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Daily worry is related to low heart rate variability during waking and the subsequent nocturnal sleep period

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Abstract

Stress and anxiety are risk factors for cardiovascular (CV) disease. Worry might be a mediator of their risks by prolonging their cognitive representation and concomitant CV activity. We hypothesized that daily stressors and worry, and trait anxiety and trait worry would be associated with high heart rate (HR) and low heart rate variability (HRV) during waking and the subsequent nocturnal sleep period, and that worry would mediate the effects of daily stressors. Low HRV and high HR are physiological risk factors for CV disease. Using an hourly diary, stressors, worry frequency and duration, and biobehavioral variables were measured during one day in 52 healthy subjects. During this time and the subsequent nocturnal sleep period, ambulatory ECG was measured. Stressors, worry and traits were related to higher HR and lower HRV during waking, and the effects of stressors and worry were extended into the sleeping period. Worry duration mediated the effects of stressors. The results were largely independent of biobehavioral variables including sleep quality. The results support the notion that worry, by prolonging CV activity, is a mediator of the CV risks of stress. They also imply a role for unconscious cognitive representation of stress.

Keywords: Stress; Perseverative cognition; Worry; Trait anxiety; Prolonged physiological activity; Heart rate variability; Sleep physiology; Cardiovascular disease

1. Introduction

Overall mortality from organic disease, particularly cardiovascular disease is co-determined by chronic psychosocial stress, including anxiety (Krantz and McCeney, 2002; Kubzansky and Kawachi, 2000; Rosengren et al., 2004; Rozanski et al., 1999; Scheier and Bridges, 1995). Worry has been argued to be an important mediator of these effects (Brosschot et al., 2005, 2006; Friedman and Thayer, 1998). There are several reasons to hypothesize this. First, in order to have substantial effects on health, the physiological effects of stress and anxiety must be prolonged, for example by slow recovery (Brosschot and Thayer, 1998; Linden et al., 1997; McEwen, 1998; Selye, 1950; Sluiter et al., 2000; Ursin, 1980; Ursin and Eriksen, 2004). Brosschot, Thayer and colleagues have hypothesized that worry might be the mediator of the prolonged physiological effects of stress, because worry theoretically may be the primary mechanism by which a person prolongs a stressor's cognitive representation, along with its physiological effects (Brosschot et al., 2005, 2006; Gerin et al., 2001). Some laboratory experiments have already yielded suggestive evidence that slow blood pressure recovery after emotional stress is due to worry or rumination (Gerin et al., 2006; Glynn et al., 2002). However, there have been no studies that tested this hypothesis in real life.

Second, worry is a core mechanism in anxiety disorders. These disorders are associated with an increased risk for cardiovascular (CV) disease. Worry might be responsible for at least a part of this risk by mediating prolonged CV activity related to anxiety. Finally, several studies have shown that trait worry as well as state worry are associated with increased physiological activation, especially CV activation (Brosschot et al., 2002; Dua and King, 1987; Gerin et al., 2006; Glynn et al., 2002; Lyonfields et al., 1995; Roger and Jamieson, 1988; Scheier and Bridges, 1995; Segerstrom et al., 1999; Suchday et al., 2004; Thayer et al., 1996; Vickers and Vogeltanz-Holm, 2003; see for review: Brosschot et al., 2006). At least one study has shown that worry predicts CV disease (myocardial infarct; Kubzansky et al., 1997).

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To summarize, worry seems to prolong the cognitive representation of stress, it is a core element in stress and anxiety, and it appears to have substantial physiological effects. These properties of worry make it a likely candidate as a mediator of prolonged activity related to stress and anxiety and a co-determinant of their cardiovascular risk.

The hallmark of a mediator of prolonged physiological responses to stressors is that it extends these responses even into periods in which stressors are absent. Sleep is perhaps the most important of these types of recuperative periods, because it covers a large part of our life and is the most critical natural episode for psychological and somatic restoration. Thus, the role of worry as a cause of prolonged cardiac activation may be even more convincing if it can be shown that its cardiac effects are prolonged during sleep at night. To date, there have been no studies showing direct effects of worry on cardiac activity during sleep. Indirectly, worry is related to poor sleep quality, which in turn is related to heart disease and general mortality (Dew et al., 2003). Moreover, during poor sleep, low levels of heart rate variability (HRV) and high levels of heart rate (HR) have been found (Hall et al., in press). A recent review (Pieper and Brosschot, 2005) showed that several types of stress were associated with prolonged cardiovascular effects during sleep. Stressful events in the past six months were associated with high sleeping HR (Ituarte et al., 1999), and frequent episodes of negative emotions were related to a higher blood pressure (BP) during sleep (Shapiro et al., 1997). Trait anxiety was also related to higher sleeping BP (Pasic et al., 1998; Raikkonen et al., 1999). There was only one experimental study of stress and sleep, that showed that anticipating an oral speech the next morning was related to low vagally-mediated HRV throughout the whole preceding sleeping period (Hall et al., 2004). The latter effect could not be explained by poor sleep quality. It is therefore possible that stress and perhaps worry can increase physiological levels without necessarily disturbing sleep quality. Studies with work stress yielded less consistent results. Three work stress studies (Schnall et al., 1998; Unden et al., 1991; Vrijkotte et al., 2000) obtained evidence of prolonged cardiovascular activity during sleep while two others did not (Fauvel et al., 2001; Goldstein et al., 1999), and a third study found an effect only when family stress was also high (Brisson et al., 1999). Pieper and Brosschot (2005) concluded that job stressors might be too specific or often not sufficiently distressing to yield effects that extend beyond the working floor.

The present study tested two main hypotheses. First, worry and stressors during the day, and trait anxiety and trait worry, are hypothesized to be associated with high HR and low HRV during both waking and subsequent nocturnal sleep. Second, it was hypothesized that – at least part of – the increased waking and sleeping cardiac levels of daily stress but also of trait anxiety and trait worry are mediated by daily worry. Low HRV is associated with increased risk of cardiovascular morbidity but also all-cause mortality, and has been proposed as a general marker for disease (Palatini and Julius, 1997; Stein and Kleiger, 1999; Task Force Guidelines, 1996; Thayer and Friedman, 2004; Tsuji et al., 1994) and high levels of HR have also been linked with all-cause mortality in several large studies (see Habib, 1999, for a review). The present study measured worry episodes and their duration, daily stressors, and several biobehavioral variables during one day using an hourly diary. Worry duration was measured in addition to the mere frequency of worry, because if worry is shown to be the mediator of prolonged activation, this will be even more the case when worry itself is prolonged. Moreover, it was previously found that worry duration is a better predictor of somatic symptoms than worry frequency (Brosschot and Van den Doef, 2006). HR and HRV (root mean square of successive differences of inter beat intervals, RMSSD) were assessed with ambulatory equipment during the day as well as the subsequent night.

2. Materials and methods

2.1. Subjects and procedure

Subjects were recruited from the general population in the area around the city of Leiden in The Netherlands by way of newspaper advertisements. They received the equivalent of 25 US dollars for their participation. Complete data were available for 52 subjects, who will be the focus of this study. Thirteen of them were men, and thirty-nine were women, aged between 15 and 65 (mean = 33.8; S.D. = 13.9). The subjects came to the laboratory between 8:00 AM and 10:00 AM. They returned questionnaires that measured trait worry, trait anxiety, age and gender that they received via the mail. Next, they were instructed about the use of the diary and an ambulatory physiological measurement device (see below). The latter apparatus signaled the subjects to complete the diary with a short 'beep' approximately every hour (plus or minus 10 min). Each hourly diary entry contained questions about stressors and worry during the preceding measurement period. The electrodes and the apparatus were attached and the subjects left the laboratory. The signals continued until 11 PM, to preclude interference with sleep onset. The next morning, the subjects indicated their sleep quality during the preceding night. Thereafter, they returned the diary and apparatus to the laboratory, were debriefed, and received their monetary compensation.

2.2. Heart rate and heart rate variability during waking and sleeping

HR and HRV were measured by the Ambulatory Monitoring System (AMS; De Geus et al., 1995; version 4.6. TD-FPP, Vrije Universiteit, Amsterdam, the Netherlands). This device has been used extensively and details of its characteristics have been published elsewhere (De Geus et al., 1995). In the present study the electrocardiogram signal was recorded using disposable pre-gelled Ag–AgCL electrodes (ConMed, New York, USA) that were placed at the jugular notch of the sternum, 4 cm under the left nipple and at the lateral right side. Using this three electrode configuration only the inter beat interval time series was available for analysis. The device detects the R-wave of the electrocardiogram and records the time in milliseconds (with one millisecond resolution). From the raw inter beat intervals the device derives and stores 30-second averages of HR (in

beats per minute) and root mean square of successive differences of inter beat intervals (in milliseconds: RMSSD), which was used as an index of HRV. The RMSSD has been shown to be a reliable index of cardiac parasympathetic influences and is recommended as a measure of vagally-mediated HRV for its simplicity (Task Force Guidelines, 1996). These parameters were averaged over the waking period and sleeping period. Thus, four variables were used: waking HR and HRV and sleeping HR and HRV.

Waking time was determined as the period between one hour *after* connecting the equipment to 1 h *before* the subject reported going to bed. The sleeping period was determined as the period between 1 h *after* going to bed to 1 h *before* waking up. If the subjects had indicated on the sleep quality questionnaire a sleep onset later than one hour after going to bed, the sleeping period was adapted by taking the estimated sleep onset time plus 1 h. The AMS also measures motility. Short periods of high motility during the night, which could reflect waking up and walking, were visually detected in the AMS data and were subsequently removed from the analyses.

2.3. Diary

The diary consisted of a maximum of 16 double-sided pages, one for each entry, which pertained to the preceding hour plus or minus 10 min. The duration varied over the entries to prevent anticipatory reactions. Each entry asked for the presence of one or more worry periods and one or more stressors during the preceding entry period, and several biobehavioral variables (see Section 2.6).

2.4. Worry and stressors

In the diary, the subject was presented with a definition of worry that was adapted from Borkovec et al. (1983): *Worry is a chain of negative thoughts, about the same or different topics that can have negative consequences for you in the future. A solution is not (yet) reached, and the same thoughts often return. It is difficult to stop when you are thinking these thoughts. They definitely engage you mentally and they are disturbing and intensive.*

Worry frequency was measured by the number of times the presence of worry was reported.

Worry duration was estimated for each worry episode by the subjects aided by a set of four time categories. They could choose which of them matched the duration of their worrying during that entry: '0–1 min', '1–5 min', '5–20 min' or 'more than 20 min'. To facilitate analysis the midpoint of these categories was used: 0.5 min, 3 min, 7.5 min and 40 min respectively, considering that the maximum duration in the last category is 60 min on average.

Stressors were assessed by asking subjects whether they had experienced one or more annoying or disturbing events in the preceding period. The number of times the presence of a stressor was reported served as the variable.

The values were counted across entries. Subjects differed with respect to the number of entries that were actually completed (mean = 11.5; standard deviation = 1.7). Thus, the absolute values were not comparable between the subjects. Therefore these variables were divided by the number of entries that were completed.

2.5. Trait anxiety and trait worry

Dispositional anxiety was measured by the Spielberger Trait Anxiety Inventory (Dutch version: Van der Ploeg et al., 1979). The Penn State Worry Questionnaire (Meyer et al., 1990; Dutch version: Van Rijsoort et al., 1999) was used to measure the tendency for excessive and uncontrollable worry. It measures trait worry as a one-dimensional construct independent from anxiety and depression, and has been stated to be useful for investigating GAD and the processes of normal and pathological worry (Behara et al., 2003). Examples of items are "I am always worrying about something" and "Once I start worrying, I can't stop". The items are scored using a 5-point Likert scale, anchored by "not at all typical" (for me) and "very typical" (for me). Both instruments are widely used, reliable and valid.

2.6. Biobehavioral variables

For every entry period the subject indicated the number of units of *coffee*, *cigarettes*, and *alcohol* consumed and the estimated amount of physical activity (climbing stairs, running, sports), the latter by a visual analogue scale (VAS) anchored by 'very little' and 'very much'. Subjects also indicated whether they had rested or snoozed during the entry period by a VAS anchored by 'not at all' and 'the whole period'. These variables too were divided by the number of entries that were completed to make them comparable across the subjects. After waking up in the morning and before returning the diary and AMS to the laboratory, the subjects indicated their approximate sleep onset and completed the Groningen Sleep Quality Scale (Meijman et al., 1988).

2.7. Analysis

The relationship between on the one hand stressors, worry frequency and worry duration and biobehavioral variables, and on the other hand HR and HRV during waking and during sleeping (1st hypothesis) was analyzed by Pearson correlation coefficients and hierarchical multiple regression analyses. For each variable, the biobehavioral variables were entered first and then stressors and worry frequency and worry duration. For the 2nd hypothesis (worry frequency and duration as a mediator of the effects of stressors) the analyses were repeated reversing the order by entering worry frequency and worry duration first and then stressors. If the effects of stressors were reduced after entering worry frequency and worry duration, it can be concluded that worry frequency and worry duration mediate, at least partly, the effects of stressors (Baron and Kenny, 1986). This was repeated for trait anxiety and trait worry instead of stressors to test whether the worry variables mediated the effects of these traits on waking and sleeping HR and HRV too. At this step, only the biobehavioral variables that had a significant bivariate correlation with a given cardiac variable were entered because the number of measured biobehavioral variables was so

large that entering them all would decrease the degrees of freedom too much for the present sample size.

The distributions of several of the variables were skewed, and differed significantly from a normal distribution according to the Kolmogorov–Smirnov Test. Some of these variables (stressors, physical activity and age) were successfully normalized by log-transformation. Variables that were still skewed (number of units of coffee, cigarettes and alcohol) were median split. Age was also median split for the convenience of presenting them together with other biobehavioral variables and gender (see Table 2). To test the associations of these latter variables with cardiac variables *T*-tests for independent samples were used. In the regression analyses they were used as binary ('dummy') variables. One extreme outlier on worry frequency was removed although this did not substantially alter the main results. Since the hypotheses were unequivocally in one direction, their tests were one-tailed. Slight differences in sample sizes are due to missing values on some of the variables. For the main analyses (effects of worry and stress on HR and HRV the sample size was held constant ($N=50$).

3. Results

3.1. Descriptive statistics and effect of life style variables

Table 1 shows the means and standard deviations of all variables that were used. As expected HR was higher during waking than during sleeping (86.4 vs. 66.5, $t(51)=17.7$, $p<001$) and HRV showed the opposite effect (29.1 vs. 51.6, $t(51)=6.0$, $p<.001$). The mean worry frequency and worry duration (.22 times and 2.0 min respectively) per hourly entry are comparable with those for high school students (.28 and 1.20, respectively (Brosschot and Van den Doef, 2006) and undergraduate students (.21 and 1.6 respectively (Verkuil et al., 2005) although the current older sample worried somewhat longer. These figures correspond with daily averages of 3.5 times and 32 min, if one multiplies the figures by 16 waking hours. Worries were marginally more often reported than stressors (.22 vs. .18, $t(51)=1.8$, $p=.07$). The values of trait worry, trait anxiety and sleep quality were in line with the literature (Van der Ploeg et al., 1979; Van Rijsoort et al., 1999; Meijman et al., 1988). Seven subjects (9.6%) met criteria for GAD according to the cut-off score suggested by Behara et al. (2003). However, the continuous scale was used instead of a GAD/non-GAD split to preserve information and because the 'GAD'-subgroup was very small.

Table 1
Means, standard deviations and range of cardiac variables during waking and sleeping; worry frequency, worry duration, and number of stressors per diary entry (per hour plus minus 10 min); sleep quality; trait anxiety and trait worry

	Mean	Standard deviation	Range
HR waking	86.4	10.1	68.2–111.1
HR sleeping	66.5	9.5	48.5–95.7
HRV waking	29.1	13.5	7.0–60.1
HRV sleeping	51.6	35.5	7.5–165.6
Worry frequency (# per entry)[a]	.22	.17	0–.71
Worry duration (min per entry)[a]	2.0	3.2	0–14.4
Nr of stressors	.18	.18	0–.82
Sleep quality	23.9	3.3	15–28
Trait anxiety	40.0	11.5	21–69
Trait worry	45.6	11.7	28–70

[a] per 60 min plus minus 10 min; Note: HR=heart rate; HRV=heart rate variability.

3.2. Effects of gender, age, life style variables, and sleep quality

The effects of gender, age and life style variables (consumption of coffee, cigarettes and alcohol) are shown in Table 2. Women had higher HR than men during waking (88.2 vs. 81.0, $t(50)=-2.4$, $p<.05$)). Older subjects (>31 years) had lower HRV than younger subjects during both waking and sleeping (25.0 vs. 33.6, $t(50)=2.4$, $p<.05$ and 38.5 vs. 65.8, $t(50)=3.0$, $p<.01$, respectively). High coffee users too had lower HRV than low users during waking and marginally during sleeping (25.3 vs. 33.9, $t(50)=2.4$, $p<.05$ and 43.6 vs. 61.7, $t(50)=1.9$, $p<.10$, respectively). Furthermore, smokers had higher HR and lower HRV than non-smokers only during the day (90.5 vs. 84.3, $t(50)=2.2$ and 24.1 vs. 31.8, $t(5)=2.0$, respectively, p's=.05). Finally, alcohol use was only related to lower HRV during sleeping (40.6 vs. 61.8, $t(50)=2.2$, $p<.05$).

The amount of physical activity was correlated with HR during waking ($r(52)=.29$, $p<.05$) while rest/snooze was marginally correlated with HRV during waking ($r(52)=.23$, $p<.10$). Sleep quality was correlated negatively with HR during sleeping ($r(51)=-.34$, $p<01$ and positively with HRV during sleeping ($\boldsymbol{r}(51)=.24$, $p<.05$).

3.3. Effects of worry frequency, worry duration, and stressors

Table 3 shows the correlation between worry frequency, worry duration, stressors, trait anxiety and trait worry on the one hand and HR and HRV during waking and sleeping hours. Worry frequency was associated with increased HR ($r(50)=.34$, $p<.01$) and lower HRV ($r(50)=-.31$, $p<.05$) during waking. Worry duration correlated with higher waking HR ($r(50)=.33$, $p<.01$) and with lower waking HRV ($r(50)=-.39$, $p<.01$). Stressors correlated positively with waking HR ($r(50)=.30$, $p<.05$), and negatively with waking HRV ($r(50)=-.26$, $p<.05$).

Next the independent effects were tested using hierarchical regression analyses. Worry frequency and duration were highly correlated ($r=.83$). To avoid collinearity the two variables were analyzed in separate tests. With respect to *waking* HR (see Table 4), after entering physical activity, gender and smoking ($F(3,47)=4.2$, $p<.01$), there was only a marginal effect left of the correlation of stressors in Table 3 ($F(1,46)=2.2$, $p<.10$) and after these biobehavioral variables and stressors were entered the effect of worry duration was also only marginally significant ($F(1,45)=1.6$, $p=.10$). The effect of worry frequency became nonsignificant ($F(1,45)=0.3$, ns; not in Table) after stressors were entered first. If worry duration was entered first after the biobehavioral variables, its effect was still significant ($F(1,46)=3.5$, $p<.05$), while that of stressors became nonsignificant ($F(1,45)=0.4$, ns; see Table 4). Worry frequency's effect was not significant after the

Table 2
Effect of biobehavioral variables on cardiac activity during waking and sleeping (means and standard deviations)

		Waking		Sleeping	
		HR	HRV	HR	HRV
Gender	Man	81.0* (8.3)	29.7 (12.7)	64.0 (11.9)	51.4(35.7)
	Female	88.2* (10.0)	28.9 (13.9)	67.3 (8.6)	51.7(35.8)
Age	(<31 years)	88.4 (9.1)	33.6* (13.4)	65.8 (9.9)	65.8** (36.1)
	(>31 years)	84.6 (10.8)	25.0* (12.5)	67.1 (9.4)	38.5** (29.8)
Coffee low	(<median)	87.4 (9.3)	33.9* (13.1)	66.3 (9.1)	61.7^{+}(39.3)
High	(>median)	85.7 (10.7)	25.3* (12.8)	66.7 (10.0)	43.6^{+}(30.4)
Smoking	(none)	84.3* (9.3)	31.8* (13.6)	65.1 (9.8)	56.9 (38.0)
	(>0)	90.5* (10.5)	24.1* (12.1)	69.1 (8.6)	41.6 (28.3)
Alcohol	(none)	88.1 (9.6)	30.5 (14.6)	65.3 (9.6)	61.8* (38.6)
	(>0)	84.6 (10.4)	27.6 (12.4)	67.9 (9.5)	40.6* (28.5)

Significance of differences between respective groups: *$p<.05$; **$p<.01$;$^{+}p<.10$; Note: HR = heart rate; HRV = heart rate variability.

biobehavioral variables were partialed out ($F(1,46)=1.5$, ns; not in Table).

For HRV during waking, the effects of stressors ($F(1,45)=3.5$, $p<.05$) as well as that of worry duration, entered thereafter ($F(1,44)=5.8$, $p<.01$), remained significant after the biobehavioral variables (age, cigarettes and coffee, rest/snooze; $F(4,46)=4.9$, $p<.001$) were entered. However, worry frequency was not significant ($F(1,44)=1.9$, ns) after entering stressors. As with waking HR, the effect of stressors became non-significant ($F(1,44)=0.2$, ns) after worry duration was entered before them ($F(1,45)=9.6$, $p<.01$). Worry frequency had a smaller effect than worry duration but still significant $F(1,45)=3.6$, $p<.05$). However the effect of stressors became non-significant ($F(1,44)=1.3$, ns) after entering worry frequency first.

For the analyses with *sleeping* HR and HRV (see Table 5), worry frequency was not used, since it had no significant bivariate effects (see Table 3). Stressors explained only a marginally significant part of variance in sleeping HR ($F(1,47)=2.3$, $p<.10$) when sleep quality was partialed out first ($F(1,48)=8.4$, $p<.01$). Worry duration's effect was not significant after stressors were entered ($F(1,46)=1.3$, ns). However, when worry duration was entered after sleep quality but before stressors, it had a significant effect ($F(1,47)=3.1$, $p<.05$), but the effect of stressors became non-significant ($F(1,46)=0.5$, ns). With respect to HRV stressors had only a marginal effect ($F(1,47)=1.7$, $p=.10$) after age and alcohol intake ($F(2,48)=6.5$, $p<.01$), whilst worry duration, entered after stressors, had a significant effect ($F(1,46)=2.8$, $p<.05$). When worry duration was entered before stressors it was significant ($F(1,47)=4.6$, $p<.05$) but the effect of stressors was eliminated ($F(1,46)=0.1$, ns; see Table 5).

Table 3
Correlation between (1) diary variables (worry frequency and worry duration, stressors), trait anxiety and trait worry and (2) cardiac activity during waking and sleeping

	Waking		Sleeping	
	HR	HRV	HR	HRV
Worry Frequency	.34**	−.31*	.16	−.17
Worry Duration	.33**	−.39**	.29*	−.28*
Stressors	.30*	−.26*	.30*	−.23^{+}
Trait worry	.29*	−.24*	.17	−.15
Trait anxiety	.24*	−.24*	.15	−.12

*p<.05; **p<.01;$^{+}p<.10$; one-tailed.
Note: HR = heart rate; HRV = heart rate variability.

3.4. Trait anxiety and trait worry

Trait anxiety and trait worry were also positively correlated with waking HR (see Table 3; $r(50)=.24$ and $r(50)=29$, respectively, p's<.05) and negatively with waking HRV (both r's (50)=.24, p's<.05), but not significantly with sleeping HR ($r(50)=.15$ and $r(50)=17$, respectively, ns) nor with sleeping HRV (($r(50)=.-12$ and $r(50)=-15$, respectively, ns). In a regression analysis, after partialing out the effects of biobehavioral variables the effects of trait anxiety on waking HR and HRV were no longer significant ($F(1,47)=1.3$, ns; $F(1,46)=1.0$,

Table 4
Waking HR and HRV: Hierarchical regression analyses of the effect of biobehavioral variables, number of stressors, worry frequency and worry duration

	Waking HR			Waking HRV		
	$r^{2:}$	F change:	partial r in last step:	r^2	F change:	partial r in last step:
Step 1	.46	4.2**		.55	4.9***	
Age[a]						−.35
Gender			.34			
Smoking			.24			−.21
Coffee						−.25
Physical exercise			−.06			
Rest/snooze						.26
Step 2	.50	2.2^{+}		.59	3.5*	
Stressors			.09			−.07
Step 3	.52	1.6^{+}		.65	5.8**	
Worry Duration			.19			−.34
Step 2	.51	3.5*		.65	9.6**	
Worry duration			.19			−.34
Step 3	.52	0.4^{ns}		.65	0.2^{ns}	
Stressors			.09			−.07

*$p<.05$; **$p<.01$; ***$p<.001$ (one-tailed for F change).
[a] Biobehavioral variables were entered for either HR or HRV analyses or both when bivariate effects (Table 2) were significant ($p<.05$); due to this alcohol during entry periods was not used.

Table 5
Sleeping HR and HRV: Hierarchical regression analyses of the effect of biobehavioral variables, number of stressors, worry frequency and worry duration

	Sleeping HR			Sleeping HRV		
	$r^{2:}$	F change:	partial r in last step:	r^2	F change:	partial r in last step:
Step 1	.39	8.4**		.46	6.5**	
Sleeping quality[a]			−.38			
Age						−.41
Alcohol						−.21
Step 2	.43	2.3^{+}		.49	1.7^{+}	
Stressors			.11			−.04
Step 3	.46	1.3^{ns}		.53	2.8*	
Worry Duration			.17			−.24
Step 2	.45	3.1*		.53	4.6*	
Worry duration			.19			−.24
Step 3	.46	0.5^{ns}		.53	0.1 ^{ns}	
Stressors			.09			−.04

$^{+}p<.10$; *$p<.05$; **$p<.01$; ***$p<.001$ (one-tailed for F change).
[a] Biobehavioral variables were entered for either HR or HRV analyses or both when bivariate effects (Table 2) were significant ($p<.05$); due to this gender and smoking, coffee, physical exercise and rest/snooze during entry periods were not used.

ns, respectively). The effect of trait worry remained significant ($F(1,47)=2.9$, $p<.05$) for waking HR and marginally significant for waking HRV ($F(1,46)=2.2$, $p<.10$). To test whether these effects were mediated by daily worry duration the latter was entered first (see previous section) resulting in a marginal effect of trait worry on waking HR ($F(1,45)=2.1$, $p<.10$) but not on HRV ($F(1,44)=0.8$, ns).

4. Discussion

4.1. Worry mediates waking and sleeping cardiac stressor effects

As hypothesized the results showed that stressors and prolonged worrying were associated with high HR and low HRV, not only during waking and but also during the subsequent nocturnal sleep period. Moreover, worry duration mediated the effects of stressors: after statistically controlling for the effects of worry duration on waking and sleeping HR and HRV the effects of stressors were virtually eliminated. These effects could only partially be explained by biobehavioral variables, including gender, age, sleep quality, and life style-related behavior during the measurement period, namely physical activity, resting or snoozing, consumption of coffee, alcohol and cigarettes. Trait worry and trait anxiety were related only to waking HR and HRV and the effects of trait anxiety were accounted for by biobehavioral variables. Thus, the effects of momentary assessed worry were superior in predicting HR and HRV. To the authors' knowledge, this is the first time that a psychological mediator of stress-related prolonged activity is reported in a real life setting. The mediator, i.e. worry, had already been recognized as a central pathogenic factor in several psychopathologies, but these results suggest that it may also play a role in the pathogenesis of somatic disorders, at least in cardiovascular disease. This role may be due to its propensity to prolong stress-related CV activity. As mentioned earlier, after a long period of neglect, there is now a growing consensus that prolonged physiological activity is key factor in the link between stress and disease (Brosschot and Thayer, 1998; Linden et al., 1997; McEwen, 1998; Selye, 1950; Sluiter et al., 2000; Ursin, 1980). A range of studies have shown prolonged cardiovascular activity related to stress, and several studies demonstrated that prolonged cardiovascular activity predicts morbidity and mortality (see Brosschot et al., 2006, for review). The current findings expand on this knowledge by suggesting that worry might mediate at least part of these prolonged effects.

4.2. Nocturnal cardiovascular activation: 'unconscious worry'?

The fact that these prolonged effects of worry were measured during nocturnal sleep is of considerable significance, since sleep is the most important restorative period of a healthy life. If stress related physiological activity is continued into this crucial period it can be truly marked as chronic and therefore a potentially high health hazard. This is especially so when it concerns types of activity that are known as prominent risk factors, such as high HR and low HRV (Palatini and Julius, 1997; Stein and Kleiger, 1999; Task Force Guidelines, 1996). Before the present study only a few studies have reported effects of stress on cardiovascular activity during the night (see Pieper and Brosschot, 2005). It is possible that these effects on sleep too are due to worry. Furthermore, the finding that stress and worry have prolonged cardiovascular effects during sleep has some intriguing theoretical implications. It points toward the possibility of unconscious cognitive representations of stress ('unconscious worry') having substantial physiological effects. Little is known about the exact nature of cognitive representations during sleep or about their potential physiological effects. Physiological effects or unconscious processing of distressing information have often been documented but are restricted to parameters bearing no direct relevance to somatic pathology such as cerebral activity, startle reflexes, skin conductance and sexual responses (e.g. Ohman and Mineka, 2001). Thus, the question remains what the nature is of stress-related cognitions during sleep, and whether these cognitions also play a role in waking life.

4.3. Worry duration and worry frequency

As expected, the effects of worry duration were more robust than those of worry frequency. Worry duration, and not frequency was significantly related to HR and HRV during sleep and mediated the effects of stressors. This is consistent with recent findings of our group that worry duration and not worry frequency was related to somatic symptoms, and a worry reduction intervention appeared to reduce somatic symptoms via a reduction in worry duration and not worry frequency (Brosschot and Van den Doef, 2006). An explanation of these findings is that, in essence, worry consists of attempts at

constructive problem solving, which may become problematic when these attempts persist in the face of apparent lack of success (Davey and Tallis, 1994). Szabo and Lovibond (2002) found that almost 50% of daily worries were seen as problem solving attempts by both low and high worriers, but the latter rated their attempts as more unsuccessful. It is possible that the duration of worry might reflect this lack of success. When duration is statistically controlled what is left is the number of attempts at problem solving. These by themselves may not have strong physiological consequences and may even be adaptive. One could argue that being aware of one's problems and concerns is healthy and adaptive as long as being aware leads to either productive problem solving or rapid disengagement. In fact, *not* being aware of one's problems would imply emotional avoidance or repression that have often been linked to increased physiological activity and worse health outcomes (Scheier and Bridges, 1995; Pennebaker et al., 1987).

4.4. Worry and anticipated stress

Worry not only mediated the effects of stressors but it also had a larger effect than stressors, implying that the stressors determined only part of the content of worrying. It is likely that the rest of this content pertained to other past or future stressors. This underscores an important limitation of conventional stress instruments that are limited to current or past events (Brosschot et al., 2005, 2006). By measuring the effects of worry one not only captures the cognitive and physiological effects of past and current stressors but also those of anticipated events. Anticipatory stress may even be the greater part of the daily stress experience for most people, even though many of the anticipated events will never happen, especially not in the case of excessive worriers such as GAD patients. Thus, worry significantly extends the assortment of stress instruments by including the effects of anticipated stress.

4.5. Worry and heart rate variability (HRV)

The finding of a link between worry and low waking and sleeping HRV extends previous findings with HRV (Brosschot et al., 2006). As mentioned, low HRV is a risk factor for CV disease and overall somatic morbidity and mortality, but it also has specific significance for psychopathology (Friedman and Thayer, 1998; Musselman et al., 1998; O'Connor et al., 2005; Thayer et al., 1998; Yeragani et al., 2002). Low HRV is an index of low parasympathetic activity, and as such also an index of disinhibition of sympathoexcitatory neural circuits that are normally under tonic inhibitory control via the prefrontal cortex. During worry and other states characterized by vigilance and arousal, priority is given to prepotent cognitive and behavioral programs, and the prefrontal cortex is taken temporarily "off-line". Parasympathetic inhibitory action is withdrawn (i.e. low HRV) and a relative sympathetic dominance associated with disinhibited defensive circuits is released. The result is a pattern of perseverations in cognitive, affective, and autonomic behavior that when sustained for long periods, can be pathogenic, somatically as well as psychologically. Psychopathological conditions such as anxiety, depression, post-traumatic stress disorder, and schizophrenia are all associated with prefrontal hypoactivity and a lack of inhibitory neural processes. This is reflected in poor habituation to novel neutral stimuli, a pre-attentive bias for threat information, deficits in working memory and executive function, and poor affective information processing and regulation (Thayer and Friedman, 2004), all of which have been linked to low HRV (Thayer and Brosschot, 2005). Together, low HRV may be the final common pathway linking psychopathology with psychosomatics, including cardiovascular disease.

4.6. Limitations

This study has several limitations that should be mentioned. First, for practical reasons it was impossible to obtain classical polysomnographical evidence of sleep. Although nocturnal awakenings were detected and removed using the motility and cardiac data of the recording system some waking periods may be missed. Thus some of the cardiac effects at night could have been due to 'waking worry' instead of 'sleeping worry'. However, substantial 'waking worry' periods would have been reflected in sleep quality, and the latter could not explain any of the effects worry. Another limitation is that worry prior to sleep onset was not measured because of the possibility of interfering with falling asleep. There could have been effects of this type of worry on the very first sleep phase. However, this was made less likely by the fact that HR and HRV data were included only from one hour after going to bed, and the motility and cardiac data did not show more signs of being awake in the first part of the sleeping period than in the later parts. Moreover, even if there would be such an effect of prior-to-sleep worry, it would not weaken the results but would mean that part of the cardiac effects during sleep have to be attributed to a yet unmeasured part of worry. Another limitation is the use of paper-and-pencil diaries and not more reliable handheld computers. It cannot be excluded that some diary entries were completed later than intended. However such a possible lack of reliability did not prevent the current results from emerging, and it is difficult to see how they could have caused them. Furthermore, the life style variables were restricted to those that have acute effects, such as smoking, coffee consumption and physical exercise, and that could therefore be confounders of the effects of stress and worry. Thus, multiple other life style factors were not measured that are known to be associated with chronic cardiac levels, such as physical fitness, body mass index, and several pharmaceutical drugs. Theoretically, their biological effects could have attenuated those of the psychological variables, but it is difficult to see how they could have explained the main findings. Finally, the wide age range of the sample is a potential limitation on the findings. The overall pattern of results support the conclusions drawn regarding worry duration, but is possible that the magnitude of those effects might vary as a function of age.

Taken together the present results suggest that stress and worry are associated with cardiac effects during waking and that these effects are extended into nocturnal sleep. The amount of time spent worrying during the day mediated the effects of

stressors. This is consistent with the view that worry, by prolonging the cardiovascular effects of stressors, may be an important mediator of their effects on the later development of cardiovascular disease. The relationship between low HRV and worry supports recent insights concerning the interconnectedness of psychopathology and somatic pathology (Thayer and Brosschot, 2005). Thus the present findings suggests a bridge that might fruitfully be explored to further illuminate the connection between psychopathology and mental health on the one hand and physical health, morbidity, and mortality on the other.

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