Restless REM sleep in insomnia disorder and its detrimental effects on regulation of emotional distress

Wassing, P.F.

2019

document version
Publisher's PDF, also known as Version of record

Link to publication in VU Research Portal

Chapter 2.

Slow dissolving of emotional distress contributes to hyperarousal

Rick Wassing[1], Jeroen S. Benjamins[1,2], Kim Dekker[1], Sarah Moens[1], Kai Spiegelhalder[3], Bernd Feige[3], Dieter Riemann[3], Sophie van der Sluis[4], Ysbrand D. Van Der Werf[5], Lucia M. Talamini[6], Matthew P. Walker[7], Frans Schalkwijk[8], and Eus J. W. Van Someren[1,9,10]

[1] Dep. of Sleep and Cognition, Netherlands Institute for Neuroscience, 1105 BA, Amsterdam, The Netherlands

[2] Dep. of Social, Health and Organizational Psychology, Utrecht University, 3584 CS, Utrecht, The Netherlands

[3] Dep. of Clinical Psychology and Psychophysiology, University Medical Center Freiburg, 79104 Freiburg, Germany

[4] Dep. of Clinical Genetics, Complex Trait Genetics, Vrije Universiteit Medical Center, 1081 HV, Amsterdam, The Netherlands

[5] Dep. of Anatomy and Neurosciences, Vrije Universiteit Medical Center, 1007 MB, Amsterdam, The Netherlands

[6] Dep. of Psychology, University of Amsterdam, 1021 WX, Amsterdam, The Netherlands

[7] Dep. of Psychology, University of California, Berkeley, CA 94720-1650

[8] Institute for Psychotherapy, 1076 AP, Amsterdam, The Netherlands

[9] Dep. of Medical Psychology, Vrije Universiteit Medical Center, 1081 HZ, Amsterdam, The Netherlands

[10] Dep. of Integrative Neurophysiology, Neuroscience Campus, Vrije Universiteit, 1081 HV, Amsterdam, The Netherlands

Abstract

The mechanisms underlying hyperarousal, the key symptom of insomnia, have remained elusive, hampering cause-targeted treatment. Recently, restless rapid-eye-movement (REM) sleep emerged as a robust signature of sleep in insomnia. Given the role of REM sleep in emotion regulation, we hypothesized that restless REM sleep could interfere with the overnight resolution of emotional distress, thus contributing to accumulation of arousal.

Participants (N = 1,199) completed questionnaires on insomnia severity, hyperarousal, self-conscious emotional distress, and thought-like nocturnal mentation that was validated to be a specific proxy for restless REM sleep (selective fragmentation: $R = 0.57$, $P < 0.001$, eye movement density: $R = 0.46$, $P < 0.01$) in 32 polysomnographically assessed participants.

The experience of distress lasting overnight increased with insomnia severity ($\beta = 0.29$, $P < 10^{-23}$), whereas short-lasting distress did not ($\beta = -0.02$, $P = 0.41$). Insomnia severity was associated with hyperarousal ($\beta = 0.47$, $P < 10^{-63}$) and with the thought-like nocturnal mentation that is specifically associated with restless REM sleep ($\beta = 0.31$, $P < 10^{-26}$). Structural equation modelling showed that 62.4% of the association between these key characteristics of insomnia was mediated specifically by reduced overnight resolution of emotional distress. The model outperformed all alternative mediation pathways.

The findings suggest that restless REM sleep reflects a process that interferes with the overnight resolution of distress. Its accumulation may promote the development of chronic hyperarousal, giving clinical relevance to the role of REM sleep in emotion regulation in insomnia, depression, and posttraumatic stress disorder.

Introduction

Both insomnia and affective disorders are among the most prevalent and burdening health concerns facing our society. Targeted prevention of people at risk, as well as identification of mechanisms of conversion, could be the most viable approach to mitigate their increasing global burden (Cuijpers *et al.* 2012). For the prevention of new-onset or recurrent affective disorders, insomnia may be the major risk factor that can be targeted best (Manber *et al.* 2008, Baglioni *et al.* 2011). About 13% of people with insomnia develop major depression disorder (MDD) within a year (Baglioni *et al.* 2011). Moreover, remission rates after cognitive behavioral therapy are 21% lower for depressed patients with abnormal sleep compared to those with relatively intact sleep (Thase *et al.* 1997). It therefore appears highly relevant to understand the mechanisms involved in the role of insomnia in disturbed emotion regulation (Baglioni *et al.* 2011). The present study addresses the roles of restless rapid-eye-movement (REM) sleep (Riemann *et al.* 2012) and chronic physiological arousal (Bonnet and Arand 2010)—characteristic of both insomnia and MDD.

While sleep contributes to the more robust consolidation of emotional memories, relative to neutral memories (Sterpenich *et al.* 2007, Wagner *et al.* 2007), their later recall is not associated with anywhere the same magnitude of subjective emotional distress, autonomic arousal, and amygdala activation (Sterpenich *et al.* 2007, Yoo *et al.* 2007, Pace-Schott *et al.* 2011, Van Der Helm *et al.* 2011). REM sleep plays an important role in this process (Gujar *et al.* 2011, Van Der Helm *et al.* 2011, Rosales-Lagarde *et al.* 2012, Spoormaker *et al.* 2012)—while not excluding a role for NREM sleep (Talamini *et al.* 2013). Naps containing REM sleep were shown to resolve emotional reactivity, whereas naps without REM sleep did not (Gujar *et al.* 2011). Furthermore, high-frequency electroencephalographic activity during REM sleep—an index of fragmented REM sleep—hinders resolution of emotional distress (Van Der Helm *et al.* 2011).

These findings are of particular interest, because meta-analysis suggests disruption of sleep continuity to be among the most robust polysomnographic signatures in insomnia (Baglioni *et al.* 2014). Two studies suggest that this fragmentation is most pronounced in REM sleep and may contribute to the development of the sleep characteristics of MDD, like increased eye movement

density (Feige *et al.* 2008, Riemann *et al.* 2012). We here use the term "restless REM sleep" to refer to REM sleep with a high number of phasic events including arousals and eye movements. These commonly occur not only in insomnia (Riemann *et al.* 2012) but also in depression (Duncan *et al.* 1979) and post-traumatic stress disorder (PTSD; Mellman *et al.* 2002, Germain 2013). If restless REM sleep interferes with the overnight resolution of emotional distress, it could contribute to its accumulation, showing as a chronically hyperaroused state. To our knowledge, the present study is the first to investigate whether chronic interference with this nocturnal process due to restless REM sleep would indeed result in a slower resolving of emotional distress and whether hyperarousal in fact represents the resulting accumulation of this distress. Of note, hyperarousal is not only present across waking and sleep in people suffering from MDD (Nofzinger *et al.* 2005), but also of key importance in the pathophysiology of primary insomnia (Nofzinger *et al.* 2004, Bonnet and Arand 2010, Riemann *et al.* 2010, Edinger *et al.* 2013), and a premorbid characteristic of people vulnerable to insomnia (Fernandez-Mendoza *et al.* 2010, Riemann *et al.* 2012).

Up till now, studies on the role of REM sleep in emotion regulation focused on basic emotions such as fear, anger and happiness. In psychological and psychiatric practice, however, self-conscious emotions, which include pride, guilt, embarrassment, humiliation and shame, are more clinically relevant. The present study focused on shame, since it may interfere most with healthy psychological functioning (Schalkwijk 2015) and was shown to be predictive of developing depression (Stuewig and Mccloskey 2005) and PTSD symptoms, including hyperarousal (Feiring and Taska 2005). By obstructing effective coping mechanisms, shame often hinders therapeutic progress, to the point that it may even lead to a negative therapeutic outcome (Van Es *et al.* 2002).

Based on the hypothesis outlined above, the first prediction is that insomnia will not only be associated with indicators of hyperarousal and restless REM sleep, but also with an increased reporting of slow resolving emotional distress. More specifically, this should be the case primarily for emotional distress lasting a day or longer, but not necessarily so for emotional distress that is resolved before the end of the day, as the latter does not involve a contribution of sleep. The second prediction is that an indicator of consolidated REM sleep will be associated with

successful overnight resolution of emotional distress, whereas restless REM sleep will interfere with this nocturnal process and result in increased reporting of long-lasting distress. The third prediction is that the more frequently people report long-lasting distress, the more likely they accumulate this into a state of chronic hyperarousal. The encompassing fourth prediction is that the association between the two more typical findings in insomnia, restless REM sleep and hyperarousal, is mediated by a slower resolution of distress induced by an emotional experience. To allow us to address these hypotheses in a large sample, we first validated a nocturnal mentation questionnaire proxy variable selectively associated with restless REM sleep in 32 people that were polysomnographically assessed for two nights. This proxy variable was subsequent assessed through internet in 1,199 participants of the Netherlands Sleep Registry (NSR), along with questionnaires on the subjective duration of emotional distress, insomnia severity, hyperarousal, major life events and a structured interview on health. Predicted associations between the variables were evaluated using multiple regression analyses and structural equation modelling.

Results

Given the limited feasibility of polysomnography (PSG) in a large sample, we first validated a questionnaire proxy variable for restless REM sleep. To do so, we systematically evaluated the association of all items of the NSR's extended implementation of the Dream Recall Frequency Scale (DRFQ; Schredl 2004) with the REM sleep arousal index (Bonnet et al. 1992) obtained from the second of two nights of PSG in 32 people (19 female, 13 male, mean (SD) 35.8 (9.0) years of age), of whom 16 had been diagnosed with Insomnia Disorder. Meta-analysis showed that variables reflecting disruption of sleep continuity are the most robust PSG signatures in insomnia (Baglioni et al. 2014), especially fragmentation of REM sleep (Feige et al. 2008, Riemann et al. 2012). Although less specific to insomnia, fragmentation occurs in NREM sleep as well (Riemann et al. 2012). Therefore, to quantify REM sleep-specific arousal density, we calculated the log-transformed ratio between REM and NREM arousal density indices derived according to the criteria of the American Sleep Disorders Association (Bonnet et al. 1992). As

reported before (Ermann *et al.* 1993), REM arousal density was associated with items on thought-like rather than dream-like nocturnal mental content. A 3-item 'nocturnal mentation' score (see Methods) correlated strongly with the REM sleep-specific arousal density index ($r(31)=0.57$, $p<0.001$), also with the nonspecific REM arousal index ($r(31)=0.41$, $p=0.02$) and moreover with the eye movement density during REM ($r(31)=0.46$, $p=0.01$) previously proposed to be consequential to REM sleep fragmentation and involved in the development of depression (Riemann *et al.* 2012). The nocturnal mentation score did not correlate with NREM arousals ($r(31)=-0.18$, $p=0.33$) or with other sleep parameters previously suggested to affect dream recall (see Antrobus 1991, Casagrande *et al.* 1995, Schredl *et al.* 1998, Nielsen 2000, Nielsen *et al.* 2001), notably the total duration of REM sleep ($r(31)=0.18$, $p=0.32$) and specific REM sleep continuity in the morning as derived from the arousal density of the last REM epoch ($r(31)=0.06$, $p=0.73$). Therefore, the nocturnal mentation score appeared useful for subsequent use as a proxy measure specifically associated with restless REM sleep in the sample of 1,199 internet-assessed participants.

N = 1,199 participants of the Netherlands Sleep Registry (891 female, 308 males, 52.1 (13.4) years of age) completed internet questionnaires. A dedicated assessment of the subjective duration of distress after a shameful experience (SDDS), was complemented by assessments on nocturnal mentation (Schredl 2004), insomnia severity (Bastien *et al.* 2001), hyperarousal (Pavlova *et al.* 2001) and major life events (Sarason *et al.* 1978), as well as an internet implemented structured interview on health (Edinger *et al.* 2004). We designed the SDDS to systematically address a range including short-lasting distress (i.e. within a day) and long-lasting distress (i.e. across one or more nights; see Methods). According to our hypothesis, consolidated REM sleep will aid the resolution of emotional distress. Therefore, restless REM sleep should selectively increase the reporting of long-lasting emotional distress but not necessarily the frequency of reporting emotional distress resolved within a day, i.e. without sleep. Factor analysis with Varimax rotation was therefore conducted to investigate whether the eight SDDS items indeed represented a latent structure of separate 'long-lasting' and 'short-lasting' distress. As predicted, these two factors were identified, representing the items "a whole day" up to "more than a week" versus "a few minutes" up to "an

hour", respectively. All questions loaded well above 0.40 on only one factor and well below 0.40 on the other, except for the question "half a day", which loaded 0.68 and 0.58 on both factors. The question may have been ambiguous (12 hours of wakefulness or including sleep) and was discarded. The two-factor structure was confirmed in a second factor analysis excluding this question. Eigenvalues were well over the Kaiser's criterion (respectively 3.64 and 2.25; table 2.1). Sampling of the two factors was adequate according to the Kaiser-Meyer-Olkin measure (KMO = 0.75). Individual KMO values for items were >0.64 and Bartlett's test indicated sufficiently strong correlations across the eight time-scales of experiencing emotional distress ($\chi^2(28)=7567.74$, $p=0.00$). Simple averages over the items included in each factor will henceforth be reported.

Table 2.1. Factor analysis distinguishes long-lasting and short-lasting emotional distress

Frequency of emotional distress lasting:	Long-lasting	Short-lasting
A few minutes	-.10	**.91**
A quarter of an hour	.07	**.96**
An hour	.35	**.84**
A whole day	**.82**	.35
Two-three days	**.91**	.18
A week	**.94**	.01
More than a week	**.87**	-.12
Eigenvalue	3.28	2.62
Variance explained	47%	37%
Cronbach's alpha	.91	.90

Factor-loadings above 0.40 are indicated with bold font-style.

Aforementioned hypotheses were evaluated with multiple regression analyses and structural equation modelling. The significance threshold was Bonferroni corrected for the total number of regression models, and set to $p < 0.003$. In search for support of the hypothesis that restless REM sleep, a key characteristic of insomnia, should selectively increase 'long-lasting' (overnight) distress, but not 'short-lasting' distress, we found that insomnia severity was specifically associated with how often emotional distress lasted overnight ($\beta = 0.29$, $t(1194) = 10.28$, $p < 10^{-23}$; figure 2.1), but not with how often the distress resolved within a day, i.e. without sleep ($\beta = -0.02$, $t(1194) = -0.82$, $p = 0.41$; all coefficients adjusted for age and sex).
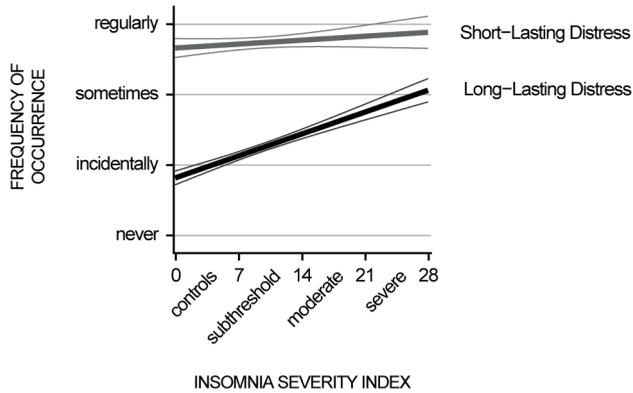
Figure 2.1. Disturbed emotion regulation in insomnia specifically concerns overnight dissolving of distress

Least squares regression line (solid lines) and 95% CI bounds (dashed lines) of association between insomnia severity and the frequency of occurrence of short-lasting (grey), and long-lasting (black) distress after a shameful experience.

The dissociation indicates a selective insufficiency of overnight resolution of emotional distress in insomnia. As expected, insomnia severity was also strongly associated with nocturnal mentation ($\beta = 0.31$, $t(1195) = 11.15$, $p < 10^{-26}$) and with hyperarousal ($\beta = 0.47$, $t(1195) = 18.01$, $p < 10^{-63}$; all coefficients adjusted for age and sex). Next, we evaluated whether the association between nocturnal mentation and hyperarousal might be mediated by insufficient overnight resolution of distress.

As predicted, the more frequently people reported nocturnal mentation, the more they experienced long-lasting distress ($\beta = 0.27$, $t(1194) = 9.65$, $p < 10^{-20}$). The association of nocturnal mentation with short-lasting distress was weak and did not reach significance after Bonferroni correction for multiple comparisons ($\beta = 0.06$, $t(1194) = 2.06$, $p = 0.04$). After demonstrating this indirect support for a possible role of restless REM sleep in the insufficiency of overnight resolution of distress, we addressed whether the resulting accumulation of unresolved distress might contribute to hyperarousal, assessed with the Self-Reported Hyperarousal Scale (Pavlova *et al.* 2001). Indeed, the more people experienced distress to last overnight, the higher their hyperarousal ratings ($\beta = 0.47$, $t(1194) = 18.12$, $p < 10^{-64}$). Short-lasting distress was not associated with hyperarousal ($\beta = 0.02$, $t(1194) = 0.68$, $p = 0.50$).
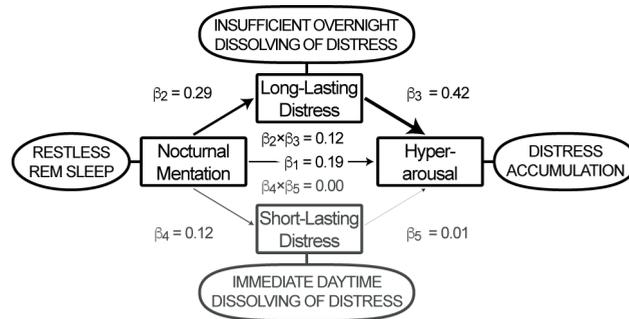
Figure 2.2. Structural Equation Model

The thought-like nocturnal mentation that is specifically associated with fragmented REM sleep and increased eye movement density appears to reflect a process that interferes with overnight dissolving of distress, resulting in its accumulation as indexed by hyperarousal. The model including data of all 1,199 participants suggests that 62.4% of the association between thought-like nocturnal mentation and hyperarousal ($\beta_1 = 0.19$, $t(1194) = 7.45$, $p < 10^{-11}$) is mediated by long-lasting distress ($\beta_2 \times \beta_3 = 0.12$, $t(1194) = 8.70$, $p < 10^{-16}$), without involvement of individual differences in the frequency of experiencing short-lasting distress ($\beta_4 \times \beta_5 = 0.00$, $t(1194) = 0.28$, $p = 0.77$).

To evaluate whether these associations might be secondary to confounding by individual differences in exposure to major life events or neurological, mental or sleep disorders other than insomnia, participants completed the NSR implementations of both the Life Experiences Survey (LES; Sarason *et al.* 1978) and the Duke Structured Interview for Sleep Disorders (DSISD; Edinger *et al.* 2004). The DSISD is a validated tool with acceptable reliability and validity for DSM-IV-TR and ICSD-2 sleep disorder diagnoses (Edinger *et al.* 2011), and its NRS implementation includes as well sections to query all current and past health issues according to ICD-10 categories. Participants had a lifetime experience of 14.9 (4.5) major life events. A neurological, mental or sleep disorder other than insomnia could not be excluded in 513 participants (see supplementary results for details). Adjusting the regression models with covariates for the number of major life events and dummy coded possible presence of these disorders, only marginally affected the estimated coefficients and their significance (see supplementary results).

Finally, we used structural equation modelling to evaluate the most likely direction of mediation between the three apparent key characteristics of insomnia. We hypothesized that the thought-like nocturnal mental content that is specifically

associated with fragmented REM sleep and increased eye movement density could reflect a process that interferes with the overnight resolution of distress, and that the consequent accumulation of distress contributes to the development of chronic hyperarousal. Indeed, the association between nocturnal mentation and hyperarousal was for a large part (62.4%) mediated selectively by long-lasting distress ($\beta_2 \times \beta_3$=0.12, t(1194)=8.70, p<10^{-16}) but not short-lasting distress ($\beta_4 \times \beta_5$=0.00, t(1194)=0.28, p=0.77; figure 2.2). Alternative models interchanging the independent, mediator and dependent variables were rejected based on their Bayesian Information Criterion (BIC), adjusted-R^2, or inferior mediation effect (supplementary table S2.1). To evaluate possible confounding, a sensitivity analysis evaluated the mediation model parameters in the subset of 686 participants that were unlikely to suffer from any neurological, mental or sleep disorder other than insomnia (see supplementary results for details): the partial mediation effect of long-lasting distress in this subsample remained selective and highly significant (figure S2.1).

Discussion

Recent studies indicate that unperturbed REM sleep beneficially contributes to resolving the distress associated with previous emotional experiences, both subjectively and objectively, at the level of limbic brain reactivity (Gujar *et al.* 2011, Van Der Helm *et al.* 2011, Rosales-Lagarde *et al.* 2012, Spoormaker *et al.* 2012). We hypothesized that this beneficial effect may be attenuated in conditions characterized by restless REM sleep (Feige *et al.* 2008, Riemann *et al.* 2012). Because hyperarousal resembles a state of chronic distress, the present study sought indirect support for the possibility that restless REM sleep interferes with the proper overnight resolving of distress after an emotional experience and thus contributes to its accumulation into a state of chronic hyperarousal in insomniacs (Bonnet and Arand 2010, Riemann *et al.* 2010).

The first prediction was a slower resolution of emotional distress in insomnia. Indeed, the more severe the insomnia people suffered, the more they experienced selectively long-lasting, but not short-lasting, emotional distress. This finding is compatible with the hypothesis that the overnight resolution of emotional distress

is compromised in insomnia, resulting in less emotional depotentiation. The second prediction was that restless REM sleep was positively associated with reporting of long-lasting distress. In order to address this question in a large population-based sample, we first showed in 32 PSG-assessed people that restless REM sleep specifically correlates with the frequency of experiencing thought-like rather than dream-like nocturnal mentation, as has been noted before to be characteristic of insomnia (Ermann *et al.* 1993). Indeed, thought-like nocturnal mentation was highly significantly associated with experiencing distress lasting overnight, but not with short-lasting distress resolving daytime. The data also supported the third prediction of the model, that the more frequently people report long-lasting distress, the more likely they are to accumulate this in a state of chronic hyperarousal. The last prediction was that the association between the two typical characteristics of insomnia, restless REM sleep and hyperarousal, is mediated by a slower resolution of distress after an emotional experience. Indeed, long-lasting distress accounted for 62.4% of the association of the thought-like nocturnal mentation that is specifically related to restless REM sleep with hyperarousal. The model outperformed all five alternative mediation models between the three variables of interest: four models explained less variance as indicated by the adjusted-R^2 and Bayesian Information Criterion (BIC); in one model these values were comparable but the mediation effect was half the size of the proposed model and accounted for only 13.3% of the association between independent and dependent variables. The findings support the hypothesis that the thought-like nocturnal mentation is specifically associated with fragmented REM sleep. Furthermore, increased eye movement density may reflect a process that interferes with overnight resolution of emotional distress, in turn promoting the development of a chronic state of hyperarousal.

Several limitations of the present study warrant further detailed investigations. First, inherent to the large sample size, restless REM sleep was not directly quantified but approximated by means of a validated questionnaire rating of thought-like nocturnal mentation. Nonetheless, fragmentation of sleep due to arousals, in particular from REM sleep, is a robust finding in people with insomnia (Feige *et al.* 2008, Riemann *et al.* 2012), and both the current study and others could show that the probability of recalling nocturnal mental content increases in

proportion to the number of arousals (Koulack and Goodenough 1975, Schredl *et al.* 1998, Riemann *et al.* 2012), especially from REM sleep (Nielsen 2005). Secondly, NREM sleep has also been implicated in the resolution of emotional distress (Pace-Schott *et al.* 2011, Talamini *et al.* 2013). Studies employing polysomnography in larger samples are needed to reveal the involvement of different sleep stages to the resolution of emotional distress. A third limitation regards the observational nature of the present study. Even though none of the alternative mediation models outperformed the model proposed here on the basis of recent findings on the role of REM sleep in emotion regulation, a more definite conclusion will require studies employing experimental manipulation of emotions and sleep. Finally, whereas there was good reason to first focus on distress induced by shame in our innovative approach to the role of sleep in self-conscious emotions rather than the basic emotions usually studied (Feiring and Taska 2005, Stuewig and Mccloskey 2005, Vandekerckhove and Cluydts 2010), our findings should not be interpreted as supporting a unique role for shame or self-conscious emotions. Future studies could address whether the duration of distress elicited by other self-conscious and basic emotions has a similar two-factor structure and if so, whether long-lasting distress from such experiences shows a similar strong association with nocturnal mentation, hyperarousal and insomnia severity.

Notwithstanding these limitations, this large sample study generated a number of important new findings. First, the present study is the first to addresses the role of sleep in the overnight resolution of distress related to self-conscious emotions, thus showing that the role of sleep in emotion regulation extends beyond the basic emotions that are usually studied. Self-conscious emotions are highly relevant in clinical psychiatry and psychology (Van Es *et al.* 2002, Schalkwijk 2011). For example, in sexually abused youth, shame contributes to risk of depression (Stuewig and Mccloskey 2005) and the maintenance of PTSD-symptoms, including hyperarousal (Feiring and Taska 2005).

Second, the findings underscore the importance of discriminating short-lasting and long-lasting distress in studies of emotion regulation. Whereas by far most studies have focused on responses *during* emotional experiences, it has been recognized already in early studies that the duration of subsequent *prolonged* responses, in a time window that can extend across sleep, are most relevant to

disease. A slow return to baseline after an emotional experience may undermine health through chronic arousal and is indeed prominent in mental disorders (cf. Linden *et al.* 1997, Brosschot 2010, Koenigsberg 2010). Based on these systematic reviews, and on our specific prediction of differential categories of short-lasting (within a day) and long-lasting (across one or more nights) distress, we generated questions to cover this range. Factor analysis confirmed that the resulting SDDS scale indeed covered separate diurnal and overnight constructs, both measured with excellent internal consistency (alpha $\geq$ 0.90). The discriminant validity of the factors was supported by their different associations with nocturnal mentation, hyperarousal and insomnia severity. The extensive structured interview on comorbidity moreover allowed us to confirm that people familiar with a mental disorder diagnosis scored higher on long-term distress ($t(1197) = 10.55$, $p < 0.001$) but did not on short-term distress ($t(1197) = 1.32$, $p = 0.19$), as compared to those without such diagnosis. Importantly, our results were not confounded by these diagnoses, as demonstrated both by multiple regression models including diagnoses as covariates, as well as by a sensitivity analysis providing a mediation model that included only participants without a neurological, mental, or sleep disorder other than insomnia. In summary, these assessments, analyses and results support the internal and external validity of the SDDS scale, providing a simple instrument for future studies on individual differences in immediate and prolonged emotional stress responses.

Third, a valuable contribution of the PSG study is that it provided a questionnaire proxy specifically associated with restless REM sleep that can easily be implemented in future population-scale studies. Arousals from all sleep stages elicit reports of mental activity that may differ depending on the assessment methodology (Antrobus 1991, Casagrande *et al.* 1995, Schredl *et al.* 1998, Nielsen 2000, Nielsen *et al.* 2001). We therefore here specifically queried both mentation with dreamlike qualities and more thought-like mentation without such qualities. We showed in the polysomnographic part that thought-like mentation specifically reflects fragmentation of REM sleep. Thought-like mentation was also related to increased eye movement density, which was previously proposed to be consequential to REM sleep fragmentation and involved in the development of depression (Riemann *et al.* 2012). Moreover, the frequency of experiencing such

thought-like mental content does not reflect fragmentation of NREM sleep, the duration of REM sleep, or the consolidation of the final REM epoch.

Finally, and most importantly, the present findings show that the overnight resolution of distress from shame is compromised in people with insomnia, that this deficit contributes to hyperarousal, and that this seems in part due to a process that is reflected in a high density of arousals and eye movements in REM sleep and concomitant thought-like nocturnal mentation. These findings reveal important associations between key characteristics of both insomnia and depression (Nofzinger *et al.* 2004, Nofzinger *et al.* 2005, Bonnet and Arand 2010, Fernandez-Mendoza *et al.* 2010, Riemann *et al.* 2010, Riemann *et al.* 2012, Edinger *et al.* 2013). Although the present study focused on insomnia, the role of restless REM sleep in emotion regulation appears highly relevant to other realms of psychiatry. Restless REM sleep is present in MDD (Duncan *et al.* 1979) and PTSD (Mellman *et al.* 2002, Germain 2013). Importantly, insomnia impedes effectiveness of depression intervention (Thase *et al.* 1997), whereas treatment of insomnia improves remission from MDD (Manber *et al.* 2008). Patients suffering from significant emotional distress and co-occurring sleep disturbances might benefit from targeted interventions to either restore consolidated REM sleep or, if not feasible, prevent the occurrence of fragmented REM sleep.

Methods

Participants

Two nights of polysomnography and the extended NSR internet version of the dream recall frequency questionnaire (DFRQ; Schredl 2004) were assessed in 32 people, 19 female, 13 male, 35.8 (9.0) mean (SD) years of age, of whom half had no sleep complaints and the other half had previously been diagnosed with Insomnia Disorder (ID). Sleep recordings were made in the Department of Psychiatry and Psychotherapy, University Medical Center of Freiburg and the questionnaire through internet. The polysomnographic study adhered to strict exclusion criteria on disorders and use of drugs including hypnotics (selection criteria and procedures according to Feige *et al.* 2008).

Large-scale questionnaire data were obtained through internet from volunteers of the Netherlands Sleep Registry (NSR). The NSR is a national platform that recruits volunteers by advertising in media (internet, television, radio, magazines, newspapers) and through flyers distributed in health care institutions and conventions. People are asked to fill out questionnaires regularly in order to help create a psychometric database to facilitate research on factors that discriminate people with insomnia from those without sleep complaints. Continued commitment of unpaid volunteers is supported by newsletters, reminder emails, and an occasional voucher lottery. The present study included data of the 1,199 participants that completed all surveys listed below. The sample consisted of 308 males and 891 females, with a mean (SD) age of 52.1 years (13.4). The Medical Ethical Committee of the Academic Medical Center of the University of Amsterdam as well as the Central Committee on Research Involving Human Subjects (CCMO), The Hague, The Netherlands, approved of unsigned informed consent because volunteers participated anonymously without revealing their full name and address and were not exposed to any intervention or behavioral constraint.

Polysomnography (PSG)

In the 32 subjects assessed with PSG, two nights were recorded between 11 pm and 7 am. Recordings included electroencephalography (EEG, C3–A2; C4–A1), electrooculography (EOG, horizontal and vertical), electromyography (EMG, submental and tibialis anterior), breathing effort, nasal airflow and oximetry. The first night served for adaptation and screening to exclude sleep apnoea and periodic limb movements. The second night was scored visually by experienced raters according to standard criteria for sleep staging and NREM and REM arousal density quantification (Rechtschaffen and Kales 1968, Bonnet *et al.* 1992). Rapid eye movements defined by fast EOG excursions (≥ 70 µV/sec) were counted to calculate their density in REM sleep.

Questionnaires

Insomnia Severity Index

The severity of insomnia complaints was assessed using the validated Insomnia Severity Index (ISI; Bastien *et al.* 2001). It contains seven questions regarding sleep difficulties, satisfaction with sleep, worries about sleep and adverse consequences of sleep problems for daily functioning and quality of life. Answer options on a five-point Likert-type scale are: "none", "mild", "moderate", "severe", and "very severe". Sum-scores range from 0 to 28 indicate insomnia severity according to the usual cut-off scores, no insomnia: ISI ≤ 7, subthreshold insomnia: 7 < ISI ≤ 14, moderate clinical insomnia: 14 < ISI ≤ 21, and severe clinical insomnia: ISI > 21. According to these criteria, insomnia was not present in 561 participants, subthreshold in 336, moderate in 229, and severe in 73.

Hyperarousal

The severity of reactive and introspective hyperarousal was acquired using the validated Self-Reported Hyperarousal Scale (Pavlova *et al.* 2001). The items describe arousal-related experiences, that have to be rated with respect to how well they apply using a 5-point Likert-type scale ("never", "seldom", "sometimes", "often", and "almost always"). Reactive and introspective hyperarousal comprise twelve items of which the sum-score can range between 0 and 48.

Deriving a proxy variable specific for restless REM sleep

The extended DRFS implemented in the Sleep Registry includes ten items; five that ask about the frequency of (1) recalling dreams during the day; (2) experiencing anxious dreams; (3) nocturnal awareness of dreams; (4) experiencing daytime mood effects of dreams and (5) sharing dreams complemented by five items (6-10) that asks about thought-like rather than dream-like nocturnal mental content. People with insomnia were found to be more likely to experience the former during REM sleep (Ermann *et al.* 1993). Answer options on a 9-point Likert-type scale are "never" , "less than once a year", "about once a year", "about two to four times a year", "about once a month", "two to three times a month", "about once a week", "several times a week" and "almost daily", and yield a score between 0 and 8. Spearman correlations were used to evaluate the association of each item with the standard nonspecific PSG REM arousal index (Bonnet *et al.* 1992), as well as with a

REM sleep-specific arousal density index calculated as the log-transformed ratio between REM and NREM arousal density indices, and with the density of eye movements during REM sleep. Items 8-10 correlated most strongly with these restless REM sleep indices and were averaged into a nocturnal mentation score.

Subjective duration of distress elicited by shameful experiences

In order to systematically quantify the subjective duration of distress elicited by shame (SDDS), participants were first introduced to examples of shameful experiences by filling out the Compass of Shame Scale (CoSS; Elison *et al.* 2006), which sketches four shame-eliciting scenarios and makes an inventory of responses. The CoSS was implemented immediately prior to the SDDS in order to facilitate reminiscences of personal shameful experiences. The SDDS asks how often it occurred that the emotional distress of a personal shameful experience lasted for eight distinct durations. Specifically, the questions were first introduced as, "You just indicated your reaction to four situations. Through these questions, you may have remembered some unpleasant situations of your own. After these situations, you may have experienced intense feelings for a short or a long time. Try to remember how long such feelings could last." They were then asked, "An intense feeling elicited by the sort of situations just described could last…" followed by eight durations ("…a few minutes", "…a quarter of an hour", "…an hour", "…half a day", "…a whole day", "…two-three days", "…a week", and "…more than a week"). Each of these eight questions had to be answered on a six-point Likert-type scale ("never", "once at most", "sometimes", "regularly", "often", and "very often"). The sequence of asking all participants to fill out the CoSS immediately prior to this assessment of distress duration served two aims. First, the fixed sequence was used to limit unexplained variance, by promoting a similar self-oriented mindset focused on the evaluation of shameful experiences in all participants. Second, the sequence was used to help participants understand the questions addressed by the SDSS and to facilitate recalling their own distress from shame by providing examples.

Major life events, neurological and mental disorders and sleep disorders other than insomnia

Given the average age and standard deviation of our large sample (52.1±13.4 years), two thirds of our sample are in the age range of about 45-64 years. In this age range, people without any morbidity are not representative; in fact, 30% can be expected to have multimorbidity (Barnett *et al.* 2012). To allow for analyses on possible confounding by individual differences in exposure to major life events and neurological, mental or sleep disorders other than insomnia, we only included NSR participants that had completed the NSR implementations of the Life Experiences Survey (Sarason *et al.* 1978) and the extended Duke Structured Interview for Sleep Disorders (DSISD; Edinger *et al.* 2004).

Statistical analyses

Factor analysis on questions about the duration of emotional distress

Factor analyses with Varimax rotation were conducted to investigate whether the eight "duration of emotional distress" items showed a two-factor structure. An initial factor analysis was used to obtain the number of factors and to select items with a factor loading above 0.40 on only one of the factors (Stevens 2009). The factor structure was verified using a second factor analysis that included only the discriminating items. Individual scores on the resulting factors were calculated as the average of the items included in each factor.

Associations of insomnia with nocturnal mentation, distress duration, and hyperarousal

Linear regression analysis was applied to evaluate the expected associations among insomnia severity, nocturnal mentation, hyperarousal, and the duration of distress factor scores. Age and gender were included as covariates in the regression analyses in case they were significantly associated with the outcome measure. To evaluate confounding by individual differences in exposure to major life events and neurological, mental or sleep disorders other than insomnia, extended regression models included these variables as covariates. A total of 15 independent regression analyses were evaluated (including those of the Structural Equation Modelling). The a priori significance threshold was therefore Bonferroni corrected and set to $p < 0.003$. Standardized beta coefficients are reported.

Structural Equation Modelling

Regression analyses were complemented by Structural Equation Modelling to evaluate whether long-lasting distress mediates the association of hyperarousal with the thought-like nocturnal mentation that is specifically associated with fragmented REM sleep. Mediation directionality of the model was investigated by comparing its adjusted R^2 and BIC with alternative models rearranging the roles of the three variables of interest as independent, dependent, or mediator variables. A sensitivity analysis evaluated the mediation model parameters in the subset of 686 participants that were unlikely to suffer from any neurological, mental or sleep disorder other than insomnia.

Acknowledgements

References

Antrobus J (1991). Dreaming: Cognitive processes during cortical activation and high afferent thresholds. *Psychol Rev* 98(1): 96-121.

Baglioni C, Battagliese G, Feige B, Spiegelhalder K, Nissen C, Voderholzer U, Lombardo C and Riemann D (2011). Insomnia as a predictor of depression: A meta-analytic evaluation of longitudinal epidemiological studies. *J Affect Disord* 135(1-3): 10-19.

Baglioni C, Regen W, Teghen A, Spiegelhalder K, Feige B, Nissen C and Riemann D (2014). Sleep changes in the disorder of insomnia: A meta-analysis of polysomnographic studies. *Sleep Med Rev* 18(3): 195-213.

Barnett K, Mercer SW, Norbury M, Watt G, Wyke S and Guthrie B (2012). Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. *Lancet* 380(9836): 37-43.

Bastien CH, Vallieres A and Morin CM (2001). Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Med* 2(4): 297-307.

Bonnet MH and Arand DL (2010). Hyperarousal and insomnia: State of the science. *Sleep Med Rev* 14(1): 9-15.

Bonnet MH, Carley D, Carskadon M, Easton P, Guilleminault C, Harper R, Hayes B, Hirshkowitz M, Ktonas P and Keenan S (1992). Asda report: Eeg arousals: Scoring rules and examples. *Sleep* 15(2): 173-184.

Brosschot JF (2010). Markers of chronic stress: Prolonged physiological activation and (un)conscious perseverative cognition. *Neurosci Biobehav Rev* 35(1): 46-50.

Casagrande M, Bertini M and Testa P (1995). Changes in cognitive asymmetries from waking to rem and nrem sleep. *Brain Cogn* 29(2): 180-186.

Cuijpers P, Beekman AT and Reynolds CF, 3rd (2012). Preventing depression: A global priority. *JAMA* 307(10): 1033-1034.

Duncan WC, Jr., Pettigrew KD and Gillin JC (1979). Rem architecture changes in bipolar and unipolar depression. *Am J Psychiatry* 136(11): 1424-1427.

Edinger JD, Kirby AC, Lineberger MD, Loiselle MM, Wohlgemuth WK and Means MK (2004). The duke structured interview schedule for dsm-iv-tr and international classification of sleep disorders. *ICSD-2 Sleep Disorder Diagnoses.*

Edinger JD, Means MK and Krystal AD (2013). Does physiological hyperarousal enhance error rates among insomnia sufferers? *Sleep* 36(8): 1179-1186.

Edinger JD, Wyatt JK, Stepanski EJ, Olsen MK, Stechuchak KM, Carney CE, Chiang A, Crisostomo MI, Lineberger MD, Means MK, Radtke RA, Wohlgemuth WK and Krystal AD (2011). Testing the reliability and validity of dsm-iv-tr and icsd-2 insomnia diagnoses. Results of a multitrait-multimethod analysis. *Arch Gen Psychiatry* 68(10): 992-1002.

Elison J, Pulos S and Lennon R (2006). Shame-focused coping: An empirical study of the compass of shame. *Social Behavior and Personality* 34(2): 161-168.

Ermann M, Peichl J, Pohl H, Schneider M and Winkelmann Y (1993). Spontanerwachen und träumen bei patienten mit psychovegetativen schlafstörungen. *PPmP Psychotherapie, Psychosomatik, medizinische Psychologie* 43(9-10): 333-340.

Feige B, Al-Shajlawi A, Nissen C, Voderholzer U, Hornyak M, Spiegelhalder K, Kloepfer C, Perlis M and Riemann D (2008). Does rem sleep contribute to subjective wake time in primary insomnia? A comparison of polysomnographic and subjective sleep in 100 patients. *J Sleep Res* 17(2): 180-190.

Feiring C and Taska LS (2005). The persistence of shame following sexual abuse: A longitudinal look at risk and recovery. *Child Maltreat* 10(4): 337-349.

Fernandez-Mendoza J, Vela-Bueno A, Vgontzas AN, Ramos-Platon MJ, Olavarrieta-Bernardino S, Bixler EO and De La Cruz-Troca JJ (2010). Cognitive-emotional hyperarousal as a premorbid characteristic of individuals vulnerable to insomnia. *Psychosom Med* 72(4): 397-403.

Germain A (2013). Sleep disturbances as the hallmark of ptsd: Where are we now? *Am J Psychiatry* 170(4): 372-382.

Gujar N, Mcdonald SA, Nishida M and Walker MP (2011). A role for rem sleep in recalibrating the sensitivity of the human brain to specific emotions. *Cereb Cortex* 21(1): 115-123.

Koenigsberg HW (2010). Affective instability: Toward an integration of neuroscience and psychological perspectives. *J Pers Disord* 24(1): 60-82.

Koulack D and Goodenough DR (1975). Dream recall and dream recall failure: An arousal-retrieval model. *Psychol Bull* 83(5): 975-984.

Linden W, Earle TL, Gerin W and Christenfeld N (1997). Physiological stress reactivity and recovery: Conceptual siblings separated at birth? *J Psychosom Res* 42(2): 117-135.

Manber R, Edinger JD, Gress JL, San Pedro-Salcedo MG, Kuo TF and Kalista T (2008). Cognitive behavioral therapy for insomnia enhances depression outcome in patients with comorbid major depressive disorder and insomnia. *Sleep* 31(4): 489-495.

Mellman TA, Bustamante V, Fins AI, Pigeon WR and Nolan B (2002). Rem sleep and the early development of posttraumatic stress disorder. *Am J Psychiatry* 159(10): 1696-1701.

Nielsen T, Kuiken D, Hoffmann R and Moffitt A (2001). Rem and nrem sleep mentation differences: A question of story structure? *Sleep and Hypnosis* 3: 9-17.

Nielsen TA (2000). A review of mentation in rem and nrem sleep: "Covert" rem sleep as a possible reconciliation of two opposing models. *Behav Brain Sci* 23(6): 851-866; discussion 904-1121.

Nielsen TA (2005). Disturbed dreaming in medical conditions. In: *Principles and practice of sleep medicine*. M. H. Kryger, T. Roth and W. C. Dement (eds.). Philadelphia, Elsevier Saunders**:** 936-945.

Nofzinger EA, Buysse DJ, Germain A, Price JC, Meltzer CC, Miewald JM and Kupfer DJ (2005). A comparison of regional cerebral metabolism across waking and nrem sleep between primary insomnia and major depression. *Sleep* 28: A232-A233.

Nofzinger EA, Buysse DJ, Germain A, Price JC, Miewald JM and Kupfer DJ (2004). Functional neuroimaging evidence for hyperarousal in insomnia. *Am J Psychiatry* 161(11): 2126-2128.

Pace-Schott EF, Shepherd E, Spencer RM, Marcello M, Tucker M, Propper RE and Stickgold R (2011). Napping promotes inter-session habituation to emotional stimuli. *Neurobiol Learn Mem* 95(1): 24-36.

Pavlova M, Berg O, Gleason R, Walker F, Roberts S and Regestein Q (2001). Self-reported hyperarousal traits among insomnia patients. *J Psychosom Res* 51(2): 435-441.

Rechtschaffen A and Kales A (1968). A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Los Angeles, CA, United States, Bethesda, Md., U. S. National Institute of Neurological Diseases and Blindness, Neurological Information Network.

Riemann D, Spiegelhalder K, Feige B, Voderholzer U, Berger M, Perlis M and Nissen C (2010). The hyperarousal model of insomnia: A review of the concept and its evidence. *Sleep Med Rev* 14(1): 19-31.

Riemann D, Spiegelhalder K, Nissen C, Hirscher V, Baglioni C and Feige B (2012). Rem sleep instability--a new pathway for insomnia? *Pharmacopsychiatry* 45(5): 167-176.

Rosales-Lagarde A, Armony JL, Del Rio-Portilla Y, Trejo-Martinez D, Conde R and Corsi-Cabrera M (2012). Enhanced emotional reactivity after selective rem sleep deprivation in humans: An fmri study. *Front Behav Neurosci* 6: 25.

Sarason IG, Johnson JH and Siegel JM (1978). Assessing the impact of life changes: Development of the life experiences survey. *J Consult Clin Psychol* 46(5): 932-946.

Schalkwijk F (2011). Emoties bij jongeren: Theorie en diagnostiek van het geweten (emotions of the young: Theory and diagnostics of the conscious). Amsterdam, Boom.

Schalkwijk F (2015). The conscience and self-conscious emotions in adolescence: An integrative approach. East Sussex, UK, Routledge.

Schredl M (2004). Reliability and stability of a dream recall frequency scale. *Percept Mot Skills* 98(3 Pt 2): 1422-1426.

Schredl M, Schafer G, Weber B and Heuser I (1998). Dreaming and insomnia: Dream recall and dream content of patients with insomnia. *J Sleep Res* 7(3): 191-198.

Spoormaker VI, Schroter MS, Andrade KC, Dresler M, Kiem SA, Goya-Maldonado R, Wetter TC, Holsboer F, Samann PG and Czisch M (2012). Effects of rapid eye movement sleep deprivation on fear extinction recall and prediction error signaling. *Hum Brain Mapp* 33(10): 2362-2376.

Sterpenich V, Albouy G, Boly M, Vandewalle G, Darsaud A, Balteau E, Dang-Vu TT, Desseilles M, D'argembeau A, Gais S, Rauchs G, Schabus M, Degueldre C, Luxen A, Collette F and Maquet P (2007). Sleep-related hippocampo-cortical interplay during emotional memory recollection. *PLoS Biol* 5(11): e282.

Stevens JP (2009). Applied multivariate statistics for the social sciences. London, UK, Routledge.

Stuewig J and Mccloskey LA (2005). The relation of child maltreatment to shame and guilt among adolescents: Psychological routes to depression and delinquency. *Child Maltreat* 10(4): 324-336.

Talamini LM, Bringmann LF, De Boer M and Hofman WF (2013). Sleeping worries away or worrying away sleep? Physiological evidence on sleep-emotion interactions. *PLoS ONE* 8(5): e62480.

Thase ME, Buysse DJ, Frank E, Cherry CR, Cornes CL, Mallinger AG and Kupfer DJ (1997). Which depressed patients will respond to interpersonal psychotherapy? The role of abnormal eeg sleep profiles. *Am J Psychiatry* 154(4): 502-509.

Van Der Helm E, Yao J, Dutt S, Rao V, Saletin JM and Walker MP (2011). Rem sleep depotentiates amygdala activity to previous emotional experiences. *Curr Biol* 21(23): 2029-2032.

Van Es SM, Kaptein AA, Bezemer PD, Nagelkerke AF, Colland VT and Bouter LM (2002). Predicting adherence to prophylactic medication in adolescents with asthma: An application of the ase-model. *Patient Educ Couns* 47(2): 165-171.

Vandekerckhove M and Cluydts R (2010). The emotional brain and sleep: An intimate relationship. *Sleep Med Rev* 14(4): 219-226.

Wagner U, Kashyap N, Diekelmann S and Born J (2007). The impact of post-learning sleep vs. Wakefulness on recognition memory for faces with different facial expressions. *Neurobiol Learn Mem* 87(4): 679-687.

Yoo SS, Gujar N, Hu P, Jolesz FA and Walker MP (2007). The human emotional brain without sleep--a prefrontal amygdala disconnect. *Curr Biol* 17(20): R877-878.

Supplementary Results

Supplementary table S2.1. Mediation effects and variance explained by three-variable structural equation models interchanging the roles of nocturnal mentation, long-lasting distress and hyperarousal as dependent, independent and mediator variables

The primary model (bold-italic font) outperformed all five alternative mediation models: four models explained less variance as indicated by the adjusted-R^2 and Bayesian information criterion (BIC); in the last model, these values were comparable but the mediation effect was half of our proposed model and accounted for only 13.3% of the association between independent and dependent variables.

Independent	Mediator	Dependent	Mediation	R^2	BIC
Nocturnal Mentation	*Long-lasting distress*	*Hyperarousal*	*.12 (62.4%)*	*.28*	*3035*
Nocturnal Mentation	Hyperarousal	Long-lasting distress	.13 (88.4%)	.26	3066
Hyperarousal	Long-lasting distress	Nocturnal Mentation	.09 (36.9%)	.13	3261
Hyperarousal	Nocturnal Mentation	Long-lasting distress	.05 (11.3%)	.26	3066
Long-lasting distress	Hyperarousal	Nocturnal Mentation	.11 (61.7%)	.13	3261
Long-lasting distress	Nocturnal Mentation	Hyperarousal	.06 (13.3%)	.28	3035

Evaluation of Confounding by Individual Differences in Exposure to Major Life Events and Neurological, Mental, or Sleep Disorders Other than Insomnia

Two approaches were taken to evaluate possible confounding of the reported associations and models by common causes related to individual differences in exposure to major life events or neurological, mental, or sleep disorders other than insomnia. As queried using the NSR implementation of the 30-item LONGSCAN version of the LES (Sarason *et al.* 1978), participants had a lifetime experience of an average (SD) of 14.9 (4.5) major life events. As queried using the NSR implementation of the DSISD (Edinger *et al.* 2009) that also includes sections to query all current and past disorders according to the categories of the 10th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), a neurological, mental, or sleep disorder other than insomnia could not be excluded in 513 participants: a neurological disorder in $n = 13$, a mental disorder in $n = 87$, another sleep disorder in $n = 318$, both a neurological and a mental disorder in $n = 2$, both a neurological disorder and another sleep disorder in $n = 8$, both a mental disorder and another sleep disorder in $n = 82$, and disorders in all three categories in $n = 3$.
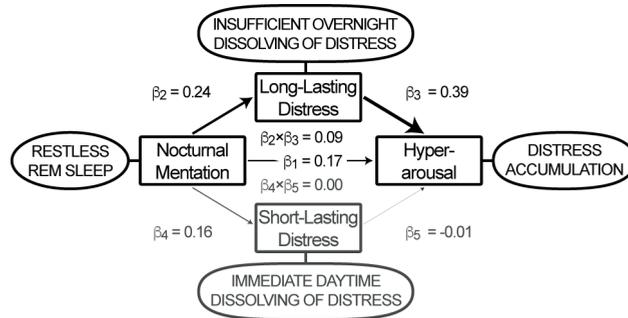
Supplementary Figure S2.1. Structural equation model restricted to 686 participants

The thought-like nocturnal mentation that is specifically associated with fragmented REM sleep and increased eye movement density appears to reflect a process that interferes with overnight dissolving of distress, resulting in its accumulation as indexed by hyperarousal. The model with restricted inclusion of only the 686 participants who were free of any neurological, mental, or sleep disorder other than insomnia suggests that 53.5% of the association between thought-like nocturnal mentation and hyperarousal ($\beta_1 = 0.17$, $t(681) = 4.98$, $p < 10^{-5}$) is mediated by long-lasting distress ($\beta_2 \times \beta_3 = 0.09$, $t(681) = 5.54$, $p < 10^{-6}$), without involvement of individual differences in the frequency of experiencing short-lasting distress ($\beta_4 \times \beta_5 = 0.00$, $t(681) = -0.38$, $p = 0.74$).

First, all regression equations evaluating bivariate associations were run once more with inclusion of covariates for the number of major life events and the dummy-coded presence of mentioned disorder categories. All significant associations remained highly significant, whereas nonsignificant associations remained non-significant. In detail, the adjusted β-coefficients and their significance were as follows. Insomnia severity remained specifically and very significantly associated with nocturnal mentation ($\beta = 0.25$, $t(1,191) = 9.16$, $p < 10^{-18}$), with hyperarousal ($\beta = 0.41$, $t(1,191) = 15.08$, $p < 10^{-46}$; all coefficients also adjusted for age and gender in both measures), and specifically with emotional distress lasting overnight ($\beta = 0.23$, $t(1,190) = 8.08$, $p < 10^{-14}$), but not with distress resolved within a day (i.e., without sleep; $\beta = -0.03$, $t(1,190) = -1.00$, $p = 0.32$; all coefficients also adjusted for age and gender). The more frequently people reported nocturnal mentation, the more frequently they experienced long-lasting distress ($\beta = 0.23$, $t(1,190) = 7.94$, $p < 10^{-14}$), but not short-lasting distress ($\beta = 0.05$, $t(1,190) = 1.85$, $p = 0.06$). The more people experienced distress that lasted overnight, the higher were their hyperarousal ratings ($\beta = 0.40$, $t(1,190) = 15.33$, $p < 10^{-47}$). Short-lasting distress was not associated with hyperarousal ($\beta = 0.02$, $t(1,190) = 0.79$, $p = 0.43$). In summary,

associations found remained highly significant when adjusting for individual differences in exposure to major life events or neurological, mental, or sleep disorders other than insomnia.

Second, to evaluate possible confounding, a sensitivity analysis evaluated the structural equation model parameters in the subset of 686 participants who were unlikely to suffer from any neurological, mental, or sleep disorder other than insomnia (511 females and 175 males; mean (SD) of 50.9 (14.1) years of age; 398 people without sleep complaints and 182 subthreshold, 83 moderate, and 23 severe insomniacs). As shown in supplementary figure S2.1, the partial mediation effect of long-lasting distress in this subsample remained selective and highly significant (53.5%; $\beta_2 \times \beta_3 = 0.09$, $t(681) = 5.54$, $p < 10^{-6}$), supporting the robustness of the findings and making it unlikely that they result from spurious correlations due to common underlying confounders.

References

Edinger JD, Wyatt JK, Olsen MK, Stechuchak KM, Carney CE, Chiang A, Krystal AD, Lineberger MD, Means MK and Radtke RA (2009). Reliability and validity of the duke structured interview for sleep disorders for insomnia screening. *Sleep* 32: A265-A265.

Sarason IG, Johnson JH and Siegel JM (1978). Assessing the impact of life changes: Development of the life experiences survey. *J Consult Clin Psychol* 46(5): 932-946.