Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research report

Poor sleep predicts symptoms of depression and disability retirement due to depression

Tiina Paunio [a,b,e,*,1], Tellervo Korhonen [c,d,i,1], Christer Hublin [e], Markku Partinen [f], Karoliina Koskenvuo [c,h], Markku Koskenvuo [c], Jaakko Kaprio [c,d,g]

[a] Public Health Genomics Unit and Institute for Molecular Medicine FIMM, National Institute for Health and Welfare, Helsinki, Finland
[b] Department of Psychiatry, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland
[c] Department of Public Health, Hjelt Institute, University of Helsinki, Helsinki, Finland
[d] Department of Mental Health and Substance Abuse Services, National Institute for Health and Welfare, Helsinki, Finland
[e] Finnish Institute of Occupational Health, Helsinki, Finland
[f] Helsinki Sleep Clinic, Vitalmed Research Centre, Helsinki, Finland
[g] Institute for Molecular Medicine FIMM, Helsinki, Finland
[h] Social Insurance Institution of Finland, Research Department, Helsinki, Finland
[i] Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland

ARTICLE INFO

ABSTRACT

Background: Disturbed sleep is associated with mood disorders. Both depression and insomnia may increase the risk of disability retirement. The longitudinal links among insomnia, depression and work incapacity are poorly known.
Methods: We examined association of self-reported sleep quality with incident symptoms of depression and disability retirement due to depressive disorders in a longitudinal population-based sample of twins ($n=12,063$ individuals). These adults were categorized by their sleep quality in 1975 and 1981, excluding individuals with depressed mood in 1975/1981. The outcomes were the Beck Depression Inventory (BDI$_{tot}$) and its subscale Negative Attitudes Towards Self (BDI$_{NATS}$) in 1990 as dichotomized measures, and the incidence of disability retirement due to depressive disorder during 1991–2004.
Results: Onset of poor sleep between 1975 and 1981 predicted incident depression (BDI$_{tot}$ OR=4.5, 95% CI: 2.7–7.4, BDI$_{NATS}$ OR=2.0, 95% CI: 1.4–2.7), while persistent poor sleep showed somewhat weaker effects (BDI$_{tot}$; OR=2.5, 95% CI: 1.0–6.0, BDI$_{NATS}$ OR=1.9, 95% CI: 1.1–3.3). Among those with few recent stressful life events, onset of poor sleep predicted strongly depression (BDI$_{NATS}$ OR=9.5, 95% CI: 3.7–24.2). Likewise onset of poor sleep by 1981 increased the risk of disability retirement due to depression (OR=2.9, 95% CI: 1.8–4.9) with a similar risk among those with persistent poor sleep (OR=2.7, 95% CI: 1.3–5.7).
Limitations: Lack of baseline diagnostic interviews; sleep quality based on self-report.
Conclusions: Poor sleep is of importance in etiology of depression and disability retirement due to depression. This emphasizes the importance of early detection and treatment of sleep disturbances.

1. Introduction

Good sleep is important for emotional well-being (Zohar et al., 2005), while acute sleep deprivation of as little as 1–2 h per night leads to problems in alertness, cognition, pain threshold, and mood (Lautenbacher et al., 2006; Van Dongen et al., 2003; Vandekerckhove and Cluydts, 2010). Symptoms of insomnia—difficulties in initiating or maintaining sleep, or non-restorative sleep accompanied by decreased daytime functioning—are frequent in the general population, with prevalence of 10–60% depending on the use of definitions and data-collection methodologies (Ohayon, 2002). Individuals reporting disturbed sleep are more likely to report emotional distress and recurrent health problems (Morin and Gramling, 1989; Katz and McHorney, 1998; Edinger et al., 2000). Insomnia and poor sleep are also risk factors for major depression, and a recent meta-analysis comprising 21 individual studies defined that initially non-depressed people with insomnia have a twofold risk to develop depression compared to people with no sleep difficulties (Baglioni et al., 2011). In depression, the electrophysiological architecture of sleep and the functional activity of different brain regions are disturbed (Riemann

et al., 2010; Kupfer, 1995; Armitage et al., 2002; Nofzinger et al., 2004). Most depression patients also report disturbances in their sleep, such as difficulties in falling asleep, waking during night or early morning awakenings (Riemann et al., 2010; Kupfer et al., 1969; Hetta et al., 1985). Thus, sleep disturbance is an important mechanism contributing to depression (Harvey, 2001).

Anxiety and depression have been identified as predictors of disability pension (Mykletun et al., 2006; Knudsen et al., 2010; Karpansalo et al., 2005). Insomnia also increases the risk of disability retirement (Sivertsen et al., 2006) and, compared to depression, has important and independent role in the process of disability retirement (Overland et al., 2008). Other risk factors of disability retirement are poor somatic health and functioning, health related risk behavior, low socioeconomic status, work and family related psychosocial factors, including stressful life events, and life dissatisfaction (Harkonmäki, 2007). The decision for disability retirement is based on thorough evaluation by experts and can be considered in a disease trajectory as a solid end point, in which the work capacity of a person has been reduced. Despite data on the risk of insomnia and depression for the disability retirement, the longitudinal relationships among insomnia, depression and disability pension due to depressive disorder are poorly known.

In the previous study of a nation-wide cohort of 18,631 adult twins, we found that poor sleep predicted life dissatisfaction, an approximation for depressed mood, in a consistent pattern with a 2–3-fold risk, while life dissatisfaction did not predict poor sleep. Thus, the temporal relationship between disturbed sleep and mood seemed to be unidirectional within a 6-year time frame.

The shared genetic component was relatively modest further supporting the hypothesis that poor sleep may have direct effects on mood (Paunio et al., 2009). In the present study we hypothesized that in healthy individuals, poor sleep increases risk for depressive symptoms and after that disability retirement due to depression. We extended our study to cover a period of three decades with survey-based data from three time points, as well as cumulative register-based information on disability pensions during three decades. Since liability to depression and poor sleep is influenced by a wide range of risk factors (Kendler and Gardner, 2001; Kendler et al., 2006) we controlled the analyses for multiple confounders, such as somatic health, stressful life events, social network, emotional support, and parental relationships. The novelty of this study is that we investigated the longitudinal relationship of poor sleep quality and changes in sleep quality with onset of depression and further to disability.

2. Materials and Methods

2.1. Sample

The Finnish Twin Cohort was compiled from the Central Population Registry consisting of all same-sex twin pairs born in Finland before 1958 with both co-twins alive in 1974 (13,888 pairs of known zygosity) (Kaprio and Koskenvuo, 2002). The project was accepted by the Ethical Committee of the University of Helsinki. The first questionnaire survey was conducted in 1975 (response rate 89%) and the second one in 1981 involving all twins in the
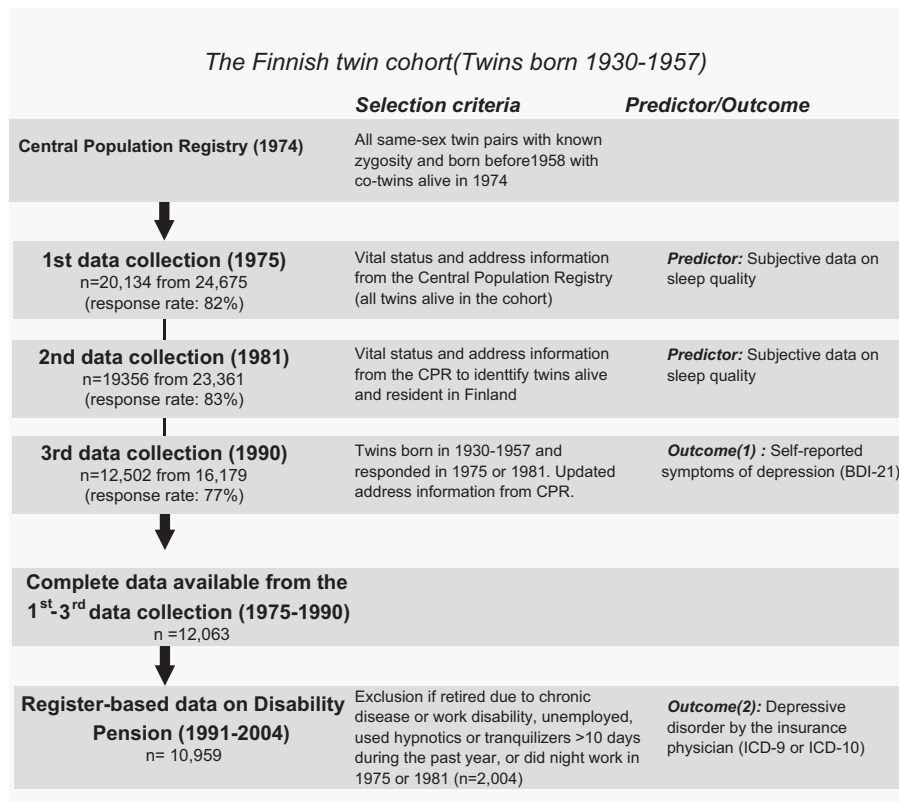

The Finnish twin cohort(Twins born 1930-1957)		
	Selection criteria	*Predictor/Outcome*
Central Population Registry (1974)	All same-sex twin pairs with known zygosity and born before1958 with co-twins alive in 1974	
1st data collection (1975) n=20,134 from 24,675 (response rate: 82%)	Vital status and address information from the Central Population Registry (all twins alive in the cohort)	*Predictor:* Subjective data on sleep quality
2nd data collection (1981) n=19356 from 23,361 (response rate: 83%)	Vital status and address information from the CPR to identtify twins alive and resident in Finland	*Predictor:* Subjective data on sleep quality
3rd data collection (1990) n=12,502 from 16,179 (response rate: 77%)	Twins born in 1930-1957 and responded in 1975 or 1981. Updated address information from CPR.	*Outcome(1) :* Self-reported symptoms of depression (BDI-21)
Complete data available from the 1st-3rd data collection (1975-1990) n =12,063		
Register-based data on Disability Pension (1991-2004) n= 10,959	Exclusion if retired due to chronic disease or work disability, unemployed, used hypnotics or tranquilizers >10 days during the past year, or did night work in 1975 or 1981 (n=2,004)	*Outcome(2):* Depressive disorder by the insurance physician (ICD-9 or ICD-10)

Fig. 1. Study flow. All same-sex twin pairs were approached in 1975 based on information from the Central Population Registry in 1974 ($n=24,675$ individuals born in 1930–1957). Out of them, 20,134 individuals participated in the questionnaire in 1974, and 19,356 individuals (from 23,361 eligible twins) in 1981. These questionnaires include data on subjective sleep quality, used as predictor in the current study. In the third data collection in 1990, twins born in 1930–1957 and responded in 1975 or 1981 were approached ($n=16,179$), out of which 12,502 responded (77%). All individuals who participated in the questionnaire completed also the BDI-21 questionnaire for self-reported symptoms of depression [Outcome (1)]. Register-based data on disability pension in 1991–2004 was collected for all those who had replayed to the 1975, 1981 and 1990 surveys ($n=12,063$), after exclusion of those who were in 1975 or 1981 retired due to chronic disease or work disability, were unemployed, or had used hypnotics or tranquilizers ($n=2004$), making the target population for the Outcome (2) (depressive disorder diagnosed by the insurance physician) to cover 10,959 twin individuals.

cohort who were still alive, including the non-respondents in 1975 (84% response rate). The third questionnaire was sent in 1990 to the younger (age 60 years or under) part of the cohort, namely twins born in 1930–1957, if they had responded to at least one of the previous surveys ($n=16{,}179$). This survey had a 77% response rate with 12,502 respondents (Kaprio and Koskenvuo, 2002). The zygosity of the twins was determined by means of a well-established, validated questionnaire (Sarna et al., 1978).

Of the 12,063 persons replying to the 1975, 1981 and 1990 surveys and providing complete data on depressive symptoms in 1990 we excluded those who were in 1975 or 1981 retired due to chronic disease or work disability, were unemployed, had used hypnotics or tranquilizers more than 10 days during the past year, or did night work ($n=2004$). Then, the sample included altogether 10,059 persons (Fig. 1). Due to variable specific missing values, the data were complete for all main variables; i.e. life satisfaction (1975, 1981, 1990), sleep quality (1975, 1981), and depressive symptoms measured using BDI (1990) for a total of 9529 persons (4263 men, 5266 women). The mean age in 1975 was 28.6 (range 18–45; SD 7.6) years. The results considering incident depressive symptoms were based on a sample of 7476 twin individuals (3327 men, 4149 women) after exclusion of those 2053 with high life dissatisfaction score (as a proxy for depressiveness) in 1975 or 1981 (936 men, 1117 women) (Table 1).

2.2. Measures

2.2.1. Outcomes

2.2.1.1. Depressive symptoms
2.2.1.1.1. Beck Depression Inventory (BDI$_{tot}$).
The 21-item Beck Depression Inventory (BDI) (Beck and Beamesderfer, 1974) was applied to measure depressive symptoms in 1990 (Varjonen et al., 1997). For the logistic regression models the participants were dichotomized as the 'non-affected' with a BDI score <17, and the 'affected' with a score ≥ 17. In estimation of the risk of self-reported depression in 1990 for disability retirement due to depressive disorder between 1991 and 2004, the BDI score <10 was considered as 'non-affected' and two alternative cut points (BDI ≥ 10 and BDI ≥ 17) as 'affected'.

2.2.1.1.2. BDI subscale Negative Attitudes Towards Self (BDI$_{NATS}$).
Items from BDI were found to consist of three factors similar to those reported in the earlier literature (Varjonen et al., 1997). Out of them, one entitled as Negative Attitude Towards Self (BDI$_{NATS}$), presented the core symptoms of depressed mood, consisting of the items on self-dislike, sense of failure, guilt feelings, mood, self-accusation, pessimism, sense of punishment, lack of satisfaction, suicidal wishes, and crying. In the same twin population Varjonen et al. (1997) reported a very high consistency ($\alpha=0.84$) for this factor while Korhonen et al. (2011) reported a high correlation with the total BDI score ($r=0.89$). The two other factors were Performance Impairment and Weight Loss or Loss of Appetite. The 'skewness' value for BDI$_{NATS}$ factor was 2.5, with high proportions of observations with value 0 ('floor effect'). Thus, also the BDI$_{NATS}$ factor score was dichotomized (low/high), with the high score being coded as 1 if the score >3 (19.7%) and the low score coded as 0. The use of dichotomous measures provides also clinically relevant cut points even if these are not equivalent to DSM-IV diagnoses.

2.2.1.2. Disability pensions due to depressive disorder.
The registry data on all retirement events, including disability pensions with depression diagnoses, during 1991–2004, was obtained from the Social Insurance Institution and the Finnish Centre for Pensions (Harkonmaki et al., 2008). Disability retirement is a form of pension given to those people who are permanently or temporarily unable to work due to a disability. In Finland, if someone is faced with a long-term illness, he/she will normally first be paid a Sickness Allowance which is payable for persons between 16 and 67 years of age. If that sickness is prolonged (over 1 year) one can apply for disability pension. Disability pensions could be granted during the follow-up period either as disability pension or as illness-based individual early retirement pension, both dependent on a medically confirmed illness, disease or injury that prevents or essentially restricts working. The definition of significantly restricted work capacity includes that work capacity is assessed to have been reduced by at least 60%, for 12 months or more. The final diagnoses causing work disability were made by the insurance physician based on the comprehensive medical information provided and using the ICD-9 and ICD-10 codes. Follow-up started from the response date to the 1990 questionnaire, and continued until onset of disability compensation, death, emigration, or end of follow-up (December 31, 2004). No essential social or pension legislative changes concerning the disability criteria were made during the follow-up period of this study. The record linkage was done by using the unique person numbers assigned to all Finnish citizens.

2.2.2. Predictors
2.2.2.1. Quality of sleep.
We measured quality of sleep in 1975 and 1981 as self-reported information by asking "Do you usually sleep well?" with five response alternatives that were "well", "rather well", "rather poorly", "poorly", and "don't know". The two time points let us create two groups of persistent good or poor sleep and two groups in which sleep quality changes, one for the worse and one for the better. To achieve this, we categorized the subjects into four groups as follows: Good–Good (sleeping well or rather well in 1975 and in 1981, $n=7058$); Poor–Good (sleeping rather poorly or poorly in 1975 but well or rather well in 1981, $n=119$); Good–Poor (sleeping well or rather well in 1975 but rather poorly or poorly in 1981, $n=219$); Poor–Poor (sleeping rather poorly or

Table 1
Proportions (%) of three BDI categories in 1990 by sleep quality in 1975–1981.

Sleep quality Change 1975→1981[c]	BDI in 1990							
	Those without life dissatisfaction in 1975 and in 1981[a] ($n=7476$)				Those with life dissatisfaction in 1975 or in 1981[b] ($n=2053$)			
	n	≤ 9	10–16	>16	n	≤ 9	10–16	>16
All	7476				2053			
Good–Good	7058	89.29	8.64	2.07	1705	72.14	19.00	8.86
Poor–Good	119	84.03	12.61	3.36	87	57.47	25.29	17.24
Good–Poor	219	68.04	21.46	10.50	185	53.51	28.11	18.38
Poor–Poor	80	65.00	27.50	7.50	76	42.11	31.58	26.32
Men[d]	3327				936			
Good–Good	3129	92.68	5.94	1.37	773	78.53	14.88	6.60
Poor–Good	61	86.89	8.20	4.92	30	66.67	20.00	13.33
Good–Poor	101	65.35	22.77	11.88	86	62.79	24.42	12.79
Poor–Poor	36	66.67	25.00	8.33	47	46.81	31.91	21.28
Women[d]	4149				1117			
Good–Good	3929	86.59	10.79	2.62	932	66.85	22.42	10.73
Poor–Good	58	81.03	17.24	1.72	57	52.63	28.07	19.30
Good–Poor	118	70.34	20.34	9.32	99	45.45	31.31	23.23
Poor–Poor	44	63.64	29.55	6.82	29	34.48	31.03	34.48

[a] Included into the sample of depression incidence.
[b] Excluded from the sample of depression incidence.
[c] Good–Good = sleeping well or rather well in 75 and 81; Poor–Good = sleeping rather poorly or poorly in 75 but well or rather well in 81; Good–Poor = sleeping well or rather well in 75 but rather poorly or poorly in 81; Poor–Poor = sleeping rather poorly or poorly in 75 and 81.
[d] Test for sex × sleep quality interaction: likelihood-ratio test LR χ^2 (3)=6.76; $P=0.08$.

poorly in 1975 and in 1981, $n=80$) (numbers among the final study sample of 7476 individuals).

2.2.3. Other measures

2.2.3.1. Life satisfaction. When estimating incident depression in 1990 we used life dissatisfaction as a proxy of pre-existing depressed mood at baseline (in 1975–1981). The questionnaire used for measurement of life satisfaction has a 4-item scale focusing on feelings of loneliness, hardness of life, happiness and anhedonia (Koivumaa-Honkanen et al., 2000; Allardt, 1973). The complete scale ranges from 4 to 20 and was used as a dichotomy so that those with score 12 or higher were coded as dissatisfied (encoded as 1 for the statistical analysis) and those below 12 as satisfied (encoded as 0) (Paunio et al., 2009; Koivumaa-Honkanen et al., 2004). In order to estimate incident depression in 1990 we excluded those who reported pre-existing depressed mood, i.e. life dissatisfaction, in 1975 or 1981 ($n=2102$), resulting in the final analysis sample of 7476 individuals. Using life dissatisfaction as a proxy for pre-existing depressiveness is justified by an earlier finding showing that high life dissatisfaction scores correlate highly with the BDI ($r > 0.60$ between these scores in 1990 survey) (Koivumaa-Honkanen et al., 2004).

2.2.3.2. Confounders. We conducted preliminary analyses for testing multiple confounders for poor sleep quality or depressed mood, which were chosen based on the earlier literature (Paunio et al., 2009; Dalgard et al., 1995; Fryers et al., 2003; Hasin et al., 2005; Koskenvuo et al., 2009). These included gender, age, marital status (0=married/cohabiting; 1=single/living alone), social class (Appelberg et al., 1991), presence of chronic somatic disease (0=none, 1=at least one chronic condition) (Romanov et al., 2003), negative stressful life events (sum-score of the 21-item Holmes–Rahe life event inventory) (Lillberg et al., 2003), smoking status (0=never,1=occasional, 2=former, 3=current smoker) (Kaprio and Koskenvuo, 1988), alcohol use (binge drinking; yes/no), leisure time physical activity based on the Metabolic Equivalent Task Score (0=sedentary, 1=moderate, 2=active) (Kujala et al., 2002), social network, emotional support, as well as mother and father relationship (Romanov et al., 2003). Most were based on data collected in 1981, but the presence of somatic disease as well as extent of social network and quality of emotional support in 1990, and life events both in 1981 and 1990. From the fully adjusted models we dropped step by step those potential confounders which were not statistically significant at level $P < 0.10$ (indicated in detail in the results as table footnotes).

2.3. Statistical analyses

In the logistic regression models we tested the strength and significance of predictive associations between sleep quality in 1975–1981 and each depression-related outcome. The Odds Ratios (OR) with 95% confidence intervals (CI) were computed first adjusting for age and sex. Multiple logistic regression models were used to adjust for the additional confounders described above. The subjects were considered as individuals but controlling for twinship. Because observations on twins within twin pairs may be correlated we used robust estimators of variance and the cluster option in Stata (version 11/SE; www. Stata.Corp, Texas, USA) in standard error estimations (Williams, 2000).

Since stressful life-events are an important risk for depressive episodes, we tested the interaction between sleep quality and life-events reported in 1990 by comparing two nested models, i.e. the one with direct effects only and the one with interaction added. The likelihood-ratio test (LR χ^2 (12)=19.9; $P=0.07$) indicated that including sleep quality × stressful life-events interaction improved

the model. This justified conducting post-hoc analysis by number of stressful life-events reported in 1990.

Because the data consisted of twins, there was a unique possibility to explore causal nature of the associations between poor sleep and depression. To test whether poor sleep predicts depressive symptoms independently of within-family confounds, we identified all twin pairs discordant for sleep quality (combined variable for 1975 and 1981) and BDI$_{NATS}$ depression in 1990 as matched cases and controls sharing the same early environment and familial background. Twin pairs discordant for sleep quality and incident BDI$_{NATS}$ depression were defined so that one twin had persistently good sleep and the co-twin had onset of poor sleep (i.e. from good in 1975 to poor in 1981 or persistently poor sleep), and one twin was depressed while his/her co-twin was not depressed. We conducted conditional logistic regression among 38 exposure-discordant and outcome-discordant pairs. These were pooled together by zygosity (test for zygosity × sleep interaction $P=0.11$). Finally, we conducted survival analyses using the Cox proportional hazards model, where the outcome (event) was register based disability pension due to depressive disorder. Disability pension development rates were calculated with survival analyses according to 1975–1981 sleep status. Hazard ratios (HR) with 95% confidence intervals (CI) associated with disability pension development were calculated with adjusted Cox proportional hazards regression models. Here, the outcome event was the disability retirement due to depression between 1991 and 2004. Drop outs from the follow-up due to death, immigration, natural retirement, disability retirement from other causes or end of follow-up at age of 65 or 31 December 2004 were censored. Because the outcome event is strongly dependent on age, the analyses were adjusted for age so that the follow-up time used in the analysis was person's age; i.e. age was the time scale in the analysis.

The assumption of proportionality of hazards was checked by examining 'log–log' plot, i.e. $-\ln\{-\ln(\text{survival})\}$ curves for categories of the variables versus $\ln(\text{analysis time})$ plots. The risk estimates (HR) from these survival analyses were adjusted for multiple confounders.

3. Results

Proportions of three BDI categories (≤ 9, 10–16, > 16) in 1990 by sleep quality in 1975–1981 are shown in Table 1, where the distributions of those without baseline 'pre-existing depression', i.e. life dissatisfaction (7476 individuals included in the analyses) and those with baseline 'pre-existing depression', i.e. life dissatisfaction (2053 individuals excluded from the analyses) are displayed.

3.1. Poor sleep increases risk for depression

We followed the effect of twice measured, self-reported sleep quality in 1975 and 1981 on incidence of depressed mood in our final sample of 7476 twins that resulted after the exclusions described earlier.

Poor sleep predicted symptoms of depression so that the risk for a BDI$_{tot}$ score of ≥ 17 was 5.5-fold among the onset of poor ('Good–Poor') sleepers (95% CI 3.5, 8.7) and 3.6-fold among the consistently poor ('Poor–Poor') sleepers (95% CI 1.5, 8.5) as compared to those sleeping consistently well ('Good–Good'). When adjusting for potential confounders the findings remained significant ('Good–Poor' OR=4.5, 95% CI 2.7, 7.4; 'Poor–Poor' OR=2.5, 95% CI 1.0, 6.0) (Table 2). The effect was particularly strong among men ('Good–Poor' OR=8.3, 95% CI 3.9, 17.6; 'Poor–Poor' OR=5.8, 95% CI 1.6, 20.9). In women, the risk remained significant in the group of 'Good–Poor' sleepers (OR=3.1, 95% CI 1.5, 6.2), while not among the consistently poor ('Poor–Poor') ones (OR=1.7, 95% CI 0.5, 5.4) (not shown in tables).

3.2. Poor sleep increases risk for core symptoms of depressed mood

In order to exclude an artifact caused by persistent symptoms of poor sleep and their correlation on some of the BDI items, we concentrated on the BDI_{NATS} domain in our subsequent analyses with a threshold of score > 3 as indicator for depressed mood.

Poor sleep predicted elevated BDI_{NATS} score in a consistent manner ('Good–Poor' OR=2.0, 95% CI 1.4, 2.7; 'Poor–Poor' OR=1.9, 95% CI 1.1, 3.3 from logistic regression adjusted for multiple confounders) (Table 3). The effect was similar in both genders being significant among those with onset of poor sleep ('Good–Poor'; men: OR=2.3, 95% CI 1.4, 3.8; women: OR=1.8, 95% CI 1.1,

2.8), but not in persistently poor sleepers (men: OR =1.9, 95% CI 0.8, 4.3; women: OR =1.9, 95% CI 0.9, 3.9) (not shown in tables).

The association between poor sleep and core symptoms of depression was replicated among 38 twin pairs which were discordant for baseline sleep quality and for 1990 BDI_{NATS} outcome. The risk of poor sleep remained elevated among those with poor sleep in 1981 irrespective of 1975 sleep quality, though not statistical significantly so (OR=1.7, 96% CI 0.9, 3.3; P=0.11) (see footnote of Table 3).

3.3. Effect of life events

Since stressful life events are an important risk for depressive episodes, as a post-hoc analysis we divided the sample according to the presence or absence of recent stressful life events at the time of measurement of BDI. This analysis was justified by an interaction between sleep quality and stressful life-events reported in 1990 (LR χ^2 (12)=19.9; P=0.07). The risk for elevated BDI_{NATS} score was 9.5 fold among those with at most one (i.e. none or one) recent stressful life events and decreasing sleep quality (95% CI 3.7, 24.2). The risk estimates of sleep quality decreased with 2–3 stressful life events, but were significant also when 4–5 stressful events were identifiable among those with onset of poor sleep quality (OR 1.6, 95% CI 1.1, 2.5) and the persistently poor sleepers (OR=3.1, 95% CI 1.5–6.2) and when 6 or more events were reported (OR 2.3, 95% CI 1.4, 4.0 and OR 2.8, 95% CI 1.3, 6.0, respectively) (Table 4).

3.4. Poor sleep and risk for disability retirement due to depression

Finally, we investigated the incidence of disability pensions between 1991 and 2004 due to diagnosed depressive disorders as related to sleep quality in 1975–1981. Poor sleep in 1981, irrespective of sleep quality in 1975, significantly increased the risk for disability retirement due to depressive disorders ('Good–Poor' HR=2.9; 95% CI 1.8, 4.9; 'Poor–Poor' HR=2.7; 95% CI 1.3, 5.7 from survival analysis adjusting for confounders) (Table 5; Fig. 2).

Table 2
Logistic regressions on sleep quality in 1975 and 1981 as predictor of at least moderate depression onset ($BDI_{tot} > 16$) in 1990 among individual twins[a].

Sleep quality 1975–1981[d]	N	Adjusted for sex and age		Adjusted for sex, age, health behaviors[b] and somatic health		Adjusted for all confounders[c]	
		OR	95% CI	OR	95% CI	OR	95% CI
Good–Good	7058	1.00		1.00		1.00	
Poor–Good	119	1.69[ns]	0.62,4.64	1.42[ns]	0.50,4.01	1.71[ns]	0.62,4.71
Good–Poor	219	5.50	3.46, 8.73	4.75[***]	2.96,7.63	4.45[***]	2.67,7.43
Poor–Poor	80	3.61	1.53, 8.48	2.81[*]	1.16,6.77	2.49[*]	1.03,5.98

**P < 0.01.

[a] Among those without life dissatisfaction in 1975 and in 1981 (score < 12) (n=7476).
[b] Smoking, alcohol use, physical activity.
[c] P < 0.10: sex, age, smoking, somatic health, social network, emotional support, father relationship, life events.
[d] Good–Good=sleeping well or rather well in 75 and 81; Poor–Good=sleeping rather poorly or poorly in 75 but well or rather well in 81; Good–Poor=sleeping well or rather well in 75 but rather poorly or poorly in 81; Poor–Poor=sleeping rather poorly or poorly in 75 and 81.
* P < 0.05.
*** P < 0.001.
[ns] P ≥ 0.05.

Table 3
Logistic regressions on sleep quality in 1975 and 1981 as predictor of BDI_{NATS}-depression in 1990[a].

Sleep quality 1975–1981[d]	N	Adjusted for sex and age		Adjusted for sex, age, health behaviors [b] and somatic health		Adjusted for all confounders[c]	
		OR	95% CI	OR	95% CI	OR	95% CI
Good–Good	7058	1.00		1.00		1.00	
Poor–Good	119	1.34[ns]	0.82,2.19	1.23[ns]	0.74, 2.04	1.28[ns]	0.77, 2.14
Good–Poor	219	2.45[***]	1.79, 3.34	2.26[***]	1.66, 3.10	1.97[***]	1.42, 2.74
Poor–Poor	80	2.62[***]	1.58, 4.32	2.22[**]	1.33, 3.71	1.92[*]	1.12, 3.29

[e]Twin pairs discordant for sleep quality and incident NATS-depression=one twin has Good–Good while his/her co-twin has Good–Poor or Poor–Poor sleep and one twin is depressed while co-twin is not depressed (38 pairs). Test for zygosity × sleep interaction: P=0.0923.
[f]Good–Poor or Poor–Poor sleep combined: OR=1.71 (0.88, 3.31; P=0.109). Test for zygosity × sleep interaction: P=0.1076.

[a] BDI_{NATS} score > 3 among those without life dissatisfaction in 1975 and in 1981 (score > 12) (n=7476).
[b] Smoking, alcohol use, physical activity.
[c] P < 0.10: sex, age, smoking, alcohol use, somatic health, social network, emotional support, father relationship, life events (1981 and 1990)
· Test for sleep × somatic health interaction: P=0.6720.
· Test for sleep × life events (1990) interaction: P=0.0695 (see Table 4).

[d] Good–Good=sleeping well or rather well in 75 and 81; Poor–Good=sleeping rather poorly or poorly in 75 but well or rather well in 81; Good–Poor=sleeping well or rather well in 75 but rather poorly or poorly in 81; Poor–Poor= sleeping rather poorly or poorly in 75 and 81.
* P < 0.05.
** P < 0.01.
*** P < 0.001.
[ns] P ≥ 0.05.

Table 4
Logistic regressions on sleep quality as predictor of BDI_{NATS}-depression onset [a] by number of stressful life-events reported in 1990[b].

Predictor Sleep quality	Stressful life-events in 1990						6 or more ($n=1744$)	
	None or one ($n=1362$)		2–3 ($n=1513$)		4–5 ($n=3931$)			
Change 1975–1981[c]	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Good–Good	1.00		1.00		1.00		1.00	
Poor–Good	0.64[ns]	0.08, 5.13	1.19[ns]	0.22, 6.59	1.04[ns]	0.49, 2.17	1.18[ns]	0.49, 2.82
Good–Poor	9.48[***]	3.71, 24.2	0.29[ns]	0.04, 2.21	1.64[*]	1.05, 2.54	2.35[**]	1.38, 3.98
Poor–Poor	3.83[ns]	0.53, 27.5	2.75[ns]	0.59, 12.8	3.07[**]	1.53, 6.16	2.79[**]	1.31, 5.98

　[a] NATS score > 3 among those without life dissatisfaction in 1975 and in 1981 (score > 12) ($n=7476$).
　[b] Adjusted for sex, age, smoking, alcohol use, somatic health, father relationship, life events in 1981, social network and emotional support.
　[c] Good–Good=sleeping well or rather well in 75 and 81; Poor–Good=sleeping rather poorly or poorly in 75 but well or rather well in 81; Good–Poor=sleeping well or rather well in 75 but rather poorly or poorly in 81; Poor–Poor=sleeping rather poorly or poorly in 75 and 81.
　[*] $P < 0.05$.
　[**] $P < 0.01$.
　[***] $P < 0.001$.
　[ns] $P \geq 0.05$.

Table 5
Survival analysis on sleep quality in 1975–1981 as predictor of disability pension due to depression in 1990–2004 ($n=8131$).

Sleep quality 1975–1981 [a]	N	Adjusted for sex		Adjusted for sex and life events		Adjusted for sex, life events and somatic health		Adjusted for sex, life events, somatic health and alcohol use	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Good–Good	7539	1.00		1.00		1.00		1.00	
Poor–Good	171	0.96[ns]	0.31,3.04	0.94[ns]	0.30, 3.00	0.90[ns]	0.28, 2.83	0.88[ns]	0.28, 2.78
Good–Poor	304	3.46[***]	2.08,5.73	3.26[***]	1.97, 5.38	2.96[***]	1.80,4.88	2.94[***]	1.79, 4.93
Poor–Poor	117	3.59[***]	1.75, 7.37	3.23[**]	1.57, 6.65	2.75[**]	1.32, 5.77	2.73[**]	1.31, 5.72

[*]$P < 0.05$.
　[a] Good–Good=sleeping well or rather well in 75 and 81; Poor–Good=sleeping rather poorly or poorly in 75 but well or rather well in 81; Good–Poor=sleeping well or rather well in 75 but rather poorly or poorly in 81; Poor–Poor=sleeping rather poorly or poorly in 75 and 81.
　[**] $P < 0.01$.
　[***] $P < 0.001$.
　[ns] $P \geq 0.05$.

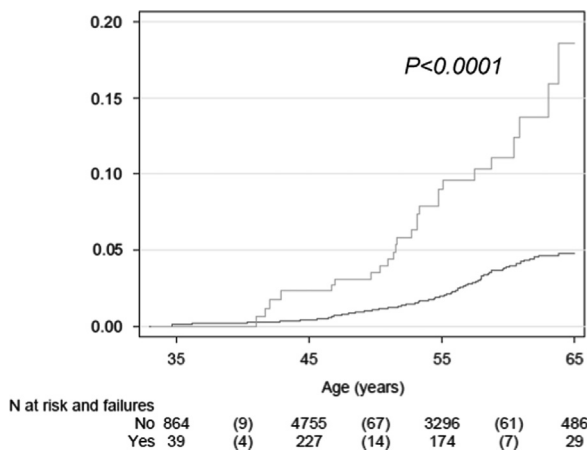| N at risk and failures							
No	864	(9)	4755	(67)	3296	(61)	486
Yes	39	(4)	227	(14)	174	(7)	29

Fig. 2. Survival analysis of work disability due to depression in 1990–2004 in relation to subjective quality of sleep in 1975 and 1981. There were no statistical differences between the analysis of the groups 'Good–Good' and 'Poor–Good' nor between 'Good–Poor' and 'Poor–Poor'. Thus, the groups 'Good–Good' and 'Poor–Good' were combined into one group 'Good' and the groups 'Good–Poor' and 'Poor–Poor' into the group 'Poor'. The difference between the groups 'Good' and 'Poor' was statistically highly significant ($P < 0.0001$, $Z=5.77$). Y axis refers to cumulative hazard to due disability.

4. Discussion

In the present study, we found that long-term poor sleep increases risk for depression and disability retirement due to depressive disorders in a sample representative for the Finnish adult population being followed systematically during many decades. The findings were statistically robust and survived also when a number of important confounders such as parental relationships, alcohol use, somatic health, stressful life events, social network, emotional support or familial influences were controlled.

4.1. Poor sleep as risk factor for depressive symptoms

After excluding individuals with high life dissatisfaction in 1975 or 1981 and while adjusting for the confounders, consistent poor sleep increased 2.5-fold the risk for general symptoms of depression in 1990. The relative risk was even higher (4.5-fold) among those whose sleep quality deteriorated during the follow-up. The association of poor sleep and depression remained elevated though was attenuated and not statistically significant after controlling for familial influences in the analysis of the discordant pairs.

In order to exclude an artifact due to correlation of symptoms of poor sleep on the complete set of the BDI items, we examined for incidence of the core affective symptomatic domain of depression. The incidence of these symptoms increased to approximately 2-fold among constantly poor sleepers and those with deteriorated sleep quality. The risk was higher in women as compared to men, who had higher risk for symptoms of BDI_{tot}. This gender difference might reflect differences in depression symptom profiles. For example, in a retrospective recall of symptoms among patients with Major Depressive Disorder symptoms of insomnia were more frequent in men while symptoms of excessive self-reproach were more frequent in women (Smith et al., 2008).

The current findings are in line with previous reports indicating that insomnia or poor sleep quality is risk factors for major depression (Riemann and Voderholzer, 2003; Riemann et al., 2010; Baglioni et al., 2011; Baglioni and Riemann, 2012). Processing of emotions involves activation of amygdala hippocampus and medial prefrontal cortex during REM-sleep (Maquet et al., 1996; Wagner et al., 2006; Maquet, 2000). Sleep has also a role in memory consolidation (Walker and Stickgold, 2004; Diekelmann et al., 2009; Meerlo et al., 2009; Tucker and Fishbein, 2009) and memories of lower emotional loading rely on early nocturnal sleep, while more amygdala-dependent emotional memory is consolidated during late sleep when REM-sleep predominates (Wagner et al., 2005). Thus, the nature of the interaction between sleep and emotions is complex and a sophisticated, symbiotic relationship appears to exist between impact of sleep on affective processing during awake and reprocessing of emotional information during the sleep (Walker and van der Helm, 2009).

Patients with primary insomnia and with major depression show symptoms of a chronically activated stress system including hyperactivity in an autonomous nervous system (Bonnet and Arand, 1998; Gorman and Sloan, 2000; Agelink et al., 2004) and in hypothalamic–pituitary–adrenal (HPA) axis (Rodenbeck et al., 2002; Backhaus et al., 2004; Muller et al., 2003). They also show sleep continuity disturbances and slow-wave sleep deficit in their sleep EEG profile, related to the HPA hyperactivity (Vgontzas et al., 1998; Wong et al., 2000; Staner et al., 2003a). However, primary insomniacs do not have any consistent abnormalities in their REM sleep (Gillin et al., 1979; Lamarche and Ogilvie, 1997; Staner et al., 2003b), which seems to succeed in processing and regulation of emotions. At transition to depression, these processes become dysfunctional in tandem with hyperactive limbic activation and hypoactivation of the prefrontal cortex. What causes this transition remains to be clarified by future studies using both experimental settings and carefully characterized longitudinal cohorts.

4.2. The effect of environment and genetic factors

The liability to depression is influenced by a wide range of risk factors that act at different stages of development. These include genetic and temperamental factors, substance abuse, as well as psychosocial adversities both early in life and in adulthood (Kendler and Gardner, 2001; Kendler et al., 2006). Psychosocial stressors, notably multiple childhood adversities, increase risk also for poor sleep (Koskenvuo et al., 2009). In the current study, associations between poor sleep quality and depressed mood remained even when the childhood relationships as well as a number of other confounders such as alcohol use, somatic health, stressful life events, social network, or emotional support were controlled. Interestingly, we found an up to 9.5-fold increased risk for the BDI_{NATS} depression in individuals who did not report recent stressful life events at the time of depression assessment. We suggest that this is due to stratifying sample by occurrence of stressful events, which then led to intensification of epidemiological evidence for risk of poor sleep predicting subsequent depression. Furthermore, the found association cannot be fully explained by shared genes or family environment, because the association between poor sleep and core symptoms of depression was replicated, albeit somewhat more weakly, among 38 twin pairs which were discordant for baseline sleep quality and for 1990 BDI_{NATS} outcome.

4.3. Risk for disability retirement due to depression

Finally, we investigated the effect of poor sleep on long-term mental health and work capacity by examining the risk for disability retirement due to depressive disorders in relation to prior poor sleep quality. Poor sleep in 1981 increased the risk of disability retirement due to depression during 1991–2004 almost 3-fold, even when we controlled for the effect of stressful life events, poor somatic health, smoking and alcohol use. To our knowledge this is also the first study in which the longitudinal link among insomnia, depression and disability pension due to depressive disorder has been demonstrated.

4.4. Strengths and limitations

One of the major strengths of the study was the size and nature of the sample, which was collected by an un-biased method, is representative for population, and has been followed systematically during decades. The large size enabled us to follow a refined analytic strategy and control for a number of potential confounders. Out of them, that for the childhood relationships with mother and father was measured only post-hoc in 1981 which may have affected the reliability of that data. However, since we excluded those with depressed mood at baseline, the time point for measurement of the childhood relationships as well, we are likely to have avoided the negative recall bias due to current state of depressive mood. Lack of cross-sectional diagnostic interview is also a clear limitation of our study, but we were able to compensate for it by including data from the disability pension register, a solid end point with both diagnostic as well as functional validity. One more limitation is that the measurement of sleep quality was based on self-report. However, subjective experiences with poor sleep quality have been found to be associated with electrophysiological architecture of sleep (Armitage et al., 1997).

5. Conclusions

Poor sleep is an independent and robust risk factor for the various symptomatic domains of depression and for disability retirement due to depressive disorder. We make a substantial contribution to the literature showing longitudinal links among poor sleep quality, incident depression and disability pension due to depressive disorders. The findings emphasize the impact of sleep on regulation of mood and the probable causative role of poor sleep quality in etiological mechanisms of mood disorder. They also evidence for the importance of early detection and treatment of poor sleep in order to prevent depression.

Conflict of interest

Dr. Korhonen and Dr. Kaprio have acted as consultants on tobacco dependence for Pfizer, Inc, in 2011-2014. Dr. Partinen has acted as a member of the Medical Advisory Board for UCB Pharma, consultant for Bioproject and obtained honoraria for speaking in medical meeting by UCB Pharma, BSK, Leiras-Nycomed and a grant to medical congress by Cephalon.

References

Agelink, M.W., Klimke, A., Cordes, J., Sanner, D., Kavuk, I., Malessa, R., Klieser, E., Baumann, B., 2004. A functional-structural model to understand cardiac autonomic nervous system (ANS) dysregulation in affective illness and to elucidate the ANS effects of antidepressive treatment. Eur. J. Med. Res. 9, 37–50.

Allardt, E., 1973. About Dimension of Welfare: An Explanatory Analysis of the Comparative Scandinavian Survey. University of Helsinki p. 1973.

Armitage, R., Hoffmann, R.F., Emslie, G.J., Weinberg, W.A., Mayes, T.L., Rush, A.J., 2002. Sleep microarchitecture as a predictor of recurrence in children and adolescents with depression. Int. J. Neuropsychopharmacol. 5, 17–228.

Appelberg, K., Romanov, K., Honkasalo, M.L., Koskenvuo, M., 1991. Interpersonal conflicts at work and psychosocial characteristics of employees. Soc. Sci. Med. 32, 1051–1056.

Armitage, R., Trivedi, M., Hoffmann, R., Rush, A.J., 1997. Relationship between objective and subjective sleep measures in depressed patients and healthy controls. Depress. Anxiety 5, 97–102.

Backhaus, J., Junghanns, K., Hohagen, F., 2004. Sleep disturbances are correlated with decreased morning awakening salivary cortisol. Psychoneuroendocrinology 29, 1184–1191.

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

Baglioni, C., Riemann, D., 2012. Is chronic insomnia a precursor to major depression? Epidemiological and biological findings. Curr. Psychiatry Rep. 14, 511–518.

Bonnet, M.H., Arand, D.L., 1998. Heart rate variability in insomniacs and matched normal sleepers. Psychosom. Med. 60, 610–615.

Beck, A.T., Beamesderfer, A., 1974. Assessment of depression: the depression inventory. Mod. Probl. Pharmacopsychiatry 7, 151–169.

Dalgard, O.S., Bjork, S., Tambs, K., 1995. Social support, negative life events and mental health. Br. J. Psychiatry 166, 29–34.

Diekelmann, S., Wilhelm, I., Born, J., 2009. The whats and whens of sleep-dependent memory consolidation. Sleep Med. Rev. 13, 309–321.

Edinger, J.D., Fins, A.I., Glenn, D.M., Sullivan Jr., R.J., Bastian, L.A., Marsh, G.R., Dailey, D., Hope, T.V., Young, M., Shaw, E., Vasilas, D., 2000. Insomnia and the eye of the beholder: are there clinical markers of objective sleep disturbances among adults with and without insomnia complaints? J. Consult. Clin. Psychol. 68, 586–593.

Fryers, T., Melzer, D., Jenkins, R., 2003. Social inequalities and the common mental disorders: a systematic review of the evidence. Soc. Psychiatry Psychiatr. Epidemiol. 38, 229–237.

Gillin, J.C., Duncan, W., Pettigrew, K.D., Frankel, B.L., Snyder, F., 1979. Successful separation of depressed, normal, and insomniac subjects by EEG sleep data. Arch. Gen. Psychiatry 36, 85–90.

Gorman, J.M., Sloan, R.P., 2000. Heart rate variability in depressive and anxiety disorders. Am. Heart J. 140, 77–83.

Harkonmäki, K., 2007. Predictors of Disability Retirement: From Early Intentions to Retirement (dissertation). University of Helsinki, Department of Public Health, The Local Government Pensions Institution, Helsinki.

Harvey, A.G., 2001. Insomnia: symptom or diagnosis? Clin. Psychol. Rev. 21, 1037–1059.

Harkonmaki, K., Silventoinen, K., Levalahti, E., Pitkäniemi, J., Huunan-Seppälä, A., Klaukka, T., Koskenvuo, M., Kaprio, J., 2008. The genetic liability to disability retirement: a 30-year follow-up study of 24,000 Finnish twins. PLoS One 3, e3402.

Hasin, D.S., Goodwin, R.D., Stinson, F.S., Grant, B.F., 2005. Epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcoholism and Related Conditions. Arch. Gen. Psychiatry 62, 1097–1106.

Hetta, J., Rimon, R., Almqvist, M., 1985. Mood alterations and sleep. Ann. Clin. Res. 17, 252–256.

Kaprio, J., Koskenvuo, M., 2002. Genetic and environmental factors in complex diseases: the older Finnish Twin Cohort. Twin Res. 5, 358–365.

Kaprio, J., Koskenvuo, M., 1988. A prospective study of psychological and socio-economic characteristics, health behavior and morbidity in cigarette smokers prior to quitting compared to persistent smokers and non-smokers. J. Clin. Epidemiol. 41, 139–150.

Karpansalo, M., Kauhanen, J., Lakka, T.A., Manninen, P., Kaplan, G.A., Salonen, J.T., 2005. Depression and early retirement: prospective population based study in middle aged men. J. Epidemiol. Community Health 59, 70–74.

Katz, D.A., McHorney, C.A., 1998. Clinical correlates of insomnia in patients with chronic illness. Arch. Intern. Med. 158, 1099–1107.

Kendler, K.S., Gardner, C.O., 2001. Monozygotic twins discordant for major depression: a preliminary exploration of the role of environmental experiences in the aetiology and course of illness. Psychol. Med. 31, 411–423.

Kendler, K.S., Gardner, C.O., Prescott, C.A., 2006. Toward a comprehensive developmental model for major depression in men. Am. J. Psychiatry 163, 115–124.

Knudsen, A.K., Overland, S., Aakvaag, H.F., Harvey, S.B., Hotopf, M., Mykletun, A., 2010. Common mental disorders and disability pension award: seven year follow-up of the HUSK study. J. Psychosom. Res. 69, 59–67.

Koivumaa-Honkanen, H., Honkanen, R., Viinamaki, H., Heikkila, K., Kaprio, J., Koskenvuo, M., 2000. Self-reported life satisfaction and 20-year mortality in healthy Finnish adults. Am. J. Epidemiol. 152, 983–991.

Koivumaa-Honkanen, H., Kaprio, J., Honkanen, R., Viinamaki, H., Koskenvuo, M., 2004. Life satisfaction and depression in a 15-year follow-up of healthy adults. Soc. Psychiatry Psychiatr. Epidemiol. 39, 994–999.

Korhonen, T., Koivumaa-Honkanen, H., Varjonen, J., Broms, U., Koskenvuo, M., Kaprio, J., 2011. Cigarette smoking and dimensions of depressive symptoms: longitudinal analysis among Finnish male and female twins. Nicotine Tob. Res. 13, 261–272.

Koskenvuo, K., Hublin, C., Partinen, M., Paunio, T., Koskenvuo, M., 2009. Childhood adversities and quality of sleep in adulthood: a population-based study of 26,000 Finns. Sleep Med. 11, 17–22.

Kujala, U.M., Kaprio, J., Koskenvuo, M., 2002. Modifiable risk factors as predictors of all-cause mortality: the roles of genetics and childhood environment. Am. J. Epidemiol. 156, 985–993.

Kupfer, D.J., 1995. Sleep research in depressive illness: clinical implications—a tasting menu. Biol. Psychiatry 38, 391–403.

Kupfer, D.J., Harrow, M., Detre, T., 1969. Sleep patterns and psychopathology. Acta Psychiatr. Scand. 45, 75–89.

Lamarche, C.H., Ogilvie, R.D., 1997. Electrophysiological changes during the sleep onset period of psychophysiological insomniacs, psychiatric insomniacs, and normal sleepers. Sleep 20, 724–733.

Lautenbacher, S., Kundermann, B., Krieg, J.C., 2006. Sleep deprivation and pain perception. Sleep Med. Rev. 10, 357–369.

Lillberg, K., Verkasalo, P.K., Kaprio, J., Teppo, L., Helenius, H., Koskenvuo, M., 2003. Stressful life events and risk of breast cancer in 10,808 women: a cohort study. Am. J. Epidemiol. 157, 415–423.

Morin, C.M., Gramling, S.E., 1989. Sleep patterns and aging: comparison of older adults with and without insomnia complaints. Psychol. Aging 4, 290–294.

Mykletun, A., Overland, S., Dahl, A.A., Krokstad, S., Bjerkeset, O., Glozier, N., Aarø, L. E., Prince, M., 2006. A population-based cohort study of the effect of common mental disorders on disability pension awards. Am. J. Psychiatry 163, 1412–1418.

Maquet, P., Peters, J., Aerts, J., Delfiore, G., Degueldre, C., Luxen, A., Franck, G., 1996. Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. Nature 383, 163–166.

Maquet, P., 2000. Functional neuroimaging of normal human sleep by positron emission tomography. J. Sleep Res. 9, 207–231.

Meerlo, P., Mistlberger, R.E., Jacobs, B.L., Heller, H.C., McGinty, D., 2009. New neurons in the adult brain: the role of sleep and consequences of sleep loss. Sleep Med. Rev. 13, 187–194.

Muller, M.B., Zimmermann, S., Sillaber, I., Hagemeyer, T.P., Deussing, J.M., Timpl, P., Kormann, M.S., Droste, S.K., Kühn, R., Reul, J.M., Holsboer, F., Wurst, W., 2003. Limbic corticotropin-releasing hormone receptor 1 mediates anxiety-related behavior and hormonal adaptation to stress. Nat. Neurosci. 6, 1100–1107.

Nofzinger, E.A., Buysse, D.J., Germain, A., Carter, C., Luna, B., Price, J.C., Meltzer, C.C., Miewald, J.M., Reynolds 3rd, C.F., Kupfer, D.J., 2004. Increased activation of anterior paralimbic and executive cortex from waking to rapid eye movement sleep in depression. Arch. Gen. Psychiatry 61, 695–702.

Ohayon, M.M., 2002. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med. Rev. 6, 97–111.

Overland, S., Glozier, N., Sivertsen, B., Stewart, R., Neckelmann, D., Krokstad, S., Mykletun, A., 2008. A comparison of insomnia and depression as predictors of disability pension: the HUNT study. Sleep 31, 875–880.

Paunio, T., Korhonen, T., Hublin, C., Partinen, M., Kivimaki, M., Koskenvuo, M., Kaprio, J., 2009. Longitudinal study on poor sleep and life dissatisfaction in a nationwide cohort of twins. Am. J. Epidemiol. 169, 206–213.

Riemann, D., Voderholzer, U., 2003. Primary insomnia: a risk factor to develop depression? J. Affect. Disord. 76, 255–259.

Riemann, D., Spiegelhalder, K., Feige, B., Voderholzer, U., Berger, M., Perlis, M., et al., 2010. The hyperarousal model of insomnia: a review of the concept and its evidence. Sleep Med. Rev. 14, 19–31.

Rodenbeck, A., Huether, G., Ruther, E., Hajak, G., 2002. Interactions between evening and nocturnal cortisol secretion and sleep parameters in patients with severe chronic primary insomnia. Neurosci. Lett. 324, 159–163.

Romanov, K., Varjonen, J., Kaprio, J., Koskenvuo, M., 2003. Life events and depressiveness—the effect of adjustment for psychosocial factors, somatic health and genetic liability. Acta Psychiatr. Scand. 107, 25–33.

Sarna, S., Kaprio, J., Sistonen, P., Koskenvuo, M., 1978. Diagnosis of twin zygosity by mailed questionnaire. Hum. Hered. 28, 241–254.

Sivertsen, B., Overland, S., Neckelmann, D., Glozier, N., Krokstad, S., Pallesen, S., Nordhus, I.H., Bjorvatn, B., Mykletun, A., 2006. The long-term effect of insomnia on work disability: the HUNT-2 historical cohort study. Am. J. Epidemiol. 163, 1018–1024.

Smith, D.J., Kyle, S., Forty, L., Cooper, C., Walters, J., Russell, E., Caesar, S., Farmer, A., McGuffin, P., Jones, I., Jones, L., Craddock, N., 2008. Differences in depressive symptom profile between males and females. J. Affect. Disord. 108, 279–284.

Staner, L., Duval, F., Haba, J., Mokrani, M.C., Macher, J.P., 2003a. Disturbances in hypothalamo pituitary adrenal and thyroid axis identify different sleep EEG patterns in major depressed patients. J. Psychiatr. Res. 37, 1–8.

Staner, L., Cornette, F., Maurice, D., Viardot, G., Le Bon, O., Haba, J., Staner, C., Luthringer, R., Muzet, A., Macher, J.P., 2003b. Sleep microstructure around sleep onset differentiates major depressive insomnia from primary insomnia. J. Sleep Res. 12, 319–330.

Tucker, M.A., Fishbein, W., 2009. The impact of sleep duration and subject intelligence on declarative and motor memory performance: how much is enough? J. Sleep. Res. 18, 304–312.

Van Dongen, H.P., Maislin, G., Mullington, J.M., Dinges, D.F., 2003. The cumulative cost of additional wakefulness: dose–response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. Sleep 26, 117–126.

Vandekerckhove, M., Cluydts, R., 2010. The emotional brain and sleep: an intimate relationship. Sleep Med. Rev. 14, 219–226.

Varjonen, J., Romanov, K., Kaprio, J., Heikkilä, K., Koskenvuo, M., 1997. Self-rated depression in 12,063 middle-aged adults. Nord. J. Psychiatry 51, 331–338.

Vgontzas, A.N., Tsigos, C., Bixler, E.O., Stratakis, C.A., Zachman, K., Kales, A., Vela-Bueno, A., Chrousos, G.P., 1998. Chronic insomnia and activity of the stress system: a preliminary study. J. Psychosom. Res. 45, 21–31.

Wagner, U., Hallschmid, M., Rasch, B., Born, J., 2006. Brief sleep after learning keeps emotional memories alive for years. Biol. Psychiatry 60, 788–790.

Wagner, U., Degirmenci, M., Drosopoulos, S., Perras, B., Born, J., 2005. Effects of cortisol suppression on sleep-associated consolidation of neutral and emotional memory. Biol. Psychiatry 58, 885–893.

Walker, M.P., van der Helm, E., 2009. Overnight therapy? The role of sleep in emotional brain processing. Psychol. Bull. 135, 731–748.

Walker, M.P., Stickgold, R., 2006. Sleep, memory, and plasticity. AnnuAnnu. Rev. Psychol. 57, 139–166.

Williams, R.L., 2000. A note on robust variance estimation for cluster-correlated data. Biometrics 56, 645–646.

Wong, M.L., Kling, M.A., Munson, P.J., Listwak, S., Licinio, J., Prolo, P., Karp, B., McCutcheon, I.E., Geracioti Jr., T.D., DeBellis, M.D., Rice, K.C., Goldstein, D.S., Veldhuis, J.D., Chrousos, G.P., Oldfield, E.H., McCann, S.M., Gold, P.W., 2000. Pronounced and sustained central hypernoradrenergic function in major depression with melancholic features: relation to hypercortisolism and corticotropin-releasing hormone. Proc. Natl. Acad. Sci. USA 97, 325–330.

Zohar, D., Tzischinsky, O., Epstein, R., Lavie, P., 2005. The effects of sleep loss on medical residents' emotional reactions to work events: a cognitive-energy model. Sleep 28, 47–54.