

Original article

Daytime symptoms in primary insomnia: A prospective analysis using ecological momentary assessment [☆]

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Abstract

Objectives: To prospectively characterize and compare daytime symptoms in primary insomnia (PI) and good sleeper control (GSC) subjects using ecological momentary assessment; to examine relationships between daytime symptom factors, retrospective psychological and sleep reports, and concurrent sleep diary reports.

Methods: Subjects included 47 PI and 18 GSC. Retrospective self-reports of daytime and sleep symptoms were collected. Daytime symptoms and sleep diary information were then collected for 1 week on hand-held computers. The Daytime Insomnia Symptom Scale (DISS) consisted of 19 visual analog scales completed four times per day. Factors for the DISS were derived using functional principal components analysis. Nonparametric tests were used to contrast DISS, retrospective symptom ratings, and sleep diary results in PI and GSC subjects, and to examine relationships among them.

Results: Four principal components were identified for the DISS: Alert Cognition, Negative Mood, Positive Mood, and Sleepiness/Fatigue. PI scored significantly worse than GSC on all four factors ($p < 0.0003$ for each). Among PI subjects DISS scales and retrospective psychological symptoms were related to each other in plausible ways. DISS factors were also related to self-report measures of sleep, whereas retrospective psychological symptom measures were not.

Conclusions: Daytime symptom factors of alertness, positive and negative mood, and sleepiness/fatigue, collected with ecological momentary assessment, showed impairment in PI versus GSC. DISS factors showed stronger relationships to retrospective sleep symptoms and concurrent sleep diary reports than retrospective psychological symptoms. The diurnal pattern of symptoms may inform studies of the pathophysiology and treatment outcome of insomnia.

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1. Introduction

Insomnia refers to the complaint of difficulty falling asleep, difficulty staying asleep, or poor sleep quality

in an individual who has adequate opportunity for sleep. However, insomnia is also used to refer to a disorder, characterized not only by nighttime sleep difficulty, but also by daytime symptoms such as fatigue or sleepiness, mood disturbances, and cognitive difficulties [1,2]. These daytime symptoms may provide clues to both the pathophysiology and risks associated with insomnia disorders. Mood symptoms are particularly relevant, given the prevalence of mood and anxiety disorders among individuals with chronic insomnia [3–5] and, conversely,

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the risk that insomnia poses for the subsequent development of syndromal psychiatric disorders [6,7]. Numerous studies in clinical samples have demonstrated that individuals with primary insomnia (PI) report more daytime symptoms of depression and anxiety than good sleeper control subjects (GSC) [8–10] even when individuals with syndromal psychiatric disorders are excluded, as reviewed by Reidel and Lichstein [11]. However, not all studies have found significant differences [12–14]. Daytime symptoms of hyperarousal are also relevant to the study of insomnia. Hyperarousal refers to an elevated state of central nervous system activity/reactivity as reflected in cognitive, emotional, or physiological domains, and is commonly viewed as a potential pathophysiological mechanism in insomnia [15]. Individuals with insomnia report symptoms consistent with increased arousal [16–18]. Perhaps, paradoxically, fatigue, low energy, and even sleepiness are also reported commonly in insomnia [19–21]. Finally, individuals with insomnia complain of impaired cognitive function that improves with treatment [22], even though objective evidence of pretreatment cognitive dysfunction is difficult to demonstrate [11,23]. At present, the direction and magnitude of relationships between sleep-related symptoms and waking symptoms in insomnia remains uncertain.

One limitation of studying daytime symptoms in insomnia is that these symptoms are typically assessed cross-sectionally, retrospectively, and in the artificial environment of the clinic. Such assessments make it difficult to examine the variability of symptoms that may occur predictably across the course of the day, or unpredictably from one day to the next. This is a particular concern with a disorder such as primary insomnia that often demonstrates considerable variability within and across days. Retrospective reports are also subject to reporting biases such as recency and severity effects; “telescoping”, in which events are recalled as more recent than they actually occurred; and differences between “counting” and “estimation” strategies for summarizing experiences [24].

Ecological Momentary Assessment (EMA) is a technique of assessing symptoms prospectively, repeatedly, and in subjects’ usual environments [24–26]. Typically, subjects complete questionnaires several times per day during the course of their usual activities. This technique can overcome many of the limitations of retrospective reports noted above. EMA has been extensively used to study phenomena as diverse as daily variation in mood and tiredness [27,28], fatigue [29,30], pain [31], coping [32], eating, smoking, and alcohol behaviors [33–36], and psychosocial correlates of ambulatory blood pressure [37]. We previously reported a pilot study using EMA to measure daytime symptoms in PI [38]. Compared to GSC, individuals with PI reported lower mean ratings, greater day-to-day variability, and differ-

ent time courses for symptom clusters which we termed Mood, Energy, Concentration, and Alertness. These clusters were determined by clinical insight rather than by statistical means. Another potential problem is that the pilot study used paper-and-pencil questionnaires for EMA; previous studies have shown that subjects do not necessarily complete such instruments at the prescribed times [39]. This problem, which can be minimized with electronic data collection devices such as hand-held computers [40], including alarms that cue subjects to complete ratings, and also provide data on actual time of data entry.

In this paper, we present exploratory analyses of EMA measures of daytime symptoms, collected using hand-held computers, in a larger sample of PI and a comparison group of GSC. The aims of this study were (1) to characterize daytime symptom factors in PI with EMA, using statistical techniques rather than clinical intuition to derive summary scales; (2) to compare these daytime symptom factors in PI and GSC; (3) to compare “standard” retrospective psychological and sleep ratings, as well as sleep diary findings in PI and GSC; and (4) to examine relationships between EMA, retrospective psychological and sleep ratings, and sleep diary findings in PI.

2. Methods

These data come from an ongoing study designed to examine mood, arousal, and pharmacologic treatment response in individuals with PI and GSC (MH24652). This study was approved by the University of Pittsburgh, Institutional Review Board, and all subjects provided informed consent. After initial eligibility screening, all participants complete a set of self-report retrospective symptom ratings followed by a 1-week in-home evaluation including sleep diary and daily symptom ratings collected on hand-held computers.

2.1. Participants

Study participants included men and women with PI and GSC, enrolled in a 3:1 ratio and aged 20–50 years. Participants were recruited through media advertisements, word of mouth, and clinical referrals. All participants were evaluated with a medical history, medication/substance history, physical examination, routine blood work, and urine drug screen; psychiatric history using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth edition (DSM-IV) (SCID) [41,42]; and sleep history using locally developed questionnaires and interviews to yield DSM-IV sleep disorder diagnoses [43]. Inclusion criteria for PI and GSC included provision of informed consent and ability to speak and understand English. For PI, additional inclusion criteria included a

current diagnosis of DSM-IV primary insomnia and a score ≥ 7 on the Pittsburgh Sleep Quality Index (PSQI) [44]. A threshold of ≥ 7 was used to ensure clinically significant complaints beyond the level of 5, which we have previously identified as distinguishing sleep disorder patients from controls. In order to approximate clinical practice, no specific quantitative criteria for sleep disturbance (e.g., average sleep latency >30 min) were used. Exclusion criteria for PI and GSC included significant or unstable medical conditions; current major syndromal mood, anxiety, psychotic, or substance use disorder; current sleep disorder (other than PI) by clinical criteria; apnea–hypopnea index >15 or periodic limb movement (PLM) arousal index >15 on one night of screening polysomnography; use of medications or substances known to affect sleep; coffee consumption (or equivalent) of >4 cups/24 h; and alcohol consumption of >14 drinks per week. Our thresholds for apnea and PLMs are higher than the value of 5 or 10 often used in clinical studies. However, some authors have noted the high frequency of apnea and PLM in insomnia samples [45,46], and have questioned their clinical significance. Therefore, we chose our cut-offs to reflect levels of apnea and PLMs that would typically elicit treatment in clinical settings. Despite our liberal inclusion criteria, the mean apnea–hypopnea index (AHI) (2.6 ± 2.6) and PLM arousal index (3.6 ± 4.6) in our PI sample were quite low and not consistent with clinical apnea or PLM disorders. Additional specific exclusion criteria for PI included a history of any major psychiatric disorder within the past 6 months. Additional specific exclusion criteria for GSC involved current or past history of PI or any major psychiatric disorder.

2.2. Measures

Baseline retrospective psychological questionnaires were designed to evaluate symptoms of mood and arousal disturbance among individuals with primary insomnia. In particular, we included measures to evaluate symptoms of depression and anxiety, as well the increased arousal often described by insomnia patients.

For all *retrospective psychological and sleep measures*, higher scores indicate greater severity of symptoms. Except where noted, the timeframe for all measures was 1 week. These measures included the following:

Inventory of Depressive Symptomatology, Self-Report Version (IDS-SR) [47]. The IDS is designed to measure symptoms of depression consistent with major depression criteria in DSM-III and DSM-IV. Validation data from over 300 patients indicates that “normal” scores are ≤ 15 , with a range of 0–90. For analyses in this paper, IDS-SR score represented the total after excluding sleep-specific items.

Beck Anxiety Inventory (BAI) [48]. The BAI is a 21-item self-report questionnaire to assess anxiety, with a

focus on somatic symptoms rather than worry. Total scores represent the sum of the four-point Likert responses and range from 0 to 63.

Penn State Worry Questionnaire (PSWQ) [49]. The PSWQ is a 16-item self-report scale designed to evaluate the tendency to worry, the intensity of worry, and the generalized nature of worry. The PSWQ focuses on the more cognitive concept of worry, as opposed to the BAI, and does not specifically address sleep symptoms. Total scores range from 0 to 90.

Hyperarousal Scale (HAS) [16]. The HAS was empirically designed to measure daytime alertness among individuals with insomnia with a “high arousal pattern”. Subjects rate the extent to which each of 26 statements is true for them, with no specific timeframe. In the original publication, a total score of ≥ 40 had a sensitivity of 90% and specificity of 100% for identifying primary insomnia versus control subjects. Total scores range from 0 to 78.

Multidimensional Fatigue Inventory (MFI) [50]. The MFI is a 20-item scale with five empirically defined subscales representing dimensions of general fatigue, physical fatigue, mental fatigue, reduced motivation, and reduced activity. Each subscale has four items rated on a five-point Likert scale. Scores for the five scales are obtained by adding individual items and range from 4 to 20. Construct validity has been evaluated with known-groups comparisons, and convergent validity supported by correlations with other fatigue measures. For these analyses, we report on the “General Fatigue” subscale only, as recommended by the scale authors when only one scale is to be used.

Pittsburgh Sleep Quality Index (PSQI) [44]. The PSQI is a 19-item self-rated questionnaire for evaluating subjective sleep quality over the previous month. The 19 questions are combined into seven clinically derived component scores, each weighted equally from 0 to 3. The seven component scores are added to obtain a global score ranging from 0 to 21, with higher scores indicating worse sleep quality.

Epworth Sleepiness Scale (ESS) [51,52]. The ESS consists of eight items, each rated from 0 to 3, that measure a subject’s “likelihood of dozing or falling asleep” in common situations of daily living. No specific timeframe is specified. The ESS has been used extensively in studies of sleep apnea and other sleep disorders. The score represents the sum of individual items, and ranges from 0 to 24.

Prospective measures of daytime symptoms and sleep included the following:

Daytime Insomnia Symptom Scale (DISS). The DISS is a measure constructed for this study. It consists of 20 visual analog scales presenting adjectives or brief phrases designed to capture the subjective experience of insomnia patients across the course of a day. The DISS includes the nine “Global Vigor and Affect” scales described by Monk et al. [53], which have previously

shown robust circadian variation in healthy subjects. We supplemented these 9 scales with 11 additional items describing mood, arousal, and cognitive efficiency. The 11 new items were selected to discriminate between insomnia patients and controls and were based on three sources of information: a chart review of chronic insomnia patients [19]; comparisons of Hopkins Symptom Checklist-90 [54] data for insomnia patients and healthy control subjects in pilot studies; and review of Thayer's Activation–Deactivation Adjective Check List (ADACL) [55], a brief instrument that assesses transitory arousal states and has been validated against psychophysiological measures of arousal. Each scale consists of a question and a horizontal line with opposite endorsements at either end (e.g., “How sleepy do you feel? Very little... Very much”). See Table 2 for a complete list of items. One scale of the 20, “Overall, how do you feel”, was not included because it did not assess any specific symptom. The DISS was completed on hand-held computer at four times per day: wake-up time, noon, 6:00 pm, and bedtime. We chose wake-up and bedtimes to capture symptoms that might immediately affect, or be affected by, sleep disturbance, and the other two time points to be approximately evenly spaced between the other two. Alarms on the computer reminded subjects to complete the noon and 6:00 pm scales. The computer displays three scales at a time on the screen, and subjects indicate their responses by tapping on the screen with a stylus along a horizontal visual analog scale. The value for that scale (from 0 to 100) is stored in hand-held computer memory, and later uploaded to personal computers for data management and analysis.

Pittsburgh Sleep Diary (PghSD) [56]. The PghSD is a diary of sleep–wake behaviors with bedtime and wake-time portions. The wake-time portion, used in the current analyses, asks when the subject went to bed and attempted to sleep; how long it took to fall asleep; when and how the subject finally awoke; estimates of total time spent awake; and three visual analog scale ratings for sleep quality, mood (calm versus tense) and alertness on awakening, each scored from 0 to 100.

The DISS and PghSD was presented in versions adapted for a commercially available hand-held computer (Handspring Visor). These hand-held computers, or personal data assistants (PDA), use the Palm OS® operating system Version 4.0.1. DISS and PghSD applications were programmed by study personnel using AppForge software (www.appforge.com) in visual basic programming language. Further details are available from the authors.

2.3. Statistical analysis

DISS data for each subject included 19 visual analog scales completed four times per day over seven days. As

an initial data reduction technique we used functional principal components analysis (FPCA) [57], which determined a factor structure for the 19 scales based on their correlation across time points, days, and subjects. Please see Appendix for details. FPCA identified four orthogonal factors (or functional principal components) that explained 67% of the variance in the 19 DISS items. The initial analysis was conducted in PI subjects alone. Factor scores were then compared across groups.

We used Wilcoxon rank-sum tests to compare PI and GSC participants on the DISS and sleep diary measures and retrospective psychological and sleep ratings. For baseline retrospective symptom assessments (IDS, BAI, HAS, PSWQ), we removed items explicitly related to sleep before calculating total scores. Within each domain of results in Table 1, we report statistical significance both without and with correction for multiple comparisons. Because of our interest in variability of daytime ratings, we also compared the mean variance in DISS scales across PI and GSC groups using the Mann–Whitney test. In order to test for potential gender differences in PI participants, we again used Wilcoxon rank-sum tests; there were too few male controls to conduct statistical comparisons between genders in GSC. Finally, we used Spearman correlation coefficients in exploratory analysis to examine the relationships between DISS factors, retrospective psychological and sleep ratings, and sleep diary measures. FPCAs of DISS data were performed using R Version 2 [58]; all other analyses were performed using SAS Version 8.2 [59].

3. Results

The sample included 47 PI participants (25 F, 22 M, 35.9 ± 9.6 years old) and 18 GSC participants (15 F, 3 M, 27.2 ± 7.9 years old). The PI sample was older (Wilcoxon rank-sum = 361, $p = 0.0002$) and included more men (Fisher's exact = 0.05) than the GSC sample. Among PI participants, 27 reported an insomnia duration of >5 years, 16 a duration of 1–5 years, and 4 a duration of 1 month to 1 year. Insomnia complaints were characterized as sleep onset insomnia ($n = 37$), sleep maintenance insomnia ($n = 41$) and early morning awakening insomnia ($n = 35$); subjects could have more than one type of complaint. Descriptively, 31/47 PI participants had mean sleep onset latency ≥ 30 min, 35/47 had mean wakefulness after sleep onset ≥ 30 min, 36/47 had mean sleep duration ≤ 6 h based on sleep history questionnaire data, and 46/47 met at least one of these criteria. Alcohol consumption averaged 2.6 ± 3.2 drinks per week in PI (range 0–12) and 0.8 ± 1.3 per week in GSC (range 0–4). Caffeine consumption averaged 1.3 ± 1.0 beverages per day in PI (range 0–5) and 1.2 ± 1.1 per day in GSC (range 0–2.9).

Subjects had good overall compliance with EMA ratings. The mean percentage of completed DISS ratings

Table 1
Ecological Momentary Assessment, retrospective psychological scales, and self-report sleep data

Measure	Control (<i>n</i> = 18)			Insomnia (<i>n</i> = 47)			Wilcoxon rank-sum test	
	Mean	SD	Med	Mean	SD	Med	<i>W</i>	<i>P</i> ^a
<i>Daytime Insomnia Symptom Scale functional principal components</i>								
Alert Cognition	9.7	10.1	11.8	−5.0	14.4	−2.9	861.0	<0.0001
Negative Mood	−12.4	12.9	−11.2	2.1	16.2	−0.4	830.0	0.0003
Positive Mood	8.2	9.2	6.3	−3.3	10.4	−2.9	304.0	<0.0001
Sleepiness/Fatigue	−10.3	8.9	−10.4	5.0	14.0	1.5	927.0	<0.0001
<i>Retrospective psychological scales</i>								
Inventory of Depressive Symptomatology	3.4	5.8	2.0	10.3	5.4	10.0	272.5	<0.0001
Beck Anxiety Inventory	1.4	1.7	1.0	3.9	4.0	3.0	398.0	0.004
Penn State Worry Questionnaire	16.3	11.9	14.0	30.1	14.1	29.0	352.0	0.0002
Hyperarousal Scale	22.4	7.3	22.0	30.0	6.2	29.0	366.5	0.0004
Multidimensional Fatigue Inventory (General Fatigue subscale)	6.9	1.9	7.0	13.2	3.4	13.0	215.5	<0.0001
<i>Self-report sleep measures</i>								
Pittsburgh Sleep Quality Index (global score)	1.9	1.1	1.5	11.0	3.5	10.0	171.0	<0.0001
Epworth Sleepiness Scale	4.4	3.5	3.5	7.4	3.8	7.0	389.0	0.002
Pittsburgh Sleep Diary								
Total sleep time (min)	464.9	60.1	461.7	370.1	66.4	378.2	837.0	<0.0001
Sleep latency (min)	8.2	5.4	5.7	30.9	24.5	24.3	224.0	<0.0001
Wake after sleep onset (min)	3.3	3.7	2.2	38.9	29.5	33.8	205.0	<0.0001
Sleep Efficiency ([Total sleep time/Time in bed] × 100; %)	97.7	1.4	97.9	83.7	10.4	86.4	932.0	<0.0001

^a All *p* values were significant at the *p* < 0.05 level after correcting for the number of comparisons within each domain (i.e., DISS functional principal components; retrospective psychological scales; self-report sleep measures); SD = standard deviation.

was $92.2 \pm 12.7\%$ (range 39.3–100%) for PI, and $92.1 \pm 12.5\%$ (range 60.7–100%) for GSC. The mean difference between target time and actual time of completion was 27.2 ± 59.0 min in PI and 23.6 ± 52 in GSC. FPCA uses all available data and does not require complete data in all subjects.

FPCA of the 19 DISS items in the PI participants identified four eigenvectors that accounted for 67% of the variation in responses across subjects. Table 2 lists the adjectives in the DISS, grouped according to their weights on the four functional principal components. The first functional principal component, labeled Alert Cognition, included five items with factor weights ≥ 0.4 : forgetful, clear-headed, able to concentrate, how much of an effort is it to do anything, and alert. The second functional principal component, labeled Negative Mood, included five items with factor weights ≥ 0.4 : anxious, stressed, tense, sad, and irritable. The third functional principal component, labeled Positive Mood, included five items with factor weights ≥ 0.4 : relaxed, energetic, calm, happy, and efficient. The fourth functional principal component, labeled Sleepiness/Fatigue, included three items with factor weights ≥ 0.4 : fatigued, sleepy, and exhausted. Of the 19 DISS items, only one, “weary”, did not load with a factor weight of ≥ 0.4 on any of the four functional principal components. Statistically significant Spearman rank-order correlations among factor scores were observed for the following pairs of factors: Alert Cognition and Negative Affect ($\rho = -0.33$, *p* = 0.02); Alert Cognition and Positive

Affect ($\rho = 0.36$, *p* = 0.01); Alert Cognition and Sleepiness/Fatigue ($\rho = -0.46$, *p* = 0.001); and Positive Affect and Sleepiness/Fatigue ($\rho = -0.31$, *p* = 0.03).

Fig. 1 illustrates the average time course of the four factors from the daily symptom diary for PI and GSC groups. For each scale, higher factor scale scores indicate a greater degree of that particular construct (i.e., a greater amount of Alert Cognition, Negative Mood, Positive Mood, and Sleepiness/Fatigue). Note that FPCA was conducted on the PI group alone, and that factor weights derived from PI alone were used to calculate scores for the factors in both groups of participants. Descriptively, the time courses for the four factors are different from one another, and PI and GSC subjects show different temporal patterns for each. For instance, on Alert Cognition, PI subjects are worst in the morning, with a slight improvement at night, whereas GSC subjects have high values in the morning, highest values during the day, and lowest values at night. On Negative Mood, the PI group has higher overall mean values than the GSC group. The two groups have similar values in the morning, but PI subjects show a small increase in the evening, whereas GSC subjects show a decrease. These differences in symptom patterns are reflected by statistically significant differences between PI and GSC subjects for all four of the DISS functional principal component scores (Table 1). The statistical differences can be interpreted as an interaction between group and time of day; the groups differ to different degrees at different times of day. We also compared the mean

Table 2

Functional principal component loading values for items on the Daytime Symptoms in Insomnia (DISS) scale in primary insomnia subjects^a

DISS Item	Daytime Insomnia Symptom Scale functional principal components			
	Alert Cognition	Negative Mood	Positive Mood	Sleepiness/Fatigue
Forgetful	-0.792	0.385	0.395	-0.313
Clear-headed	0.742	0.064	0.213	0.025
Concentrate ^b	0.742	0.154	0.246	0.034
Effort ^c	-0.677	0.173	0.368	0.122
Alert	0.457	0.187	0.160	-0.324
Weary	-0.367	-0.038	-0.286	0.337
Anxious	0.114	0.750	-0.027	0.142
Stressed	0.144	0.703	-0.135	0.093
Tense	-0.011	0.698	-0.178	-0.146
Sad	0.014	0.696	0.007	0.105
Irritable	-0.335	0.581	0.146	-0.025
Relaxed	-0.042	-0.18	0.808	-0.001
Energetic	0.118	0.251	0.706	-0.221
Calm	0.040	-0.362	0.687	0.252
Happy	-0.0001	-0.144	0.658	0.176
Efficient	0.373	0.316	0.427	-0.139
Fatigued	0.208	0.148	-0.051	0.948
Sleepy	-0.050	0.038	0.120	0.880
Exhausted	-0.121	0.076	0.077	0.841

^a Except as indicated, items are of the form, "How ____ do you feel?"

^b Actual wording: "How well are you able to concentrate?"

^c Actual wording: "How much of an effort is it to do anything?"

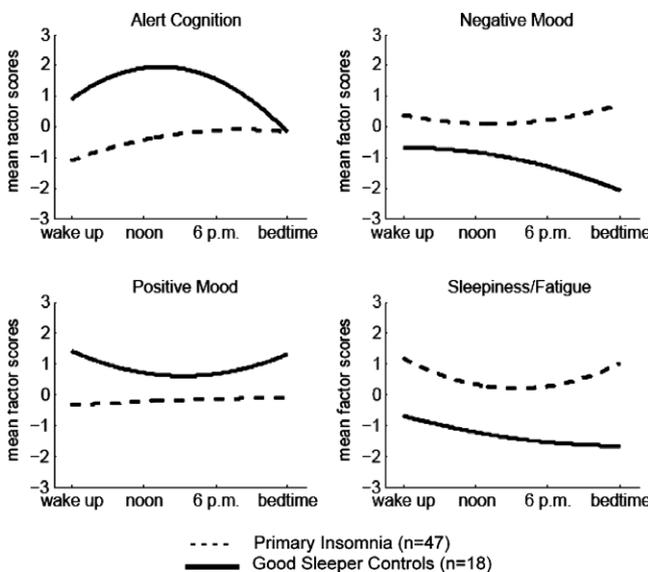


Fig. 1. Group mean data for functional principal components of the Daytime Insomnia Symptom Scale (DISS). Values represent fitted standardized factor scale scores for each group. Because these represent standardized scale scores, the y-axis scales do not have specific units. Higher scores indicate a greater level of the construct for each scale (i.e., higher level of Alert Cognition, more Negative Mood, more Positive Mood, greater Sleepiness/Fatigue). Group differences for each functional principal component was statistically significant at $p < 0.001$, indicating a different levels and time courses between insomnia (dashed line) and control (solid line) groups.

variance of DISS scales across days in PI and GSC groups. This measure captures day-to-day variability of the scale, but addresses the entire day's composite scale score rather than variability at individual time points within the day. Only the Sleepiness/Fatigue scale showed significantly greater variance among PI than GSC (0.271 ± 0.063 versus 0.392 ± 0.136 ; $W = 567$, $p = 0.05$).

Significant differences were also found among PI and GSC groups for all retrospective psychological and sleep ratings and sleep diary measures (Table 1). Thus, the PI sample endorsed more depressed, anxious, worried mood, a greater tendency toward hyperarousal, and more sleepiness and fatigue. As expected, group differences in PSQI scores, Epworth scores, and sleep diary ratings of sleep latency, total sleep time, wakefulness after sleep onset, and sleep efficiency were also highly significant (Table 1), even after correction for multiple comparisons.

To explore the potential impact of gender on DISS and retrospective data, we compared male and female PI subjects. Across the domains and specific measures in Table 1, only one measure showed significant gender differences. Women reported higher scores on the PSWQ than men (33.8 ± 12.1 versus 25.9 ± 15.4 , $W = 434$, $p = 0.05$). DISS scales showed no gender differences.

The correlation between DISS factors and retrospective psychological symptom measures among PI subjects showed a plausible pattern of relationships that differed among the four factors (Table 3). Alert cognition correlated negatively with the IDS. Negative mood positively correlated with scores on the IDS and BAI. Positive mood correlated inversely with scores on the IDS, HAS, and MFI General Fatigue Scale. Sleepiness/Fatigue correlated positively with the MFI General Fatigue subscale. Overall, 7/20 possible correlations between DISS factors and retrospective psychological rating scales had ρ values ≥ 0.30 , corresponding to p values of < 0.05 .

Correlations between different DISS factors and self-report sleep measures again showed different patterns (Table 3). Positive Mood and Sleepiness/Fatigue DISS factors were significantly related to the PSQI total score, but the other two DISS factors were not. Somewhat unexpectedly, negative mood, but not sleepiness/fatigue, correlated with the ESS. With regard to sleep diary correlations, the Alert Cognition and Negative Mood factors were significantly related to the diary measure of sleep latency in the expected direction; Positive Mood correlated with sleep efficiency; and Sleepiness/Fatigue correlated positively with wakefulness after sleep onset, and negatively with sleep efficiency. Overall, 8/24 possible correlations between DISS factors and self-report sleep measures had ρ values ≥ 0.30 .

In contrast to the above findings, when we examined exploratory correlations between the retrospective

Table 3
Correlations between DISS factor scores, retrospective psychological scales, and self-report sleep measures in insomnia patients ($n = 47$)

Measure	Daytime Insomnia Symptom Scale functional principal components			
	Alert Cognition	Negative Mood	Positive Mood	Sleepiness/Fatigue
<i>Retrospective psychological scales</i>				
Inventory of Depressive Symptomatology	-0.32*	0.43**	-0.30*	0.25
Beck Anxiety Inventory	-0.13	0.49***	-0.20	-0.22
Penn State Worry Questionnaire	-0.05	0.12	-0.27	0.19
Hyperarousal Scale	-0.15	0.19	-0.30*	-0.06
Multidimensional Fatigue Inventory (General Fatigue subscale)	-0.26	0.25	-0.35*	0.53***
<i>Self-report sleep measures</i>				
Pittsburgh Sleep Quality Index (global score)	-0.27	0.08	-0.32*	0.34*
Epworth Sleepiness Scale	0.23	-0.34**	0.01	-0.04
Pittsburgh Sleep Diary				
Sleep latency (min)	-0.35*	0.30*	-0.23	0.26
Total sleep time (min)	0.02	-0.01	0.25	-0.20
Wake after sleep onset (min)	-0.01	-0.01	-0.20	0.40**
Sleep Efficiency (%)	0.16	-0.09	0.30*	-0.39**

Statistically significant correlations (Spearman's rho) are indicated by bold font.

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$.

psychological symptom measures and sleep measures, none of the 30 possible correlations had ρ values ≥ 0.30 (data not shown). Retrospective psychological symptom scales were not related to either the PSQI or any of the prospective sleep diary measures.

4. Discussion

Daytime symptoms of insomnia, collected four times per day with ecological momentary assessment methodology, provided evidence for four functional principal components, representing Alert Cognition, Positive Mood, Negative Mood, and Sleepiness/Fatigue. These component scores differed significantly between insomnia and good sleeper subjects, and were related to some but not all traditional psychological and sleep measures. DISS components were more closely related to sleep symptoms than were the retrospective psychological symptom measures. Although these results are exploratory in nature, given the relatively small sample size, they suggest that ecological momentary assessment of daytime symptoms in insomnia may help to better characterize the insomnia syndrome and its consequences, and may be a useful tool for outcome studies.

Individuals with insomnia typically present with symptoms of depression and anxiety that are greater than those of good sleeper controls but less severe than those in individuals with syndromal mood and anxiety disorders [11]. We found that PI and GSC groups differed on traditional retrospective self-report measures of mood disturbance, including the IDS and the BAI. The two groups also differed on measures designed to

measure the construct of hyperarousal, such as Regestein's Hyperarousal Scale and the PSWQ. Although PI and GSC differed significantly on most retrospective psychological rating scales, the level of symptoms in the PI group was typically less than that seen for clinical populations with mood or anxiety disorders. For example, a score of ≤ 15 on the IDS-SR is considered "normal", and 16–24 "mild" depression [47]; scores of 0–7 on the Beck Anxiety Inventory are generally taken to indicate "minimal" anxiety, and scores of 8–15 mild anxiety [48]. Even if sleep-related symptoms are added back to the reported scores, our sample would not reach levels seen in mood or anxiety disorder patient samples. Overall, then, the current sample is consistent with the common conceptualization of insomnia as a condition characterized by low-level mood disturbance and increased arousal [16–18].

Given the small but highly significant differences between PI and GSC on psychological symptom measures, it is reasonable to ask whether EMA contributes any novel information. Insomnia sufferers commonly report variability of sleep and daytime symptoms both within and across days [19,60]; therefore, EMA may be a particularly useful way to characterize this aspect of their complaints. Most retrospective measures do not capture the course of symptoms within a day or variability from 1 day to the next. Field studies with similar instruments, such as the Positive Affect–Negative Affect Scale (PANAS) [27,61], have demonstrated that different components of mood and arousal show different patterns of diurnal variation, even in healthy subjects. Like the PANAS, the DISS identified separate factors for positive and negative mood, which appear to be func-

tionally distinct dimensions across a wide range of conditions and situations [62]. Because the four DISS scales were derived by factor analysis with Varimax rotation, it is not surprising that correlations among the scales were modest, with ρ values ranging from 0.10 to 0.46 (i.e., shared variance of 1–21%). The magnitude of these correlations was similar to those observed between DISS scales and retrospective ratings, and supports the distinction between the four domains.

FPCA is a particularly useful method for characterizing the DISS factors because it accounts not only for how individual symptoms are related to one another in a general sense, but also accounts for variation over time, even after accounting for within-subject variability. Inspection of Fig. 1 clearly demonstrates that differences between PI and GSC groups occurred not only in terms of mean symptom levels, but also in terms of diurnal variation patterns. Thus, diurnal patterns of symptoms may constitute a novel and informative method of characterizing the daytime experiences of individuals with insomnia. In addition, daytime symptom patterns could constitute useful and meaningful outcome measures for treatment studies. We also found greater variability of ratings across days in PI versus GSC for the Sleepiness/Fatigue scale, but not for the other scales. This differs somewhat from our earlier findings, where we reported greater day-to-day variability for all EMA measures in PI versus GSC [38]. However, the very different statistical methods used in the two papers are likely to account for this discrepancy. Our earlier analyses in a much smaller group of subjects used analyses of variance (ANOVAs) on logically derived factors, with each time point within a day taken as a separate measure. FPCA, used in the current paper, models the data taking into account the pattern of variability within and across days.

The validity of the DISS scales is supported by their plausible relationships with the retrospective rating scales. The Positive Mood and Negative Mood scales of the DISS were most strongly related to retrospective scales with similar dimensions of anxiety, depression, and arousal. The Negative Mood scale, in particular, appears to capture symptoms of anxious arousal. The Alert Cognition Scale of the DISS correlated negatively with the depression scale, suggesting that “mood” disturbances in insomnia may be driven, in part, by cognitive complaints. The Sleepiness/Fatigue factor of the DISS was correlated with two common retrospective measures of daytime sleepiness and fatigue. Given that this last factor showed the largest magnitude difference between PI and GSC, and that it was related to 3/6 self-report sleep scales, Sleepiness/Fatigue appears to be a particularly salient symptom dimension for PI subjects.

The important contribution of EMA measures of daytime symptoms is further suggested by correlations

with retrospective and daily self-report sleep ratings. A total of 8/24 correlations between DISS factors and sleep ratings had ρ values >0.30 (i.e., p value <0.05), whereas none of the 30 correlations between traditional retrospective and sleep ratings reached this value. Although none of the observed correlations would reach statistical significance after strictly controlling for the number of comparisons, the observed relationships warrant further examination. Some of the difference between EMA and retrospective symptom measure correlations with sleep diary data may be a function of different timeframes and different times of administration. Retrospective symptom and sleep measures were administered during baseline evaluations, 1–2 weeks before the concurrent collection of DISS and sleep diary data. Furthermore, most of the retrospective ratings had timeframes of the past week, although some do not specify a timeframe (e.g., HAS, ESS) and some had a 1-month frame (e.g., PSQI). The DISS inquires about current symptoms, and the sleep diary inquires about sleep the night before. Therefore, retrospective symptom ratings may not correlate as well as DISS with sleep diary ratings because of differences in timeframe. However, 2/4 DISS scales correlated with the PSQI (with a reporting frame of 1 month), while none of the retrospective symptom rating scales did. Therefore, a difference in timeframe seems less plausible as a sole explanation for the difference between retrospective and EMA-based symptom correlations with sleep measures. A previous study has shown that daily ratings of stress are related to self-report sleep measures, and that this relationship is mediated by daily ratings of pre-sleep arousal [63]. Thus, daily symptom reports may be more closely related to sleep reports than more general symptom ratings. In this regard, it is also interesting that, despite the widely recognized association between mood disturbances and sleep, we did not find strong direct relationships between these categories of measures in the retrospective ratings.

Some correlations that might have been expected were not observed. For instance, the PSWQ was not related to any of the DISS scales or any of the sleep ratings, despite the fact that worry is hypothesized to be related to insomnia (e.g., [64]). The ESS did not correlate with the DISS Sleepiness/Fatigue scale. This may relate to the fact that the ESS relates to perceived sleepiness in specific situations which the subject may or may not encounter in a specific day, while the DISS is a momentary assessment.

The PI was older and included relatively more men than the GSC group. Therefore, group comparisons must be interpreted with caution. It is possible that larger, age-matched samples will differ less robustly on retrospective or DISS measures; in the current sample of PI subjects, age was significantly correlated with Alert

Cognition ($\rho = 0.30$, $p = 0.04$) and Negative Mood ($\rho = 0.46$, $p = 0.001$), but not with Sleepiness/Fatigue or Positive Mood ($\rho = 0.01$ for each). On the other hand, we did not find significant sex differences on the DISS, sleep diary, or retrospective rating scales within the PI group. Larger samples would also be useful for confirmatory data analyses. Because of the small sample size and the limitations of FPCA, factors in these analyses were derived only from PI and not from the entire sample of PI and GSC.

The selection criteria for our sample of PI subjects differed somewhat from those used in most pharmacologic and cognitive-behavioral treatment studies. In particular, our sample was selected by DSM-IV criteria without additional specification of “quantitative” criteria based on self-report, diaries, or polysomnography. Criteria such as sleep latency >30 min, wakefulness after sleep onset >30 min, and sleep time <6 h are commonly employed in the literature [65]. Our more general criteria were selected in order to obtain a sample more similar to that typically seen in clinical practice, where specific quantitative criteria are not likely to be used. Nevertheless, we found that our sample would meet common severity definitions often used in clinical studies. In a similar fashion, we set high thresholds for exclusion due to apnea or PLMs with arousal, which raises the possibility that our findings might be different in a more highly selected insomnia sample. However, the actual mean AHI and PLM arousal index values in our sample were very low, making comorbid apnea and PLM disorder unlikely confounders of our findings.

Future analyses should include larger, better-matched samples as well as examination of treatment effects. The relationship between DISS and self-report or polysomnographic measures will also be examined in subsequent analyses. DISS data could be particularly informative for examining the directionality of sleep-daytime symptom ratings. In other words, concurrent DISS and sleep diary data could address the strength of potentially causal relationships and whether the magnitude of association is greater between sleep and subsequent daytime symptoms, or between daytime symptoms and subsequent sleep.

We have recently reported alterations in regional glucose metabolism during non-rapid eye movement (NREM) sleep in subjects with PI compared to GSC [66], suggesting a pattern of hyperarousal during sleep among those with insomnia. The DISS could be used to determine whether alterations in regional glucose metabolism during sleep or wakefulness are related to daytime symptom patterns. For instance, lower scores on the Alert Cognition scale may be related to the observed relative hypometabolism in pre-frontal regions during wakefulness in PI; the Negative and Positive Mood Scales to relative hypermetabolism in brainstem, limbic, medial temporal, and anterior cingulate regions

during sleep; and the Sleepiness/Fatigue Scale to relative hypermetabolism in brainstem structures or hypometabolism in frontal regions during sleep. Such studies could help to further clarify the pathophysiology underlying insomnia and its morbidity.

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Appendix. Details of functional principal components analysis

Functional principal components analysis (FPCA) is a specific form of functional data analysis (FDA) [67]. FDA refers to a set of exploratory data analysis techniques that combine elements of longitudinal data analysis (LDA) and nonparametric data smoothing techniques to examine the temporal structure of longitudinal data. Unlike LDA techniques, such as mixed models, which assume a specific “shape” to the data, FDA relies on smoothing techniques to estimate time courses and within-subject correlation. Prior to FPCA in the current study, we smoothed data for individual subjects over the course of each day. (In particular, we used mixed-model B-spline regressions. Three quadratic B-spline basis functions with equally spaced knots resulted in good model fits. Further information is available upon request from the authors.) These mixed models provide a flexible estimate of time courses and within-subject variability across multiple time points and over multiple days. Factor estimates can then be determined from these models, utilizing the information on changes over time within subjects. After B-spline mixed models were fit to the DISS data, an FPCA analysis was performed, resulting in four eigenfunctions that explained 67% of the variation in smoothed responses across subjects. Varimax rotation of the four eigenfunctions was used to estimate the final standardized functional principal components. FPCA was conducted in PI subjects alone because there appeared to be little overlap between groups on raw DISS scores, the size of the GSC group was relatively small, and FPCA do not readily accommodate modeling across multiple groups. The identified functional principal component loadings for individual items on the DISS data were used to obtain four factor scores for each individual subject across the week of data collection. Factor scores could then be compared among insomnia and control subjects.

References

- [1] Edinger JD, Bonnet MH, Bootzin RR, Doghramji K, Dorsey CM, Espie CA, et al. Derivation of research diagnostic criteria for insomnia: report of an American Academy of Sleep Medicine Work Group. *Sleep* 2004;27(8):1567–96.
- [2] American Academy of Sleep Medicine. The international classification of sleep disorders, second edition (ICSD-2): diagnostic and coding manual. 2nd ed.; 2005.
- [3] Buysse DJ, Reynolds CF, Hauri PJ, Roth T, Stepanski EJ, Thorpy MJ, et al. Diagnostic concordance for DSM-IV sleep disorders: a report from the APA/NIMH DSM-IV field trial. *Am J Psychiatry* 1994;151(9):1351–60.
- [4] Ohayon MM. Prevalence of DSM-IV diagnostic criteria of insomnia: distinguishing insomnia related to mental disorders from sleep disorders. *J Psychiatr Res* 1997;31(3):333–46.
- [5] Ohayon MM, Caulet M, Lemoine P. Comorbidity of mental and insomnia disorders in the general population. *Compr Psychiatry* 1998;39(4):185–97.
- [6] Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. *Biol Psychiatry* 1996;39(6):411–8.
- [7] Riemann D, Voderholzer U. Primary insomnia: a risk factor to develop depression? *J Affect Disord* 2003;76:255–9.
- [8] Kales A, Caldwell AB, Soldatos CR, Bixler EO, Kales JD. Biopsychosocial correlates of insomnia. II. Pattern specificity and consistency with the Minnesota multiphasic personality inventory. *Psychosom Med* 1983;45(4):341–56.
- [9] Mendelson WB, Garnett D, Gillin JC, Weingartner H. The experience of insomnia and daytime and nighttime functioning. *Psychiatry Res* 1984;12(3):235–50.
- [10] Morin CM, Gramling SE. Sleep patterns and aging: comparison of older adults with and without insomnia complaints. *Psychol Aging* 1989;4(3):290–4.
- [11] Riedel BW, Lichstein KL. Insomnia and daytime functioning. *Sleep Med Rev* 2000;4(3):277–98.
- [12] Bonnet MH, Arand DL. 24-Hour metabolic rate in insomniacs and matched normal sleepers. *Sleep* 1995;18(7):581–8.
- [13] Seidel WF, Ball S, Cohen S, Patterson N, Yost D, Dement WC. Daytime alertness in relation to mood, performance, and nocturnal sleep in chronic insomniacs and noncomplaining sleepers. *Sleep* 1984;7(3):230–8.
- [14] Sugarman JS, Stern JA, Walsh JK. Daytime alertness in subjective and objective insomnia: some preliminary findings. *Biol Psychiatry* 1985;20:741–50.
- [15] Perlis ML, Smith MT, Pigeon WR. Etiology and pathophysiology of insomnia. In: Kryger MH, Roth T, Dement WC, editors. *Principles and practice of sleep medicine*. Philadelphia: Elsevier Saunders; 2005. p. 714–25.
- [16] Regestein QR, Dambrosia J, Hallett M, Murawski B, Paine M. Daytime alertness in patients with primary insomnia. *Am J Psychiatry* 1993;150(10):1529–34.
- [17] Coren S, Mah KB. Prediction of physiological arousability: a validation of the arousal predisposition scale. *Behav Res Ther* 1993;31(2):215–9.
- [18] Coren S. Prediction of insomnia from arousability predisposition scores: scale development and cross-validation. *Behav Res Ther* 1988;26(5):415–20.
- [19] Moul DE, Nofzinger EA, Pilkonis PA, Houck PR, Miewald JM, Buysse DJ. Symptom reports in severe chronic insomnia. *Sleep* 2002;25(5):553–63.
- [20] Hauri PJ. Cognitive deficits in insomnia patients. *Acta Neurol Belg* 1997;97(2):113–7.
- [21] Means MK, Lichstein KL, Epperson MT, Johnson CT. Relaxation therapy for insomnia: nighttime and day time effects. *Behav Res Ther* 2000;38(7):665–78.
- [22] Krystal AD, Walsh JK, Laska E, Caron J, Amato DA, Wessel TC, et al. Sustained efficacy of eszopiclone over 6 months of nightly treatment: results of a randomized, double-blind, placebo-controlled study in adults with chronic insomnia. *Sleep* 2003;26(7):793–9.
- [23] Fulda S, Schulz H. Cognitive dysfunction in sleep disorders. *Sleep Med Rev* 2001;5(6):423–45.
- [24] Stone AA, Shiffman S, DeVries MW. Ecological momentary assessment. In: Kahneman D, editor. *Well-being: the foundations of hedonic psychology*. New York: Russell Sage Foundation; 2000. p. 26–39.
- [25] Stone AA. Ecological momentary assessment (EMA) in behavioral medicine. *Ann Behav Med* 1994;16(3).
- [26] Bolger N, Davis A, Rafaeli E. Diary methods: capturing life as it is lived. *Annu Rev Psychol* 2003;54:579–616.
- [27] Watson D, Wiese D, Vaidya J, Tellegen A. The two general activation systems of affect: structural findings, evolutionary considerations, and psychobiological evidence. *J Pers Soc Psychol* 1999;76(5):820–38.
- [28] Kahneman D, Krueger AB, Schkade DA, Schwarz N, Stone AA. A survey method for characterizing daily life experience: the day reconstruction method. *Science* 2004;306(5702):1776–80.
- [29] Stone AA, Broderick JB, Porter LS, Krupp L, Gyns M, Paty J, et al. Fatigue and mood in chronic fatigue syndrome patients: results of a momentary assessment protocol examining fatigue and mood levels and diurnal patterns. *Ann Behav Med* 1994;16:228–34.
- [30] Curran SL, Beacham AO, Andrykowski MA. Ecological momentary assessment of fatigue following breast cancer treatment. *J Behav Med* 2004;27(5):425–44.
- [31] Stone AA, Smyth JM, Pickering T, Schwartz J. Daily mood variability: form of diurnal patterns and determinants of diurnal patterns. *J Appl Soc Psychol* 1996;26:1286–305.
- [32] Stone AA, Schwartz JE, Neale JM, Shiffman S, Marco CA, Hickcox M, et al. A comparison of coping assessed by ecological momentary assessment and retrospective recall. *J Pers Soc Psychol* 1998;74(6):1670–80.
- [33] Carels RA, Douglass OM, Cacciapaglia HM, O'Brien WH. An ecological momentary assessment of relapse crises in dieting. *J Consult Clin Psychol* 2004;72(2):341–8.
- [34] Wegner KE, Smyth JM, Crosby RD, Wittrock D, Wonderlich SA, Mitchell JE. An evaluation of the relationship between mood and binge eating in the natural environment using ecological momentary assessment. *Int J Eat Disord* 2002;32(3):352–61.
- [35] Shiffman S, Gwaltney CJ, Balabanis MH, Liu KS, Paty JA, Kassel JD, et al. Immediate antecedents of cigarette smoking: an analysis from ecological momentary assessment. *J Abnorm Psychol* 2002;111(4):531–45.
- [36] Litt MD, Cooney NL, Morse P. Ecological momentary assessment (EMA) with treated alcoholics: methodological problems and potential solutions. *Health Psychol* 1998;17(1):48–52.
- [37] Kamarck TW, Janicki DL, Shiffman S, Polk DE, Muldoon MF, Liebenauer LL, et al. Psychosocial demands and ambulatory blood pressure: a field assessment approach. *Physiol Behav* 2002;77(4–5):699–704.
- [38] Levitt H, Wood A, Moul DE, Hall M, Germain A, Kupfer DJ, et al. A pilot study of subjective daytime alertness and mood in primary insomnia participants using ecological momentary assessment. *Behav Sleep Med* 2004;2(2):113–31.
- [39] Stone AA, Shiffman S, Schwartz JE, Broderick JE, Hufford MR. Information in practice. *BMJ* 2002;321:1193–4.
- [40] Koop A, Mosges R. The use of handheld computers in clinical trials. *Control Clin Trials* 2002;23:469–80.
- [41] First M, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM-IV axis I disorders-patient edition (SCID-I/P). Version 2.0 ed. New York: New York State Psychiatric Institute; 1995.

- [42] First MB, Gibbon M, Spitzer RL, Williams JBW. Structured clinical interview for DSM-IV axis I disorders SCID I: clinician version, administration booklet. Washington (DC): American Psychiatric Press; 1997.
- [43] American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-IV-TR). 4th ed., text revision ed. Washington (DC): American Psychiatric Association; 2000.
- [44] Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. *Psychiatry Res* 1989;28:193–213.
- [45] Lichstein KL, Riedel BW, Lester KW, Aguillard RN. Occult sleep apnea in a recruited sample of older adults with insomnia. *J Consult Clin Psychol* 1999;67(3):405–10.
- [46] Youngstedt SD, Kripke DF, Klauber MR, Sepulveda RS, Mason WJ. Periodic leg movements during sleep and sleep disturbances in elders. *J Gerontol A, Biol Sci Med Sci* 1998;53(5):M391–4.
- [47] Rush AJ, Gullion CM, Basco MR, Jarrett RB, Trivedi MH. The inventory of depressive symptomatology (IDS): psychometric properties. *Psychol Med* 1996;26(3):477–86.
- [48] Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol* 1988;56:893–7.
- [49] Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the Penn state worry questionnaire. *Behav Res Ther* 1990;28(6):487–95.
- [50] Smets EMA, Garssen B, Bonke B, Haes de JCJM. The multidimensional fatigue inventory (MFI); psychometric qualities of an instrument to assess fatigue. *J Psychosom Res* 1995;39:315–25.
- [51] Johns MW. Reliability and factor analysis of the Epworth sleepiness scale. *Sleep* 1992;15(4):376–81.
- [52] Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;14(6):540–5.
- [53] Monk TH. A visual analogue scale technique to measure global vigor and affect. *Psychiatry Res* 1988;27:89–99.
- [54] Derogatis LR, Lipman RS, Rickels K, Uhlenhuth EH, Covi L. The Hopkins symptom checklist (HSCL): a self-report symptom inventory. *Behav Sci* 1974;19:1–15.
- [55] Thayer RE. Factor analytic and reliability studies on the Activation–Deactivation Adjective Check List. *Psychol Rep* 1978;42(3 PT 1):747–56.
- [56] Monk TH, Reynolds CF, Kupfer DJ, Buysse DJ, Coble PA, Hayes AJ, et al. The Pittsburgh sleep diary. *J Sleep Res* 1994;3:111–20.
- [57] Ramsay J, Silverman BW. Functional data analysis. 2nd ed. New York: Springer; 2005.
- [58] R Development Core Team. A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2005.
- [59] SAS Institute I. SAS/STAT Software Version 8. Cary, NC: SAS Institute, Inc.; 2000.
- [60] Carey TJ, Moul DE, Pilkonis P, Germain A, Buysse DJ. Focusing on the experience of insomnia. *Behav Sleep Med* 2005;3(2):73–86.
- [61] Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol* 1988;54(6):1063–70.
- [62] Watson D, Clark LA. Measurement and mismeasurement of mood: recurrent and emergent issues. *J Pers Assess* 1997;68(2):267–96.
- [63] Morin CM, Rodrigue S, Ivers H. Role of stress, arousal, and coping skills in primary insomnia. *Psychosom Med* 2003;65(2):259–67.
- [64] Harvey AG, Tang NK, Browning L. Cognitive approaches to insomnia. *Clin Psychol Rev* 2005;25(5):593–611.
- [65] Lichstein KL, Durrence HH, Taylor DJ, Bush AJ, Riedel BW. Quantitative criteria for insomnia. *Behav Res Ther* 2003;41(4):427–45.
- [66] Nofzinger EA, Buysse DJ, Germain A, Price JC, Miewald JM, Kupfer DJ. Functional neuroimaging evidence for hyperarousal in insomnia. *Am J Psychiatry* 2004;161(11):2126–31.
- [67] Ramsay JO, Silverman BW. Applied functional data analysis. Methods and case studies. New York: Springer; 1997.