Sleep Medicine Reviews 36 (2017) 71–81

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

THEORETICAL REVIEW

# Insomnia heterogeneity: Characteristics to consider for data-driven multivariate subtyping

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ARTICLE INFO

*Article history:*
Received 11 January 2016
Received in revised form
24 August 2016
Accepted 26 October 2016
Available online 9 November 2016

*Keywords:*
Insomnia
Subtype
Phenotype
Internet
Questionnaires
Traits
Life events
Multivariate methodology
Latent class analysis
Disease history

SUMMARY

Meta-analyses and systematic reviews have reported surprisingly few consistent insomnia-characteristics with respect to cognitions, mood, traits, history of life events and family history. One interpretation of this limited consistency is that different subtypes of insomnia exist, each with its own specific multivariate profile of characteristics. Because previously unrecognized subtypes will be differentially represented in individual studies and dilute effect sizes of subtype-dependent characteristics of importance, they are unlikely to be reported consistently in individual studies, let alone in meta-analyses. This review therefore aims to complement meta-analyses by listing previously reported psychometric characteristics of insomnia, *irrespective* of the degree of consistency over studies. The review clearly indicates that characteristics of insomnia may not be limited to sleep. Reports suggest that at least some individuals with insomnia may deviate from people without sleep complaints with respect to demographics, mental and physical health, childhood trauma, life events, fatigue, sleepiness, hyperarousal, hyperactivity, other sleep disorders, lifetime sleep history, chronotype, depression, anxiety, mood, quality of life, personality, happiness, worry, rumination, self-consciousness, sensitivity, dysfunctional beliefs, self-conscious emotion regulation, coping, nocturnal mentation, wake resting-state mentation, physical activity, food intake, temperature perception and hedonic evaluation. The value of this list of characteristics is that 1) internet has now made it feasible to asses them all in a large sample of people suffering from insomnia, and 2) statistical methods like latent class analysis and community detection can utilize them for a truly bottom–up data-driven search for subtypes. The supplement to this review provides a blueprint of this multivariate approach as implemented in the Sleep registry platform (www.sleepregistry.nl), that allows for bottom–up subtyping and fosters cross-cultural comparison and worldwide collaboration on insomnia subtype finding – and beyond.


## Introduction

Insomnia is a very common health problem that affects between six and 33% of the population – depending on classification criteria [1]. The DSM-5 defines insomnia disorder (ID) as the subjective experience of difficulty initiating sleep, maintaining sleep and/or early morning awakening, for at least three nights a week for three consecutive months, while there is adequate opportunity for

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http://dx.doi.org/10.1016/j.smrv.2016.10.005

**Abbreviations (including Supplement)**

| | |
|---|---|
| 4DSQ | four-dimensional symptom questionnaire |
| ACS | action control scale |
| ADHD | attention deficit hyperactivity disorder |
| APS | arousal predisposition scale |
| APSQ | anxiety and preoccupation about sleep questionnaire |
| ARSQ | Amsterdam resting state questionnaire |
| ASRS | ADHD self-report scale |
| ASQ | autism spectrum quotient |
| BCPQ | bedtime counterfactual processing questionnaire |
| BIS/BAS | behavioral inhibition system/behavioral activation system |
| CES-D | Center for epidemiological studies – depression |
| CIDI | composite international diagnostic interview |
| CoSS | compass of shame scale |
| DBAS | dysfunctional beliefs and attitudes about sleep |
| DFD | daytime functioning diary |
| DIS | difficulty initiating sleep |
| DMS | difficulty maintaining sleep |
| DRFS | dream recall frequency scale |
| DSISD | Duke structured interview for diagnosing sleep disorders |
| DSM-IV | diagnostic and statistical manual of mental disorders, fourth edition |
| DSM-IV-R | diagnostic and statistical manual of mental disorders, fourth revised edition |
| DSM-IV-TR | diagnostic and statistical manual of mental disorders, fourth edition text-revision |
| DSM-5 | diagnostic and statistical manual of mental disorders, fifth edition |
| EEG | electroencephalography |
| EMA | early morning awakening |
| ESS | Epworth sleepiness scale |
| ETSRS | experienced temperature sensitivity and regulation survey |
| FFM | five factor model |
| FIRST | Ford insomnia response to stress test |
| FSS | fatigue severity scale |
| GRS | global rumination scale |
| HADS | hospital anxiety and depression scale |
| HAS | hyperarousal scale |
| HSP | highly sensitive person |
| ICD-10 | international classification of diseases, tenth edition |
| ICSD | international classification of sleep disorders |
| ICSD2 | international classification of sleep disorders, second edition |
| ICSD3 | international classification of sleep disorders, third edition |
| ID | insomnia disorder |
| IDS | inventory of depressive symptoms |
| IPIP | international personality item pool |
| IRLSSG | international restless legs syndrome study group |
| ISI | insomnia severity index |
| MASQ | mood and anxiety symptom questionnaire |
| MCTQ | Munich chronotype questionnaire |
| MFI | multidimensional fatigue inventory |
| NSR | Netherlands sleep registry |
| OSAS | obstructive sleep apnea syndrome |
| PANAS | positive and negative affect scale |
| PHQ-9 | patient health questionnaire |
| PI | perfectionism inventory |
| PLMD | periodic leg movement disorder |
| PLMS | periodic leg movements in sleep |
| PSAS | pre-sleep arousal scale |
| PSQI | Pittsburgh sleep quality index |
| PSWQ | Penn State worry questionnaire |
| PVT | psychomotor vigilance task |
| RAND-36 | 36-item short form survey from the rand medical outcomes study |
| REM | rapid eye movement |
| RLS | restless legs syndrome |
| RRS | ruminative responses scale |
| S-ASQ | short autism spectrum quotient |
| SCS | self-consciousness scale |
| SD | standard deviation |
| SF-36 | 36-item short form survey from the RAND medical outcomes study |
| SPQ-BR | schizotypal personality questionnaire-brief revised |
| SR | sleep registry |
| TCI | temperament and character inventory |
| TEPS | temporary experience of pleasure scale |
| TFEQ | three factor eating questionnaire |
| WSQ | web screening questionnaire |

undisturbed sleep and the complaints are also not adequately explained by other mental or physical problems. A further requirement is that the sleep problems contribute to subjective impairments in social, occupational, educational, academic, behavioral, or other important areas of functioning. ID has a strong impact on quality of life and is a risk factor for development of other disorders, including depression [2]. It shows a moderate heritability, suggesting that it should be possible to find markers of vulnerability in, for instance, genetic or brain imaging studies. Such biomarkers could provide clues on the mechanisms and pathways that underlie the disorder and consequently provide the basis needed to develop rational and more effective treatments than presently available [3].

Unfortunately, it turned out to be remarkably difficult to pinpoint biomarkers that are consistent over multiple studies from multiple research groups. One possible reason for the variability of findings would be if different studies have recruited a different distribution of subtypes from a heterogeneous sample. Given the large percentage of the population that suffers from ID, it is not unlikely that multiple subtypes could exist, just like the diversity of causes, pathways and diagnoses we are now able to discern for 'senile dementia', which a century ago was regarded a single disorder. Indeed, the existence of insomnia subtypes has gained support from studies showing that several of the adverse health consequences may be specific to the subtype of insomnia that comes with chronic short sleep [4,5].

The aim to define different types of insomnia based on *sleep characteristics* has a long history. Subtypes like initial, middle, late and mixed insomnia have been proposed, based on dominant complaints. The most often used complaint-based subtype classification focuses on difficulty initiating sleep (DIS); difficulty maintaining sleep (DMS) and early morning awakening (EMA). These different complaints of insomnia are reflected in psychometric scales to quantify the severity like the insomnia severity index [6]. It has seemed attractive to label people according to their dominant complaint [7,8], like 'sleep onset insomnia' for those that present with DIS predominantly. Common classifications like psychophysiological, paradoxical and idiopathic insomnia

complement sleep-related complaints with for example specific psychological processes and the age of onset [9–11]. Subtypes of insomnia have been proposed in the major nosologies that include classification of sleep disorders. Whereas the DSM (III-R, IV and IV-TR) diagnostic system of the American psychiatric association described only a few insomnia diagnoses [12–14], the International classification of sleep disorders (ICSD and ICSD-2) delineated numerous primary and secondary insomnia subtypes [9,10]. A seminal study on the different nosologies including their subtypes however concluded that the reliability and validity was so poor that they did not improve diagnostic accuracy and that alternate diagnostic paradigms for insomnia classification should be considered [11]. Both the DSM-5 and the ICSD3 abandoned further subtyping of chronic insomnia [15,16].

It has been insufficiently explored however whether clearer subtypes of insomnia could emerge when sleep characteristics are complemented by *non*-sleep characteristics. Such consideration has been proven to be valuable in other disorders. For example, a systematic review on subtypes of depression suggests that optimal discrimination may not be accomplished by focusing on the familiar defining symptoms of depression only [17]. Likewise, it has been shown that the use of neuropsychological and temperament scales makes it possible to discriminate subtypes among people diagnosed with attention deficit/hyperactivity disorder (ADHD) [18,19]. It is thus conceivable that different insomnia subtypes could have identical sleep complaints, yet differ on non-sleep characteristics. Indeed, recent imaging findings on brain structural correlates of insomnia severity in people with depression, anxiety, both, or none, show that seemingly similar sleep complaints are associated with individual differences in quite different brain areas, depending on the affective disorder phenotype [20].

Which *non*-sleep characteristics may be of relevance for insomnia? Meta-analyses and systematic reviews have reported surprisingly *few consistent* insomnia characteristics with respect to cognition [21], mood [2], traits [22], history of life events [23], family history [24,25], polysomnography [26], sleep microstructure [27], brain imaging [28], and genetics [29]. One interpretation of this limited consistency is that there are in fact no consistent biomarkers in insomnia because they don't exist other than in the subjective realm. It may also be that our current arsenal of assessment tools is still too limited or too insensitive to find them. A third possibility that would make the finding of consistent biomarkers more difficult because of heterogeneity, is that presently unrecognized different subtypes of insomnia exist, *each with its own specific multivariate profile of trait-like personality characteristics, cognitions, mood, sleep microstructure, brain imaging and genetic markers*. Because these subtypes may or may not differ with respect to subjective complaints about sleep *per se*, the historical focus mostly or even exclusively on different sets of sleep complaints may have impeded their successful definition and discrimination [11].

We considered the possibility that insomnia comes in different subtypes of pathophysiology that are reflected in traits and other stable characteristics, and not necessarily also in specificity of sleep complaints. If such subtypes exist and participants are not recognized and classified accordingly during the recruitment phase of a study, mixed samples may dilute or even alter effects. The representation of subtypes may then differ between studies making the effects even weaker in meta-analyses and systematic reviews. This review therefore aims *to list previously reported psychometric characteristics of insomnia, irrespective of the degree of consistency* over studies. We argue that if at least some studies found people with ID to differ from controls on an outcome measure, even an inconsistently reported deviation may be of value in discriminating subtypes.

At present, there is limited support for insomnia being either a homogeneous disorder or a heterogeneous disorder. We consider the view of insomnia as a homogeneous disorder to represent the null hypothesis that we have to adhere to until there is sufficient strong, reliable and converging support for subtypes. In general, statistical approaches can be of help for refuting a null hypothesis, but cannot ultimately prove a null hypothesis – it is always conceivable that the relevant discriminating variables have not yet been identified, measured and included in analyses. Within these restrictions however, the null hypothesis would be in a better position if adequate algorithms of latent class analysis or community detection cannot find any support for subtypes even in a very large sample of subjects assessed on a very wide range of variables.

The supplement to this review therefore *outlines an approach for data-driven discovery of such insomnia subtypes* by means of large-scale multivariate psychometric assessment through internet, as currently implemented in the Netherlands (Netherlands sleep registry, NSR, www.sleepregistry.nl) and awaiting translation in different languages and use in other countries.

The present manuscript thus not only provides a broad overview of previously reported characteristics that were found to deviate in at least some samples of people suffering from chronic insomnia, but in its supplement also provides a list of common validated instruments used to assess these characteristics. Moreover, it provides a concise evaluation of our experience with the Dutch version of the Sleep registry, which has been running for some years now. Translated versions for international use are pending. Finally, the supplement provides an overview of key principles and details about application. Concertedly, the topics discussed will thus provide a valuable reference for investigators of individual differences in people suffering from ID, whereas the supplement will be valuable reference for users of the Sleep registry assessment tool.

## Characteristics associated with insomnia

Studies were identified via literature searches using PubMed and Google scholar, supplemented by searches in online available sleep conference proceedings. Key search terms included: 'insomnia' paired with each of the words listed in the headers of the 17 paragraph headers in italics below. The searches resulted in a very large number of results. For example, 'insomnia AND personality' resulted in over 800 hits on PubMed and over 80.000 hits on Google scholar. Rather than embarking a virtually intractable effort to summarize all findings in all domains, we selected exemplary studies and reviews that listed different findings – and in keeping with the aim of the present review to report insomnia characteristics irrespective of the degree of consistency over studies. Below, we discuss 17 domains of characteristics that have emerged in at least some reports to be of relevance to insomnia. We include, if known, their possible relevance to identify insomnia subtypes. Although we have tried to prevent any bias towards discriminating more relevant versus less relevant characteristics, we have to acknowledge that our non-systematic review approach may have missed characteristics of relevance. The open structure of the Sleep registry assessment tool described in the supplement however allows for their implementation might such characteristics show up.

### *Life history: demographics, mental and physical health, trauma and life events*

Numerous studies have reported demographic characteristics of people suffering from insomnia. Females for example have a higher risk to have or develop insomnia; a meta-analysis concluded an

odds ratio of 1.41 [30]. This ratio seemed to be very consistent over age and quite independent of the specific criteria used to define insomnia. Moreover, the higher risk of women to develop insomnia was confirmed by another review looking into risk factors at later age, which in itself is risk factor for insomnia as well [31]. Another risk factor for insomnia is low socioeconomic status. A 20 year longitudinal study showed that in lower socioeconomic classes particularly chronic insomnia complaints were more prevalent [32]. Accordingly, a multivariate characterization of insomnia subtypes requires a systematic assessment of a person's demographic characteristics.

Childhood adversity increases the risk of sleep problems in adulthood. It has been suggested that physical, emotional and sexual abuse all are associated with global sleep pathology and that this relationship is mediated by neuroticism [33,34]. Epigenetic effects of early life adversity are thought to contribute to the risk of developing disorders in adulthood, including insomnia [35]. A specific subtype of insomnia related to trauma has even been proposed [23]. Assessment of subsequent, post-childhood, stressful life events remains important as well, as they may trigger the onset of an epoch of insomnia [23,36]. The most common life events related to insomnia fall into the categories of family, health, and work-school events. Sixty-five percent of these precipitating events had a negative valence [9]. Analogue to the diathesis-stress theories of depression, an individuals' sensitivity to develop insomnia after stressful events is likely to depend on their genetic make-up [37].

ID often coincides with other morbidities [38] which are increasingly present with advancing age [39] and add to intrinsic ageing effects on sleep, due to, among others, functional changes in the suprachiasmatic nucleus and the effectiveness of its major Zeitgeber of light [40–42]. With respect to one's health history, a review concluded that both depressed mood and physical illness predict more insomnia later in life [31]. Given the relationship of childhood adversity, life events and mental and physical health with insomnia and given the vast variance that develops in a population on these factors, it seems paramount to consider these characteristics when investigating insomnia subtypes.

*Sleep timing, duration, subjective quality and complaints*

Although this article focuses on non-sleep characteristics that could serve as possible discerning factors in subtyping insomnia, we do acknowledge that sleep characteristics will remain important when investigating subtypes. Previous subtyping endeavors, including our own [8], have tried to subtype insomnia based on symptoms such as sleep timing, sleep duration, subjectively reported sleep quality and complaints. Although sleep characteristics alone may not be sufficiently discriminating in insomnia, it remains relevant to assess recent sleep quality and severity of insomnia complaints according to the recommendations for a standard research assessment of insomnia [43].

*Fatigue, sleepiness, hyperarousal and hyperactivity*

People with insomnia differ considerably regarding the daytime aspects of their complaints [44]. Some may experience daytime fatigue [45,46]. Within a group of fatigued subjects, some may be sleepy as well, i.e., have the tendency to fall asleep easily during the day, whereas others may be fatigued without being able to find relief from a nap simply because they cannot fall asleep. In this respect, people suffering from chronic insomnia often differ markedly from sleep deprived people without sleep complaints. Fatigue can be further divided into different dimensions that are differently associated with insomnia severity [47]. A key feature that will vary in an insomnia population is the level of generalized *hyperarousal*, as indicated by increased body temperature, resting metabolic rate, cortisol secretion and sympathetic tone [48,49]. Interestingly, hyperarousal seems a premorbid characteristic of subjects vulnerable to insomnia rather than a consequence of insomnia [50]. It has been proposed that hyperarousal involves structural and functional deviations in brain circuits involved in hedonic evaluation and inhibition, resulting in an insufficient capacity to disengage from two primary functions of the brain: environmental monitoring and action preparation [51]. Related to the concept of hyperarousal is the finding that sleep-onset insomnia is present in part of the people suffering from Attention deficit hyperactivity disorder that may involve a phase-delayed circadian rhythm [52–54].

*Sleep disorders*

Other sleep disorders are important when considering characteristics for a multivariate discrimination of insomnia subtypes. For an overview, see Sutton [55]. Sleep disorders that frequently coincide with ID or contribute to insomnia complaints are restless leg syndrome (RLS) and obstructive sleep apnea syndrome (OSAS). Narcolepsy, circadian rhythm disorders and REM sleep behavior disorder (RBD) can contribute to insomnia complaints as well.

*Lifetime sleep history*

People with insomnia differ with respect to the age of onset and life chart of their sleep complaints. Structural interviews like the Duke structured interview for diagnosing sleep disorders (DSISD) [56] cover past sleep problems to some extent in order to evaluate the early childhood onset criterion for idiopathic insomnia. For a multivariate characterization of insomnia subtypes it may be of value to assess sleep-related experiences, problems and perceptions in a greater level of detail, including a person's earliest childhood memories of sleep and the sleep environment, complaints and disturbances, possible causes of disturbed sleep across lifetime, overall lifetime quality of sleep, temporal patterns of sleep complaints, and familial presence of insomnia. The estimated timing of the first episode of insomnia is moreover essential in studies on causal associations between insomnia and mood disorders [2,57–63]. Surprisingly, a literature search did not yield a validated detailed and comprehensive sleep history survey. As will be discussed in the supplement, the Sleep registry implements a newly developed survey to access one's lifetime sleep history.

*Chronotype*

The diagnosis of insomnia is largely dependent on subjectively reported problems, that may be indiscriminable from the symptoms of other disorders. For example, people with a delayed sleep phase can easily be misdiagnosed with insomnia [7,64]. Sleep complaints may also result from mild discrepancies between chronotype and socially desirable scheduled sleep timing. Not being able to fall asleep in time or waking up too early could be indicative of a circadian sleep problem rather than being symptomatic of insomnia.

*Depression, anxiety and mood*

Depression and anxiety are closely linked to insomnia [58–60]. In people diagnosed with major depressive disorder, symptoms commonly include either insomnia or hypersomnia. In case–control studies targeting primary ID, depressive and anxious symptoms are usually reported to be systematically higher than in control subjects, and not seldom above clinical cut-offs. The few

studies that matched cases and controls, could accomplish this only by discarding many volunteering people with ID in the recruitment phase [65–67].

The link between insomnia and mood symptoms occurs not only in parallel, but also across time. Insomnia increases the risk of developing depression [2,57] and in turn depressive symptoms also predict more sleep complaints later in life [31]. A similar relationship between insomnia and anxiety has been suggested [61–63]. Some studies suggest a bidirectional association across time for relationship between insomnia on the one hand and anxiety and depression on the other hand [62]. Other studies however suggest more specific lead-lag associations. In one study in adolescents, insomnia tended to precede depression, but rather follow anxiety [58]. The opposite orders – insomnia preceding anxiety or depression preceding insomnia – were less likely. A study in elderly people reported that specifically sleep onset insomnia predicted depression three years later [59]. In conclusion, it seems highly relevant for any investigation of insomnia subtypes to not only assess momentary symptoms of depression and anxiety, but also the sequential time courses of periods of disturbed mood and periods of insomnia.

*Quality of life, happiness*

The presence and severity of insomnia has shown to not only affect negative emotions like depression and anxiety, but also affects positive emotions like happiness, well-being, satisfaction and quality of life in a negative way [46,68–71], for a review see Kyle et al. [72]. Of note, quality of life, satisfaction with life and happiness do not necessarily represent the other end of a continuum towards depressive symptoms, and need separate assessment. Assessing the 'positive' dimension seems relevant in studies on subtypes of insomnia. One study for example found four separate clusters of insomnia patients, defined by specific combinations of not only sleep and daytime complaints, but also of health-related quality of life [46].

*Personality*

Several studies investigated personality profiles in people suffering from insomnia. As reviewed by van de Laar et al. [22], the overall conclusion is that, on average, people with insomnia score high on the internalizing characteristics of harm avoidance, self-transcendence and neuroticism, and score low on the dimensions of self-directedness, novelty seeking and reward dependence [73–77]. It remains to be determined whether specific personality profiles predispose to the development of insomnia, or reversely, chronic insomnia affects the way items in personality questionnaires are answered. The former possibility is most interesting given the association of personality characteristics with individual differences in brain structure and brain function. For example, both sleep vulnerability and the introversion that characterizes insomnia have been linked to low gray matter density in the orbitofrontal cortex [8,51,78]. Interestingly, the extent to which deviation from an average personality profile occurs, may depend on the diagnostic type of insomnia [22,79,80].

The terms 'personality' and 'temperament' are often used interchangeably. However, 'temperament' may have a more constitutional, genetic and biological basis than personality, and its modification by subsequent environment and development then shape 'personality' [81] and may therefore be considered separately as well when investigating insomnia subtypes. Another important aspect of individual differences, that may not be fully captured by traditional scales to assess personality, is how people tend to respond to stressful situations. Self-regulation competences determine the extent to which a stressful situation affects well-being and health. People with insomnia differ with respect to the way they cope with stressors ranging from tiredness [45] to life events [82].

Perfectionism is another personality characteristic of importance to assess, since it has repeatedly been associated with insomnia [83–89]. Within the concept of perfectionism, separate factors have been proposed, that can be differentially associated with insomnia. Two studies suggested that insomnia is specifically related to the factor of socially prescribed perfectionism which refers to the perception that others prescribe the person to be perfect [83,90]. A longitudinal study showed predictive value of perfectionism for the development of insomnia, and noted that it seemed mediated by emotional distress [85], underscoring the relevance of multivariate assessment to understand mechanisms of insomnia.

Although seldom studied, there is some support for the relevance of personality characteristics in subtyping insomnia. For example, the characteristic of threat sensitivity, representing Gray's behavioral inhibition system (BIS), is higher in psychophysiological insomnia than in idiopathic insomnia [80]. High threat sensitivity is associated with insufficient right frontal inhibition during stage 2 sleep, as indicated by a low relative right frontal EEG alpha power [91]. High threat sensitivity may promote the onset of insomnia [92], early morning awakening [93] and, in interaction with compromised emotion regulation capacity, its associated increase in the risk of developing psychopathology [61,94]. Accordingly, its assessment may be of value in studies that try to predict the subtype of people with insomnia most likely to convert to another mental disorder.

*Worry, rumination, self-consciousness and sensitivity*

The tendency to experience repetitive thoughts, notably worry and rumination, has long been recognized to be highly important in several mental disorders including insomnia [95]. In the last decade, these cognitive processes have been investigated more specifically for the symptoms of insomnia [96–98]. Indeed, one of the most characteristic, cross-cultural, robust and age-independent complaints of people suffering from insomnia is the inability to initiate and maintain sleep because of excessive and uncontrollable, often negatively toned, cognitive activity during the pre-sleep period [96]. Worry and rumination are distinguishable processes, of which the latter seems most relevant to insomnia [98]. Worry concerning one's self-perception has also been called self-consciousness. When investigating repetitive thoughts, and more specifically worry and rumination, often there is a strong emphasis on thoughts with negatively valenced content. Self-evaluative worry has indeed been associated with disturbed sleep [99]. If interpreted within the hyperarousal model of insomnia, thoughts however don't have to be confined to negative content, and can pertain to general intrusive thoughts as well, thus favoring a broader definition of rumination in the study of insomnia [100]. Moreover, whereas it is often presumed that people with insomnia are too self-conscious about their own sleep disturbance, it has not been addressed whether this is specific to sleep or rather reflects enhanced self-consciousness in general. It may even be considered to what extent enhanced self-consciousness is a consequence of enhanced sensory processing in general, i.e., not specific for inward directed attention. In contrast to sleep-deprived good sleepers, people with insomnia may have enhanced rather than attenuated sensory processing [51,65,101]. Studies on subtypes of insomnia would thus do well to include integrated assessments of sensory sensitivity in general, of inward directed attention in general, and of inward directed attention specifically at bedtime.

*Dysfunctional beliefs*

Sleep-related cognitions such as faulty beliefs and expectations, worry, and attentional bias are thought to perpetuate and exacerbate insomnia [102], even though it is equivocal whether their reduction in cognitive behavioral therapy mediates sleep improvements [103,104]. Interestingly, the extent to which people have dysfunctional beliefs and attitudes about sleep (abbreviated to DBAS in a specific questionnaire, see Supplement) may differ for specific insomnia patient groups, the diagnostic type of insomnia, their presenting symptoms and even treatment responses [105–107]. A study that discriminated insomnia subtypes based on subscales of the DBAS questionnaire showed that they differed with respect to insomnia severity, use of medication, comorbid depression and anxiety and daytime sleepiness, and moreover showed different responses to cognitive behavior therapy [107]. Subtyping may also be relevant to understand individual differences in treatment response: a higher overall level of DBAS predicts a larger response to cognitive behavior therapy [105].

*Self-conscious emotion regulation and coping*

A recent review concluded that insomnia is characterized by dysfunctional emotional reactivity, which could also be involved in the relationship between insomnia and depression [2,108]. Whereas experimental studies often address merely basic emotions, we notice that self-conscious emotions, including pride, guilt, embarrassment, humiliation and shame, are oftentimes most relevant in psychological and psychiatric practice. Indeed, insomnia severity is associated with the extent to which people report self-conscious emotions before going to sleep [109]. Maladaptive coping strategies with negative self-conscious emotions can have severe consequences for mental health [110] and interfere with therapeutic progress [111]. A recent study showed that people with insomnia are specifically compromised in the overnight resolving of distress caused by self-conscious emotions, whereas they do not differ from controls in the daytime resolving of such distress [112]. The specific overnight deficit suggests some kind of non-adaptive sleep. Indeed, mediation models suggested that the deficit was driven by restless REM-sleep (with dense arousals and eye movements) and, importantly, contributed strongly to the development of chronic hyperarousal, which is probably the most robust characteristic of insomnia. It thus seems important for studies on insomnia subtypes to include assessments of emotion regulation and coping, preferably not limited to basic emotions but including the more clinically relevant self-conscious emotions.

*Nocturnal mentation*

People suffering from insomnia are characterized by altered nocturnal mentation. On the one hand, ongoing thoughts and rumination during the night may contribute to the characteristic 'sleep state misperception' [113]. On the other hand, there are several reports on altered dream recall. Although people suffering from insomnia were reported to have a normal dream recall frequency after being awaken from REM sleep, they have less dream recall than good sleepers after spontaneous awaking from REM sleep [114]. Moreover, dream reports after spontaneous awaking from REM sleep contained more abstract dream thoughts and less visible dream action [114].

As compared to these sleep-lab assessments, a more feasible measure for the large-scale assessment that is necessary for bottom–up subtype finding may be the retrospective dream recall people have the next day. Several studies suggest an association between self-reported awakenings and retrospective dream recall frequency that are both higher in people suffering from insomnia [115–118]. Dream recall frequency might thus even represent a proxy indicator of fragmented sleep [112,117,119,120]. Interestingly, in contrast to the still common belief that mental content is specific to REM sleep, Foulkes [121] recognized that awakenings from all sleep stages elicit reports of mental activity if more liberal criteria are applied, instead of specifically asking about 'dreams'. Accordingly, enhanced ongoing thought-like nocturnal mentation during sleep [122] may be involved in the underestimation of time asleep that is characteristic for many people with insomnia [113]. Interestingly, a recent study [112] found that particularly the frequency of recalling thought-like nocturnal mentation, rather than the frequency of recalling dream-like nocturnal mentation, represents a proxy indicator of the restless REM-sleep that is so characteristic of insomnia [120,123]. It thus seems essential not only to ask about dreams, but also about ongoing thought-like nocturnal mentation.

*Wake resting state mentation*

In addition to nocturnal mentation, daytime wake mentation may differ between subtypes of insomnia. Several of the domains discussed above assess wake mentation specifically associated with insomnia, like worry, rumination, self-consciousness and cognitive arousal. In both healthy volunteers and numerous patient groups including insomnia [124], a recent surge of functional MRI studies have shown the value of quantifying the brain's resting state functional connectivity. Importantly, the emerging functional connectivity patterns are associated with the mental content reported immediately after the MRI assessment [125]. The Amsterdam resting state questionnaire (ARSQ) can be used to reliably quantify mental content in several factors including discontinuity of mind, theory of mind, self, panning, sleepiness, comfort, and somatic awareness [126,127]. Several of these factors are associated with insomnia severity [128] as well as with personality characteristics [127], which themselves could be discerning characteristics of different insomnia subtypes, as mentioned above. It thus seems valuable to assess wake resting state mentation in studies pursuing bottom–up subtype finding within samples of people with insomnia.

*Lifestyle: physical activity and food intake*

There is a well-established association between habitual physical activity and sleep parameters in the general population. Several studies specifically addressed insomnia (reviewed in [129]). Whereas a poor night of sleep impedes next day's exercise, and reversely the acute effect of a single bout of exercise on next night's sleep may be limited, exercising three times a week for four months improved sleep continuity and duration, but not sleep onset latency [130]. A 6-month intervention study implementing $\geq$150 min of moderate-to vigorous-intensity physical activity per week showed a clinically relevant decrease in insomnia severity [131]. A 3-year long population-based questionnaire study following up a large sample of elderly people showed that frequent physical activity, i.e., five or more days/week reduces the prevalence and incidence of insomnia, again acting mostly on difficulties maintaining sleep [132]. Interestingly, the extent to which people lack sufficient physical activity may depend on the diagnostic type of insomnia; those with psychophysiological insomnia are less physically active [133].

In the general population, the quality, duration and timing of sleep are bidirectionally associated with nutrient intake [134–136]. On the one hand, food choices affect sleep [137] and diet-induced

weight loss can improve sleep [138]. On the other hand, short and poor sleep may affect food intake (for a concise overview, see [20]). Insufficient sleep tends to increase caloric intake by several mechanisms, including more time for eating, psychological distress, greater sensitivity to food reward, disinhibited eating, more energy needed to sustain extended wakefulness, and changes in appetite hormones [139].

Less is known about the relevance of food intake for insomnia. Interestingly, people with insomnia tend to have a low caloric intake rather than the increased caloric intake typical of insufficient sleep in people without insomnia [140]. Moreover, low or excessive carbohydrate and protein intake are differentially associated with difficulties initiating versus maintaining sleep [141].

It can thus be recommended for studies on subtypes of insomnia to include assessments of both habitual physical activity and habitual food intake.

*Body temperature*

There is a well-established association between body temperature and sleep parameters in the general population. Sleep onset is facilitated on the descending part of the 24-hour core body temperature rhythm, whereas wakefulness is promoted once temperature starts to increase again in the early morning. Indeed, a phase-delayed temperature rhythm may be involved in sleep onset insomnia, whereas a phase-advanced temperature rhythm may be involved in problems with early morning awakening [7]. Sleep maintenance insomnia has not been associated with the phase of the temperature rhythms, but rather with high nocturnal core body temperature [7]. Sleep is not only affected by core body temperature, but also by skin temperature. Whereas sleep is impeded in extreme cold or heat, it is also sensitive to spontaneous fluctuations in skin temperature within the thermoneutral zone, or manipulations within that range [142]. A recent study moreover showed that people with insomnia may differ with respect to their subjectively experienced body temperature and behavioral and autonomic thermoregulation. In brief, people with insomnia 1) are more likely to experience fatigue if temperature deviates from the thermoneutral zone, 2) are more likely to feel cold especially internally and at their proximal skin area (trunk), and 3) have a stronger sense of their own autonomic and behavioral thermoregulatory responses [143]. The latter finding once more suggests that it is of value to complement measures of specific sensitivity with an assessment of sensory sensitivity in general, as discussed above for findings about worry, rumination and self-consciousness.

*Hedonic evaluation*

It has recently been found that at least some people with insomnia have an insufficient capacity to reliably judge whether the temperature of the sleeping environment was comfortable [128]. Moreover, using the ARSQ to quantify resting-state mental content, insomnia severity was found to be negatively associated with comfort sensing [126]. The judgment of comfort is part of the brain's hedonic evaluation domain that strongly involves the orbitofrontal cortex [144,145]. Interestingly, several structural brain imaging studies indicate more orbitofrontal gray matter in people that habitually sleep longer than they consider strictly necessary [146], while people with a low gray matter density in a part of their orbitofrontal cortex are vulnerable to early morning awakening [8], insomnia [66,147], fragmented sleep [148] and low perceived sleep quality [149].

## Conclusion

The provided overview aimed to address the domains of non-sleep characteristics that have been reported in at least some studies to deviate in people suffering from insomnia. We discussed the possibility that discrepancies between studies and failure of replication could indicate heterogeneity and differentially sampled distributions of unrecognized subtypes, each with its own specific multivariate profile of relatively stable characteristics. Because previously unrecognized subtypes will be differentially represented in individual studies and dilute effect sizes of subtype-dependent characteristics of importance, they are unlikely to be reported consistently in individual studies, let alone in meta-analyses. This review therefore aimed to complement meta-analyses by listing previously reported psychometric characteristics of insomnia, *irrespective* of the degree of consistency over studies. The review clearly indicates that characteristics of insomnia are not limited to sleep. Reports suggest that at least some subtypes of people suffering from insomnia may deviate from those without sleep complaints with respect to demographics, mental and physical health, childhood trauma, life events, fatigue, sleepiness, hyperarousal, hyperactivity, other sleep disorders, lifetime sleep history, chronotype, depression, anxiety, mood, quality of life, personality, happiness, personality, worry, rumination, self-consciousness, sensitivity, dysfunctional beliefs, self-conscious emotion regulation, coping, nocturnal mentation, wake resting-state mentation, physical activity, food intake, temperature perception and hedonic evaluation.

The value of this list of characteristics is that 1) internet has now made it feasible to assess them all in a large sample of people suffering from insomnia, and 2) statistical methods like latent class analysis and community detection can utilize them for a truly bottom–up data-driven search for subtypes. The supplement to this review provides a blueprint of this multivariate approach with commonly used surveys and questionnaires as implemented in the Sleep registry platform (www.sleepregistry.nl), that allows for bottom–up subtyping and fosters cross-cultural comparison and worldwide collaboration on insomnia subtype finding.

**Practice points**

1. Discrepancies and failure of replication in studies on discerning characteristics of insomnia disorder could indicate heterogeneity and differentially sampled distributions of unrecognized subtypes.
2. Data-driven multivariate subtype discovery is possible with statistical techniques like latent class analysis and community detection if sufficiently large datasets on relevant characteristics are available.
3. Characteristics that could discriminate subtypes are not necessarily limited to sleep-related variables, or may not even include sleep-related variables.
4. Characteristics that could discriminate subtypes may well include personality traits and history of diseases and life events, which reflect individual differences in brain structure and function.
5. It is possible to assess such characteristics in large samples by means of internet, thus unveiling the feasibility for efforts on data-driven insomnia subtype finding.

**Research agenda**

1. The top-down classification of insomnia subtypes, as proposed in previous diagnostic nosologies, should be complemented and compared with bottom–up classification strategies.
2. The multivariate dataset obtained in the Sleep registry approach in the Netherlands approaches the numbers needed for bottom–up subtype finding.
3. It would be of great value if the multivariate data collection approach of the Sleep registry could be adopted by several sleep research groups that can invest time in recruitment and promotion of their continued commitment.
4. Once insomnia subtypes can be identified robustly, a small set of the most discriminating questions may be developed into a practical tool for fast subtype estimation.
5. Once insomnia subtypes can be identified robustly, more homogeneous subpopulations should be selected in studies on genetic predispositions, brain structure and function, and individually optimized treatment.

## Conflicts of interest

The authors do not have any conflicts of interest to disclose.

## Acknowledgements

This work was supported by the Netherlands Organization for Scientific Research (NWO), The Hague, The Netherlands (VICI innovation grant number 453-07-001); the Dutch Technology Foundation STW, which is the applied science division of NWO, and the Technology Programme of the Ministry of Economic Affairs (Perspective Programs NeuroSIPE, project 10738 and OnTime, project 12188); the FP7-PEOPLE-ITN-2008 Marie Curie Actions Networks for Initial Training (ITN) funding scheme, grant number 238665, project Neuroendocrine Immune Networks in Ageing (NINA); and by the European Research Council (ERC-ADG-2014-671084 INSOMNIA). We would like to express our gratitude to Nico Veenman for advice, brainstorm sessions, and generally sharing knowledge on a myriad of information technology topics along the whole process of building the Sleep registry. Moreover, we are very thankful and appreciate all (continued) efforts taken by international colleagues Iuliana Hartescu, Jacob Itzhacki, Corrado Garbazza, Michał Jarkiewicz, Teresa Rebelo Pinto, Joy Perrier, Noemi Tesler, Tina Sundelin, Kai Spiegelhalder, Lyudmila Korostovtseva, Marija Bakotic, Laura Palagini, and Katerina Nikalopoulou in translating the Sleep registry to English, Spanish, Italian, Polish, Portugese, French, German, Swedish, Russian, Croatian and Greek to be able to facilitate cross-cultural comparison and cooperation. The study was performed at the Department of Sleep and Cognition, Netherlands Institute for Neuroscience.

## Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.smrv.2016.10.005.

* The most important references are denoted by an asterisk.

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