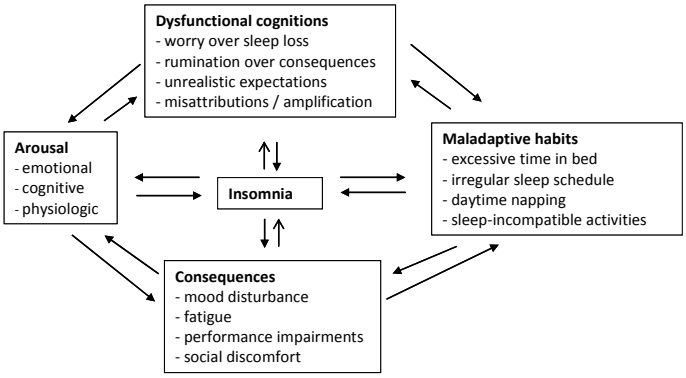

Figure 2.2 A model of chronic insomnia, based on a model by Morin (1993). This model describes the interaction between cognitions, behavior, behavioral consequences and arousal in perpetuating insomnia.

There are several different theories to explain personality but – unfortunately – there is no unifying concept. Personality traits are generally assessed by personality tests, which can be based on theories, empirical work, or a combination of both. In Table 2.1, various personality traits that are discussed in this paper are listed. Table 2.2 shows examples of often-used personality tests, together with psychometric properties such as test–retest reliability. It also lists which personality traits are assessed by each test.

In the present paper we review relevant studies that deal with the role of personality in insomnia. We discuss findings on personality traits in different types of insomnia and studies that distinguish different insomnia types (partly) based on personality traits. In addition, studies comparing personality profiles in insomnia versus other sleep disorders are examined. Personality traits may also influence the effects of cognitive behavioral therapy for insomnia. Finally, we discuss the hypothetical etiological role that personality may play in the development of insomnia.

Research methods

PubMed was searched up to July 2009, using a combination of both Medical Subject Headings (MeSH) terms and free text words. First, all papers dealing with insomnia were identified using either 'Insomnia' or 'Sleep Initiation and Maintenance Disorders' as search terms. We then identified a subset of papers, using the following terms: personality, personality tests, personality traits, personality inventory, personality assessment or personality correlates. In addition, a selection of the most important personality tests was used as specific search terms: Minnesota Multiphasic Personality Inventory, Cattell Personality Factor Questionnaire, Neo-Five Factor Personality Inventory, Temperament Character Inventory and Zuckerman–Kuhlman Personality Questionnaire. The initial search yielded 596 articles. The selection was limited to papers published after 1967 in English, Dutch, French or German.
We screened the abstracts of the papers found, to retrieve those research articles that specifically dealt with the topic of insomnia and personality. Only articles in which personality traits were measured with self-report questionnaires were selected. Papers referring to so called projective personality tests (i.e., personality tests based on responses to ambiguous scenes, words or images) were excluded, because of the low reliability and validity of these tests. Although there are various clinical classification systems that cover insomnia (e.g. ICSD, diagnostic and statistical manual of mental disorder-III (DSM-III) or DSM-IV) (ASDA, 1990; APA, 2000; APA, 1980; ASDC, 1979), in many studies classification criteria were either unofficial or not mentioned. We decided not to exclude these studies in our present. Eventually, we retrieved the full text from 38 articles that contained relevant information for the reviewed topic.

Table 2.2 Psychometric properties of personality tests.

Personality test	Internal Consistency (α)	Test-retest Reliability	Personality traits measured
NEO FFI	.73 - .87 (Holden & Fekken, 1994)	.68 - .86 (Costa & McCrae, 1992)	Openness; Conscientiousness; Extraversion; Agreeableness; Neuroticism
MMPI I	not reported	.55 - .88 (Rosen, 1953)	Hypochondriasis; Depression; Hysteria; Psychopathic Deviate; Masculinity-Femininity ; Paranoia ; Psychasthenia ; Schizophrenia; Hypomania; Social introversion
MMPI II	.34 - .87 (Butcher, et al., 1989)	.58 - .92 (Butcher, et al., 1989)	
KSP	.40 - .87 (Gustavsson, et al., 2000)	.53 - .73 (Kampe, et al., 1996)	Somatic Anxiety; Psychic Anxiety; Psychasthenia; Inhibition of Agression; Impulsiveness; Monotony Avoidance; Detachment; Social Desirability; Socialization; Irritability; Suspicion; Verbal Aggression; Muscular Tension; Guilt; Indirect Aggression
EPI	.74 - .91 (Eysenck & Eysenck, 1968)	.84 - .97 (Eysenck & Eysenck, 1968)	Extraversion; Neuroticism
TCI	.49 - .87 (Pelissolo & Lépine, 2000)	.51 - .82 (Gourion, et al., 2003)	Novelty Seeking; Harm Avoidance; Reward Dependence; Persistence; Self-directedness; Cooperativeness; Self-transcendence
ZKPQ	.72 - .86 (Zuckerman, et al., 1993)	.76 - .84 (Zuckerman, et al., 1993)	Neuroticism-Anxiety; Activity; Sociability; Impulsive Sensation-Seeking; Aggression-Hostility
F-MPS	.77 - .93 (Frost, et al., 1990)	not reported	Personal standards perfectionism; Concern over mistakes; Parental expectations; Parental criticism; Doubts about actions; Order and Organization

NEO FFI: Neuroticism Extraversion Openness Five Factor Inventory; MMPI: Minnesota Multiphasic Personality Inventory; KSP: Karolinska Scales of Personality; EPI: Eysenck personality inventory; TCI: Trait and Character Inventory (French version); ZKPQ : Zuckerman-Kuhlman Personality Questionnaire (ZKPQ); F-MPS: Frost Multidimensional 'perfectionism' Scales.

Personality traits in insomnia

The study of the role of personality traits in insomnia is complicated by the reciprocal interactions between sleep symptoms, comorbid DSM axis-I disorders such as depression, personality traits and personality disorders. Certain personality traits are predisposing for axis-I disorders. However, personality tests are also variably influenced by those disorders, and results are therefore more or less 'state-dependent'. 'State-dependency' refers to instability of personality measurements over time, in contrast to 'trait-dependency' which implies stable personality factors.
The presence of a personality disorder has consequences for the measurements of personality traits. In other words, the presence of a personality disorder makes it more difficult to reliably assess the interaction between personality traits and insomnia. Moreover, while some tests assess the normal range in personality variations (such as the NEO FFI), others measure both normal and pathological traits (like the often-used Minnesota Multiphasic Personality Inventory (MMPI)).
The intricate relationship between personality traits, personality disorders, insomnia and axis-I diagnoses underscores the importance of approaching insomnia subgroups differently, and to distinguish between insomnia with and without psychiatric comorbidity in particular.

'General' insomnia

Unfortunately, in many personality studies in insomniacs, well-defined subdiagnoses were not provided. In this paragraph, we discuss those studies in which a precise sleep disorder diagnosis was lacking. In most studies, the MMPI was used, and these results are summarized in Tables 2.3 and 2.4.
The personality traits of insomniacs were first studied in 1975 by Coursey, although the personality traits of 'good' and 'poor' sleepers had already been investigated before this time (Coursey, 1975). Coursey described a personality pattern of general dissatisfaction and sensitivity to anxiety, obsessive worrying and hypochondriacal concerns, differentiating subjects with insomnia from normal sleepers (see also Table 2.3). In addition to these findings, 'internalization' has been put forward as an important personality aspect of insomniacs (Kales, Caldwell, Preston, Healey & Kales, 1976). Insomniacs were described to 'keep emotions to themselves' instead of externalizing negative affect by acting-out and showing anger or aggressive behavior. This tendency to internalize was also described in other papers (Levin, Bertelson & Lacks, 1984; Kalogjera-Sackellares & Cartwright, 1997). In another study, insomniacs showed more neurotic and anxious symptomatology than control subjects (Shealy, Lowe & Ritzler, 1980).
A constant finding in insomnia patients is a tendency to be overconcerned (lacking self-confidence and having greater doubts about action) (Levin, Bertelson & Lacks, 1984; Lundh, Broman, Hetta & Saboonchi, 1994; Vincent & Walker, 2000). These personality traits are typically associated with perfectionism and self-imposed strain. The

importance of these latter factors in chronic insomnia has been emphasized by several authors (Lundh et al., 1994; Vincent & Walker, 2000; Lundh, Broman & Hetta, 1995).
More recent studies demonstrated that 76–86% of insomniacs have one or more MMPI-scales in the pathological range (Table 2.4) (Kales et al., 1976; Roth, Kramer & Lutz, 1976; Kales, Caldwell, Soldatos, Bixler & Kales, 1983; Tan, Kales, Kales, Soldatos & Bixler, 1984). It was generally concluded that insomniacs tended to show a pathological concern over bodily functioning, dissatisfaction, 'histrionic somatization' and 'neuroticism'. Interestingly, when patients with comorbid sleep apnea, periodic limb movement disorder (PLMD) or substance abuse were excluded, a much smaller percentage (58%) of insomnia patients showed abnormal MMPI profiles (Carskadon et al., 1976). PLMD may be associated with more pathological elevations on the MMPI than other sleep disorders, which may partially explain these results (Aikens, Vanable, Tadimeti, Caruana-Montaldo & Mendelson, 1999).
A study by Seidel et al. (1984) did not find significant MMPI differences between insomniacs and controls. There may be several explanations for this finding. For one, differences may be due to small sample sizes (see e.g., Table 2.3), which is important when assessing multiple MMPI-subscales. There may also have been significant inhomogeneity in selected patient groups. Seidel et al. specifically excluded patients with psychiatric disorders, which may have 'normalized' to some degree the insomnia patient sample with respect to personality characteristics (Ford & Kamerow, 1989; Greene, Gwin & Staal, 1997).

Age effects

In one study it was found that elderly insomniacs showed less pathological elevations on the MMPI than younger patients (Roehrs, Lineback, Zorick & Roth, 1982). The authors extended this finding to hypothesizing that insomnia associated with psychiatric comorbidity is more often found in younger insomnia patients. This is supported by the fact that insomnia in the elderly may be related to other risk factors that are relatively specific to this group, such as increased prescription drug use and somatic disorders (Pallesen et al., 2002) and a lack of physical activity (Morgan, 2003).

Table 2.3 Significant elevations of Minnesota Multiphasic Personality Inventory (MMPI)* I and II clinical scales in insomniacs, when compared to controls.

MMPI scales Type	Ins(n)	C(n)	Ref	Hs	D	Hy	Pd	Mf	Pa	Pt	Sc	Ma	Si
Recruited													
insomniacs	10	10	Mendelson, Garnett, Gillin & Weingartner,1984	_	↑	_	_	_	_	_	_	_	↑
chronic insomniacs	29	27	Seidel, et al., 1984	_	_	_	_	X	_	_	_	_	X
sleep onset insomniacs	49	26	Levin, Bertelson & Lacks, 1984	↑	↑	↑	↑	X	_	↑	_	_	_
chronic insomniacs	18	18	Coursey, 1975	↑	↑	↑	_	_	_	↑	_	_	_
sleep onset insomniacs	40	40	Shealy, Lowe & Ritzler, 1980	↑	↑	↑	_	_	↑	↑	↑	_	_
sleep onset insomniacs	12	12	Freedman & Sattler, 1982	_	_	↑	_	_	_	↑	↑	_	_
sleep state misperception subjects	7	7	Salin-Pascual, Roehrs, Merlotti, Zorick & Roth, 1992	_	_	↑	_	X	_	_	_	_	_
objective insomniacs	7	7	Salin-Pascual, Roehrs, Merlotti, Zorick & Roth, 1992	↑	↑	_	_	X	_	_	_	_	_
Referred													
psychophysiological insomniacs	16	16	Schneider-Helmert, 1987	↑	↑	↑	↑	_	↑	↑	↑	_	_
chronic insomniacs	279	100	Kales, Caldwell, Soldatos, Bixler & Kales, 1983	↑	↑	↑	↑	_	↑	↑	↑	_	X
primary insomniacs	16	16	Niemcewicz, et al., 2001	↑	↑	↑	_	_	_	↑	_	_	X
Referred and recruited													
sleep state misperception subjects	9	9	Bonnet & Arand, 1997	↑	↑	_	↑	_	_	↑	↑	_	_
psychophysiological insomniacs	22	22	Hauri & Fisher, 1986	_	_	↑	_	_	_	_	_	_	_
insomniacs with dysthymic disorders	19	22	Hauri & Fisher, 1986	↑	↑	↑	_	_	↑	↑	_	↓	_

* The MMPI is designed to measure pathological, not general personality traits; Ins = insomniacs; C = controls; Ref = article reference;↑ significantly higher in insomniacs;↓ significantly lower in insomniacs; _ no significant finding; X scale not included in research; Hs = Hypochondriasis; D = Depression; Hy = Hysteria; Pd = Psychopathic deviation; Mf = Masculinity/femininity; Pa = Paranoia; Pt = Psychasthenia; Sc = Schizophrenia; Ma = Hypomania; Si = Social introversion.

Insomnia subgroups based on personality traits

Through cluster analysis of results on personality tests, researchers have attempted to identify different types of insomnia (Hauri, 1983; Sexton-Radek, Urban & Pichler-Maury, 2007; Pailhous, Benoit, Goldenberg, Bouard & Payant, 1988; Edinger, Stout & Hoelscher, 1988). Again, these types of analyses have been based mainly on MMPI code types. MMPI code types are based on the two or three MMPI-subscales that are elevated the most. Using this approach, different researchers have identified two, up to nine different insomnia subgroups. Cluster analyses based on MMPI code types have been criticized because of specific methodological issues (Butcher &Tellegen, 1978). Especially the studies yielding large numbers of insomnia subgroups have to be interpreted with caution. However, in some instances this approach has resulted in meaningful distinctions. For example, Edinger et al. (1988) described two types of insomniacs based on MMPI results: 'type 1' patients were more willing to admit personal faults and shortcomings, were less psychologically defended, had fewer somatic concerns and were more activated/aroused. 'Type 2' insomnia was characterized by a clearly defined 'neurotic' mean profile. In addition, it was concluded that 'type 1' patients benefited less from behavioral therapy than 'type 2' patients.

Insomnia with psychiatric comorbidity

Insomnia patients often suffer from comorbid psychiatric disorders, such as depression. In fact, psychiatric disorders are among the most common diagnoses in insomnia patients visiting a sleep disorder center (Buysse et al., 1994). Personality research is scarce in patients with well-defined comorbid insomnia however. Against expectations, Hauri and Fisher (1986) showed that insomniacs with dysthymic disorders had personality profiles that have often been described as typical for insomniacs in general (see also Table 2.3). The only remarkable finding was a significantly lower score on the MMPI 'hypomania'-scale in the insomniacs with dysthymic disorders. It is likely that these scores were partly state-dependent, reflecting the symptoms of dysthymia. Piccione, Tallarigo, Zorick, Wittig and Roth (1981) compared psychiatric patients with and without insomnia. Only the MMPI-scale 'psychasthenia' proved to be different in the two groups, and was increased in the patients with insomnia. The researchers hypothesized that a disposition to anxiety and worrying is typical for psychiatric patients with comorbid insomnia. On the other hand, the higher 'psychasthenia' score in insomniacs could also reflect the consequences of insomnia. This has been put forward by authors who stated that the generally higher 'psychasthenia'-scores in the insomnia sample were largely due to items that refer to the typical symptoms of insomnia, such as difficulty to regain lost sleep, fatigue, and concentration difficulties (Lundh et al., 1995).

Primary, psychophysiological and paradoxical insomnia

In a number of studies, the insomnia diagnoses were well codified, including primary insomnia or more specific diagnoses such as psychophysiological insomnia and paradoxical insomnia. In primary insomnia, high 'neuroticism', 'internalization', high concern over bodily functioning, social introversion, dissatisfaction and tendencies for 'histrionic somatization' have been reported by different authors (Wang, Zhu, Pan, Hu & Wang, 2001; Engel & Engel-Sittenfeld, 1980; Mendelson, Garnett, Gillin & Weingartner, 1984; Freedman & Sattler, 1982; Niemcewicz et al., 2001). One study reported no difference in 'neuroticism' between primary insomniacs and normal subjects, but attributed this to a loss of power because of the specific statistical techniques used (Voss, Kolling & Heidenreich, 2006).

Psychophysiological insomnia

Findings in psychophysiological insomniacs have been more divergent. Some studies reported that personality traits of psychophysiological insomniacs were very similar to normal controls (Lundh LG, Broman JE & Hetta J, 1995; Hauri P & Fisher J, 1986). Contrasting findings came from a more recent study in which it was concluded that psychophysiological insomniacs were generally more pessimistic, fearful, shy and more easily fatigued than controls (de Saint Hilaire, Straub & Pelissolo, 2005). It was stated that the personality profile of patients featured qualities that are even characteristic of personality disorders (Cloninger, Svrakic & Przybeck, 1993). Schneider-Helmert (1987) suggested that personality traits of psychophysiological insomniacs were very similar to subjects with psychosomatic disorders in general. He concluded that patients were more sensitive, controlling, somatizing and more 'introverted' when compared to normal sleepers. Similar to subjects with less precisely defined insomnia, 'internalization' was prevalent in subjects with psychophysiological insomnia.

Paradoxical insomnia

Psychophysiological insomniacs were not only compared to normal sleepers, but also to patients with paradoxical insomnia (i.e., sleep state misperception). Theoretically, patients with sleep state misperception focus more on their somatic complaints and might be less introspective, canalizing psychological tensions through somatic complaints. Indeed, in paradoxical insomnia, trends were found toward higher 'neuroticism', 'extraversion' scores, and higher scores on the MMPI-scale 'hysteria' (Dorsey & Bootzin, 1997; Bonnet & Arand, 1997; Salin-Pascual, Roehrs, Merlotti, Zorick & Roth, 1992). These scores may reflect a truly different personality phenotype between psychophysiological and paradoxical insomnia, although the findings should be interpreted with caution because of the small samples' sizes (7–9 subjects per group).

Recruited and referred insomniacs

Depending on the research design, studies have included insomnia patients who were referred to a sleep clinic, or were actively recruited from the general population. With respect to personality research, this may actually be an important distinction. Stepanski et al. (1989) showed that personality traits of recruited insomniacs were more 'in the normal range' when compared to referred patients. There were no between-group differences in sleep parameters such as total sleep time or sleep latency, so differences were not explained by the possibility that referred patients simply had a more severe form of insomnia. The hypothesis that referred patients more often have psychiatric comorbidity was ruled out as well: when the data was reanalyzed after excluding patients with comorbid insomnia, similar results were found (Stepanski et al., 1989). In other studies using the MMPI, clear differences between referred and recruited subjects were not found (see Tables 2.3 and 2.4). These discrepancies may be based on differences in the composition of the study cohorts. Although the prevalence of insomnia is generally about 1.5 times higher in females, the study by Stepanski et al. included a clear overrepresentation of males (32 men and 18 women in both referred and recruited groups) (Sutton, 1997). Whilst future research may shed more light on this topic, it at least underscores the importance of clearly defining the study cohort, including the method of including the subjects.

Insomnia and other sleep disorders

In one study, the MMPI was applied to patients with psychophysiological and comorbid insomnia, as well as patients with PLMD or obstructive sleep apnea (OSA) (Aikens et al., 1999). The patients with psychiatric disorders and those with PLMD were quite similar in outcome, and prone to dysthymia accompanied by generalized anxiety and interpersonal detachment. Psychophysiological insomniacs and OSA patients had fewer MMPI elevations. This resemblance between personality profiles between patients with psychophysiological insomnia and OSA is interesting, but may also raise some doubts on the specificity of the MMPI when doing personality research in insomnia.

Personality and treatment response

Studies have not only focused on the role of certain personality traits as a possible etiological factor for insomnia, but also on the influence of personality on treatment outcome, especially cognitive behavioral treatment (CBT). Most studies did find an association between baseline personality characteristics and treatment results. Lacks and Powlishta (1989) found that a lower number of MMPI-scales in the pathological range correlated with better CBT outcomes. Shealy et al. (1980) found that patients who improved by relaxation and stimulus-control treatment, scored lower on MMPI scales 'hysteria', 'hypomania' and 'schizophrenia', but higher on 'depression' and 'psychopathic deviation'.

Table 2.4 Most frequent pathological elevations of MMPI* scales in insomniacs.

MMPI scales Type	Ins(n)	Ref	Hs	D	Hy	Pd	Mf	Pa	Pt	Sc	Ma	Si
Recruited												
sleep onset insomniacs	49	Levin, Bertelson & Lacks, 1984		↑		↑	X		↑			
Referred												
primary insomniacs	86	Engel & Engel-Sittenfeld, 1980	↑	↑	↑				↑			
insomniacs	50	Roth, Kramer & Lutz, 1976	↑	↑	↑							
insomniacs	100	Tan, Kales, Kales, Soldatos & Bixler, 1984	↑	↑	↑				↑			
chronic insomniacs	104	Tsushima & Ingolfsdottir, 2004	↑	↑	↑				↑			
chronic insomniacs	279	Kales, Caldwell, Soldatos, Bixler & Kales, 1983		↑	↑				↑			X
Referred and recruited												
insomniacs	124	Kales, Caldwell, Preston, Healey & Kales, 1976	↑	↑	↑	↑			↑	↑		
chronic insomniacs	65	Carskadon, et al, 1976	↑	↑	↑		X					

* The MMPI is designed to measure pathological, not general personality traits; Ins = insomniacs; Ref = article reference; ↑ most frequent pathological elevations in these scales; X scale not included in research; Hs = Hypochondriasis; D = Depression; Hy = Hysteria; Pd = Psychopathic deviation; Mf = Masculinity/femininity; Pa = Paranoia; Pt = Psychasthenia; Sc = Schizophrenia; Ma = Hypomania; Si = Social introversion.

Conversely, those who failed treatment generally had higher scores on 'hypomania' and 'schizophrenia'. In another study, non-depressed elderly insomniacs who positively responded to treatment (e.g., sleep restriction and relaxation therapy) at three month follow-up scored lower on NEO FFI scales 'extraversion' and 'openness' (Bliwise, Friedman, Nekich & Yesavage, 1995). According to the authors, this may imply that elderly poor sleepers who could be described as conventional, rigid and unimaginative reported greater success.

Edinger et al. (1988) found that non-depressed insomniacs who benefited from behavioral treatment showed a clearly defined 'neurotic' profile. On the other hand, patients with less benefit from CBT showed trends toward 'more willing to admit personal faults and shortcomings' and showed more vulnerability and less guardedness. Furthermore, they showed less signs of somatic concerns. In addition, there may be a link with physiological parameters as this group reported to be more activated and aroused as well (Edinger et al., 1988). The findings on prediction of treatment outcomes may be difficult to interpret because of several issues. Most importantly, different scores on certain personality scales, such as 'depression' and 'extraversion' may primarily reflect the severity of the subjective insomnia complaints. This is supported by the fact that three scales in the study by Shealy et al. (1980) decreased significantly after treatment. Furthermore, 'extraversion' is an example of a trait that is influenced by axis-I disorders. For example, it was found that a decrease in depressive symptomatology after treatment generally results in higher scores on 'extraversion' (Griens, Jonker, Spinhoven & Blom, 2002). Patients with more severe insomnia complaints – hypothetically causing lower scores on the 'extraversion'-scale and higher scores on the 'depression'- scale – may improve more after CBT, because they have less sleep time to start with. In this case, personality characteristics do not directly predict treatment outcome, but only reflect more severe sleep complaints. On the other hand, Lacks and Powlishta (1989) found that patients with chronic insomnia who had fewer MMPI-scales in the pathological range, had better behavioral treatment outcomes, at least in patients without comorbid psychiatric disorders. This may seem contradictory to the earlier reported findings by Shealy et al. (1980), but may also imply that there is a certain 'optimum' for disease severity to show improvement by CBT. While more severe insomnia complaints may be related to relatively good CBT response, too severe associated psychological complaints may render a single behavioral therapeutic approach insufficient.

The role of personality in the etiology of insomnia

The 'internalization' hypothesis

As discussed, insomniacs typically show signs of high 'neuroticism' and traits associated with perfectionism. They also tend to show anxiety related to different areas, such as worrying about health, worrying about making mistakes (which might lead to

selfimposed strain) and low self-esteem. Finally, insomniacs seem to be more introverted and express negative feelings less easily. In the 'internalization' hypothesis based on early studies by Kales et al. (1976), it is described how an 'internalization' process could account for a state of constant emotional arousal. Chronic insomniacs tend to handle stress and conflicts by keeping emotions to themselves and not expressing negative feelings. This may cause emotional arousal, consequently leading to physiological activation, which may then interfere with initiating or maintaining sleep (Kales et al., 1976). Direct evidence for this 'internalization' hypothesis has not been provided yet.

Most studies describe an association between personality traits and insomnia, but it remains unclear whether certain personality traits are either predisposing to or caused by insomnia. It is known that insomnia causes daytime dysfunction which theoretically may lead to insecurity, less stability in coping with everyday problems and withdrawal from social interaction. Also, daily problems in functioning might lead the patient to worry about mistakes and to put more effort (self-imposed strain) in daily tasks than normal controls. Longitudinal studies are needed to shed more light on the cause-effect interactions between personality and insomnia.

Research models of personality traits in insomnia

It remains uncertain whether personality traits in insomnia are reflecting unique psychological dimensions. For instance, Leblanc and colleagues show that 'neuroticism' is highly correlated with anxiety and depressive feelings (Leblanc et al., 2007). These results cast doubt on the assumption that high 'neuroticism' in insomnia is a true individual psychological dimension, as it may also merely reflect a more generic distress profile. A recent prospective study showed that perfectionism is related to both pre-existing and future insomnia, but its role was relatively weak (Jansson-Fröjmark & Linton, 2007). When emotional distress was accounted for, perfectionistic features did not significantly contribute in explaining pre-existing and future insomnia. The authors hypothesized that a third factor, such as elevated arousal might explain the higher scores on perfectionism and the higher rates of insomnia.

This hypothesis is related closely to one model of insomnia, in which it is proposed that insomnia is caused by physiological hyperarousal. Support for this hypothesis has been found in several autonomous, neuroendocrine, neuroimmunological, electro-physiological and neuroimaging studies, demonstrating increased levels of arousal in primary insomnia during both night and daytime (Riemann et al., 2009). However, also in this area of research, uncertainty about the causal directions remains.

A psychobiological approach

Personality traits and physiological factors are not single predisposing factors for insomnia, but play an interactive role in the onset and perpetuation of sleep problems.

Recent research showed that perfectionism is related to increased physiological stress in response to achievement stress (Besser, Flett, Hewitt & Guez, 2008). Experimentally induced failing on a task produced increased systolic blood pressure among perfectionists, especially those who had poorer performance to begin with, and who had received negative feedback about this performance (Besser et al., 2008). Hypothetically, in insomniac patients, perfectionism may play a mediating role in inducing (more) physiological arousal when confronted with the 'failure to sleep'. In turn, this physiological arousal may further increase the feeling of failure to sleep.

Another link between personality traits and arousal mechanisms in insomnia came from a small event-related potential study using a distractor task. A correlation was found between mismatch negativity amplitudes and impulsivity scores in insomniacs (Wang et al., 2001).

Riemann et al. (2009) recently proposed a synthesis model in which primary insomnia is not purely a psychological disorder but can be conceptualized as a psychobiological disorder, in which psychological and biological processes are highly interdependent and interrelated.

Discussion

The role of personality in insomnia is complex, and many areas of uncertainty remain. In general, insomniacs show signs of high 'neuroticism' and traits associated with perfectionism. However, the exact causal relations are unclear as of yet. Hypothetically, certain personality features could definitely play a predisposing role. But just as well, the same features could be a consequence of the insomnia and its detrimental effect on daytime functioning. In other words, if the latter is the case, personality differences between insomniacs and controls might rather be state-dependent instead of trait-dependent.

The association between insomnia and psychiatric disorders is another issue which complicates the drawing of clear-cut conclusions on the influence of personality in the development of chronic insomnia. Some studies showed that the exclusion of psychiatric disorders in an insomnia group 'normalizes' personality measurements. This could be further proof that insomnia with and without psychiatric comorbidity are separate clinical phenotypes. However, this could also further strengthen the idea that personality measurements in insomnia are highly state-dependent and therefore strongly influenced by the presence of psychiatric comorbidity. This underscores the importance to describe in detail the presence of axis-I and personality disorders in future studies.

Even if there is a predisposing role of personality in insomnia, there seems to be an important overlap between concurrent emotional distress and personality measurements, for example with 'neuroticism' and feelings of anxiety and depression. Indeed, when controlling for concurrent emotional distress, the role of perfectionism in

particular becomes much weaker. This raises the question whether certain personality traits in insomniacs are really reflecting unique psychological dimensions, or are – again – a consequence of emotional distress and concurrent physiological arousal.

Many studies on personality in insomnia used only small sample sizes (see Tables 2.3 and 2.4). This is an important factor, and may explain some of the contrasting findings between studies. Most personality tests yield several different subscales, and power-calculations for future studies should take this fact into account.

So far, most studies on personality and insomnia had an epidemiological focus and aimed at finding clinically meaningful correlations.

However, the investigation of possible pathophysiological mechanisms could be a better approach to further unravel the links between personality and insomnia. For example, there is some evidence showing a relation between arousal and personality traits. As discussed earlier, in a study measuring physiological arousal during experimentally induced task-failures, perfectionism was associated with increased arousal levels (Besser et al., 2008). Perfectionism is often associated with putting (too) much effort in achieving goals. Likewise, insomniacs often report that they put much effort in trying to get to sleep. This process is also described in the attention–intention–effort pathway model, in which normal sleep is a relatively automatic process and may be inhibited by focused attention and by direct attempts to control its expression (Espie, Broomfield, MacMahon, Macphee & Taylor, 2006). Hypothetically, 'perfectionism' may play a predisposing role in elevating the focused attention to the process of falling asleep. When facing ''failure to sleep'', the perfectionistic patient may subsequently try to exert control to achieve the objective of falling asleep. This might result in an increase of physiological arousal, which further prevents the onset of sleep, initiating the vicious cycle of chronic insomnia (Riemann et al., 2009).

Future research studies may follow various avenues. In order to examine the exact relationship between insomnia and personality, longitudinal studies are urgently needed. In such studies, personality characteristics should be assessed next to other factors such as concurrent feelings of anxiety, depression and measures of physiological arousal. As shown in this review, several small studies suggest that certain personality traits interact with physiological arousal at the onset and perpetuation of insomnia. Therefore, future research should not focus on personality as a single predisposing factor for insomnia, but assess it as a part of a larger group of interacting psychological and physiological factors involved in the predisposition to and perpetuation of chronic insomnia. Specifically, perfectionism might be a personality variable of interest for insomnia research. Future longitudinal studies might focus on a hypothetical relationship between perfectionism, the attention–intention–effort pathway and physiological arousal in insomniacs.

The relative contribution of personality traits and physiological arousal to the perpetuation of chronic insomnia is likely to be different for every patient. This may have implications for treatment: for example to focus more on either psychological or physiological factors. Treatment studies suggested that insomnia patients who reported

higher arousal levels show less improvement through psychological treatment. This supports the hypothesis that there may be important interindividual differences regarding the importance and role of either biological or psychological factors in the etiology and perpetuation of the insomnia complaints. Future studies may give more insight in the benefits of a more personally tailored treatment, in which psychological as well as physiological aspects are considered.

Practice points

1. Personality traits may affect the emotional impact of insomnia. However, there is a lack of longitudinal studies clarifying the nature of the relationship between personality traits and insomnia.
2. Personality measurements are not only 'trait-dependent' but also 'state-dependent'. Data suggests that even if personality plays a role in the development of insomnia, its association with other factors, such as emotional distress and complaints of anxiety and depression is strong.
3. Many insomniacs display signs of 'neuroticism', 'internalization', anxious concerns and traits associated with perfectionism.
4. Insomniacs who reported to be more activated and/or aroused may have less benefit from behavioral treatment. This supports the hypothesis that there are individual differences between insomniacs regarding the importance and role of psychological and biological factors in the initiation and perpetuation of insomnia complaints.

Research agenda

1. Perform longitudinal personality studies in patients with insomnia, and clarify the causal relationship between personality traits and insomnia.
2. These studies should include well-defined and precise insomnia (sub)diagnoses, and also take into account other psychological and physiological factors that may play a causal role.
3. Study personality differences between patients with positive and negative cognitive behavioral treatment results.
4. Study the effect of 'tailored' treatment strategies in CBT non-responders, adjusting for personality characteristics, and incorporating other factors as well, for example targeting varying levels of physiological arousal.

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Chapter 3

Subjective sleep characteristics in insomnia with and without psychiatric comorbidity

van de Laar, M., Pevernagie, D., van Mierlo, P. & Overeem, S. (2014). Subjective sleep characteristics in primary insomnia versus insomnia with comorbid anxiety or mood disorder. Sleep and Biological Rhythms, 13, 41-48.

Abstract

We assessed subjective sleep measures in a cohort of 146 patients with chronic insomnia and hypothesized that these measures may differ depending on the presence as well as the type of comorbid psychiatric disorders. All patients were consecutively referred to a third line sleep medicine center and underwent an extensive clinical intake by both a sleep physician and a psychologist. Psychodiagnostics were performed according to the DSM-IV criteria. Subjective sleep was assessed by sleep diaries and the insomnia severity index. Insomniacs with anxiety disorders showed a relatively higher total sleep time and higher sleep efficiency than the two other groups. Furthermore, the number of awakenings was higher and time in bed after the final awakening was lower in patients with comorbid anxiety disorders when compared to the two other groups. Although subjective total bedtimes were comparable, patients with comorbid anxiety disorders on average reported a striking 2 hours more sleep per night and around a 20% higher sleep efficiency than patients with comorbid mood disorders. Patients with comorbid mood disorders showed a trend towards a higher Insomnia Severity Index-score when compared to primary insomniacs. Insomniacs with comorbid anxiety disorders presented with a markedly higher sleep efficiency and total sleep time. On the other hand, these patients described more fragmented sleep. Our findings may have practical implications for more tailored cognitive behavioral treatment in insomniacs with and without different types of psychiatric comorbidity.

Introduction

Insomnia is a highly prevalent disorder that is known for its negative effect on daytime functioning (Komada et al., 2012). Clinically, there are several different subtypes. The term primary insomnia is used when symptoms cannot be attributed to a medical or psychiatric cause, while in comorbid insomnia the sleep complaint is accompanied with mental disorders. Comorbid insomnia comprises about 50% of insomnia patients referred to a sleep clinic (Buysse et al., 1994; Mahendran, Subramaniam & Chan, 2007).
Insomnia is characterized by problems in the initiation of sleep, early morning awakenings, maintenance of sleep and/or nonrestorative sleep. In the clinical evaluation of insomnia, a sleep diary can give insight in the subjective severity of problems in initiating and maintaining sleep. The sleep diary is a self-report of individual sleep and wake times, usually over a period of one to two weeks. Several sleep measures can be derived from this method, including total bed time (TBT), total sleep time (TST), wake after sleep onset (WASO) and number of awakenings (NOA). These sleep measures provide a good indication of the subjective disturbance of several different aspects of sleep.
Studies on objective sleep measures have been a main topic in primary and comorbid insomnia. In primary insomniacs polysomnographic measures showed a reduced sleep duration, lower sleep efficiency and an increased arousal index when compared to normal controls (Voderholzer, Al-Shajlawi, Weske, Feige & Riemann, 2003). In depressed insomniacs and patients with panic disorders a lower sleep efficiency, lower total sleep time and a longer sleep onset latency and more wakefulness in the total sleep period were found when compared to normal controls (Papadimitriou & Linkowski, 2005; Saletu-Zyhlarz et al., 2002). Patients with generalized anxiety disorders also generally showed longer sleep latency, increased time awake and reduced sleep efficiency (Papadimitriou & Linkowski, 2005). Concluding, it seems that objective measures of insomnia are very comparable between patients with and without different types of comorbid psychiatric disorders.
Although subjective perception of sleep disruption is likely to differ between primary and comorbid insomnia, research on sleep diary differences between these groups is scarce. Kohn and Espie (2005) compared patients with primary and comorbid insomnia on several subjective and objective sleep variables. Based on the results, the authors suggested that primary and comorbid insomnia may be on a continuum of insomnia severity, rather than categorically distinct. There were no differences in (self-reported) sleep variables between primary and comorbid insomniacs. Note, that in this study the group of comorbid insomniacs was not further specified although examination of insomniacs with specific subtypes of comorbid psychiatric disorders would clinically be highly relevant. Sleep diary studies in comorbid insomnia subtypes may reveal differences in the severity of subjective sleep disturbances, as well as insight in specific characteristics of the reported insomnia complaint.

Because anxiety and mood disorders are the most common psychiatric disorders in insomniacs, we specifically focus on these two comorbid groups in the present study (Buysse et al., 1994; Mahendran et al., 2007). We hypothesized that there are clear differences in nature and severity of subjective sleep variables depending on presence and type of psychiatric comorbidity and that patients with comorbid psychiatric disorders will generally show more severe insomnia.

Methods

General study design and setting

We performed a cohort study comprising consecutive patients seen in Sleep Medicine Centre Kempenhaeghe, a tertiary referral centre. Patients were referred for further examination of insomnia complaints and included between June 2010 and May 2011. All patients had a complaint of chronic insomnia with symptoms lasting at least 3 months. Patients between 18 and 65 years of age were included if they did not work in shifts and did not suffer from a current psychotic disorder or had a history of developmental disorders. Subjects were medically examined by a sleep physician. If there were signs of another primary sleep disorder besides insomnia, additional diagnostic studies – such as polysomnography – were performed. Patients with a somatic disease or other sleep disorder that could explain the insomnia were excluded (e.g. sleep apnea, restless legs syndrome, epilepsy, chronic pain). Patients with alcohol or drug abuse were also excluded. Groups were defined according to the presence of psychiatric comorbidity. The classification of primary insomnia was based on the DSM-IV criteria (APA, 2000). Patients using hypnotic medication were kept in the analyses, as all patient groups used this type of medication to a comparable degree. Antidepressant or anxiolytic medication was only used by some patients with psychiatric comorbidity, and as these drugs may influence sleep, these patients were excluded from further analyses. The study design was approved by the local medical ethical committee and all participants gave written informed consent.

Psychopathology

Semi-structured interview for mental disorders

All patients were examined by a trained clinical psychologist following the criteria of the DSM-IV (APA, 2000). This was achieved through a semi-structured interview for psychiatric disorders comprising 16 screening questions referring to the main types of DSM axis-I disorders, including different types of anxiety and mood disorders (Hoogduin, 1999). Insomniacs suffering from more than one type of psychiatric disorder were excluded.

Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) is a 14-item screening instrument, measuring severity of depression and anxiety symptoms (Zigmond & Snaith, 1983; Spinhoven et al., 1997). The questionnaire contains a separate depression and anxiety scale. Each scale is evaluated by seven items on a four-point Likert Scale.

Sleep variables

Sleep diary

All patients filled in a sleep diary during one week, recording each bedtime and time of getting out of bed. Furthermore, patients recorded the time spent in bed, either awake or sleeping. Afterwards, several variables were extracted from the sleep diaries, as defined in Table 3.1 (Morin, 1993).

Table 3.1 Sleep diary characteristics

Total bed time (TBT)	Time spent in bed during the night
Total sleep time (TST)	Time slept during the night
Sleep efficiency (SE)	Proportion of time in bed actually asleep
Sleep onset latency (SOL)	Time from moment in bed to first sleep
Wake after sleep onset (WASO)	Amount of awake time after falling asleep for the first time
Number of awakenings (NOA)	Number of awakenings during the night
Time in bed after awakening (TIBAA)	Time spent in the bed after the final awakening
Total daytime sleep (TDS)	Time slept during the day

Insomnia Severity Index

The Insomnia Severity Index (ISI) is a seven-item validated questionnaire assessing the nature, severity and impact of insomnia (Morin, 1993; Morin, Belleville, Bélanger & Ivers, 2011). A five-point Likert scale is used to rate each of these items, yielding a total score ranging from 0–28. Scores are classified in four severity categories: (0–7): absence of insomnia, (8–14): mild insomnia symptoms, (15–21): moderate insomnia, (22–28): severe insomnia. This questionnaire is an important addition to the sleep diary, because besides nighttime variables, daytime impact is assessed.

Data analysis

Data were analyzed using SPSS 20 for Windows. To examine possible differences in independent demographic and general clinical characteristics between primary insomniacs, patients with comorbid mood disorders and patients with comorbid anxiety disorders, χ^2 tests and Kruskal–Wallis tests were performed. Kruskal–Wallis tests were also used to compare the three diagnostic groups on various sleep variables. Because of the unequal group sizes Tamhane post-hoc analyses were performed to

identify specific differences between the separate subgroups. Bonferroni corrections for multiple testing were applied.

Results

General sample characteristics

Figure 3.1 represents the inclusion/exclusion flowchart. More than half of the insomniacs showed a form of psychiatric comorbidity (51% of the total). As expected, mood disorders (31%) and anxiety disorders (26%) were most common and therefore selected for further analysis (Buysse et al., 1994; Mahendran et al., 2007). Other psychiatric disorders included undifferentiated somatoform disorder/burnout (14%), undifferentiated somatoform disorder/chronic fatigue syndrome (14%), adaptation disorder (12%) and ADHD (6%). Of the 63 patients with comorbid mood and anxiety disorders, 30% used antidepressants or anxiolytics and were excluded. Two patients (9%) with a primary mood disorder in addition suffered from an anxiety disorder and four patients (19%) with a primary anxiety disorder suffered from a mood disorder as well, and these six were excluded. The final group consisted of 107 primary insomniacs, 20 insomniacs with comorbid mood disorder and 19 insomniacs with comorbid anxiety disorder. Specific subtypes of mood and anxiety disorders in our research population are shown in Table 3.2.

Table 3.2 Psychiatric diagnoses in research population (N=39)

	Type of DSM-IV diagnosis	N (%)
Mood disorders (N=20)	Depressive disorder	16 (41%)
	Dysthymic disorder	4 (10%)
Anxiety disorders (N=19)	Generalized anxiety disorder	8 (21%)
	Panic disorder	5 (13%)
	Social phobia	3 (8%)
	Posttraumatic stress disorder	1 (3%)
	Obsessive compulsive disorder	1 (3%)
	Anxiety disorder not otherwise specified	1 (3%)

Demographic data and clinical characteristics

There were no significant differences in age and gender between the three insomnia subgroups, so confounding effects of these factors on between group differences in sleep characteristics are not likely (Table 3.3). As expected, patients with comorbid mood and anxiety disorders clearly showed higher HADS-scores than primary insomniacs.

Insomnia characteristics

There were no differences in the duration of insomnia and sleep medication use between the three insomnia groups (Table 3.3). Patients with comorbid mood disorders showed a trend towards higher ISI-scores compared to primary insomniacs.

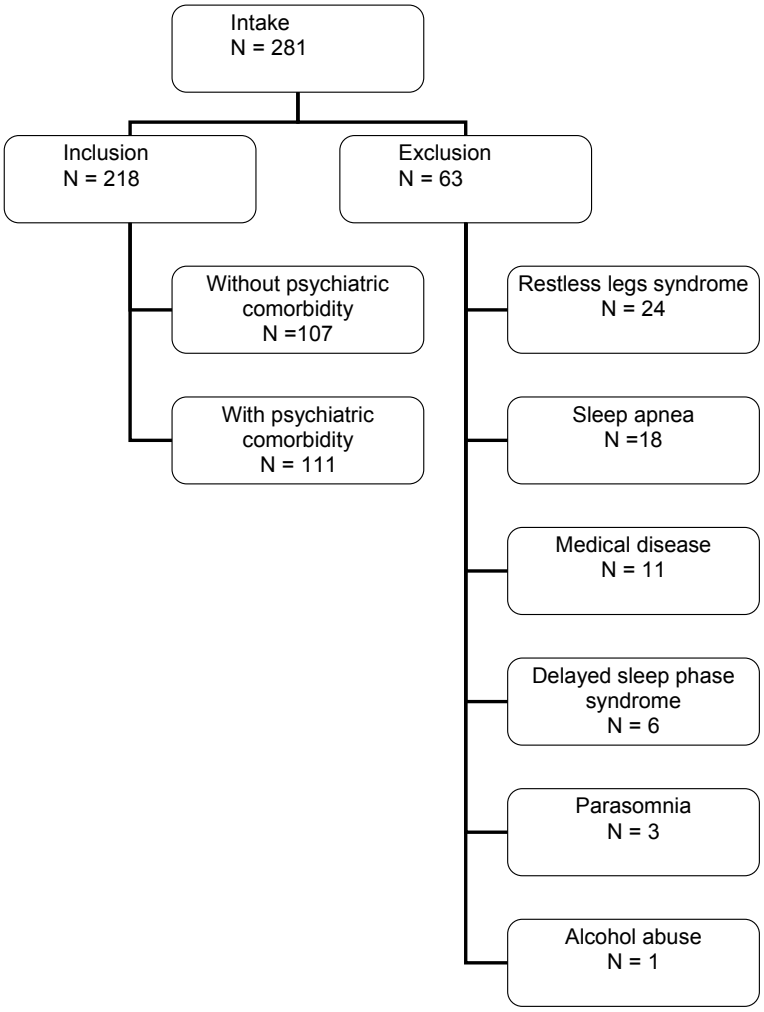

Figure 3.1 Flowchart of patients initially referred for diagnosis of insomnia complaint.

Table 3.3 Demographic, clinical and insomnia characteristics in chronic primary insomniacs and insomniacs with specified psychiatric comorbidity.

	Primary insomnia	With comorbid mood disorder	With comorbid anxiety disorder	P[1]	Post-hoc analyses[2]
N	107	20	19		
Age (years)	44.1 ± 11.8 (18.0-65.0)	45.8 ± 9.7 (24.0-64.0)	40.4 ± 11.2 (23.0-63.0)	.289	
Male (N)	34 (32%)	9 (45%)	7 (37%)	.503	
HADS (total score)	10.4 ± 4.5 (1.0-22.0)	19.5 ± 4.9 (13.0-34.0)	17.7 ± 4.6 (10.0-27.0)	.000**	PI < WCM, WCA
Insomnia duration (years)	10.3 ± 12.1 (0.3-64.0)	13.2 ± 13.0 (0.8-45.0)	10.3 ± 9.7 (1.0-32.0)	.644	
Using sleep medication (N)	62 (58%)	14 (70%)	8 (42%)	.209	
Insomnia severity index (score)	19.9 ± 4.1 (10.0-28.0)	22.7 ± 3.0 (15.0-27.0)	20.7 ± 3.9 (13.0-26.0)	.011*	PI < WCM
Total bed time (hours)	8.5 ± 0.9 (6.1-10.9)	9.0 ± 1.6 (7.0-14.0)	8.7 ± 0.7 (7.1-10.3)	.294	
Total sleep time (hours)	5.0 ± 1.3 (1.5-7.9)	3.9 ± 1.9 (0.0-6.8)	5.9 ± 0.8 (4.6-8.1)	.001**	PI, WCM < WCA
Sleep efficiency (%)	58.9 ± 14.6 (18.5-85.8)	45.8 ± 23.6 (0.0-84.9)	67.9 ± 10.8 (48.4-93.5)	.003**	PI, WCM < WCA
Sleep onset latency (hours)	1.2 ± 0.7 (0.0-4.0)	1.9 ± 1.5 (0.3-6.1)	1.0 ± 0.6 (0.0-2.2)	.080	
Wake after sleep onset (hours)	1.1 ± 0.7 (0.0-3.1)	0.8 ± 0.9 (0.0-3.3)	1.3 ± 0.7 (0.2-2.5)	.056	
Total daytime sleep (hours)	0.0 ± 0.1 (0.0-.9)	0.0 ± 0.2 (0.0-0.8)	0.1 ± 0.2 (0.0-0.7)	.400	
Number of awakenings	1.3 ± 1.0 (0.0-4.7)	0.9 ± 1.0 (0.0-3.6)	2.4 ± 1.6 (0.1-5.3)	.003**	PI, WCM < WCA
Time in bed after awakening (hours)	1.1 ± 0.8 (0.0-4.0)	1.9 ± 1.6 (0.0-5.1)	0.6 ± 0.6 (0.0-2.3)	.006*	PI, WCM > WCA

Continuous data are shown as mean ± SD (min - max); categorical data as number (% of total),[1] chi square test χ or Kruskal-Wallis tests, * P ≤ .05, ** P ≤ .003 (.05/14), [2] Post-hoc testing using Tamhane test, HADS = Hospital Anxiety and Depression Scale, PI = Primary insomnia, WCM = Insomnia with comorbid mood disorder, WCA = Insomnia with comorbid anxiety disorder.

Sleep diary variables

Primary insomniacs and patients with comorbid depressive disorders showed comparable sleep diary characteristics. However, specific differences were found between these two groups and patients with comorbid anxiety disorders. Patients with comorbid anxiety disorders showed a substantially higher total sleep time (TST) and sleep efficiency (SE) than the other two groups (Table 3.3). On average, they slept 2 hours longer and showed a 20% higher SE than patients with comorbid mood disorders. Also, there was a trend for insomniacs with comorbid anxiety disorders staying shorter in bed after final awakening. However, patients with comorbid anxiety disorders showed a higher number of awakenings (NOA) when compared to primary insomniacs and insomniacs with comorbid mood disorders. They reported two to three times as many awakenings during the night when compared to primary insomniacs and insomniacs with comorbid mood disorders, respectively. There were no significant correlations between HADS anxiety or depression subscales and sleep diary variables (Table 3.4).

Table 3.4 Correlations between HADS depression or anxiety scale and sleep diary variables.

Sleep variables	HADS anxiety scale		HADS depression scale	
	Pearson's rho	*p*	*Pearson's rho*	*p*
Total bed time	.008	.93	.002	.98
Total sleep time	.079	.35	-.107	.20
Sleep efficiency	.099	.24	-.098	.24
Sleep onset latency	-.075	.37	.038	.65
Wake after sleep onset	-.068	.42	-.047	.57
Total daytime sleep	.064	.45	-.028	.74
Number of awakenings	-.041	.63	-.070	.41
Time in bed after awakening	-.042	.62	.008	.93

Data shown are Pearson's rho correlation coefficient, with associated significance level. No significant correlations were found.

Discussion

In line with our hypothesis, there were clear variations in the nature and severity of subjective sleep variables in our cohort of insomniacs depending on the presence and type of comorbid psychiatric disorder. In our study, patients with comorbid anxiety disorders showed a higher subjective SE and longer TST when compared to the other two groups. Although total bedtime (TBT) was comparable, subjective TST and SE were substantially higher in patients with comorbid anxiety disorders (amounting to 2 hours more sleep per night and a 20% higher SE than patients with comorbid mood disorders). While there was a clear difference in TST and SE, the ISI score was comparable between groups, indicating that although nighttime variables suggest a less severe insomnia phenotype in patients with comorbid anxiety disorders, they

experience a similar impact of their sleep disorder. A possible explanation would be that patients with comorbid anxiety disorders worry more about their sleep and tend to seek medical help in the presence of less severe nighttime sleep problems. There was no relationship between the severity of anxiety or depressive complaints and sleep diary variables.

In our study, the NOA was higher in insomniacs with comorbid anxiety disorders, with two to three times more awakenings than the other groups. On the other hand, the wake after sleep onset was not significantly different, which suggests that the time spent awake in bed between the onset of sleep and final awakening was comparable. We conclude that the experience of a highly fragmented sleep is probably the most important insomnia complaint in patients with comorbid anxiety disorders. Time in bed after awakening was shorter in patients with comorbid anxiety disorders. This might yet be another indication of the longer sleep duration in patients with comorbid anxiety disorders. However, it may also reflect a better sleep hygiene with a tendency to get out of bed earlier after the final awakening.

While sleep diary variables were comparable, there was a trend towards a higher ISI-score in insomniacs with comorbid mood disorders when compared to primary insomniacs. The ISI includes items referring to daytime complaints such as fatigue, concentration problems and mood problems, often reported by depressed patients in general. Therefore, a possible explanation is that the higher ISI-score reflects depressive symptomatology instead of greater subjective insomnia severity. Another explanation might be that insomniacs with comorbid mood disorders tend to interpret their sleep problems more negatively and in effect suffer more from comparable nighttime sleep problems.

Because of the cross-sectional design, no cause and effect relationships can be established between insomnia, psychiatric disorders and sleep variables from our data. In addition, the relatively small sample sizes of the groups with comorbid psychiatric disorders precluded an evaluation of possible sleep differences in more specific subgroups, such as different types of anxiety disorders. Future research including larger subgroups of insomniacs with psychiatric comorbidity may be able to answer such questions.

All our variables are based on self-report measures. In the future, it would be interesting to examine and compare additional polysomnographic measures in insomniacs with and without mood and anxiety disorders to evaluate whether our findings can also be generalized to objective sleep measures. Studies on objective sleep measures showed comparable findings in primary insomniacs and insomniacs with different types of mood and anxiety disorders (low sleep efficiency, low total sleep time, high number of awakenings, long time awake in the bed) (Voderholzer et al., 2003; Papadimitriou & Linkowski, 2005; Saletu-Zyhlarz et al., 2002). However, these studies only focused on differences between these groups and normal controls, and did not examine differences between primary and comorbid insomniacs. Studying both objective and subjective measures of sleep may provide insight in the role of sleep

(mis)perception in the experience and presentation of subjective insomnia complaints in these groups.

Edinger et al. (2009) compared the effectiveness of cognitive behavioral treatment for insomnia (CBT-I) between primary insomniacs and insomniacs with comorbid psychiatric disorders with the main conclusion that CBT-I produced similar benefits for both groups across most sleep diary and actigraphy measures. Our findings might have therapeutic consequences for cognitive behavioral treatment of different types of insomnia. Stimulus control refers to a behavioral method in which a patient is advised to get up and move to another room when sleep-onset does not occur within 15 minutes (Morin & Espie, 2003). Because patients with anxiety disorders report more frequent awakenings this method might have an adverse effect, creating very restless nights, frequently getting out and back into the bed. Sleep restriction might be more suitable for these patients. In this method, creating a temporary mild state of sleep deprivation not only helps to bring about a faster sleep onset, but also a greater sleep continuity and quality (Morin & Espie, 2003). In primary insomniacs and patients with comorbid mood disorders stimulus control might be more efficient, especially after the final awakening. Because these patients generally spend 1 to 2 hours in bed after the final awakening (which is a striking 2 to 3 times as much as patients with anxiety disorders) getting up out of bed earlier might be even more important in order to “re-associate” the bed with sleep instead of lying awake. The fact that patients with comorbid anxiety disorders generally show a longer subjective sleep time and a higher sleep efficiency, but still an ISI-score comparable to depressed patients might imply a more negative attribution towards sleep in the first group. Therefore in the treatment of these patients special attention could be given to cognitive therapeutic interventions aiming to reduce magnification and catastrophizing of sleep problems.

In contrast with our hypothesis, comorbid insomniacs do not seem to experience more severe subjective sleep problems in general. Future longitudinal research might focus on the cause and effect relationships between subjective insomnia complaints and psychiatric disorders. The effect of tailored cognitive behavioral treatments for insomnia with and without psychiatric comorbidity would be a relevant research focus.

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Chapter 4

General quality of life in insomnia with and without psychiatric comorbidity

van de Laar, M., Pevernagie, D., Van Mierlo, P. & Overeem, S. (2016). Correlates of general quality of life are different in patients with primary Insomnia as compared to patients with insomnia and psychiatric comorbidity. Psychology, Health and Medicine, 22: 172-183

Abstract

Chronic insomnia is known to have a negative influence on quality of life (QOL). To date, most studies on chronic insomnia have focused on health-related aspects of QOL. General QOL, which is a different construct, has not been studied in detail. Moreover, it is not known which factors are associated with general QOL in insomnia, and whether the presence of mental disorders, a condition known as comorbid insomnia, affects these variables. The present study focused on identifying sleep and psychosocial variables that might be associated with general QOL in primary and comorbid insomnia. Personality traits, coping variables, anxiety and depressive symptoms, fatigue and subjective sleep variables were assessed in 218 consecutive well-characterized patients with primary and comorbid insomnia, referred to a third line centre for sleep medicine. In primary insomnia, higher extraversion and lower discrepancies in social support were associated with higher QOL. Surprisingly, insomnia severity was not significantly associated with QOL in this group. However, lower fatigue, which can be seen as an important daytime consequence of insomnia was correlated with higher QOL in patients with primary insomnia. In both insomnia groups, low anxiety and depressive symptoms and low fatigue were associated with higher general QOL. In contrast with the primary insomnia group, lower insomnia severity was correlated with higher QOL in patients with comorbid insomnia. These results stress the importance of assessing and treating daytime fatigue in insomnia. In primary insomnia, improving social support might be an important treatment goal. Furthermore, this study supports the concept that treatment of insomnia should not be neglected in patients with comorbid insomnia. Indeed, both insomnia and indices of psychiatric disease are strongly associated with general QOL in this condition.

Introduction

Chronic insomnia is accompanied with problems in daytime functioning and is known to have a negative influence on health-related quality of life (QOL) (Kyle, Morgan & Espie, 2010). Most research on QOL in insomnia has focused on health-related QOL. In a recent review, Kyle et al. (2010) mentioned the importance to distinguish between general QOL and health-related QOL in insomnia. General QOL has a broader definition and encompasses more than the impact of disease on everyday functioning. It is defined as individuals' perceptions of their position in life, in the context of the culture and personal values and in relation to their goals, expectations, standards and concerns (Herrman et al., 1993). However, research on the effects of insomnia on general QOL is scarce.

It is presently unknown which factors are associated with general QOL in insomnia. However, several determinants for QOL have been identified in other chronic disorders. Relationships between personality, coping strategies, perceived social support and QOL have been found in previous studies (Bennett et al., 2001; Garnefski, Koopman, Kraaij, & Ten Cate, 2009; Masthoff, Trompenaars, Van Heck, Hodiamont, & De Vries, 2007; Schoofs, Bambini, Ronning, Bielak, & Woehl, 2004). These factors might also be associated with QOL in patients with insomnia. When examining these factors, insomnia patients with and without psychiatric comorbidity should be considered as separate entities because QOL is strongly influenced by the presence of psychiatric disorders (Ishak et al., 2011; Olatunji, Cisler, & Tolin, 2007). Therefore in this explorative pilot study we hypothesized that, besides insomnia severity, psychosocial factors such as personality, coping style and perceived social support might differentially be associated with general QOL in insomnia patients with and without psychiatric disorders.

Methods

General study design and setting

We performed a cross-sectional study comprising patients referred to Kempenhaeghe, a tertiary center for sleep medicine. All patients had a complaint of chronic insomnia (>3 months). Patients were included between June 2010 and May 2011. Criteria for primary insomnia were based on the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV (American Psychological Association, 2000), as the DSM-V was not yet published at the time of data collection. Primary insomnia was diagnosed based on complaints of difficulty initiating or maintaining sleep or nonrestorative sleep, with the sleep disturbance (or associated daytime fatigue) causing clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Comorbid insomnia was diagnosed based on the same criteria as primary insomnia but with the additional presence of a current psychiatric disorder based on the DSM-IV. Patients between 18 and 65 years of age were included if they did not work in shifts and did not have a history of developmental disorders or severe psychopathology (e.g. psychotic disorders). They were medically examined and polysomnography was performed when an organic sleep disorder was suspected from the medical interview performed by a sleep specialist. Full polysomnography was done in-lab, according to the current standards of the American Academy of Sleep Medicine. Other – organic-sleep disorders were diagnosed based upon the ICSD-2 criteria. Those with a somatic disease (e.g. epilepsy, chronic pain) or other sleep disorder (e.g. sleep disordered breathing, restless legs syndrome, periodic limb movement disorder) that could explain at least part of the insomnia were excluded. Patients with alcohol or drug abuse were also excluded. Patients willing to participate in the study signed an informed consent. The study design was approved by the local medical ethical committee.

Quality of life

World Health Organization quality of life (WHO QOL)-bref

As the dependent variable we used the general QOL score from the WHO QOL-bref self-report questionnaire (WHO QOL Group, 1998). General QOL is defined as the computation of the 'overall QOL' and 'general health' items of this questionnaire. These items are rated on a five-point Likert scale (low score of one to high score of five). The internal consistency of the WHO-QOL-bref varies between $\alpha = .75$ and $\alpha = .89$ (Chiu et al., 2006; Lin, Hwang, Chen & Chu, 2007).

Psychopathology

Semi-structured interview for mental disorders

All patients were psychologically examined by a clinical psychologist, and diagnosed according to the DSM-IV, with the aid of a semistructured interview covering the entire range of mental disorders (American Psychological Association, 2000; Hoogduin, 1999).

Hospital Anxiety and Depression Scale (HADS)

The HADS is a 14-item screening instrument, measuring severity of depression and anxiety symptoms (Spinhoven et al., 1997; Zigmond & Snaith, 1983). The questionnaire contains a separate depression and anxiety section, evaluated by seven items each on a four point Likert Scale. Internal consistency ranges between $\alpha = .67$ and $\alpha = .90$. (Bjelland, Dahl, Haug, & Neckelmann, 2002).

Sleep variables

Sleep log

All patients filled in a sleep log during one week. They had to describe the bedtime and time of getting up out of bed. Furthermore they filled in the time spent in bed, awake and sleeping. From this, the following estimated variables were extracted: total bed time, total sleep time, sleep efficiency, sleep onset latency and wake after sleep onset. Patients also filled out questions on the duration of insomnia complaints and current (sleep) medication use.

Insomnia severity index (ISI)

The ISI is a 7-item questionnaire assessing the nature, severity and impact of insomnia (Morin, 1993; Morin, Belleville, Bélanger & Ivers, 2011). A five-point Likert scale is used to rate each of these items, yielding a total score ranging from 0 to 28. Scores can be classified in four severity categories: (0–7): absence of insomnia, (8–14): mild insomnia symptoms, (15–21): moderate insomnia, (22–28): severe insomnia. The internal consistencies range from $\alpha = .90$ to $\alpha = .91$ (Morin et al., 2011).

Personality

Neuroticism extraversion openness five factor inventory (NEO FFI)

The NEO FFI is a short version of the neuroticism extraversion openness personality inventory revised. The NEO FFI contains 60 items, tapping five personality domains, also known as the 'Big Five': neuroticism, extraversion, openness, agreeableness and conscientiousness. The definition of these five broad factors was based on empirical, data-driven research (Costa & McCrae, 1992). Each domain is evaluated by 12 items and a five-point Likert scale is used to rate these items. The internal consistencies of the subscales of the Dutch NEO-FFI are comparable to those of the American NEO-FFI and range between $\alpha = .68$ and $\alpha = .86$ (Hoekstra, Ormel & De Fruyt, 2003).

Trait and character inventory (TCI) short form

The TCI short form is a Dutch short version of the temperament and character inventory. It is comparable to the original version of the TCI and measures the same personality dimensions (Cloninger, Przybeck, Svrakic & Wetzel, 1994; Duijsens, Spinhoven, Goekoop, Spermon & Eurelings-Bontekoe, 2000). Research showed that the original and shortened scales correlate highly and there were no differences in mean scale scores between the two versions (Duijsens & Spinhoven, 2006). The short version contains 105 items and measures seven personality trait dimensions. These can be divided in four temperaments (novelty seeking, harm avoidance, reward dependence and persistence) and three characters (self- directedness, cooperativeness and self-

transcendence). Each dimension is evaluated by 15 items and rated on a five-point Likert Scale. Internal consistencies range between α = .69 and α = .85 (Duijsens & Spinhoven, 2006).

Coping

Cognitive emotion regulation questionnaire (CERQ)

The CERQ includes nine conceptually distinct subscales, each consisting of four items referring to what somebody thinks after the experience of threatening or stressful events. Likert-type items ranging from one [(almost) never] to five [(almost) always] are rated so that higher scores represent greater use of the coping strategy. The following cognitive emotion regulation strategies were measured: self-blame, acceptance, focus on thought/rumination, positive refocusing, refocus on planning, positive reappraisal, putting into perspective, catastrophizing and blaming others. Internal consistencies are in most cases well over α = .70 and in many cases even over α = .80 (Garnefski & Kraaij, 2007).

Social support

Social support list (SSL)

Social support was measured by the van Sonderen SSL (Timmerman, Emanuels-Zuurveen & Emmelkamp, 2000). The SSL is divided into the SSL-I (amount of social support), the SSL-D (discrepancies between amount of social support and desired amount of social sup-port and the SSL-N (amount of negative interactions). Total scores of SSL-I and SSL-D range from 34 to 136, total score of SSL-N from 7 to 28. The internal consistencies of the subscales are satisfactory, with alpha values ranging from 70 to .86 (Timmerman et al., 2000).

Fatigue

Checklist individual strength (CIS) fatigue severity subscale

The CIS is a 20-item questionnaire and measures the following four aspects of fatigue during the previous two weeks: fatigue severity, concentration problems, reduced motivation and reduced activity. The fatigue severity subscale contains eight items and the total subscale score ranges between 8 and 56 (Vercoulen, Alberts & Bleijenberg, 1999). The internal consistency for the fatigue severity subscale is α = .88 (Vercoulen et al., 1994).

Data analysis

Data was analyzed using SPSS 20 for Windows. Descriptive statistics were first used to characterize the sample. Mann–Whitney U tests and χ^2 tests were used to compare general QOL, baseline demographic characteristics and insomnia characteristics between patients with primary and comorbid insomnia. Spearman correlations were applied to analyze relations between sleep variables, psychosocial variables and general QOL. Linear regression was used to identify significant factors that were independently associated with general QOL in patients with and without psychiatric comorbidity. Factors with an uncorrected p-value for the correlation below .01 were entered in the regression analyses. Multicollinearity diagnostics were performed for both regression models, showing no signs of multicollinearity among the independent variables.

Results

General sample characteristics

Over the study period, a total of 281 patients referred to the sleep center signed informed consent for the study. Of these patients, 62 subjects were excluded because of the presence of a somatic disease or another sleep disorder that could explain insomnia. One patient was excluded because of alcohol abuse (Figure 4.1). The final group with insomnia comprised 218 patients; 107 patients with primary insomnia and 111 patients with comorbid insomnia. Specific subtypes of the comorbid psychiatric disorders are described in Table 4.1.

Table 4.1 Specific psychiatric diagnoses in research population (N=111)

DSM-IV cluster	Specific type of DSM-IV diagnosis	Frequency
Mood disorders (N=34)	Depressive disorder	27
	Dysthymic disorder	4
	Bipolar disorder	3
Anxiety disorders (N=29)	Generalized anxiety disorder	13
	Panic disorder	8
	Posttraumatic stress disorder	3
	Social phobia	3
	Obsessive compulsive disorder	1
	Anxiety disorder not otherwise specified	1
Somatoform disorders (N=28)	Undifferentiated somatoform disorder	28
Adjustment disorders (N=13)	Adjustment disorder	13
Attention-deficit and disruptive behavior disorders (N=7)	ADHD	7

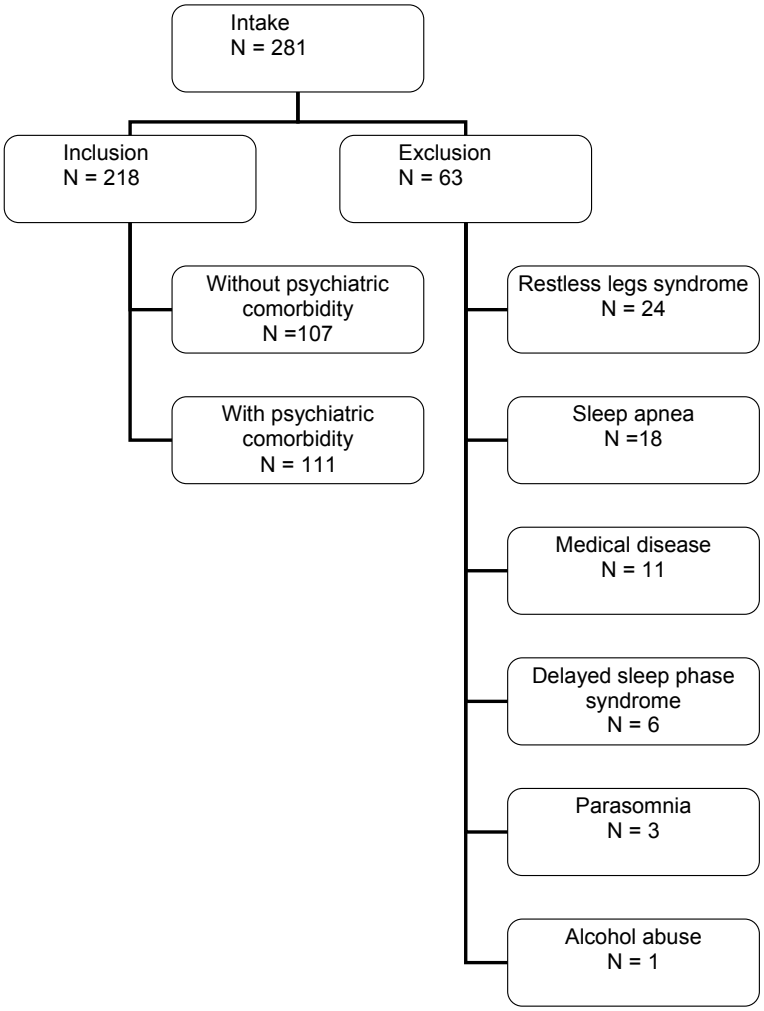

Figure 4.1 Flowchart of patients initially referred for diagnosis of insomnia complaint.

Characteristics of the sample, QOL and insomnia variables in patients with and without psychiatric comorbidity are presented in Table 4.2. Patients with psychiatric comorbidity had significantly lower scores on general QOL than primary insomniacs. Insomnia severity was significantly higher in the first group. To examine whether insomnia severity was a confounding variable in the general QOL difference between patients with and without psychiatric comorbidity, we performed an ANCOVA analysis controlling for insomnia severity, age and gender (Table 4.3). General QOL was still significantly different between the two groups after controlling for these covariates.

Table 4.2 Quality of life, baseline demographic characteristics and insomnia characteristics in patients with primary and comorbid insomnia.

Variables	Primary insomniacs (N = 107)	Comorbid insomniacs (N = 111)	P [1]
WHO QOL-bref			
general quality of life	6.8 ± 1.4 (3-10)	5.4 ± 1.6 (2-9)	.000*
Age	44.1 ± 11.8 (18-65)	43.8 ± 10.6 (21-64)	.737
Gender (male/female)	34/73 (32%/68%)	41/70 (37%/63%)	.423
Sleep variables			
Insomnia severity index	20.2 ± 4 (10-28)	21.0 ± 3.8 (12-28)	.035*
Insomnia duration (years)	10.3 ± 12.1 (.3-64)	12.1 ± 11.4 (.3-52)	.110
Total bed time (hours)	8.5 ± .9 (6.1-10.9)	8.7 ± 1.3 (6.2-14.0)	.156
Total sleep time (hours)	5.0 ± 1.3 (1.5-7.9)	5.0 ± 1.6 (0-8,4)	.760
Sleep efficiency (%)	58.9 ± 14.6 (18.5-85.8)	57.6 ± 18.7 (0-93.5)	.970
Sleep onset latency (hours)	1.2 ± .7 (0-4)	1.5 ± 1.2 (0-6.1)	.233
Wake after sleep onset (hours)	1.2 ± .7 (0-3.1)	1.1 ± .8 (0-4.3)	.717
Sleep medication use (y/n)	62/45 (58%/42%)	67/44 (60%/40%)	.717

Data are mean ± SD (range), [1] Chi-square test χ^2 or Mann-Whitney U test α, * = significant on a P≤.05 level , WHO QOL-bref = World Health Organization Quality of Life abbreviated version.

Table 4.3 Analysis of covariance (dependent variable is QOL)

	Degrees of freedom	Mean of squares	F-value
Model	4	153.3	18.8
Control variables			
-Insomnia severity index	1	42.1	20.6*
-Age (years)	1	1.2	.6
-Gender (male/female)	1	7.3	3.6
Psychiatry (yes/no)	1	80.9	39.6*

adjusted R^2 = .246 * P<.001

Primary insomnia

Correlational analyses showed that higher anxiety and depressive symptoms and higher fatigue were significantly associated with lower general QOL. Higher discrepancies in social support were also significantly associated with lower general QOL whilst higher amount of social support was associated with higher general QOL. High Extraversion was associated with higher general QOL. Surprisingly, insomnia severity and other sleep variables including sleep medication use, did not correlate significantly. Also, none of the coping variables had significant correlations with general QOL. Remarkably, in primary insomnia, neither insomnia severity nor the other sleep variables were correlated with general QOL. Multiple regression analyses showed that scores on the HADS, CIS-fatigue scale, NEO FFI Extraversion and SSL-discrepancies in social support, significantly and independently explained the variance in general QOL (see Table 4.4).

Table 4.4 Multiple linear regression model between psychosocial and sleep variables and quality of life in primary insomnia (N=107)

Variables	B	SE	β	t	95% CI for B	
					Lower Bound	Upper Bound
Constant	8.825	1.320		6.686	6.207	11.444
HADS	-.055	.025	-.177*	-2.197	-.104	-.005
CIS-fatigue	-.047	.011	-.346**	-4.438	-.068	-.026
NEO FFI Extraversion	.043	.020	.186*	2.182	.004	.083
SSL-interactions	.005	.009	.056	.590	-.013	.024
SSL-discrepancies	-.035	.011	-.283**	-3.028	-.057	-.012

adjusted R^2 =.373, df =5, * P≤.05, ** P≤.01, HADS = Hospital Anxiety and Depression Scale, CIS = Checklist Individual Strength, NEO FFI = Neuroticism, Extraversion Openness Five Factor Inventory, SSL = Social Support List

Comorbid insomnia

Correlational analyses showed that higher anxiety and depressive symptoms were associated with lower general QOL. In contrast with the results in the primary insomnia group, higher insomnia severity was significantly associated with lower general QOL. None of the other sleep variables including sleep medication use were significantly associated with general QOL. Patients with higher fatigue generally showed lower general QOL. Finally, high negative social interactions were associated with lower general QOL. Multiple regression analyses showed that scores on the HADS, ISI and CIS-fatigue significantly and independently explained the variance in general QOL (see Table 4.5).

Table 4.5 Multiple linear regression model between psychosocial and sleep variables and quality of life in comorbid insomnia

Variables	B	SE	β	t	95% CI for B	
					Lower Bound	Upper Bound
Constant	11.751	.881		13.346	10.005	13.497
HADS	-.073	.018	-.323**	-3.979	-.109	-.036
Insomnia Severity Index	-.089	.035	-.214*	-.2565	-.158	-.020
CIS-fatigue	-.056	.017	-.272**	-3.249	-.091	-.022
SSL-negative interactions	.047	.036	-.102	-1.301	-.118	.025

adjusted R^2 =.373, df =4, * P ≤ .05, ** P ≤ .01, HADS = Hospital Anxiety and Depression Scale, CIS = Checklist Individual Strength, SSL = Social Support List

Discussion

Our study is the first to examine the association between psychosocial and sleep variables and general QOL in a group of well-defined primary and comorbid insomniacs. We showed that several sleep and psychosocial factors are differentially associated

with general QOL in these two groups. General QOL was lower and insomnia severity was higher in comorbid insomniacs. The difference in general QOL between primary and comorbid insomniacs remained significant after controlling for insomnia severity and other possible confounders, which is in line with results from earlier studies (Lichstein, Durrence, Bayen & Riedel, 2001; Sarsour, Morin, Foley, Kalsekar & Walsh, 2010). This highlights the importance of the presence of psychiatric comorbidity in respect to general QOL in insomniacs and supports the development of two separate association models for general QOL in primary and comorbid insomnia.

General QOL and sleep variables vs. daytime functioning

In both insomnia groups, higher fatigue, which is potentially a consequence of chronic insomnia, was associated with lower general QOL. Surprisingly, there was no association between insomnia severity and general QOL in patients with primary insomnia, while in comorbid patients, higher insomnia severity was significantly associated with general QOL. In both groups, none of the sleep diary variables were associated with general QOL, which suggests weak linkage between sleep diary variables and daytime functioning. This is in line with results from a study by Omvik et al. (2008), who found that the correspondence between improvements in sleep and improvements in daytime functioning due to treatment was poor. Attention towards the sleep problem and self-monitoring might be more important in the experience of daytime consequences of insomnia than subjective sleep variables.

General QOL and social support

In our study, social support seems to be an important aspect associated with general QOL in primary insomniacs, which is in line with research in depressed patients (Kuehner & Buerger, 2005). An explanation for this relationship might be that the presence of sufficient social support is somehow protective for the negative consequences of insomnia on daytime functioning. Another explanation might be that lack of social support is an important consequence of insomnia because patients often report to become less socially active as a result of fatigue and other daytime consequences. Longitudinal research might contribute to a better understanding of the causal relationship between general QOL, social support and daytime consequences in primary insomnia.

General QOL and personality

Extraversion was associated with a higher general QOL in our sample. Presumably, patients who are more outgoing and extraverted can better resist the negative daytime consequences of primary insomnia than introverted patients. However, because extraversion is known to be influenced by current emotional state, another explanation

might be that introversion is an important consequence of insomnia which impairs perceived QOL.

General QOL and depressive and anxiety symptoms

In both groups, the severity of depressive and anxiety symptoms was strongly associated with general QOL. In contrast with primary insomnia patients, the severity of insomnia was also associated with general QOL in comorbid insomniacs. Surprisingly, none of the psychosocial variables were associated with general QOL in these patients. It might be that anxiety and depressive symptoms exert dominant effects on general QOL in these patients and that – as a consequence – other psychosocial variables are masked by the presence of these symptoms.

General conclusion and treatment suggestions

From our findings we conclude that insomnia should be an important independent treatment goal in comorbid insomniacs and should not be regarded as a mere epiphenomenon of psychiatric morbidity. These results are in line with earlier investigations which showed that adjuvant cognitive behavioral therapy of insomnia in depressed patients concurrent with treatment of depression enhanced treatment outcomes of both depression and insomnia (Manber et al., 2008).

The results from the present study hint towards personalized management of chronic insomnia. Assessing discrepancies in social support and identifying possible negative consequences of insomnia on social relations might guide independent treatment goals.

These goals might be related to the enhancement of social activity in primary insomniacs. Special attention should be given to primary insomniacs with low extraversion. As a result of daytime insomnia consequences, these patients might be more prone to show passive behavior. This might lead to a vicious circle creating a lack of exposure to external resources that provide distraction and positive reinforcement. As a consequence they might develop a higher focus on negative daytime effects of insomnia leading to more passive behavior.

The use of only two items of the WHO-QOL bref might be seen as a limitation of the study. However, using more specific measures of QOL, such as psychological health and social relationships dimensions as outcome variables also creates methodological issues. For example, variables such as the HADS and SSL show great overlap with items of the psychological health and social relationships-dimensions of the QOL-bref. To avoid this, we decided to use a general measure of QOL, defined by general health and overall QOL.

Because of the cross-sectional design, no cause and effect relationships can be established between insomnia severity, psychosocial variables and general QOL from our data. Future longitudinal studies should focus on the possible causality between insomnia severity, lack of social support, extraversion and general QOL. Moreover,

therapeutic trials should include fatigue as a daytime measure of functioning in the evaluation of treatment effect in primary insomnia. Also, the influence of cognitive processes such as attention towards the sleep problem, on general QOL might be interesting to examine. The present study has focused on the – highly heterogenic-group of patients with comorbid psychiatric disorders. It will be important for future studies to examine whether the correlations we found between insomnia severity, HADS-score and general QOL in the present study are also generalizable to specific comorbid psychiatric disorders.

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Chapter 5

Psychiatric comorbidity and coping predict cognitive behavioral treatment effect

van de Laar, M., Pevernagie, D., Van Mierlo, P. & Overeem, S. (2015). Psychiatric comorbidity and aspects of cognitive coping negatively predict outcome in cognitive behavioral treatment of psychophysiological insomnia. Behavioral Sleep Medicine, 13, 140-156.

Abstract

Cognitive behavioral treatment is the gold standard treatment for insomnia, although a substantial group does not respond. We examined possible predictors for treatment outcome in psychophysiological insomniacs, with a focus on the presence of clearly defined psychiatric comorbidity. This was a longitudinal uncontrolled case series study comprising 60 patients with chronic psychophysiological insomnia consecutively referred to a tertiary sleep medicine center, to receive cognitive behavioral treatment for insomnia (CBT-I). Remission of insomnia was defined as a posttreatment.

Insomnia Severity Index score below 8. As an alternative outcome, we used a clinically relevant decrease on the Insomnia Severity Index (drop of >7 points). Personality, coping, and social support questionnaires were assessed before the start of the treatment and were compared between treatment responders and nonresponders. To examine whether these variables were predictive for negative treatment outcome, logistic regression analyses were applied. Treatment nonresponders had a significantly higher prevalence of psychiatric comorbidity. Logistic regression analyses showed that the presence of psychiatric comorbidity was strongly predictive for negative treatment outcome (odds ratios: 20.6 and 10.3 for the 2 outcome definitions). Additionally, higher scores on the cognitive coping strategy called “refocus on planning” were associated with worse CBT-I outcome. Current psychiatric comorbidity is strongly predictive for negative treatment outcome. The presence of a psychiatric disorder must therefore be one of the leading arguments in the choice of treatment modalities that are being proposed to patients with insomnia.

Introduction

Insomnia is a highly prevalent disorder that is known to have a negative influence on daytime functioning (Komada et al., 2012). Some patients have "pure" psychophysiological insomnia, but the disorder is often accompanied by mental disorders (Buysse et al., 1994; Mahendran, Subramaniam & Chan, 2007). Cognitive behavioral treatment (CBT-I) to target the vicious circle of maladaptive behavior around sleep, negative cognitions, and physiological arousal, is generally described as the gold standard treatment for insomnia in patients with and without psychiatric comorbidity (Edinger et al., 2009; Morin & Espie, 2003; Sanchez-Ortuno & Edinger, 2012).

The 3-P model by Spielman and Glovinsky (1991) describes how predisposing, precipitating, and perpetuating factors play an important role in the development of chronic insomnia. In this model, personality and social factors are mentioned as possible predisposing factors, while psychiatric disorders can be precipitating events. Finally, cognitive aspects such as rumination can be perpetuating factors for chronic insomnia. As these psychological aspects play an important role in the development and maintenance of insomnia, they may also be associated with CBT-I treatment effect.

Past research that aimed to identify predictors of CBT-I treatment response mainly focused on the general group of primary insomnia, without comorbidity. Psychiatric comorbidity often was an explicit exclusion criterion, or the presence of mental disorders was not clearly defined. However, there are indications that psychiatric comorbidity may be related to treatment effect. For example, in a study by Gagné and Morin (2001), depressive symptoms in older adults with insomnia predicted more negative treatment outcome. In other studies, higher baseline anxiety scores and psychological distress predicted worse treatment response (Belleville & Morin, 2008; Morgan, Thompson, Dixon, Tomeny & Mathers, 2003). Edinger et al. (2009) compared the effectiveness of CBT-I between primary insomniacs and insomniacs with comorbid psychiatric disorders. This study mainly focused on nighttime symptoms of insomnia, with the main conclusion that CBT-I produced similar benefits for both groups across most sleep diary and actigraphy measures. It would be interesting to examine whether patients with psychiatric comorbidity would respond similarly to CBT-I when focusing on the important daytime consequences of insomnia. The Insomnia Severity Index (ISI) is a relevant instrument in this respect, covering both nighttime and daytime symptoms of insomnia (Morin, 1993; Morin, Belleville, Bélanger & Ivers, 2011).

The role of personality has been examined in previous research on predictors of treatment effect. A lower number of MMPI scales in the pathological range, and lower scores on MMPI scales for hysteria, hypomania, and schizophrenia, correlated with better CBT-I outcomes (Lacks & Powlishta, 1989; Shealy, Lowe & Ritzler, 1980). In another study, nondepressed elderly insomniacs who positively responded to treatment (e.g., sleep restriction and relaxation therapy) at three-month follow-up scored lower on Neuroticism Extraversion Openness Five Factor Inventory (NEO FFI) scales for extraversion and openness (Bliwise, Friedman, Nekich & Yesavage, 1995).

Edinger, Stout and Hoelscher (1988) found that nondepressed insomniacs who benefited from behavioral treatment showed a clearly defined neurotic profile. It remains unknown how personality characteristics interact with the presence of psychiatric comorbidity to predict treatment response in insomnia.
Cognitive factors have also been identified as possible predictors of treatment effect. For example, patients with relatively high levels of unhelpful sleep-related beliefs showed better clinically significant improvement (Edinger, Carney & Wohlgemuth, 2008). Two studies on patients with persistent insomnia showed that reductions in negative sleep-related beliefs were associated with positive CBT-I treatment response (Edinger, Wohlgemuth, Radtke, Marsh & Quillian, 2001; Morin, Blais & Savard, 2002). A related psychological construct that might be interesting to examine is cognitive coping. Cognitive coping refers to what someone thinks after experiencing a negative event (Garnefski & Kraaij, 2007). Patients who tend to ruminate or catastrophize might be more prone to have negative sleep-related beliefs after experiencing several nights of bad sleep. Because patients with high levels of negative sleep-related beliefs are known to show better improvement after sleep therapy, high scores on cognitive coping factors such as rumination and catastrophizing might be subject characteristics that might be related to a better treatment effect (Edinger et al., 2008).
Although social factors have not been examined in previous research on predictors of treatment effect in insomnia, a lack of social support might induce elevated stress levels and consequently have a negative influence on CBT-I outcome. This hypothesis is supported by research on the relationship between social support and insomnia: a low level of social support was one the factors associated with overreporting of sleep difficulties and underestimation of sleep efficiency (Jackowska, Dockray, Hendrickx & Steptoe, 2011).
The aim of the present study was to identify psychosocial predictors for the outcome of cognitive behavioral treatment of psychophysiological insomnia with and without clearly defined psychiatric disorders. We hypothesized that the presence of psychiatric comorbidity, personality characteristics, certain aspects of cognitive coping (i.e., rumination and catastrophizing), and lack of social support are associated with treatment effect. Identifying important predictors for treatment effect might guide the choice for type of treatment and help to develop and implement new treatment strategies for CBT-I treatment nonresponders in the future.

Research methods

Setting and general study design

We performed an explorative longitudinal uncontrolled case series study in patients with psychophysiological insomnia, seen at the Kempenhaeghe Center of Sleep Medicine, a tertiary referral center. Patients were included between March 2010 and

December 2011. Psychodiagnostic and sleep variables were assessed at baseline and at the end of treatment, three months after. All subjects gave written informed consent. The study design was approved by the local medical ethical committee.

Inclusion and exclusion, baseline assessment

We followed the diagnostic criteria for psychophysiological insomnia of the International Classification of Sleep Disorders, second edition (ICSD-2; AASM, 2005). All subjects had a complaint of chronic insomnia (> 3 months). Patients between 18 and 65 years of age were included if they did not work in shifts and did not have a history of developmental disorders or severe psychopathology (e.g., psychotic disorders). They were medically examined and polysomnography was performed when an organic sleep disorder was suspected from the medical interview, performed by a sleep specialist. Those with a somatic disease or other sleep disorders that could explain (part of) the insomnia (e.g., sleep apnea, restless legs syndrome, epilepsy, chronic pain) were excluded. Patients with alcohol or drug abuse were also excluded.
All patients were psychologically examined by a clinical psychologist, and diagnosed according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV), with the aid of a semistructured interview covering the entire range of mental disorders (American Psychological Association, 2000; Hoogduin, 1999). Those patients who were diagnosed with comorbid psychopathology and who were not currently treated for their psychiatric disorder were counselled to contact their general physician for a referral for psychological treatment.

Intervention

All patients followed standardized cognitive behavioral treatment for insomnia (Morin & Espie, 2003). Interventions included: psychoeducation, sleep hygiene, progressive relaxation, sleep restriction, stimulus control and cognitive therapy targeting negative thoughts and beliefs around sleep. CBT-I started with six weekly treatment sessions, followed by two treatment sessions after one and three months. In the last two sessions, the longer-term effect of the treatment strategies on the insomnia complaint was evaluated and the prevention of a possible relapse was discussed.

Treatment Outcome

The primary definition of treatment response was based on a posttreatment ISI below 8, which is a validated remission criterion (Morin et al., 2011). As an alternative indicator of treatment response, we used a decrease in ISI score of more than 7 points, which was shown to be a moderate, but clinically relevant, improvement (Morin et al., 2011).

Outcome Variables

The following questionnaires were assessed at baseline and at the end of CBT-I (i.e., after 3 months from start).

Sleep Variables

Sleep log

All patients filled in a sleep log during one week. They had to describe the bedtime and time of getting up out of bed. Furthermore they filled in the time spent in bed, awake and sleeping. From this, the following estimated variables were extracted: total sleep time, sleep efficiency, and sleep onset latency.

Insomnia Severity Index (ISI)

The ISI is a 7-item questionnaire assessing the nature, severity and impact of the sleep problems (Morin, 1993; Morin et al., 2011). A five-point Likert scale is used to rate each of these items, yielding a total score ranging from 0 to 28. Scores can be classified in four severity categories: (0–7): absence of insomnia; (8–14): mild insomnia symptoms; (15–21): moderate insomnia; (22–28): severe insomnia.

Personality

Neuroticism Extraversion Openness Five Factor Inventory (NEO FFI)

The NEO FFI is a short version of the Neuroticism Extraversion Openness Personality Inventory Revised (NEO PI R). The NEO FFI contains 60 items, tapping five personality domains, also known as the Big Five: neuroticism, extraversion, openness, agreeableness, and conscientiousness. The definition of these five broad factors were based on empirical, data-driven research (Costa & McCrae, 1992). Each domain is evaluated by 12 items, and a five-point Likert scale is used to rate these items. The Dutch version of the NEO FFI has good psychometric properties (Hoekstra, Ormel & De Fruyt, 2003). The internal consistencies of the subscales of the Dutch NEO FFI are comparable to those of the American NEO FFI and range between ¸ α= 68 and ¸ α= .86, while indices of validity range between r =.50 and r =.84, reflecting correlations with questionnaires measuring similar personality characteristics (Hoekstra et al., 2003).

Temperament and Character Inventory (TCI) Short-Form

The TCI Short Form is a Dutch short version of the Temperament and Character Inventory. It is comparable to the original version of the TCI and measures the same personality dimensions (Cloninger, Przybeck, Svrakic & Wetzel, 1994; Duijsens, Spinhoven, Goekoop, Spermon & Eurelings-Bontekoe, 2000). In previous research, original and shortened scales correlated highly and there were no differences found in

mean scale scores between the two versions (Duijsens & Spinhoven, 2006). The short version contains 105 items and measures seven personality trait dimensions. These can be divided into four temperaments (novelty seeking, harm avoidance, reward dependence, and persistence) and three characters (self-directedness, cooperativeness, and self-transcendence). Each dimension is evaluated by 15 items and rated on a five-point Likert Scale. The TCI Short Form has good psychometric properties. Internal consistencies range between α=.69 and α=.85. Test–retest correlation coefficients range between r=.71 and r=.90 (Duijsens & Spinhoven, 2006).

Coping

Cognitive Emotion Regulation Questionnaire (CERQ)

The CERQ includes nine conceptually distinct subscales, each consisting of four items referring to what somebody thinks after the experience of threatening or stressful events. Likert-type items ranging from 1 (almost never) to 5 (almost always) are rated so that higher scores represent greater use of the coping strategy. The following cognitive emotion regulation strategies were measured: self-blame, acceptance, focus on thought/rumination, positive refocusing, refocus on planning, positive reappraisal, putting into perspective, catastrophizing, and blaming others. The psychometric properties of the CERQ have been proven to be good with Cronbach's alpha coefficients in most cases well over .70 and in many cases even over .80 (Garnefski & Kraaij, 2007).

Anxiety and depressive symptoms

Hospital Anxiety and Depression Scale (HADS)

The HADS is a 14-item screening instrument, measuring severity of depression and anxiety symptoms (Spinhoven et al., 1997; Zigmond & Snaith, 1983). The questionnaire contains a separate depression and anxiety scale. Each scale is evaluated by seven items on a four-point Likert Scale.

Social Support

Social Support List (SSL)

Social support was measured by the van Sonderen Social Support List (SSL; Timmerman, Emanuels-Zuurveen & Emmelkamp, 2000). The SSL is divided into the SSL-I (amount of social support), the SSL-D (discrepancies between amount of social support and desired amount of social support), and the SSL-N (amount of negative interactions). Total scores of SSL-I and SSL-D range from 34 to 136, total score of SSL-N from 7 to 28. The internal consistencies of the subscales are satisfactory, with alpha values ranging from .70 to .86 (Timmerman et al., 2000).

Fatigue

Checklist Individual Strength (CIS) fatigue severity subscale The CIS is a 20-item questionnaire and measures the following four aspects of fatigue during the previous two weeks: fatigue severity, concentration problems, reduced motivation, and reduced activity. The fatigue severity subscale contains 8 items and the total subscale score ranges between 8 and 56 (Vercoulen, Alberts & Bleijenberg, 1999).

Data Analysis

Data was analyzed using SPSS 20 for Windows. Descriptive statistics were used to characterize the sample. Baseline demographic and clinical characteristics of treatment responders and nonresponders were compared using Mann-Whitney U tests and chi-square tests. Bonferroni correction was applied to adjust for multiple testing. Forward logistic regression analyses were performed to identify significant factors predicting negative treatment response (i.e. posttreatment ISI score remaining above 8, or decrease of less than 7 points on the ISI). Multicollinearity diagnostics were performed for both regression models, showing no signs of multicollinearity among the independent variables.

Results

General sample characteristics

Figure 5.1 represents the inclusion/exclusion flowchart. Fifty-one percent of the patients seen in our center during the inclusion period were willing to participate in the treatment study. There were no significant differences in baseline demography, sleep, personality, coping, social support, and fatigue scores between the patients who were and were not willing to participate. Of the 110 patients willing to participate, 71% were eligible for the treatment study. Of those who were not eligible, 7 subjects had spontaneous remission from insomnia before the start of the CBT-I. One patient had already participated in an earlier CBT-I treatment. In 11 patients the main complaint concerned the comorbid psychiatric condition (e.g., depressive or anxious symptoms). Thirteen patients did not meet the criteria for psychophysiological insomnia (i.e., no negative thoughts/emotions around sleep or physiological arousal). Within the group of patients eligible for CBT-I, 18 subjects dropped out of treatment. There were no significant differences on demographic variables, baseline sleep variables, presence of psychiatric disorders, and severity of anxiety and depressive symptoms between treatment dropouts and patients who finished treatment (Table 5.1). The final cohort to be analyzed therefore comprised 60 patients (19 men, 41 women, age 43.8 ± 11.6 years; range 20–64 years).

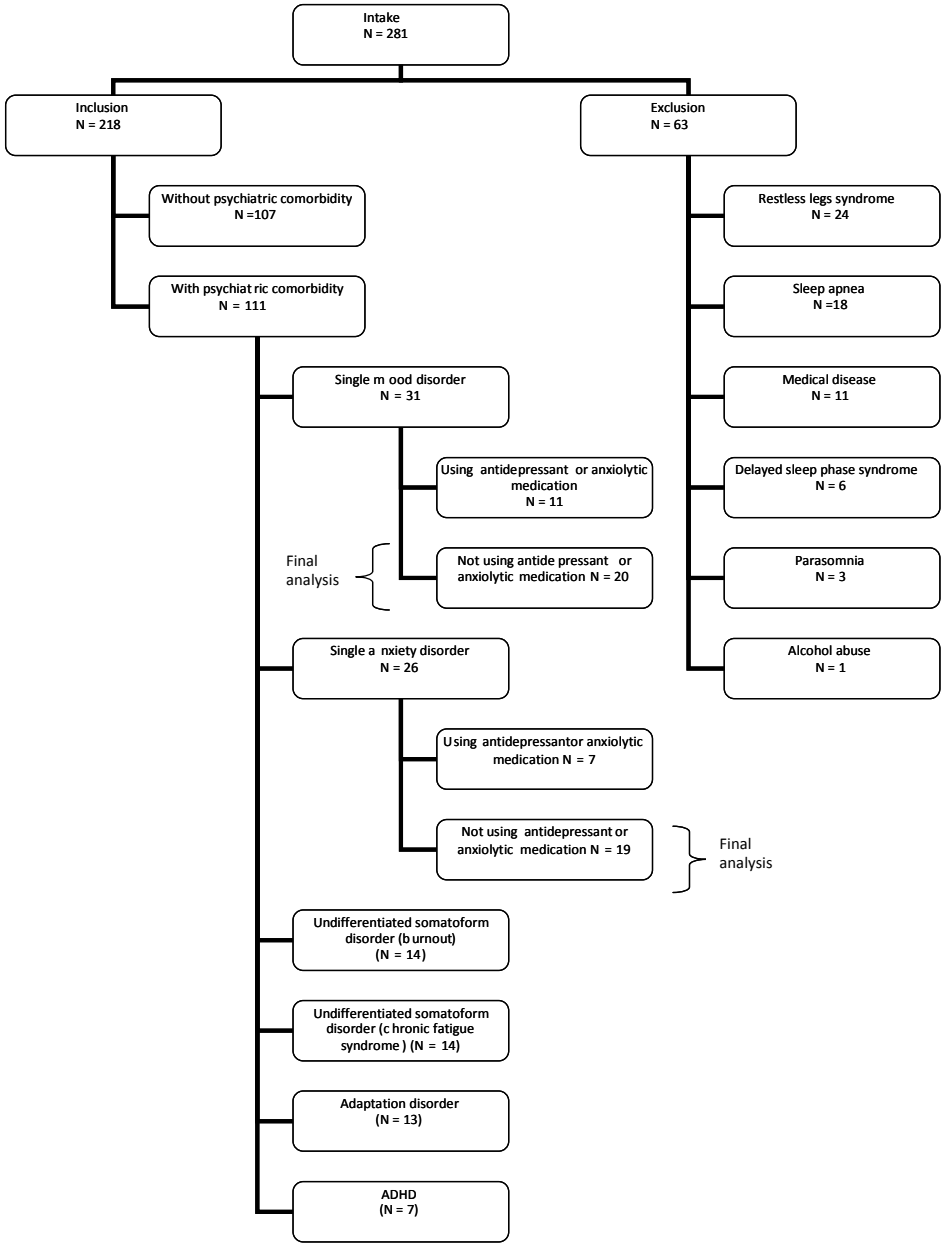

Figure 5.1 Flowchart of patients initially referred for diagnosis of insomnia complaint.

Table 5.1 Clinical characteristics of treatment dropouts and patients who finished CBT-I.

	Patients who finished CBT-I (N =60)	Treatment dropouts (N=18)	P[1]
Age (years)	43.8 ± 11.6	43.4 ± 10.6	.873
Sex (males)	19 (32%)	6 (33%)	1.00
Psychiatric comorbidity (%)	30 (50%)	8 (44%)	.790
Insomnia severity index	20.6 ± 4	21.7 ± 2.6	.361
Sleep efficiency (%)	55.6 ± 15.9	60.1 ± 21.9	.107
Sleep onset latency (hours)	1.4 ± 1	1.2 ± 1	.296
Total sleep time (hours)	4.8 ± 1.4	5.1 ± 1.8	.108
HADS	13.6 ± 6.1	13.1 ± 6.2	.686

Data are mean ± SD / number (%), [1] Chi-square test χ^2 or Mann-Whitney U test α, HADS = Hospital Anxiety and Depression Scale

Thirty patients (30%) had a comorbid psychiatric disorder (for details on the DSM-IV diagnoses and psychiatric treatment, see Table 5.2). The largest group (26.7%) comprised patients with undifferentiated somatoform disorder, followed by major depressive disorder (16.7%) and adaptation disorder (13.3%). Eleven of the 30 patients with comorbid mental disorders (36.7%) were under current psychotherapy and/or using medication for their mental disorder. Comorbid insomniacs who were not currently treated for their psychiatric disorder were advised to contact their general physician for a referral for psychological treatment. After the intake procedure, seven patients (23.3%) were referred to a psychologist by their general physician and started psychological treatment for their psychiatric disorder parallel to CBT-I. Twelve patients (40%) did not receive treatment for their mental disorder already and were not referred by their general physician. These patients were not motivated for a psychological intervention or medication use for their psychiatric problem and/or wanted to have their sleep problem treated first before they wanted to consider a referral.

Table 5.2 Psychodiagnostics and psychiatric treatments in insomniacs with psychiatric comorbidity (N=30).

DSM-IV Axis-I diagnosis	N	Psychotherapy	Medication	Combination therapy	Referral[1]	No current therapy or referral
Major depressive disorder	5 (16.7%)	-	-	-	1	4
Dysthymic disorder	1 (3.3%)	-	-	-	-	1
Bipolar disorder	3 (10%)	-	1	1	1	-
Panic disorder	2 (6.7%)	1	-	-	1	-
Generalized anxiety disorder	3 (10%)	-	-	-	1	2
Social anxiety disorder	2 (6.7%)	1	-	-	-	1
Undifferentiated somatoform disorder	8 (26.7 %)	4	-	-	2	2
Adaptation disorder	4 (13.3 %)	1	-	-	1	2
ADHD	2 (6.7%)	1	1	-	-	-

[1] Referral for psychiatric treatment, coordinated by general physician, ADHD = Attention Deficit Hyperactivity Disorder

Treatment outcome

Table 5.3 shows sleep variables and depressive and anxiety symptoms before and after treatment. In the overall group, the mean ISI-score at baseline was 20.6 points, indicating moderately severe insomnia. After treatment, the mean ISI-score significantly decreased to 8.3 points (i.e., subthreshold insomnia). The mean sleep efficiency significantly increased from 55.8% to 76.5%. Mean sleep onset latency decreased from 1.4 hours to .6 hours and total sleep time increased from 4.8 hours to 5.8 hours per night. The mean HADS-score significantly decreased from 13.6 to 10.3. Mean outcomes on sleep variables and HADS scores significantly improved also when patients with and without psychiatric comorbidity were analyzed separately.

Table 5.3 Sleep variables and anxiety and depressive symptoms before and after CBT-I.

		Before treatment	After treatment	P[1]
Total group (N=60)	Insomnia severity index	20.6 ± 4	8.3 ± 5.4	.000 *
	Sleep efficiency (%)	55.8 ± 16.4	76.5 ± 13.1	.000 *
	Sleep onset latency (hours)	1.4 ± 1.1	.6 ± .4	.000 *
	Total sleep time (hours)	4.8 ± 1.4	5.8 ± 1.2	.000 *
	HADS	13.6 ± 6.1	10.3 ± 6.4	.000 *
Patients without psychiatric comorbidity (N=30)	Insomnia severity index	20.3 ± 4.3	5.1 ± 3.4	.000 *
	Sleep efficiency (%)	56.2 ± 13.6	80.9 ± 11.6	.000 *
	Sleep onset latency (hours)	1.3 ± .9	.4 ± .3	.000 *
	Total sleep time (hours)	4.8 ± 1.3	6.1 ± 1.1	.000 *
	HADS	9.9 ± 4	6.9 ± 4	.005
Patients with psychiatric comorbidity (N=30)	Insomnia severity index	20.8 ± 3.7	11.6 ± 5.2	.000 *
	Sleep efficiency (%)	55.5 ± 18.8	72.5 ± 13.3	.000 *
	Sleep onset latency (hours)	1.4 ± 1.2	.7 ± .5	.001 *
	Total sleep time (hours)	4.7 ± 1.5	5.5 ± 1.2	.001 *
	HADS	17.3 ± 5.5	13.8 ± 6.4	.003 *

Data are mean ± SD, [1] Wilcoxon signed rank test α, * P ≤ .003 (.05/15), HADS = Hospital Anxiety and Depression Scale.

Differences Between CBT-I Responders and Nonresponders

After CBT-I, 53% (n=32) of the study population showed an ISI score below 8, and 68% (n=41) showed a decrease in ISI-score of more than 7 points. In Tables 5.4 and 5.5, clinical and psychological outcomes are compared between responders and nonresponders, using the 2 different response criteria. Using either criterion, the presence of psychiatric comorbidity was significantly higher in the nonresponders to CBT-I: about 20–30% of treatment responders had current psychiatric comorbidity, compared to over 80% of nonresponders. The strong effect of psychiatric comorbidity on CBT-I response was also evident when comparing patients with and without psychiatric comorbidity: 83% of the patients without psychiatric comorbidity showed an ISI-score of <8 versus only 23% in patients with psychiatric comorbidity.

Table 5.4 Pre-treatment differences between responders (Insomnia Severity Index score <8) and nonresponders.

	CBT-responders (N=32)	CBT nonresponders (N=28)	P[1]
Age (years)	43.1 ± 12.0	44.6 ± 11.2	.568
Sex (males)	12 (38%)	7 (25%)	.299
Current psychiatric disorder	*7 (22%)*	*23 (82%)*	*.000 **
Previous psychiatric disorder	7 (22%)	8 (29%)	.550
Sleep efficiency (%)	55.6 ± 14.6	55.6 ± 17.6	.767
Sleep onset latency (hours)	1.3 ± .8	1.4 ± 1.3	.668
Total sleep time (hours)	4.8 ± 1.4	4.7 ± 1.4	.795
HADS	11.3 ± 5.1	16.3 ± 6.0	.002
Insomnia Severity Index	19.8 ± 4.5	21.5 ± 3.2	.170
CIS (fatigue)	41.8 ± 10.6	45.4 ± 7.4	.202
NEO FFI			
Neuroticism	32.5 ± 6.2	38.4 ± 7.0	.003
Extraversion	39.1 ± 6.1	37.4 ± 5.9	.335
Openness	37.8 ± 7.2	36.8 ± 5.4	.864
Agreeableness	44.9 ± 4.6	45.3 ± 5.0	.953
Conscientiousness	44.9 ± 5.2	44.4 ± 5.1	.738
Trait and Character Inventory			
Novelty seeking	6.6 ± 3.1	6.3 ± 2.7	.591
Harm Avoidance	7.3 ± 3.5	10.2 ± 3.6	.003
Reward dependence	9.9 ± 3.2	10.4 ± 3.1	.698
Persistence	9.2 ± 2.9	9.2 ± 2.9	.952
Self-directedness	12.4 ± 2.0	9.6 ± 4.7	.041
Cooperativeness	13.0 ± 2.3	12.8 ± 3.2	.982
Self-transcendence	2.3 ± 2.8	4.0 ± 3.9	.060
CERQ			
Self-blame	8.7 ± 1.9	11.2 ± 3.9	.017
Acceptance	11.0 ± 3.0	11.5 ± 3.4	.726
Rumination	10.7 ± 3.3	13.1 ± 3.2	.010
Positive refocusing	9.1 ± 3.6	9.8 ± 2.9	.429
Refocus on planning	12.6 ± 3.6	14.2 ± 2.3	.063
Positive reappraisal	10.8 ± 3.7	11.7 ± 2.9	.219
Putting into perspective	10.7 ± 3.3	11.2 ± 3.4	.503
Catastrophizing	6.6 ± 2.2	6.7 ± 1.6	.718
Other blame	6.7 ± 2.5	6.5 ± 1.8	.809
Social Support List			
Social support	78.6 ± 14.0	78.0 ± 16.1	.744
Negative social interactions	10.3 ± 2.4	11.4 ± 3.6	.307
Social support discrepancies	47.8 ± 10.7	55.5 ± 19.1	.296

Data are mean ± SD / number (%), [1] Chi-square test χ^2 or Mann-Whitney U test α, * P≤.001 (.05/34), HADS = Hospital Anxiety and Depression Scale, CIS = Checklist Individual Strength, NEO FFI = Neuroticism, Extraversion Openness Five Factor Inventory, CERQ = Cognitive Emotion Regulation Questionnaire

Table 5.5 Pre-treatment differences between responders (Insomnia Severity Index decrease >7 points) and nonresponders

	CBT-responders (N=41)	CBT nonresponders (N=19)	P[1]
Age (years)	42.8 ± 11	45.9 ± 12.7	.283
Sex (males)	15 (37%)	4 (21%)	.229
Current psychiatric disorder	*14 (34%)*	*16 (84%)*	*.000 **
Previous psychiatric disorder	9 (22%)	6 (32%)	.423
Sleep efficiency (%)	55.3 ± 14.8	56.4 ± 18.6	.584
Sleep onset latency (hours)	1.4 ± 1.1	1.2 ± .7	.904
Total sleep time (hours)	4.8 ± 1.4	4.8 ± 1.3	.861
HADS	12.3 ± 5.8	16.3 ± 5.8	.019
Insomnia Severity Index	20 ± 4.4	21.7 ± 2.7	.263
CIS (fatigue)	42.6 ± 9.7	45.3 ± 8.3	.336
NEO FFI			
Neuroticism	33.9 ± 6.8	38.1 ± 7.3	.057
Extraversion	38.5 ± 6.2	37.9 ± 5.8	.793
Openness	37.6 ± 7	36.8 ± 5	.911
Agreeableness	45.3 ± 4.7	44.7 ± 5.1	.416
Conscientiousness	44.8 ± 5.2	44.4 ± 4.9	.861
Trait and Character Inventory			
Novelty seeking	6.4 ± 3	6.6 ± 2.7	.898
Harm Avoidance	8.1 ± 3.7	9.9 ± 3.7	.082
Reward dependence	9.2 ± 3	9.2 ± 2.6	.565
Persistence	9.2 ± 2.6	9.2 ± 3	.779
Self-directedness	11.8 ± 3.1	9.6 ± 4.8	.238
Cooperativeness	13.3 ± 2.1	12.1 ± 3.6	.081
Self-transcendence	2.7 ± 3	3.9 ± 4.1	.231
CERQ			
Self-blame	9.3 ± 2.8	11 ± 3.7	.150
Acceptance	11.5 ± 3.2	10.7 ± 3.1	.314
Rumination	11.5 ± 3.6	12.6 ± 3.1	.295
Positive refocusing	9.4 ± 3.3	9.5 ± 3.3	.873
Refocus on planning	12.8 ± 3.4	14.4 ± 2.3	.081
Positive reappraisal	11.2 ± 3.6	11.1 ± 2.6	.987
Putting into perspective	11 ± 3.2	10.8 ± 3.6	.981
Catastrophizing	6.7 ± 2.1	6.6 ± 1.6	.859
Other blame	6.8 ± 2.3	6.3 ± 1.9	.492
Social Support List			
Social support	77.5 ± 14.3	80.1 ± 16.3	.697
Negative social interactions	10.3 ± 2.9	11.7 ± 3.2	.125
Social support discrepancies	49.1 ± 13.2	56.2 ± 19.3	.348

Data are mean ± SD / number (%), [1] Chi-square test χ^2 or Mann-Whitney U test α, * P ≤ .001 (.05/34), HADS = Hospital Anxiety and Depression Scale,, CIS = Checklist Individual Strength, NEO FFI = Neuroticism, Extraversion Openness Five Factor Inventory, CERQ = Cognitive Emotion Regulation Questionnaire.

Regression analyses: Psychosocial predictors of treatment response

Factors with an uncorrected p value below .2 when comparing responders versus nonresponders were entered in the regression analyses. Separate forward regression analyses showed that the presence of psychiatric comorbidity was strongly predictive

for a negative outcome (Table 5.6). A higher CERQ cognitive coping dimension, refocus on planning, was slightly predictive for an absence of complete remission (Table 5.6).

Table 5.6 Forward multivariate logistic analysis results: summary of regression results.

Negative treatment outcome (Insomnia Severity Index score remaining above 8)

Variables	Coefficient	Odds ratio	SE	Wald	df	95% CI	P
Psychiatric comorbidity (y)	3.0	20.6	.7	17.6	1	5.0-84.4	.000 **
Refocus on planning	.2	1.3	.1	4.5	1	1.0-1.6	.033 *

Negative treatment outcome (decrease less than 7 points on the Insomnia Severity Index)

Variables	Coefficient	Odds ratio	SE	Wald	df	95% CI	P
Psychiatric comorbidity (y)	2.3	10.3	.7	10.8	1	2.6-41.4	.001 **

SE = standard error, df = degrees of freedom, * P ≤ .05 ** P ≤ .01, CI =confidence interval

Influence of psychiatric treatment

We examined whether there was a difference in treatment response between insomniacs who were and were not treated for their comorbid psychiatric disorder parallel to the CBT-I and found no significant differences between the two groups (Table 5.7). Furthermore, there were no significant differences in baseline demography, sleep, or psychological factors between the patients who were and were not treated for psychiatric comorbidity.

Table 5.7 Differences in CBT-I treatment response between comorbid insomniacs who were and were not in parallel treatment for their psychiatric comorbidity

	Patients treated for a comorbid psychiatric disorder (N= 18)	Patients not treated for a comorbid psychiatric disorder (N=12)	P[1]
ISI below 8 after treatment	6 (33%)	1 (8%)	.113
ISI reduction of > 7 points	9 (50%)	5 (42%)	.654

[1] Chi-square test χ^2, * P ≤ .025 (0.5/2)

Discussion

We studied the influence of psychiatric comorbidity, personality, coping, and social characteristics on cognitive behavioral treatment effect for insomnia, showing that the presence of a psychiatric disorder and high scores on the cognitive coping strategy called “refocus on planning” are predictive for a negative CBT-I outcome. In our sample,

83% of the patients with psychophysiological insomnia without psychiatric comorbidity achieved remission after CBT-I, reflected as an ISI-score of <8 after CBT-I. This is in line with earlier data on CBTI treatment effects (Riemann & Perlis, 2009). This contrasts sharply with the finding that only 23% of insomniacs with psychiatric comorbidity achieved remission, even though sleep log measures did improve in this group. Using forward regression modelling, the presence of comorbid psychiatric disorders also predicted worse CBT-I treatment effect, with odds ratios of 20.6 and 10.3 on the respective definitions of negative treatment outcome. Given the fact that 50% of our sleep center sample of insomniacs had psychiatric comorbidity, the influence on treatment outcome is of great clinical importance.

In contrast with our findings, Edinger et al. (2009) found no differences in effectiveness of CBT-I between patients with and without psychiatric comorbidity across most nocturnal sleep measures. However, in the same study, they describe that more than 75% of the patients with primary insomnia subjectively reported normal sleep quality after CBT-I versus roughly 20% in the group with comorbid psychiatric disorders. These results are therefore in line with our data. As insomnia is largely a subjective disorder, we primarily used the Insomnia Severity Index as an outcome measure, which may give a better indication of treatment effect compared to looking at wake after sleep onset or other nighttime sleep measures.

Our data suggest that the effects of CBT-I in patients with comorbid psychiatric disorders are rather limited. An explanation for this might be that these patients are less likely to follow the treatment recommendations and therefore have a less favorable treatment response. Therefore, it could be that adequate timing of CBT-I (i.e., parallel with or after treatment of the psychiatric disorder) may improve treatment outcome. However, through exploratory analyses we could not confirm that patients who followed parallel treatment of their psychiatric disorder were more likely to show a positive CBT-I treatment response. In any case, adherence to CBT-I is important to monitor and stimulate where possible.

It may be that a concurrent psychiatric disorder is an active perpetuating factor for the insomnia complaint. Given the influence of psychiatric comorbidity on treatment outcome, it is striking that a large proportion of patients with psychiatric diagnoses were nevertheless not motivated for (parallel) treatment of the mental disorder. One could speculate that patients who are less motivated for treatment of their comorbid psychiatric disorder might show less improvement in CBT-I because they show different personality characteristics or coping strategies. However, we did not find any such differences. In clinical practice, actively informing patients about the limited effects of CBT-I in the presence of psychiatric disorders is important to manage expectations, and—more importantly—motivate patients as much as possible to seek psychiatric treatment.

The cognitive coping strategy called refocus on planning turned out to be a small but significant predictor of CBT-I treatment effect, with a high refocus being predictive for not reaching remission of insomnia. This is remarkable, as in previous research refocus

on planning was shown to have negative relationships with measures of depression and anxiety, while 80% of the nonresponders in our study showed comorbid psychiatric disorders versus 20–30% of the group of responders (Janoff-Bulman, 1992). Theoretically, one would expect that the problem-focused strategy of refocus on planning might help the patient to define clear goals in cognitive behavioral treatment and might promote structured and active behavior leading to positive change. This paradoxical finding might be explained by the intention-attention-effort pathway theory of insomnia by Espie et al. (2006). According to this theory normal sleep is a relatively automatic process that may be inhibited by focused attention and direct attempts to control its expression. Insomniacs with greater refocus on planning might be more prone to consciously trying to actively solve and control sleep problems, leading to worse sleep.

In contrast with our findings, An, Park, Jang and Chung (2012) showed that responders had significantly higher reward dependence scores on the TCI. This discrepancy might be due to differences in the treatment program, as important differences in length of treatment and general treatment effect can be identified. In our study, treatment consisted of six primary treatment sessions and two sessions after 1 and 3 months, instead of only four sessions. Furthermore, our response rate was 83% in psychophysiological insomniacs without psychiatric comorbidity versus 52% in the study by An et al. (2012). Our treatment results are more in line with earlier large treatment effect studies (Riemann & Perlis, 2009).

Based on previous research findings, we hypothesized that cognitive coping characteristics such as rumination and catastrophizing might be predictive for more positive CBT-I treatment response (Edinger et al., 2008). However, we could not find an association between these cognitive coping factors and treatment outcome. It therefore seems that maladaptive thoughts about sleep are very specific and not linked to a general cognitive coping style. Similarly, we expected that lack of social support would be related to CBT-I treatment response, but we could not find a relationship between social support and treatment results. Although previous research data suggests that a lack of social support is associated with a more negative perception of sleep, this factor does not seem to influence treatment outcome negatively (Jackowska et al., 2011).

There were no significant differences between treatment dropouts and patients who finished CBT-I. Ong, Kuo and Manber (2008) found that short sleep duration was associated with increased risk of early termination from CBT-I. This discrepancy may be related to differences between the two study samples. For example, Ong et al. included patients with comorbid organic sleep disorders that might be associated with the insomnia complaint (e.g., restless legs syndrome and sleep apnea).

Our outcomes are based on a longitudinal follow-up of a clinical sample of insomnia patients, following a standard clinical program of insomnia diagnosis and treatment. One limitation of this approach is the fact that not all patients were examined by polysomnography. However, as stated above, the subjective assessment of both night

and daytime consequences of insomnia is a more clinically relevant indicator of severity than primary sleep measures. Psychiatric disorders were diagnosed by experienced clinical psychologists guided by a semistructured interview. However, no internationally validated formal instrument was applied. Future investigations may focus on the longitudinal follow-up of a larger group of insomnia patients with psychiatric comorbidity to further examine the relationship with treatment outcome. In addition, standardized treatment of concurrent psychiatric disorders should be applied in future studies, to assess the effects on insomnia treatment outcome.

In summary, insomniacs with comorbid psychiatric disorders are less likely to respond to CBT-I than insomniacs without psychiatric comorbidity. Parallel treatment of the psychiatric disorder may be associated with better treatment outcome. The presence of a psychiatric disorder must therefore be one of the leading arguments in the choice of treatment modalities that are being proposed to patients with insomnia. This study stresses the importance of motivating patients with comorbid psychiatric disorders to engage in (parallel) treatment for their psychiatric disorder and inform them about the limited effects of cognitive behavioral treatment for insomnia when a comorbid psychiatric disorder is present. Furthermore, extra attention might be given to acceptance-based techniques in patients with high refocus on planning.

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Chapter 6

Phenotypes of sleeplessness

van de Laar, M., Leufkens, T., Bakker, B., Pevernagie, D. & Overeem, S. (2017). Phenotypes of sleeplessness: stressing the need for psychodiagnostics in the assessment of insomnia. Psychology, Health and Medicine, Jan 30:1-9 (Epub ahead of print).

Abstract

Insomnia is a too general term for various subtypes that might have different etiologies and therefore require different types of treatment. In this explorative study we used cluster analysis to distinguish different phenotypes in 218 patients with insomnie, taking into account several factors including sleep variables and characteristics related to personality and psychiatric comorbidity. Three clusters emerged from the analysis. The “moderate insomnia with low psychopathology”-cluster was characterized by relatively normal personality traits, as well as normal levels of anxiety and depressive symptoms in the presence of moderate insomnia severity. The “severe insomnia with moderate psychopathology”-cluster showed relatively high scores on the Insomnia Severity Index and scores on the sleep log that were indicative for severe insomnia. Anxiety and depressive symptoms were slightly above the cut-off and they were characterized by below average self-sufficiency and less goal-directed behavior. The “early onset insomnia with high psychopathology”-cluster showed a much younger age and earlier insomnia onset than the other two groups. Anxiety and depressive symptoms were well above the cut-off score and the group consisted of a higher percentage of subjects with comorbid psychiatric disorders. This cluster showed a “typical psychiatric” personality profile. Our findings stress the need for psychodiagnostic procedures next to a sleep-related diagnostic approach, especially in the younger insomnia patients. Specific treatment suggestions are given based on the three phenotypes.

Introduction

Insomnia cannot be regarded as a uniform sleep disorder to be treated with a single intervention (Krystal, 2005). The clinical and scientific community is increasingly becoming aware of the idea that insomnia is a too general term for a number of subtypes consisting of different sleep complaints and having different causes (Sánchez-Ortuño, Edinger & Wyatt, 2011). As a consequence, the effectiveness of treatment is likely to be dependent on the subtype of insomnia. The presence of psychiatric comorbidity may be a very relevant factor in the 'phenotyping' of insomnia. A clear assessment of psychiatric comorbidity is important because approximately half of the patients presenting at a sleep clinic were shown to suffer from comorbid psychiatric conditions (Mahendran, Subramaniam & Chan, 2007). Moreover, insomnia patients with psychiatric comorbidity have shown to respond less well to cognitive behavioral treatment for insomnia (CBT-I) (van de Laar, Pevernagie, van Mierlo & Overeem, 2015).

In the past decades, several researchers have attempted to empirically identify naturally occurring insomniac subtypes through cluster analysis (van de Laar, Verbeek, Pevernagie, Aldenkamp & Overeem, 2010). Edinger, Stout & Hoelscher (1988) defined 14 clusters and concluded that their results support the existence of multiple, clinically discrete insomnia subtypes. Previous mental health issues, assessed by self-report questionnaires were included in their cluster analysis. However, ongoing psychiatric disorders were not assessed. It was suggested to prospectively use structured clinical interviews for the assessment of Diagnostic and Statistical Manual of Mental Disorders (DSM)-categories as well as psychometric instruments (Edinger et al., 1988). Fernandez-Mendoza et al. (2011) found two subtypes of insomnia also based on cluster analysis. Using polysomnography, they distinguished patients with objective short and patients with objective normal sleep duration. In the first group, a psychological profile typical for medical outpatients was found, while the second group showed anxious-ruminative traits and poor coping skills (Fernandez-Mendoza et al., 2011). While any treatments for mental health problems were checked at the intake, actual psychiatric comorbidity was not appropriately assessed. Hauri (1983) defined 9 clusters of insomnia based on personality characteristics, the Zung Depression Index and sleep variables. He also included age of onset of the insomnia complaint in the analyses. The DSM-III was used to classify different psychiatric disorders in the population. Patients with major affective disorders were excluded from the analysis. The psychiatric diagnoses were based on retrospective data of psychiatric symptoms without using structured diagnostic methods at the time.

While the presence of psychiatric comorbidity is likely to be an important factor, none of the cluster analysis studies have as yet included actual psychiatric disorders in the assessment of insomnia. In this explorative study we examined whether different phenotypes of insomnia can be distinguished in a population in which current

psychiatric comorbidity was appropriately assessed through semi-structured interviews. Next to the presence of psychiatric comorbidity, factors related to sleep, personality, fatigue and severity of anxiety and depression were taken into account.

Methods

General study design and setting

We performed a cross-sectional study comprising patients referred to Kempenhaeghe, a tertiary center for sleep medicine. All patients had a complaint of chronic insomnia (>3 months). Patients were included between June 2010 and May 2011. Criteria for insomnia were based on the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV (i.e. complaints of difficulty initiating or maintaining sleep or nonrestorative sleep, with the sleep disturbance (or associated daytime fatigue) causing clinically significant distress or impairment in social, occupational or other important areas of functioning) (American Psychological Association, 2000). The current version of the DSM (DSM-V) was not yet available at the time of the data collection. Patients between 18 and 65 years of age were included if they did not work in shifts and did not have a history of developmental disorders or severe psychopathology (e.g. psychotic disorders). They were medically examined and polysomnography was performed when an organic sleep disorder was suspected from the medical interview, performed by a sleep specialist. Those with a somatic disease or other sleep disorder that could explain (part of) the insomnia (e.g. sleep apnea, restless legs syndrome, epilepsy, chronic pain) were excluded. Patients with alcohol or drug abuse were also excluded. Patients willing to participate in the study signed an informed consent. The study design was approved by the local medical ethical committee.

Psychopathology

Semi-structured interview for mental disorders

All patients were psychologically examined by a clinical psychologist, and the presence or absence of psychiatric comorbidity was assessed based on the criteria of the DSM-IV, with the aid of a semistructured interview covering the entire range of mental disorders (American Psychological Association, 2000; Hoogduin, 1999).

Hospital Anxiety and Depression Scale (HADS)

The HADS is a 14-item screening instrument, measuring severity of depression and anxiety symptoms (Spinhoven et al., 1997; Zigmond & Snaith, 1983). The questionnaire contains a separate depression and anxiety scale. Each scale is evaluated by 7 items on a four point Likert Scale.

Sleep variables

Sleep log

All patients filled out a sleep log during one week. They had to graphically define bedtime and time of getting up out of bed. Furthermore they filled in the time spent in bed, awake and sleeping. From this, the following estimated variables were extracted: total sleep time (TST), sleep efficiency (SE) and sleep onset latency (SOL).

Insomnia Severity Index (ISI)

The ISI is a 7-item questionnaire assessing the nature, severity and impact of insomnia (Morin, 1993; Morin, Belleville, Bélanger & Ivers, 2011). A five-point Likert scale is used to rate each of these items, yielding a total score ranging from 0-28. Scores can be classified in four severity categories: (0-7): absence of insomnia, (8-14): mild insomnia symptoms, (15-21): moderate insomnia, (22-28): severe insomnia.

Personality

Neuroticism Extraversion Openness Five Factor Inventory (NEO FFI)

The NEO FFI is a short version of the Neuroticism Extraversion Openness Personality Inventory Revised (NEO PI R). The NEO FFI contains 60 items, tapping five personality domains, also known as the "Big Five": neuroticism, extraversion, openness, agreeableness and conscientiousness. The definition of these five broad factors was based on empirical, data-driven research (Costa & McCrae, 1992). Each domain is evaluated by 12 items and a five-point Likert scale is used to rate these items. The Dutch version of the NEO FFI has good psychometric properties (Hoekstra, Ormel & De Fruyt, 2003). The internal consistencies of the subscales of the Dutch NEO-FFI are comparable to those of the American NEO-FFI and range between α=.68 and α=.86, while indices of validity range between r =.50 and r =.84, reflecting correlations with questionnaires measuring similar personality characteristics (Hoekstra et al., 2003).

Trait and Character Inventory (TCI) Short Form

The TCI Short Form is a Dutch short version of the Temperament and Character Inventory. It is comparable to the original version of the TCI and measures the same personality dimensions (Cloninger, Przybeck, Svrakic & Wetzel, 1994; Duijsens, Spinhoven, Goekoop, Spermon & Eurelings-Bontekoe, 2000). Research showed that the original and shortened scales correlate highly and there were no differences found in mean scale scores between the two versions (Duijsens & Spinhoven, 2006). The short version contains 105 items and measures seven personality trait dimensions. These can be divided into four temperaments (novelty seeking, harm avoidance, reward dependence and persistence) and three characters (self-directedness, cooperativeness

and self-transcendence). Each dimension is evaluated by 15 items and rated on a five-point Likert Scale. The TCI Short Form has good psychometric properties. Internal consistencies range between α=.69 and α=.85. Test-retest correlation coefficients range between r =.71 and r =.90 (Duijsens & Spinhoven, 2006).

Fatigue

Checklist Individual Strength (CIS) fatigue severity subscale

The CIS is a 20-item questionnaire and measures the following four aspects of fatigue during the previous two weeks: fatigue severity, concentration problems, reduced motivation and reduced activity. The fatigue severity subscale contains 8 items and the total subscale score ranges between 8 and 56 (Vercoulen, Alberts & Bleijenberg, 1999). The psychometric properties of the CIS have proven to be good with a Cronbach's alpha coefficient of .9 for the total scale (Vercoulen et al., 1994).

Data analysis

We performed a cluster analysis on all data types that were either numerical (e.g. age, total sleep time) or binary (e.g. gender). The selected data sources were: presence of psychiatric comorbidity, age, gender, age of onset, Insomnia Severity Index, total sleep time, sleep efficiency, sleep onset latency, neuroticism, extraversion, openness, agreeableness, conscientiousness, harm avoidance, self-directedness, HADS and CIS-8. All data were normalized to have zero mean and unit standard deviation over the complete pool of 218 subjects. Missing data were replaced by the pool average (or zero, after normalization). Clustering was performed through the k-medoids method as implemented in the Matlab Clustering Toolbox made available by Janos Abonyi (http://nl.mathworks.com/matlabcentral/fileexchange/7486-clustering-toolbox). The k-medoids method assigns k examples (in this case, subjects) as cluster representatives (or medoids). Each subject out of the pool was assigned to that cluster that has the 'closest' representative, where 'close' is defined by the sum-squared distance between the normalized data values for the subject to be assigned and the cluster representative. The clustering method aims to minimize the average distance between the subjects to be clustered and the chosen medoids.
The chosen Matlab script uses the Voronoi iteration method to find the optimal set of medoids:

1. k subjects are chosen at random to serve as medoids
2. Each subject is assigned to its nearest medoid, forming k clusters
3. In each cluster, the subject that minimizes the sum of distances within the cluster is made the new medoid for that cluster
4. Repeat from 2 until there is no further change in medoids.

We performed k-medoid clustering for k = 2.10. The final choice of the number of clusters (3) was made based on visual inspection and confirmed by the Dunn Index, which reached a maximum at 3 clusters. Personality scores on the NEO FFI and TCI Short Form and CIS- fatigue scores in the three clusters were compared to the norm scores of the general Dutch population (Hoekstra et al., 2003; Duijsens et al., 2000; Vercoulen et al., 1999).

Results

General sample characteristics

A total group of 281 patients signed an informed consent. The inclusion flowchart is shown in Figure 6.1. Of the initial 281 patients, 62 subjects were excluded because of the presence of a somatic disease or another sleep disorder that could explain insomnia. One patient was excluded because of alcohol abuse. The final group with insomnia comprised 218 patients; 107 patients without psychiatric comorbidity and 111 patients with psychiatric comorbidity. General characteristics of the total sample, sleep variables and other variables of interest are presented in Table 6.1. Specific subtypes of the comorbid psychiatric disorders are described in Table 6.2.

Cluster analysis

Three groups were identified through partitional cluster analyses (Figure 6.2). Age, age of onset, total sleep time, sleep efficiency and harm avoidance were clear distinguishing characteristics between the three clusters. In Figure 6.3 these variables are depicted in a star diagram. The “moderate insomnia with low psychopathology”-cluster was characterized by low harm avoidance scores when compared to the other two clusters. The “severe insomnia with moderate psychopathology”-cluster mainly showed low scores on total sleep time and sleep efficiency, while the “early onset insomnia with high psychopathology”-cluster was characterized by lower age and lower age of onset.

Comparing specific variables between clusters

Age, duration of insomnia and age of onset

In Table 6.3, the mean scores and standard deviations of different variables are shown as well as general characteristics of the groups identified through cluster analysis. The mean age of patients in the “early onset insomnia with high psychopathology”-cluster was around 10 years younger than in the other two groups. Although these patients had younger age, they reported a longer duration of the insomnia complaint (around 5 to 7 years longer than in the other two clusters). Age of onset in these patients was a striking 16 years lower than in the other two clusters.

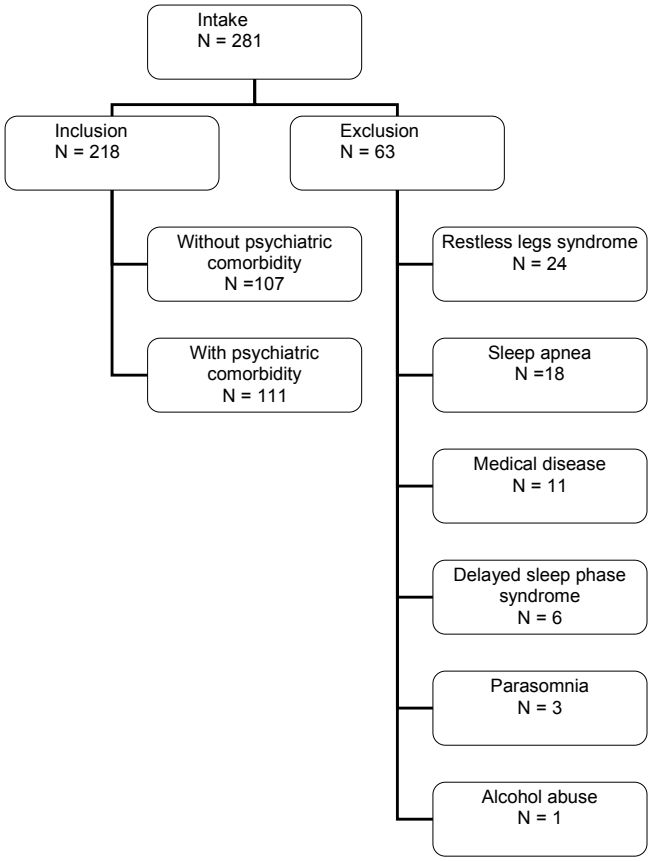

Figure 6.1 Flowchart of patients initially referred for diagnosis of insomnia complaint.

Table 6.1 Baseline demographic characteristics and insomnia characteristics.

Variables	Total study sample (N=218)
Age (years)	44.0 ± 11.2 (18-65)
Gender (male/female)	75/143 (34%/66%)
Sleep variables	
Insomnia severity index	20.4 ± 4 (10-28)
Insomnia duration (years)	11.2 ± 11.8 (.3-64)
Total sleep time (hours)	5.0 ± 1.5 (0-8.4)
Sleep efficiency (%)	58.3 ± 16.8 (0-93.5)
Sleep onset latency (hours)	1.3 ± 1.0 (0-6.1)
Sleep medication use (y/n)	129/89 (59%/41%)

Data are mean ± SD (range) or frequency (percentage)

Table 6.2 Specific psychiatric diagnoses in research population (N=111).

DSM-IV cluster	Specific type of DSM-IV diagnosis	Frequency
Mood disorders (N=34)	Depressive disorder	27
	Dysthymic disorder	4
	Bipolar disorder	3
Anxiety disorders (N=29)	Generalized anxiety disorder	13
	Panic disorder	8
	Posttraumatic stress disorder	3
	Social phobia	3
	Obsessive compulsive disorder	1
	Anxiety disorder not otherwise specified	1
Somatoform disorders (N=28)	Undifferentiated somatoform disorder	28
Adjustment disorders (N=13)	Adjustment disorder	13
Attention-deficit and disruptive behavior disorders (N=7)	ADHD	7

Table 6.3 Characteristics of the three clusters

Variables	Moderate insomnia with low psychopathology (N=97)	Severe insomnia with moderate psychopathology (N=59)	Early onset insomnia with high psychopathology (N=62)
Age (years)	46.1 ± 10.3 (23-65)	48.2 ± 9.9 (24-64)	36.6 ± 10.2 (18-64)
Gender (male/female)	33/64 (34%/66%)	19/40 (32%/68%)	23/39 (37%/63%)
Sleep variables			
Insomnia severity index	19.2 ± 3.8 (11-28)	22.7 ± 3.4 (10-28)	20.2 ± 3.7 (13-28)
Insomnia duration (years)	8.6 ± 8.5 (.3-40)	10.5 ± 12.4 (.3-64)	15.8 ± 14.1 (.3-52)
Age of onset (years)	37.4 ± 11.0 (6.0-60.0)	37.7 ± 13.2 (0-61.0)	20.9 ± 12.2 (0-47.7)
Total sleep time (hours)	5.3 ± 1.3 (2.1-8.1)	3.6 ± 1.3 (0-6.8)	5.7 ± 1.0 (2.1-8,4)
Sleep efficiency (%)	63.4 ± 13.5 (29.7-88.0)	41.5 ± 14.7 (0-66.4)	65.8 ± 11.9 (27.4-93.5)
Sleep onset latency (hours)	1.0 ± .7 (0-2.8)	2.3 ± 1.3 (.5-6.1)	1.2 ± .7 (0-2.9)
Sleep medication use (y/n)	54/43	37/22	38/24
Personality			
NEO FFI			
Neuroticism	30.6 ± 6.3 (16-44)	36.1 ± 7.5 (22-49)	42.0 ± 6.0 (29-57)
Extraversion	40.2 ± 5.4 (28-52)	36.3 ± 6.8 (21-55)	35.6 ± 7.3 (21-52)
Openness	36.9 ± 5.7 (24-55)	38.6 ± 7.4 (23-57)	35.6 ± 7.0 (21-56)
Agreeableness	45.5 ± 4.7 (29-57)	45.5 ± 5.4 (31-56)	43.0 ± 4.9 (31-54)
Conscientiousness	47.1 ± 4.8 (37-58)	42.1 ± 5.6 (28-56)	41.2 ± 5.2 (26-54)
TCI (Short-Form)			
Harm Avoidance	6.8 ± 3.5 (0-14)	10.2 ± 3.2 (3-15)	11.0 ± 3.7 (4-15)
Self-Directedness	13.4 ± 2.0 (3-15)	10.6 ± 3.4 (3-15)	8.1 ± 3.6 (1-13)
Anxiety and depressive symptoms			
Psychiatric disorder (y/n)	34/63 (35%/65%)	34/25 (58%/42%)	43/19 (69%/31%)
HADS	10.5 ± 4.9 (1-22)	14.8 ± 6.9 (3-34)	18.6 ± 6.6 (6-37)
Fatigue			
CIS-8	41.1 ± 10.0 (14-56)	47.7 ± 8.2 (22-56)	45.3 ± 8.0 (25-56)

Data are mean ± SD (range) or frequency (percentage)

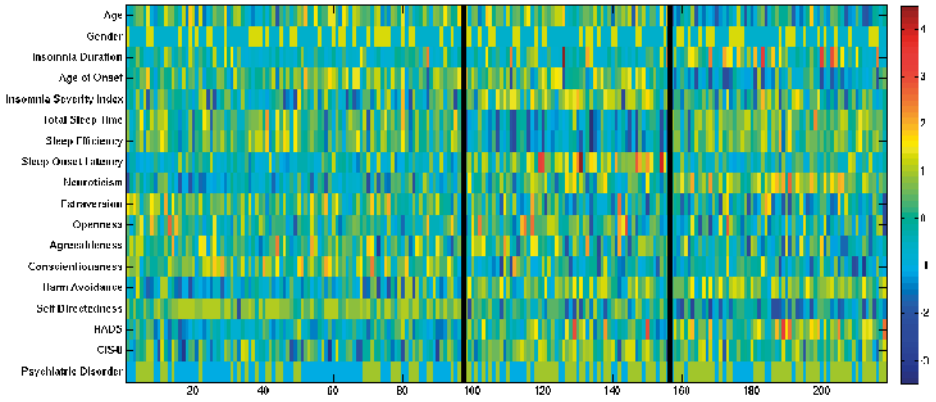

Figure 6.2 Heat diagram after partitional cluster analysis. Each column (numbered on the horizontal axis) represents one patient, whereas each row (named on the vertical axis) represents a patient characteristic. Colors indicate the (normalized) numerical values of the characteristics, red indicating an above average value, blue a below average value. Note that Gender and Psychiatric Disorder have binary values, where high (1) represents male gender or the presence of a psychiatric disorder. Patients are grouped together according to the result of the cluster analysis, where the black vertical lines indicate the boundaries between the three clusters. Note that although Psychiatric Disorder is shown along with the other characteristics, it has not been used in the formation of the clusters.

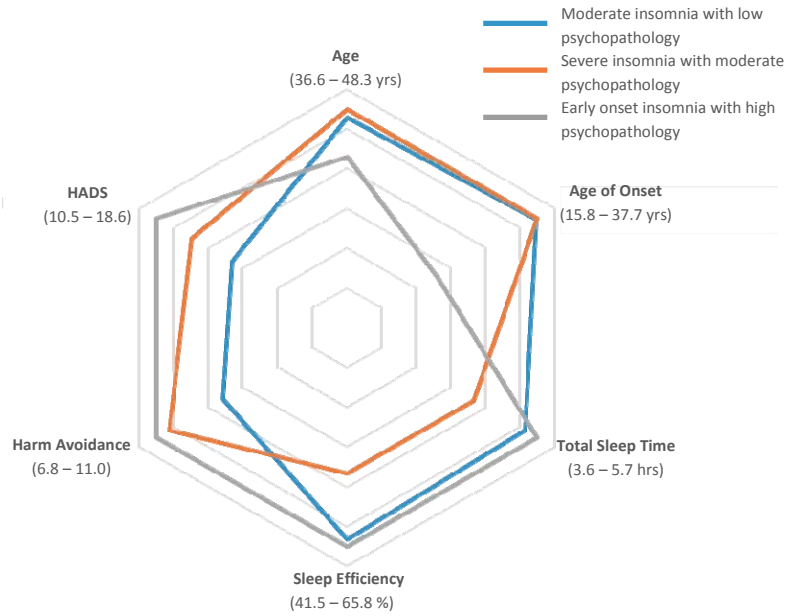

Figure 6.3 Star diagram of the most distinguishing characteristics of the three clusters.

Psychiatric comorbidity

The “moderate insomnia with low psychopathology”-cluster was mainly characterized by the relatively low percentage of patients with comorbid psychiatric conditions, comprising 35% of patients in this group. In the other two clusters, rates of psychiatric disorders were much higher, ranging from 58% in the “severe insomnia with moderate psychopathology”-cluster to 69% in the “early onset insomnia with high psychopathology”-cluster. This was also translated into the differences in HADS-scores. In the “severe insomnia with moderate psychopathology”-cluster, the mean HADS score is slightly above the cut-off range for psychiatric disorders (i.e. 11), while in the “early onset insomnia with high psychopathology”-cluster the mean HADS score is well above the cut-off range.

Sleep variables

In accordance with our findings in the heat diagram, the “severe insomnia with moderate psychopathology”-cluster showed low sleep efficiency scores, with a mean score of 41.5% which was more than 20% lower than the sleep efficiency scores in the other two clusters. The total sleep time per night in this cluster was 1.7 hours shorter than in the “moderate insomnia with low psychopathology”-cluster and a striking 2.1 hours shorter than in the “early onset insomnia with high psychopathology”-cluster. The mean sleep onset latency in the “severe insomnia with moderate psychopathology”-cluster was generally twice as long as in the other two clusters. In accordance with this, the mean ISI-score in this cluster was indicative for severe insomnia, while the scores in the other two clusters fell within the moderate insomnia range.

Personality variables

Table 6.4 shows the mean scores of the personality variables and corresponding norm scores for the general Dutch population. The ”early onset insomnia with high psychopathology”-cluster was characterized by high neuroticism, low extraversion, low conscientiousness, high harm avoidance and low self-directedness when compared to the general population. In contrast, the “moderate insomnia with low psychopathology”-cluster showed normal scores on all personality variables. The “severe insomnia with moderate psychopathology”-cluster showed normal scores on all NEO FFI-variables. On the TCI-Short Form this group scored above average on harm avoidance and below average on self-directedness.

Fatigue

All three clusters showed a very high mean CIS-fatigue score when compared to normal controls.

Table 6.4 Norm scores of the personality variables in the three clusters

Variables	Moderate insomnia with low psychopathology (N=97)	Severe insomnia with moderate psychopathology (N=59)	Early onset insomnia with high psychopathology (N=62)
NEO FFI			
Neuroticism	30.6 (5)	36.1 (6)	42.0 (8) *
Extraversion	40.2 (5)	36.3 (4)	35.6 (3) *
Openness	36.9 (6)	38.6 (6)	35.6 (5)
Agreeableness	45.5 (6)	45.5 (6)	43.0 (5)
Conscientiousness	47.1 (6)	42.1 (4)	41.2 (3) *
TCI (Short-Form)			
Harm Avoidance	6.8 (Average)	10.2 (Above average)*	11.0 (High)*
Self-Directedness	13.4 (Average)	10.6 (Below average)*	8.1 (Low)*

Data are mean scores (stanines based on general population norm scores/ score in comparance with general population norm scores (Hoekstra et al., 2003; Duijsens et al, 2000), NEO FFI: norm score 1 is very low, norm score 2 and 3 are low, norm scores 4, 5 and 6 are average, norm scores 7 and 8 are high, norm score 9 is very high; * = score outside the normal range.

Discussion

To our knowledge, this is the first study in which phenotypes of insomnia are distinguished not only based on several sleep, psychological and personality variables, but also on the presence of psychiatric disorders based on semi-structured interviews performed by a clinical psychologist. We found three phenotypes of insomnia. Age of onset of insomnia and severity of anxiety and depressive symptoms as well as subjective sleep variables strongly defined the three clusters.

The “moderate insomnia with low psychopathology”-cluster was characterized by normal scores on personality inventories, as well as normal levels of anxiety and depressive symptoms in the presence of moderate insomnia severity. This group shares features with a cluster in the earlier study by Hauri (1983), described as “psychophysiological insomnia”. This group had moderate insomnia complaints and psychologically these patients appeared somewhat dissatisfied and tense (probably by the insomnia complaint itself) but otherwise quite normal (Hauri, 1983).

Our “severe insomnia with moderate psychopathology”-cluster showed relatively high scores on the Insomnia Severity Index, indicating severe insomnia. The scores on the sleep diary variables corroborated the scores on the ISI. Subjective sleep efficiency was around 20% lower than in the other two groups. The subjective total sleep time was 12 to 14 hours less per week than in the other two groups and subjective sleep onset latency was generally two times higher than in the other groups. The elevated score on harm avoidance and below average score on self-directedness can be interpreted as lower self-sufficiency and less goal-directed behavior. Anxiety and depressive

symptoms were slightly above the cut-off. This group may be similar to the “insomnia in depleted neurotic patients”-cluster in the study done by Hauri (1983). Low energy levels were typical for this cluster in combination with a very poor sleep throughout the night and a “neurotic” psychological profile which corresponds to a higher harm avoidance score and elevated HADS-score in this group in our study.

Although we did not measure objective sleep parameters for verification of total sleep time, the “severe insomnia with moderate psychopathology”-cluster could hypothetically represent a distinct entity within the primary insomnia group, referred to as paradoxical insomnia (previously known as sleep state misperception) (American Academy of Sleep Medicine, 2005). The extremely low subjective sleep time in combination with the specific pattern of psychometric variables supports this hypothesis. For instance, Fernandez-Mendoza et al. (2011) found that patients with sleep misperception showed Minnesota Multiphasic Personality Inventory (MMPI)-2 personality profiles characterized by “depressive mood, rumination, anxiety, intrusive thoughts, and poor resources for coping with stress”, which is parallel to the elevated HADS-score, elevated Harm Avoidance score and low Self-directedness score within this cluster in our study.

The “early onset insomnia with high psychopathology”-cluster showed a much younger age of onset of the insomnia than the other two groups. These patients were generally a striking 16 to 17 years younger when their insomnia complaints started, their current age was 10 to 12 years younger than the other two groups while reporting 1,5 to almost 2 times longer insomnia duration. Furthermore this group showed anxiety and depressive symptoms well above the cut-off score and showed a higher percentage of subjects with comorbid psychiatric disorders. Scores on personality inventories showed a “typical psychiatric” personality profile of high neuroticism, low extraversion, low conscientiousness, high harm avoidance and low self-directedness. This is in line with earlier personality research in patients with psychiatric disorders without specified insomnia. In these studies, patients with depressive disorders and anxiety disorders showed low extraversion, high neuroticism, high harm avoidance and low self-directedness (Harkness, Bagby, Joffe & Levitt, 2002; Cloninger, Zohar, Hirschmann & Dahan, 2012; Weinstock & Whisman, 2006; Bienvenu, Hettema, Neale, Prescott & Kendler, 2007). The finding that lower age and a lower age of onset of insomnia was accompanied with higher psychiatric comorbidity (which is expressed in our “early onset insomnia with high psychopathology”-cluster) is in line with the results from a study by Roehrs, Lineback, Zorick and Roth (1982). They found that elderly insomniacs showed less pathological elevations on the MMPI than younger patients. The authors hypothesized that insomnia associated with psychiatric comorbidity is more often found in younger insomnia patients. This is supported by the fact that insomnia in older patients may be related to other risk factors that are relatively specific to this group, such as increased prescription drug use and somatic disorders and a lack of physical

activity (Pallesen et al., 2002; Morgan, 2003). Our “early onset insomnia with high psychopathology”-cluster corresponds best with the “Insomnia associated with dysthymia”-cluster in the study by Hauri et al. (1983). Psychologically, these patients were unhappy and depressed and although patients with major affective disorders (e.g. depressive disorder, bipolar disorder) were specifically excluded in this study, the large majority of these patients had been classified as insomniacs associated with affective disorders.

Our findings may have important clinical implications. They stress the need for psychodiagnostic procedures next to a sleep-related diagnostic approach, especially in the younger insomnia patients. Special attention should be given to the application of conventional semi-structured interviews and tailored interventions, focusing on the improvement of sleep and simultaneously treating possible comorbid psychiatric conditions in this group. In an earlier study, treating both problems at the same time (i.e. depression through pharmacological treatment and insomnia by cognitive behavioral treatment) has shown to increase treatment effect related to mood and sleep variables (Manber et al., 2008).

In the present study, we observed that insomnia subtypes are not only characterized by the presence of psychiatric comorbidity, but also by subjective severity of insomnia and age of onset. Future investigations should focus on possible cluster differences in cognitive behavioral treatment effect. It is plausible that sleep misperception is more prevalent in the “severe insomnia with moderate psychopathology”-cluster, which might imply the application of more tailored interventions in this group. Intensive sleep retraining is a promising new technique in the treatment of insomnia, specifically targeting a decrease of sleep misperception (Harris, Lack, Kemp, Wright & Bootzin, 2012). More specifically, with this technique, patients are awoken during sleep and given direct feedback about when sleep occurs. In this way, they learn to perceive sleep in a more accurate way. It would be interesting to examine whether patients in this cluster particularly respond better or faster to intensive sleep retraining than to traditional cognitive behavioral therapy. Our study mainly focused on subjective measures and psychological aspects. In future research it would be worthwhile to include objective measures as well, to examine whether the subjective differences in severity of insomnia can also be verified by polysomnography results.

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Chapter 7

General discussion

General discussion

In this thesis, several research questions have been addressed concerning the complex relationship between insomnia, psychiatric disorders and psychosocial factors. An overview of these questions and the conclusions that can be drawn based on our research are described in this discussion. It stresses the importance of clear psychodiagnostic procedures in insomnia as well as the assessment of personality traits and coping strategies. Furthermore, predictors of treatment results and practical implications for tailored treatment are discussed. Additionally, recommendations for future research are given.

7.1 Can insomnia subgroups be identified based on psychological differences?

A main finding in our research is that insomnia patients with and without psychiatric comorbidity are very different in relation to several psychological and sleep-related aspects. Personality traits, subjective sleep variables and factors correlated with quality of life vary significantly across patients with and without psychiatric comorbidity

In the introduction, personality traits are described as one of the predisposing factors for chronic insomnia, based on the 3P-model by Spielman and Glovinsky (1991). We also described that personality research in insomnia is often hampered by the bidirectional relationship between comorbid mental disorders and personality traits. Therefore, it is important to distinguish between patients with and without psychiatric comorbidity when personality traits are assessed in patients with insomnia.

Our research confirms that there is no general personality type in insomniacs and that earlier personality studies must be interpreted with caution, as insomnia proves to be a heterogeneous condition. The 3P model in which personality can be seen as one of the predisposing factors of insomnia might be too simplistic. Because most personality traits are state-dependent, there might be a more complex interplay between these traits and insomnia. In other words: some insomniacs may show different personality traits because insomnia itself has a negative effect on daytime functioning and results in fatigue, anxiety and concentration problems. They might become more introverted and more neurotic because of these complaints.

Based on our results we conclude that the causal relationship in which specific personality traits are predisposing for the development of insomnia might be questioned. Primary insomniacs generally showed normal personality profiles, which was confirmed in the cluster analysis. The cluster “moderate insomnia with low psychopathology” showed normal scores on personality questionnaires when compared to norm scores in the general population, while the cluster "early onset insomnia with high psychopathology” showed personality profiles typical for patients with psychiatric disorders. Personality however might play an indirect role in the perpetuation of insomnia in general. According to a recent model by Harvey, Gehrman and Espie (2014) it is plausible that neuroticism plays a mediating role in which it

increases stress reactivity and negative associations around sleep. More research is needed to investigate this mechanism.

Differences between patients with and without psychiatric comorbidity are not only found in personality traits but also when assessing subjective sleep variables. These variables vary strongly according to the presence and type of comorbid psychiatric disorders. Patients with anxiety disorders generally show less severe subjective sleep complaints based on a sleep log, while patients with depressive disorders showed a trend towards higher insomnia severity index-scores. We hypothesized that patients with comorbid anxiety disorders might worry more about their sleep and tend to seek medical help in the presence of less severe nighttime sleep problems.
Our research shows that factors correlated with quality of life are different among patients with and without psychiatric comorbidity. In patients without psychiatric comorbidity, social support is correlated with a higher quality of life along with higher extraversion. Insomnia severity is only negatively correlated with general quality of life in patients with psychiatric comorbidity, while fatigue is negatively correlated with general quality of life in patients with primary insomnia.

7.2 Do psychological differences have implications for diagnostic procedures in insomnia?

Our investigation shows that more than half of the patients with insomnia presenting in a sleep clinic suffer from comorbid psychopathology. Through cluster analysis we found that younger patients with insomnia show more severe psychopathology, so additional attention towards psychodiagnostics is needed in this group. Our research corroborates the notion that there is an important interplay between insomnia and psychiatric disorders. The application of psychodiagnostics in patients presenting with insomnia complaints is essential. It is important to advise these patients to seek help for their psychiatric disorders in parallel with the treatment of their sleep complaints. On the other hand, sleep and sleep behaviors should always be assessed in patients with psychiatric disorders. Knowledge of insomnia and the treatment of this sleep disorder might contribute to better treatment results for patients with psychiatric disorders and insomnia.

Overall, our study results suggest that the current terminology used in the DSM-V and ICSD-3 (i. e. “insomnia disorder”) is too general. There are strong differences between insomnia patients with and without comorbid mental disorders in sleep variables and personality characteristics. Also, different treatment modalities can be suggested based on the presence of comorbid mental disorders. The relationship between psychiatric disorders and insomnia is often very complex and the DSM-IV term “insomnia due to mental disorder” implies a causal relationship between the mental disorder and insomnia while in clinical practice a relationship as such is often difficult to determine.

Because of this complex relationship, a more fitting term was proposed during the 2005 NIH conference, namely “comorbid insomnia”) (NIH, 2005). The advantage of using this diagnostic entity is that it does not imply a causal relationship between the mental disorder and insomnia, but the use of it does guide the clinician in paying attention towards possible perpetuating mechanisms for the insomnia. In conclusion, we suggest that a distinction between primary and comorbid insomnia and using these terms as different nosological entities can be helpful in clinical practice.

7.3 Do psychological differences predict CBT-I treatment effect in insomnia?

We found that cognitive behavioral treatment of insomnia can be significantly hampered by current psychiatric comorbidity. Thus it should be avoided to raise over-optimistic expectations about the effects of CBT-I in patients suffering from comorbid psychiatric disorders. As described in the above, concurrent treatment for comorbid psychiatric conditions is essential to gain optimal treatment results. Although our results show that treatment effects are negatively influenced by the presence of psychiatric disorders, adding CBT-I to regular treatment of psychiatric disorders has shown to increase treatment results. For example, Manber et al. (2008) found that adding CBT-I to treatment for depression enhances depression outcome and alleviates insomnia symptoms in patients with major depressive disorders. This indicates that patients with psychiatric disorders might still benefit from CBT-I, as long as both treatments are given concurrently.

Patients scoring high on refocus on planning show worse CBT-I treatment results. An explanation for this finding can be found in the intention-attention-effort pathway theory by Espie et al. (2006). In this theory, normal sleep is a relatively automatic process that may be inhibited by focused attention and direct attempts to control its expression. Patients with greater refocus on planning might be more prone to consciously trying to actively solve and control sleep problems, leading to worse sleep. Adding acceptance-based techniques might help these patients in exerting less control over sleep and create more relaxation and less rumination, leading to better treatment results.

7.4 Can CBT-I be more “tailored” based on psychological differences?

Several treatment suggestions can be made based on our research on sleep variables and quality of life. Insomnia patients with comorbid anxiety disorders may benefit more from sleep restriction than from stimulus control therapy, because they report more frequent short awakenings and stimulus control might create very restless nights. Stimulus control might be more efficient for primary insomniacs and patients with comorbid mood disorders because these patients generally spend 1 to 2 hours in bed after the final awakening. Getting up out of bed earlier might help “re-associate” the

bed with sleep instead of lying awake. Especially in patients with comorbid mood disorders this is a challenge, because these patients generally have more difficulty to push themselves towards activity. It is important to plan an extra session to discuss the possible meaningful or relaxing activities they can plan to substitute the time they spend lying awake in the bed in the morning. In primary insomniacs enhancing social support might contribute to a higher general QOL and better treatment effect. In this group, special attention should be given towards the assessment and treatment of fatigue as a specific and separate treatment goal next to the decrease of insomnia complaints.

Next to the presence and type of psychiatric comorbidity, individual differences in coping variables might also guide more tailored interventions. Moreover, assessment of coping strategies might help to assess the chance of improvement through CBT-I. In patients scoring high on refocus on planning an addition of acceptance and commitment therapy (ACT) and mindfulness based interventions might enhance CBT-I treatment effect. Recent studies show that these are promising techniques that might complement CBT-I. For example, Hertenstein et al. (2014) showed that CBT-I nonresponders showed significant improvement in quality of life and subjective sleep quality after ACT. Also, Wong et al. (2016) showed that adding four sessions of mindfulness-based techniques to regular CBT-I enhanced treatment effect as shown in total sleep time, wake after sleep onset and sleep efficiency, but also on actigraphy results and the insomnia severity index. Figure 7.1 represents a flow chart in which recommendations are given for additional intake procedures and treatment modalities for insomnia patients based on our study results.

7.5 Implications for future research

Future longitudinal research might focus on the cause and effect relationships between subjective insomnia complaints and psychiatric disorders. These studies should include well-defined and precise insomnia (sub)diagnoses, and also take into account other psychological and physiological factors that may play a causal role. Furthermore, they should focus on the benefits of implementing more tailored interventions based on type of psychiatric comorbidity. Examples of these interventions might be the introduction of extra sessions focusing on the sleep restriction method in patients with anxiety disorders and more attention towards motivating patients with comorbid mood disorders to get up earlier out of bed and creating meaningful activities in the morning instead of lying in the bed awake. Also, measures of quality of life should be included in the evaluation of treatment effect. Moreover, therapeutic trials should include fatigue as a daytime measure of functioning in the evaluation of treatment effect in primary insomnia. The effect of adding cognitive behavioral interventions targeting (social) activation on quality of life should be investigated. Also, the positive effects of adding

acceptance and commitment therapy and mindfulness-based strategies should be explored in specific cohorts of insomnia patients with an active cognitive coping style.

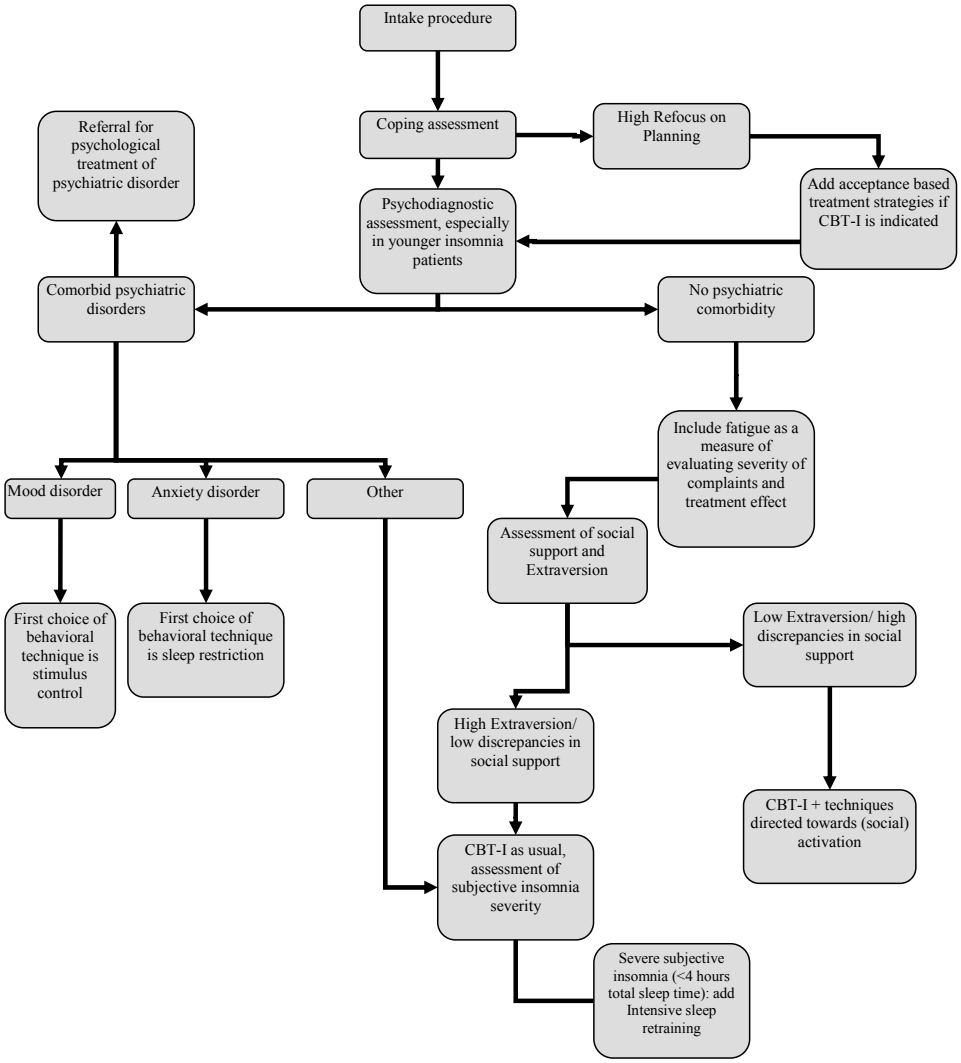

Figure 7.1 Flowchart of research and treatment suggestions after referral for insomnia.

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Summary

Summary

The present thesis describes the complex relationship between insomnia, psychiatric comorbidity and other psychosocial factors. It highlights the importance of psycho-diagnostics in the evaluation of chronic insomnia. Furthermore, it describes how personality and coping research might attribute to an understanding of different phenotypes of insomnia as well as support the enhancement of quality of life in patients with insomnia and might guide the prediction of treatment results.

Chapter 1 is the general introduction of this thesis and describes the background of our study and research questions. The pathophysiology, nosological classification and treatment of insomnia and the relationship with personality traits and psychiatric disorders are discussed.

In **chapter 2** "The role of personality traits in insomnia" we reviewed studies on insomnia and personality and concluded that neuroticism, internalization and anxious personality traits characterize insomniacs in general. However, due to a lack of longitudinal data and other methodological issues, such as small sample sizes and lack of psychodiagnostics it was difficult to conclude whether these personality traits are predisposing for insomnia. Specific differences in personality traits might just as well be a consequence of insomnia. In addition, certain personality traits may be related to the response to (cognitive) behavioral treatment. We also stressed that personality should not be viewed as a single predisposing factor, but should be assessed as a part of a larger group of interacting psychological and physiological factors involved in the predisposition to and perpetuation of chronic insomnia. For future research we recommended longitudinal studies including different psychosocial variables and clear psychodiagnostic assessment of the research population.

In **chapter 3** "Subjective sleep characteristics in insomnia with and without psychiatric comorbidity" we discussed differences between subjective sleep diary variables between three groups. We found that patients with psychiatric comorbidity do not necessarily show more severe subjective complaints. Patients with comorbid anxiety disorders showed a sleep efficiency that was significantly higher than patients with primary insomnia. Also they showed a sleep efficiency-score that was more than 20% higher than patients with comorbid mood disorders. While subjective total bedtimes were comparable, the total sleep time was on average 2 hours longer in patients with comorbid anxiety disorders than in patients with comorbid mood disorders. We also found evidence that the main problem in patients with comorbid anxiety disorders involves sleep fragmentation. These results show that tailored CBT-I treatment may vary according to the presence and type of psychiatric comorbidity. Patients with comorbid anxiety disorders might benefit more from sleep restriction while patients

with primary insomnia and comorbid depressive disorders might show better results through stimulus control procedures.

In **chapter 4** "General quality of life in insomnia with and without psychiatric comorbidity" we examined psychosocial factors and sleep variables and their possible contribution to a higher quality of life in insomniacs. We found that the association of these variables with general quality of life (QOL) varies according to the presence of psychiatric comorbidity. Remarkably, the ISI-score was not associated with QOL in primary insomniacs. On the other hand, fatigue was negatively associated with QOL and seems to be more important for general well-being than subjective sleep diary measures such as sleep efficiency or total sleep time in both groups. High discrepancies in social support and low Extraversion are associated with lower QOL in primary insomniacs. Including an assessment of these factors during intake procedures might guide more tailored treatments in which (social) activation might enhance QOL in these patients. In patients with comorbid insomnia, insomnia severity (ISI-score) was negatively associated with QOL as well as the anxiety and depressive symptoms (HADS-score). This stresses the importance of adding CBT-I elements in the treatment of psychiatric disorders in patients who also suffer from insomnia.

Chapter 5 "Psychiatric comorbidity and coping predict cognitive behavioral treatment effect" focused on the prediction of CBT-I treatment effect by examining personality traits, coping and social support. We found that the presence of a comorbid psychiatric disorder predicts worse treatment results. In our results we found a trend that patients who are following current treatment for their comorbid psychiatric disorder might benefit more from CBT-I than patients who are not engaging in current psychological treatment for the comorbid psychiatric disorder. Also, we found that high refocus on planning independently predicts worse CBT-I treatment results. If a comorbid psychiatric disorder is present, we suggest that it is better to integrate cognitive behavioral treatment for insomnia with psychological treatment for the comorbid psychiatric disorder and not exclusively treat the insomnia problem. Adding specific treatment strategies focusing on the decrease of controlling behavior and thoughts around sleep en promoting acceptance of the sleep problem might gain better treatment results in patients with high refocus on planning.

In **chapter 6** "Phenotypes of sleeplessness: stressing the need for psychodiagnostics in the assessment of insomnia" we used cluster analysis to distinguish different phenotypes in patients with insomnia. Our findings stress the need for psycho-diagnostic procedures next to a sleep-related diagnostic approach, especially in younger insomnia patients. We identified three clusters. The "moderate insomnia with low psychopathology"-cluster was characterized by relatively normal personality traits, as well as normal levels of anxiety and depressive symptoms in the presence of moderate insomnia severity. The "severe insomnia with moderate psychopathology"-

cluster showed relatively high scores on the Insomnia Severity Index and scores on the sleep log that were indicative for severe insomnia. Anxiety and depressive symptoms were slightly above the cut-off and they were characterized by below average self-sufficiency and less goal-directed behavior. The “early onset insomnia with high psychopathology”-cluster showed a much younger age and earlier insomnia onset than the other two groups. Anxiety and depressive symptoms were well above the cut-off score and the group consisted of a higher percentage of subjects with comorbid psychiatric disorders. This cluster showed a “typical psychiatric” personality profile. Specific treatment suggestions are given based on the three phenotypes.

In **Chapter 7** we discussed the implications of our findings for clinical practice. We concluded that there are strong personality and subjective sleep differences in patients with and without psychiatric comorbidity. Also, there are other factors correlated with general quality of life depending on the presence of psychiatric comorbidity. Therefore, the term insomnia disorder is much too broad and we suggested the introduction of the term comorbid insomnia. Especially in younger patients with insomnia, psychodiagnostics are very important. These patients often show more comorbid psychiatric disorders. Patients with comorbid psychiatric disorders show less positive treatment results after CBT-I and we recommend a parallel treatment of the psychiatric disorder when starting with CBT-I. Based on our results we conclude that patients with anxiety disorders might benefit more from sleep restriction and that extra attention should be given towards stimulus control in patients with insomnia and comorbid mood disorders. Adding new promising techniques such as acceptance commitment therapy (ACT) and mindfulness-based treatment might enhance treatment effect in specific groups of patients who respond less well to CBT-I. Future research should focus on the benefits of implementing tailored interventions based on type of psychiatric comorbidity and cognitive coping style.

Samenvatting

Samenvatting

In dit proefschrift wordt de complexe relatie tussen insomnie, psychiatrische comorbiditeit en andere psychosociale factoren beschreven. Het belang van psychodiagnostiek in de evaluatie van chronische insomnie wordt benadrukt. Verder wordt in dit proefschrift beschreven hoe onderzoek naar persoonlijkheid en coping kan bijdragen aan het begrip van verschillende fenotypes van insomnie, hoe het de kwaliteit van leven kan vergroten in insomniepatiënten en hoe het kan helpen bij het voorspellen van behandelresultaten.

Hoofdstuk 1 is de algemene introductie van dit proefschrift en beschrijft de achtergrond van onze studie en de onderzoeksvragen. De pathofysiologie, nosologische classificatie en behandeling van insomnie en de relatie met persoonlijkheidstrekken en psychiatrische stoornissen worden besproken.

In **hoofdstuk 2** "The role of personality traits in insomnia" hebben we onderzoeken ten aanzien van insomnie en persoonlijkheid gereviewd en concludeerden we dat neuroticisme, internalisatie en angstige persoonlijkheidstrekken kenmerkend zijn voor insomniepatiënten in het algemeen. Echter, door een gebrek aan longitudinale data en andere methodologische problemen, zoals kleine groepsgroottes en gebrek aan psychodiagnostiek, was het lastig om te concluderen of deze persoonlijkheidstrekken predisponerend zijn voor insomnie. Het is even waarschijnlijk dat specifieke verschillen in persoonlijkheidstrekken een consequentie zijn van de insomnie. Bepaalde persoonlijkheidstrekken zijn verder mogelijk gerelateerd aan (cognitief) gedragstherapeutisch behandeleffect. We benadrukten ook dat persoonlijkheid niet als enkelvoudig predisponerende factor gezien zou moeten worden, maar als een onderdeel van een grotere groep interacterende psychologische en fysiologische factoren die betrokken zijn in de predispositie en het onderhouden van chronische insomnie. Ten aanzien van toekomstig onderzoek adviseerden we onderzoeken uit te voeren met een longitudinale opzet waarbij aandacht is voor verschillende psychosociale variabelen en duidelijke psychodiagnostiek binnen de onderzoeksgroep.

In **hoofdstuk 3** "Subjective sleep characteristics in insomnia with and without psychiatric comorbidity" beschreven we verschillen in subjectieve slaapdagboekvariabelen tussen drie groepen. We vonden dat patiënten met psychiatrische comorbiditeit niet per definitie ernstigere subjectieve klachten laten zien. Patiënten met comorbide angststoornissen hadden een significant hogere slaapefficiëntie dan patiënten met primaire insomnie. Ook hadden zij een slaapefficiëntiescore die meer dan 20% hoger was dan bij patiënten met comorbide stemmingsstoornissen. Terwijl subjectieve bedtijden vergelijkbaar waren, was de totale slaaptijd 2 uur langer bij patiënten met comorbide angststoornissen in vergelijking met patiënten met comorbide stemmingsstoornissen. Een van de resultaten was ook dat het grootste

probleem bij patiënten met comorbide angststoornissen te maken heeft met slaapfragmentatie. Deze gegevens laten zien dat CGT-I behandeling kan variëren afhankelijk van de aanwezigheid van psychiatrische comorbiditeit en het type bijkomende psychiatrische stoornis. Patiënten met bijkomende angststoornissen zouden meer baat kunnen hebben bij slaaprestrictie, terwijl patiënten met primaire insomnie en comorbide stemmingsstoornissen betere resultaten zouden kunnen behalen door middel van stimuluscontrole procedures.

In **hoofdstuk 4** "General quality of life in insomnia with and without psychiatric comorbidity" onderzochten we psychosociale factoren en slaapvariabelen en hun mogelijke bijdrage aan een hogere kwaliteit van leven bij insomniepatiënten. We vonden dat het verband tussen deze variabelen en de algemene kwaliteit van leven varieerde, afhankelijk van de aanwezigheid van psychiatrische comorbiditeit. Opmerkelijk was dat de ISI-score niet samenhing met QOL in primaire insomniepatiënten. Er was een negatief verband aanwezig tussen vermoeidheid en QOL en vermoeidheid lijkt een belangrijkere factor te zijn voor algemeen welbevinden dan subjectieve slaapdagboekvariabelen zoals slaapefficiëntie en totale slaaptijd. Dit geldt voor beide groepen. Hoge discrepanties in sociale steun en lage extraversie hangen samen met een lagere kwaliteit van leven in primaire insomniepatiënten. Het toevoegen van een onderzoek naar deze factoren tijdens de intake kan bijdragen aan meer op maat gemaakte behandelingen waarbij (sociale) activatie de kwaliteit van leven kan vergroten bij deze patiënten. Bij patiënten met comorbide insomnie was de ernst van de insomnie (ISI-score) negatief geassocieerd met kwaliteit van leven en ditzelfde gold voor de angst- en stemmingsklachten (HADS-score). Dit benadrukt het belang van het toevoegen van CGT-I elementen aan de behandeling van patiënten met psychiatrische stoornissen die ook last hebben van insomnie.

In **Hoofdstuk 5** "Psychiatric comorbidity and coping predict cognitive behavioral treatment effect" werd de focus gelegd op voorspellers van CGT-I behandeleffect door onderzoek naar persoonlijkheidstrekken, coping en sociale steun. We vonden dat de aanwezigheid van een comorbide psychiatrische stoornis voorspellend was voor slechtere behandelresultaten. We vonden een trend dat patiënten die gelijktijdig een behandeling kregen voor hun comorbide psychiatrische stoornis meer positief effect zouden kunnen hebben van de CGT-I dan patiënten die deze psychologische behandeling niet kregen. Eén van onze resultaten was verder dat een hogere focus op planning voorspellend was voor slechtere CGT-I behandelresultaten. Als er een bijkomende psychiatrische stoornis aanwezig is adviseren we integratie van CGT-I in een behandeling van deze psychiatrische stoornis in plaats van het alleen behandelen van de insomnie. Het toevoegen van specifieke behandelstrategieën die gericht zijn op het verminderen van controlerend gedrag en gedachten rondom slaap en die de acceptatie van het slaapprobleem bevorderen kunnen voor betere behandelresultaten zorgen bij patiënten die snel geneigd zijn zich te richten op planning.

In **hoofdstuk 6** “Phenotypes of sleeplessness: stressing the need for psychodiagnostics in the assessment of insomnia” gebruikten we een clusteranalyse om verschillende fenotypes van insomnie te kunnen onderscheiden. Onze bevindingen benadrukken het belang van psychodiagnostiek naast een slaapgerelateerde aanpak, vooral bij jongere insomniepatiënten. We identificeerden drie clusters. Het “matige insomnie met lage psychopathologie”-cluster kenmerkte zich door relatief normale persoonlijkheids-trekken en een normaal niveau van angst- en stemmingsklachten in aanwezigheid van matig ernstige insomnieklachten. Het “ernstige insomnie met matige psycho-pathologie”-cluster liet relatief gezien hoge scores zien op de ISI en slaapdagboek-variabelen die indicatief waren voor ernstige insomnie. Angst- en stemmingsklachten bevonden zich qua ernst net boven de drempelwaarde en dit cluster kenmerkte zich door beneden gemiddelde zelfredzaamheid en minder doelgericht gedrag. Het “vroeg begin van de insomnie met hoge psychopathologie”-cluster had een veel lagere leeftijd en hierbij begon de insomnie eerder dan bij de andere twee groepen. Angst- en stemmingsklachten scoorden sterk boven de drempelwaarde en de groep bestond uit een hoger percentage patiënten met comorbide psychiatrische stoornissen. Dit cluster had een persoonlijkheidsprofiel wat typisch is voor patiënten met psychiatrische stoornissen. Op basis van deze drie clusters worden er specifieke aanbevelingen voor de behandeling gegeven.

In **hoofdstuk 7** bespraken we de implicaties van onze bevindingen voor de klinische praktijk. We concludeerden dat er sterke persoonlijkheids- en subjectieve slaapverschillen bestaan tussen patiënten met en zonder psychiatrische comorbiditeit. Ook zijn er verschillende factoren die samenhangen met kwaliteit van leven afhankelijk van de aanwezigheid van psychiatrische comorbiditeit. Daarom is de term “insomniestoornis” te breed en stellen we voor om de term “comorbide insomnie” te gebruiken. Vooral bij jongere insomniepatiënten is psychodiagnostiek erg belangrijk. Deze patiënten hebben vaker comorbide psychiatrische stoornissen. Patiënten met bijkomende psychiatrische stoornissen hebben minder positieve behandelresultaten na CGT-I en we adviseren parallelle behandeling van de psychiatrische problematiek bij het starten van de CGT-I. Aan de hand van onze resultaten concluderen we dat patiënten met bijkomende angststoornissen mogelijk meer baat hebben bij slaaprestrictie en dat er bij patiënten met primaire insomnie en bijkomende stemmingsstoornissen extra aandacht zou moeten worden gegeven aan stimulus controle. Het toevoegen van nieuwe, veelbelovende technieken zoals acceptance commitment therapy (ACT) en mindfulness therapie zou het behandeleffect kunnen vergroten bij specifieke patiëntgroepen die minder goed op CGT-I reageren. Toekomstig onderzoek zou zich kunnen richten op de voordelen van het implementeren van op maat gemaakte behandelingen aan de hand van het type psychiatrische comorbiditeit en cognitieve copingstijl.

Valorisation

Valorisation

Relevance

Insomnia is a very prevalent disorder, affecting 9–10% of the general population in the United States (Ancoli-Israel & Roth, 1999). Chronic insomnia has shown to increase the risk for developing a major depressive disorder and it decreases psychological wellbeing and quality of life (Zammit et al., 1999; Idzikowski, 1996). Insomnia is associated with a substantial direct and indirect burden on society. Outpatient visits and medication are examples of the direct negative effects. Lost productivity and accidents are examples of indirect negative consequences on society (Martin, Aikens & Chervin, 2004).

Target groups

The results of this thesis are relevant for patients with insomnia, (general) physicians, specialized sleep physicians and psychiatrists. Our results stress that general physicians and psychiatrists should be aware of the negative effect of insomnia in patients with psychiatric disorders and should advice separate and parallel treatment for insomnia in these patients. For sleep physicians and other experts in the field of sleep medicine this thesis indicates that there should be attention towards clear psychodiagnostics and parallel treatment for patients with comorbid psychiatric disorders. Sleep therapists can assess coping strategies in patients with insomnia and provide more tailored treatment based on this assessment.

Activities and innovation

The results of this thesis contributed to improvement of insomnia care in several ways.

Literature review

The literature review in Chapter 2 contributes to an understanding of the fact that chronic insomnia is a very broad diagnostic category. It highlights the importance of clear psychodiagnostics in evaluation and treatment of insomnia.

Group differences in subjective sleep variables

Chapter 3 shows that the differences in sleep variables found between groups with and without psychiatric comorbidity might guide a more tailored treatment of insomnia. Our results indicate that a stronger focus on certain treatment strategies might enhance treatment effects in patients with and without psychiatric comorbidity. Thus, psychodiagnostic procedures can be helpful not only in understanding the etiology of insomnia in the individual patient, but also in guiding specific insomnia treatment procedures.

Enhancing general quality of life in specific insomnia subgroups

Chapter 4 gives insight in the correlates of general quality of life in patients with and without psychiatric comorbidity. It highlights the importance of the assessment of fatigue when treating primary insomnia. Results show that insomnia severity has a strong correlation with general quality of life in patients with psychiatric disorders. Therefore insomnia should be treated separately next to the psychiatric disorders. Also, attention should be given to the assessment of social support in patients with insomnia. Enhancing social activity and support might lead to a higher general quality of life.

Predicting cognitive behavioral treatment (CBT) effect

The results shown in chapter 5 contribute to a better understanding of predictors of cognitive behavioral treatment effect. They show that patients with psychiatric comorbidity have less benefit of CBT-I and that expectation management is important in this group. Also, the clinician should pay attention towards the treatment of the comorbid psychiatric disorder. Treating both disorders simultaneously might increase CBT-I effect. An addition of mindfulness-based strategies might enhance treatment effect in patients with an active cognitive coping style.

Phenotypes of insomnia

Chapter 6 shows that three groups of insomnia patients with different clinical features can be distinguished. These features might guide more tailored assessment and treatment. Factors such as age, psychiatric comorbidity and sleep variables have shown to be important distinguishing variables. Especially in younger patients, the need for psychodiagnostic procedures next to a sleep-related diagnostic approach is stressed.

Implementation

Summarized this thesis provides more insight in the specific differences between insomnia subgroups and helps the clinician to choose and implement more tailored treatment strategies. It also broadens the scope of treatment by highlighting factors that have not yet been implemented in standard CBT-I. For example, social activation might be more important in patients with insomnia than previously thought. Exploring the social environment of the patient and specifically targeting the passive behavior that is often seen in patients with chronic insomnia might enhance treatment effect. An assessment of coping strategies and the addition of mindfulness-based strategies to regular CBT-I is another example of a possibility to increase treatment effect, especially in patients who show a very active coping style.

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Dankwoord

Dankwoord

Als “niet in hart en nieren”-onderzoeker maar echte praktijkman heb ik veel op doorzettingsvermogen moeten doen en het is een lange weg geweest, maar het is nu klaar. Met positieve gevoelens kijk ik terug op de samenwerking met een aantal collega’s die me hebben bijgestaan in het onderzoek dat heeft geleid tot dit proefschrift. Zonder jullie was dit alles niet mogelijk geweest.

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Curriculum vitae

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Merijn van de Laar werd op 25 september 1979 geboren in Weert en groeide hier ook op. Na het behalen van zijn VWO-diploma in 1997 aan het Bisschoppelijk College te Weert, volgde hij de studie psychologie in Maastricht met als afstudeerrichting biologische psychologie (neuropsychologie). Vervolgens werkte hij achtereenvolgens bij de GGzE ouderenzorg, HSK Eindhoven en het Maaslandziekenhuis in Sittard. Ondertussen maakt hij de gedragstherapie-opleiding af. In 2006 begon hij met de GZ-opleiding en werkte hij 2 jaar lang bij het Catharina-ziekenhuis en verpleeghuis “de Sterren” in Eindhoven. Na het behalen van zijn diploma als GZ-psycholoog startte hij met werken bij Kempenhaeghe Centrum voor Slaapgeneeskunde. Vanaf 2013 ging hij daarnaast werken bij de Universiteit Maastricht aan de huisartsopleiding. Hier is hij inmiddels curriculumcoördinator en docent gedragswetenschapper. Verder voert hij zijn eigen praktijk “Slaappraktijk Eindhoven” waarin hij eerstelijnszorg biedt aan patiënten met verschillende typen slaapproblematiek.

Merijn van de Laar was born on the 25th of September 1979 and grew up here as well. After graduating his secondary school education in 1997 at the Bisschoppelijk College in Weert, he studied psychology in Maastricht and graduated in biological psychology (neuropsychology). After this, he worked at the GGzE department of elderly care, HSK Eindhoven and the Maasland hospital in Sittard. Meanwhile he finished the postgraduate study of behavioral therapy. In 2006 he started the postgraduate program to become a registered mental health psychologist. During this two-year program, he worked at the Catharina hospital and nursing home “de Sterren” in Eindhoven. After his graduation, he started working at Kempenhaeghe Center for Sleep Medicine. In 2013 he also started working at Maastricht University at the postgraduate program for general physicians. He is currently curriculum coordinator and teacher of behavioral sciences at Maastricht University. Also, he has his own practice “Slaappraktijk Eindhoven” in which he offers primary health care to patients with different types of sleep problems.

List of publications

List of publications

Regarding this thesis

1. van de Laar, M., Verbeek, I., Pevernagie, D., Aldenkamp, A. & Overeem, S. (2010). The role of personality traits in insomnia. Sleep Medicine Reviews, 14, 61-68.
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Other publications

1. Verbeek, I. & van de Laar, M. (2008). Behandeling van langdurige slapeloosheid. Bohn Stafleu van Loghum, Houten.
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