# The Relationship Between **Spectral Changes in Heart Rate** Variability and Fatigue

Yvonne Tran<sup>1</sup>, Nirupama Wijesuriya<sup>3</sup>, Mika Tarvainen<sup>2</sup>, Pasi Karjalainen<sup>2</sup>, and Ashley Craig<sup>3</sup>

<sup>1</sup>Centre in Health Technologies, University of Technology, Sydney, Australia, <sup>2</sup>Department of Physics, University of Kuopio, Finland, <sup>3</sup>Rehabilitation Studies Unit, Northern Clinical School, Faculty of Medicine, The University of Sydney, Australia

Abstract. Fatigue is a prevalent problem in the workplace and a common symptom of many diseases. However, its relationship with the autonomic nervous system, specifically with sympathetic arousal, needs clarification. The objective of this study was to determine the association between fatigue and heart rate variability (HRV). HRV is regarded as an indicator of the autonomic regulation activity of heart rate, specifically sympathetic and parasympathetic activity. Spectral changes in low-frequency (LF; 0.04–0.15 Hz) and high-frequency (HF; 0.15-0.4 Hz) components of HRV have been reported to be associated with distressing conditions such as hemorrhagic shock, acute myocardial infarction, elevated anxiety, and depressed mood. While HRV changes have been found in persons with chronic fatigue syndrome, its association with fatigue in healthy individuals still needs clarification. HRV was assessed in a total of 50 participants who were asked to perform a task until becoming fatigued. Low-frequency HRV activity increased, while indices of parasympathetic modulation such as RMSSD and pNN50 remained stable as participants experienced fatigue, suggesting that fatigue in healthy individuals may be associated with increased sympathetic arousal. In addition, employing multiple regression analyses, we could positively associate the change in LF/HF HRV ratio from baseline to fatigue with factors such as emotional stability, warmth and tension and negatively associate it with social boldness and self-reported levels of vigor.

Keywords: drowsiness, fatigue, heart rate variability, stress, sympathetic activity

# Introduction

Fatigue is a prevalent problem in society (Åkerstedt et al., 2004; Bultmann, Kant, Kasl, & Beurskens, 2002) and is known to be related to increased risks of accidents in the workplace and on the road (Arnedt, Geddes, & Maclean, 2005; Connor et al., 2002; Dinges, 1995; Dinges et al., 1997; Lal & Craig, 2001; Lamond & Dawson, 1999; Nilsson, Nelson, & Carlson, 1997; Philip et al., 2003). Fatigue is believed to be a major factor contributing to fatal road crashes in occupational drivers (Phillip, 2005). For instance, research in Australia has found that workers employed in the transport and storage industries have the highest rate of work-related road deaths (15.5 per 100,000), and fatigue is thought to be a major factor causing these accidents (Mitchell, Driscoll, & Healey, 2004). Fatigue is also a common complaint and symptom associated with many diseases such as sleep apnoea (George, 2004), chronic fatigue syndrome (Boneva et al., 2007), depressive and anxiety-based disorders (Friedman & Thayer, 1998; Fuhrer & Wessely, 1995), trait anxiety and stress (Craig, Tran, Wijesuriya, & Boord, 2006), and lifethreatening diseases such as cancer and heart failure (Åkerstedt et al., 2004; Mills, Parker, Dimsdale, Sadler, & Ancoli-Israel, 2005).

A promising area for understanding processes involved with fatigue involves studying the changes in heart rate variability (HRV) associated with fatigue. HRV is a measure of autonomic activity that describes variations in the heart rate (Malik, 1996). As concluded by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (Malik, 1996), the power spectral analysis of HRV provides a measure of the autonomic modulation of heart rate. Overall HRV is traditionally measured by analyzing the standard deviation of the normal to normal heart rate intervals (SDNN). Spectral analysis of HRV provides three components, which are very low frequency (0.003-0.04; VLF), low frequency (0.04-0.15; LF) and high frequency (0.15–0.40; HF). While VLF has not been considered a reliable measure (Malik, 1996), LF reflects both sympathetic and vagal (parasympathetic) heart rate control; HF is driven by respiration and provides an estimate of parasympathetic or vagal modulation of heart rate (Malik, 1996). Studies have shown increased power in the LF band (and sometimes simultaneous decreases in the HF component) to be associated with distress and anxiety (Dishman et al., 2000; Friedman & Thayer, 1998; Lucini, Norbiato, Clerici, & Pagani, 2002) and depressive mood (Rottenberg, Wilhelm, Gross & Gotlib, 2002). Additionally, Kawachi, Sparrow, Vokonas, and Weiss (1995) showed reduced HRV associated with anxiety in 581 men, while Yeragani et al. (1993) found decreased HRV in panic-disordered patients (Malik, 1996).

A few studies have examined the association between HRV and fatigue. Disturbance in autonomic function in the sympathetic component of the HRV has been linked to fatigue in persons with multiple sclerosis (Flachenecker et al., 2003) and with chronic fatigue syndrome (Yoshiuchi, Quigley, Ohashi, Yamamoto, & Natelson, 2004). Sluiter and colleagues found reproducibility in HRV variables in chronic fatigue participants. Verwey and Zaidel (1999) conducted a study in which 26 drivers performed a simulated driving task for over 2 h. They found that the LF component of HRV (0.1 Hz) was related to drowsiness. Ahsberg, Gamberale, and Gustafsson (2000) performed a study in which 20 male and 20 female adults participated in a vigilance task. Among many other measures they found that HRV increased more when associated with a vigilance task compared to a proofreading task. Egelund (1982) studied HRV in 8 participants while they drove for around for 4 h (comprised of short 2-km drives interspersed with short breaks) on a highway in the afternoon and found that the LF spectrum component of the HRV (that is, 0.04–0.15 Hz) increased as the subjects became fatigued, though he found no association between fatigue and overall HRV. Apparies, Riniolo, and Porges (1998) studied HRV during driving in 24 truck drivers over a period of 8 to 10 h. Heart rate increased and HRV decreased over the period of the driving shift, suggesting also an increase in sympathetic activity.

The majority of studies that have investigated HRV changes associated with fatigue suggest that fatigue is associated with reduced HRV or an increased LF component and thus perhaps increased sympathetic activity. However, most of these studies have utilized low numbers of participants, lowering the confidence one would have in their conclusions, and few have studied spectral changes of HRV associated with fatigue in healthy subjects. Furthermore, few if any have investigated factors that contribute to changes in HRV as a person fatigues. Therefore, the aims of this study were (1) to investigate HRV spectral changes that occur in healthy participants as they fatigued during a boring simulated driving task; and (2) to investigate psychological and demographic determinants that contribute to HRV change associated with fatigue.

## Methods

#### Participants

A total of 50 participants (23 females and 27 males) were randomly selected from a large group of university students, staff, and general community. The participants' mean age was 32 years (SD = 12.5 years, range 18 and 55

Journal of Psychophysiology 2009; Vol. 23(3):143-151

years). Participants were only admitted into the study if they were currently healthy (as determined by the preinterview), held a current drivers license, and reported having had no prior brain disease or sleep disorders (self-reported). They were asked to refrain from alcohol consumption for 24 h and caffeine consumption for 12 h prior to the study, which was approved by the institution's research ethics committee. Participants were entered into the study only after informed consent.

#### Procedure

The design of the study involved an experiment in which the electrocardiogram (ECG) of participants was assessed at baseline (measure 1 or M1), after 5 min of driving (measure 2 or M2), and immediately after the subjects showed first signs of fatigue (measure 3 or M3). Following M3, the task (simulated driving task) was terminated.

After giving the participants time to relax and adjust to the environment of the laboratory, participants were given psychological and physiological premeasures. A battery of questionnaires were given to participants to complete. This included the Chalder Fatigue Scale (CFS; Chalder et al., 1993), which measures aspects of mental and physical fatigue and provides an overall indicator of fatigue. It was used to assess fatigue before and after the monotonous task. The scale has been shown to have high reliability and validity. They also completed the Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1971) before the driving task. An assessment of personality was also conducted using the primary factors of the 16 Personality Factor (16PF) questionnaire (Cattell, Eber, & Tatsuoka, 1986). To determine the health status of the group, an assessment of lifestyle health was measured using the Lifestyle Appraisal Questionnaire (LAQ; Craig, Hancock, & Craig, 1996), and sleepiness propensity was measured by the Epworth Sleepiness Scale (ESS; Johns, 1991). All these questionnaires have been shown to be reliable and to have acceptable validity.

The completion of the psychological battery was followed by physiological premeasures such as height, weight (BMI), blood pressure, and a 5-minute assessment of resting ECG to establish resting baseline HR and HRV (M1). The participants were then given time to familiarize themselves with the task by undertaking a practice run on the driving simulator. Once participants felt confident that they were able to steer the simulated car and no longer felt the task to be novel, the task was begun. Throughout the task, the faces of the participants were captured on video.

Participation in the task was terminated 5 min after the participants began to show physical signs of fatigue (such as head nodding and eyeblink duration). Immediately after the task, participants completed the CFS again to determine the extent of self-reported fatigue. Each participant was tested individually in a temperature- (20–23 °C) and light-controlled room. All participants were tested during one of

two periods of the day (9.00-12.00 a.m. and 2.00-5.00 p.m.) in order to control the potential confounding influence of circadian rhythms. These two periods have been shown to be similar in circadian rhythm influence (Bear, Connors, & Paradiso, 2001). However, it is important to note that the subjects who were assessed in the 9.00-12.00 a.m. period were found to have lower levels of pretask self-reported fatigue than those assessed in the 2.00–5.00 p.m. period (difference in the Chalder Fatigue Scale of 9.4 in the morning compared to 13.9 in the afternoon session; p < .05). This difference in alertness level over time is similar to what has been predicted by the Three Process Model of Alertness Regulation (Åkerstedt & Folkard, 1995). Although both groups may have started at different levels of self-reported fatigue, the change in the levels of self-reported fatigue during the monotonous task was not significantly different between the morning and afternoon groups, and the mean time it took the groups to fatigue was also not significantly different (Wijesuriya, Tran, & Craig, 2007). In addition, repeated measures ANOVA from M1 to M3 found no significant differences in HR, LF, HF, and LF/HF between the groups assessed in the morning and afternoon sessions (p = .33, .52, .49 and .38, respectively).

#### Heart Rate Variability Analysis

In this study, the electrocardiogram was recorded using the Biosemi Active Two data acquisition system (Biosemi.com). Two surface flat-type Ag-AgCl Biosemi<sup>TM</sup> Active (Biosemi. com) electrodes were placed on the left side of the chest region. The ECG signal was acquired at a sample rate of 2048 Hz. A resting baseline ECG of 5 min was recorded for each participant before the commencement of the driving task. The R-R interval (ms) was detected from each ECG recording by using an adaptive QRS complex detection algorithm. All analyzed R-R data segments were selected so that they were 5 min in length (300 s) in order to avoid variance in results. The low frequency trend was removed from each R-R segment by using a smoothness priors based detrending method with smoothing parameter  $\lambda = 500$  (Tarvainen, Ranta-aho, & Karjalainen, 2002). The R-R interval sequence is a nonequidistantly sampled time sequence and must be converted to an equidistantly sampled sequence before spectral analysis. This was accomplished by utilizing a 4 Hz cubic spline interpolation.

Time- and frequency-domain variables of HRV (HR, RR, SDNN, pNN50, RMSSD, LF, HF, and LF/HF) were then calculated (Malik, 1996). All the calculations were done by using Matlab<sup>®</sup> (The MathWorks, Inc.) environment. In the frequency domain, the power spectrum estimates were calculated using both an FFT-based method (Welch's periodogram) and an autoregressive (AR) modeling-based method (Marple, 1987). In Welch's periodogram, a 100-s window with 50% overlap was used. In AR spectrum estimate, a model order 20 was used (the decision of which was made based on three common model order selection criteria). In both spectrum estimation methods, the spectrum was divided into three frequency bands, i.e., very low frequency (VLF): 0–0.04 Hz, low frequency (LF): 0.04–0.15 Hz, and high frequency (HF): 0.15–0.4 Hz. VLF was not used in the analysis. The LF and HF data are also presented in a normalized format, that is, the individual spectra is divided by the total spectral band, as this has been shown to optimize the LF and HF data (Jaffe, Fung, & Behrman, 1994). The LF/HF ratio was also used to indicate sympathovagal balance.

#### The Simulated Driving Task

Vigilance level or alertness/arousal has proved to decrease with fatigue (Campagne, Pebayle, & Muzet, 2004). A simulated driving task was used in this study as a vigilance task. Simulated driving tasks are used in fatigue studies, both in clinical and research settings as they provide a measure to detect fatigue by means of decreased vigilance (George, 2004). In this study we used the Divided Attention Steering Simulator (DASS) (Stowood Scientific Instruments, Oxford, UK), according to the manufacturer's instructions. The DASS has been used reliably in other studies (Phillip et al., 2003). The program measures decreasing vigilance/fatigue by means of increased deviation of steering the car and poor reaction time. The aim of the task was to steer an image of a car down the center of the road using a game steering wheel (Grandprix 1, Thrustmaster, Alta Loma, CA, USA). During the task, the digits, which changed randomly, were displayed at the corner of the screen. To test vigilance and reaction time, we required the subjects required to identify the number "2" when it appeared by pressing a button on the same side of the steering wheel as it appeared on the screen (Turkington, Sircar, Allgar, & Elliott, 2001). The task was considered monotonous because the participants were required to drive at slow speeds for an extended period of time in a noise-, stimulus-, and temperature-controlled laboratory.

#### Fatigue Symptoms

As in our prior related studies (Craig et al., 2006; Wijesuriya, et al., 2007), fatigue was defined as the consistent appearance of physical facial symptoms such as nodding and yawning (validated by video analysis), or when eye closure during blinking became prolonged (at least 400 ms). A Biosemi Active Two system (Biosemi.com) was used to measure eye activity via an electrooculogram (EOG). Two pairs of active electrodes were placed across the eyes diagonally to measure EOG activity. Other studies (Caffier, Erdmann, & Ullsperger, 2003) have found that alert eye closure during a blink occurs for around 200 ms (range: 100 to 300 ms) increasing to around 300 ms during fatigue (range: 200 to 450 ms). Therefore, closure times of at least 400 ms during eyeblinks were considered evidence that the subject was definitely experiencing fatigue. Behavior and facial expressions of the participants were also observed during the task through video monitoring, for signs of fatigue, such as tired eyes, prolonged eye closure, and head nodding. This experiment was set up to be a 2-h task, whereby the participants were stopped by the researcher 5 min after subjects began to show definite signs of fatigue (i.e., nodding off, prolonged eye closure, or when a subject drove off the road for more than 15 s). As stated above, subjects were video recorded during the task and detection of the fatigue related state was independently assessed by two trained observers. A 90% agreement on video monitoring occurred between the two raters, suggesting that the video analysis component of the physiological measure was a reliable assessment.

#### Analysis

All analyses were performed using Statistica software (Version 7, Statsoft, Tulsa, OK, USA). Statistical power for the study was determined to be in the range of 50% to 98% given the moderate to large effect sizes found (e.g., effect size for overall CFS = .7; for HRV normalized LF = .43; for HRV normalized HF = .54). High statistical power of around 80% increases confidence in the study findings. Factorial repeated measures ANOVAs were conducted in order to determine spectral differences in HRV for the 50 participants between baseline (M1), 5 min after the start of the task (M2), and when the subjects were found to have fatigued (M3). All three measures consisted of periods of 5 min of HRV data. While HR was continuously measured throughout the task, only the above three periods (baseline or M1, 5 min into the task or M2, and after subjects fatigued or M3) of 5 min were reported and analyzed in order to determine the effect of fatigue on HRV activity. Data for two participants were removed from the time interval M2 and one from the time interval M3 due to poor HR signals. Their HRV data were substituted with means for the multiple regression analyses. To determine the unique contribution of the demographic and psychological factors to HRV, all psychological and relevant demographic variables were then entered into a series of forward deletion multiple regression analyses (entry criteria set at F of 1.5), with the dependent variable being change in LF/HF (calculated as LF/HF M3 minus LF/HF M1). The aim of the performing a regression analysis was to establish the strongest combination of factors that contributed to HRV variation. Certain factors were not entered because of the problem of multicollinearity (Tabachnik & Fidell, 1996), in which variables that are highly correlated should not be entered together into the regression. Therefore, the Total POMS score (highly correlated with the POMS subcomponent scores), the secondary 16PF factors (highly correlated with the 16PF Primary factors), and the POMS Fatigue score were not entered into the regression analysis.

### **Results**

Premeasure psychological and physiological results found that the LAQ scores (mean = 13.8, SD = 6; 95%CI: 12.1-15.6) for the sample suggest that the group of 50 drivers was within the normal healthy range with the LAQ mean and 95% confidence intervals, falling well below the unhealthy range (> 20 for people aged 20 to 50 years) (Craig et al., 1996). This is also suggested by the mean scores for blood pressure (mean systolic/diastolic BP = 118/70; SD = 10/11), heart rate (mean HR = 71, SD = 11), and body mass index (mean BMI = 23.9, SD = 3.5). The group was also found to have "normal" levels of mood states as measured by the POMS (McNair et al., 1972). This was the case for anxiety (sample mean = 10.6, SD = 6; POMS norm of around 13–14 for adult males and females), depressive mood (sample mean = 9.7, SD = 11; POMS norm of around 13-15 for adult males and females), and fatigue (sample mean = 10, SD = 5; POMS norm of around 10-11 for adult males and females). The group's mean sleepiness score (mean ESS = 8.1; SD = 3.9) was found to be similar to normative values (Johns, 1991). Age was not found to correlate significantly with any of the HRV measures. Furthermore, testing for differences between males (n = 27) and females (n = 23) using t-test procedures on the normalized LF and HF measures did not result in any consistent significant differences.

Table 1 shows the mean self-reported Chalder Fatigue Scale (CFS) broken into its subtraits of mental and physical fatigue. CFS scores increased as the subjects completed the simulator task, and this increase was significant (e.g., overall CFS: t = 4.1, df = 49, p < .05), suggesting the participants fatigued as a consequence of simulated driving over the time period of the task. Furthermore, blink rates (blinks per minute) of the group taken at 5 min into the task and at the time they were asked to stop driving was shown to have significantly increased from 15.98 to 24.5 (t = -5.11, p < .001).

*Table 1.* Descriptive values (mean [*SD*] CI) for the Chalder Fatigue Scale (CFS), total CFS score, and physical and mental CFS breakdowns

Measure	Pretask (SD) 95%CI	Posttask (SD) 95% CI	р
Chalder	12.08 (6.92) 10–14	16.78 (7.91) 14.5–19	.00015
Chalder Physical	7.82 (4.43) 6.6–9.1	11.20 (5.18) 9.7–12.7	.00003
Chalder Mental	4.42 (3.03) 3.5–5.3	5.58 (3.31) 4.6–6.5	.0105

Table 2 shows mean values for the R-R, SDNN, pNN50, RMSSD, the LF/HF ratios, the absolute and normalized values for LF and HF spectrum for baseline (M1), after the first 5 min in the task (M2), and when subjects began to

	pNN50
	RMSSD
	LF (ms)
	LF norm
	HF (ms)
	HF norn
43-151.	LF/HF r
siology 2009.23:1	Table 3
hophys	Persona
of Psyc	16 PF A 16 PF C
0	

Table 2. Descriptive values (Mean [SD] CI) for HR and HRV measures for M1 (pretask), M2 (5 min into task) and M3 (onset of fatigue symptoms)

Measure	Pretask(SD) 95% CI	5 min ( <i>SD</i> ) 95% CI	Posttask(SD) 95% CI	р
R-R (ms)	865.7 (144) 824–906	862.6 (125) 827–898	845.5 (131) 808–882	.0122
SDNN	46.7 (29) 38–55	43.6 (22) 37–50	49.4 (25) 42–56	.1472
pNN50	20.1 (22.0) 13.9–26.4	19.0 (18.1) 13.7–24.2	18.1 (18.0) 12.9–23.3	.1736
RMSSD	50.1 (41.4) 38.3–61.8	46.1 (32.0) 36.8–55.4	50.2 (36.8) 39.7–60.8	.3492
LF (ms)	1179 (1520) 748–1612	1037 (1217) 683–1390	1581 (1792) 1067–2096	.0180
LF normalized score	50.1 (15) 45–54	52.8 (15) 48–57	56.6 (15) 52–61	.0030
HF (ms)	1415 (2612) 673–2157	980 (1639) 504–1456	1218 (1789) 704–1732	.1274
HF normalized score	43.6 (16) 39–48	40.6 (15) 36–45	35 (17) 30–40	.0002
LF/HF ratio	1.5 (1.3) 1.2–1.9	1.7 (1.5) 1.3–2.2	2.4 (2.3) 1.7–3.1	.0081

3. Multiple regression summary for change in LF/LH (from M1 to M3). R = 0.58,  $R^2 = 0.33$ ; F(5, 44) = 4.47, p < 100.01. Semipartial correlations are shown (Spc), as is the amount each factor individually contributes to the dependent variable (Spc<sup>2</sup>)

Personality traits	β	SE β	В	t value	p value	Spc	Spc <sup>2</sup>
16 PF A (warmth)	0.21	0.13	0.27	1.6	.11	0.20	3.9%
16 PF C (emotional stability)	0.34	0.14	0.50	2.4	.02	0.29	8.5%
16PF H (social boldness)	-0.46	0.13	-0.52	-3.5	.001	-0.43	18.6%
16PF Q4 (tension)	0.28	0.15	0.40	1.9	.07	0.23	5.3%
POMS Vigor	-0.25	0.14	-0.11	-1.8	.07	-0.23	5.1%

show definite signs of fatigue (M3). The R-R values in the time domain over the monotonous task significantly decreased (F = 4.6, df = 2.94; p < .05), and significant differences existed between baseline R-R and R-R taken during M3 (Scheffé test p < .05). The significant R-R decrease means that heart rate increased as fatigue increased. The overall HRV (SDNN) scores and parasympathetic indices pNN50 and RMSSD, did not significantly change from pre to post over the fatiguing task. Absolute and normalized LF both showed significant increases from M1 to M3 (F = 4.2, df = 2.94; p < .05 and F = 6.2, df = 2.94; p < .05, respectively). Scheffé test showed significant differences between M1 and M3. Absolute HF was not significantly different from pre- to postfatigue task; however, normalized HF did show a significant decrease between M1 and M3 and M2 and M3 (F = 6.1, df = 2.94; p < .05). Figure 1 shows the significant influence of the fatiguing task on LF and HF values (Wilks  $\lambda = 0.74$ , F(4, 44) = 4.44, p = .009). The LF/HF ratio significantly increased over the task (F =5.1, df = 2.94; p < .01), and the significant differences existed between baseline LF/HF ratio (M1) and the LF/HF ratio when subjects fatigued (M3) (Scheffé test p < .05).

A stepwise multiple regression analysis was performed to isolate possible demographic and psychological determinants of the HRV. The dependent variable was the change in LF/HF ratio (from M1 to M3). The forward deletion multiple regression was run until the strongest five variables had been isolated that contributed to fatigue. Semipartial correlations (Spc) and the amount of variance that each variable contributed to the fatigue outcome measures (Spc<sup>2</sup> as a percentage value) are also provided. Table 3 shows the regression statistics for change in LF/HF with the five variables contributing 34% to the LF/HF ratio from baseline to alert (R = .58,  $R^2 = .34$ , F(5, 44) = 4.47, p < .58.01). Only two of these variables were significant: emotional stability (contributing 8.5% with high emotional stability scores relating to greater change in LF/HF ratio from M1 to M3) and social boldness (contributing 18.6% with high levels of social boldness related to lower levels of change in LF/HF ratio from pre- to posttask).



*Figure 1.* Normalized values for LF versus HF components of the HRV data over the time of the fatiguing task. Time M1 is the pretask measure, Time M2 is the 5 min measure and Time M3 is the posttask HRV measure.

# Discussion

The participants in this study were found to experience significantly increased levels of fatigue as a result of completing the monotonous driver simulator task. This conclusion was supported by the significantly and substantially increased self-reported CFS levels of fatigue as well as the increased physical symptoms of fatigue (such as increased eyeblinks). A major purpose of this study was to determine whether healthy participants experienced changes in spectral HRV as they fatigued. The findings provide strong evidence that fatigue is associated with increased LF values (both absolute LF and normalized LF) and decreased normalized HF values. There was also a significant increase in the LF/HF ratio (M1 to M3). However, absolute HF as well as other parasympathetic indices such as pNN50 and RMSSD were shown to be stable from pre- to posttask (see Table 2). These findings suggest that sympathetic activity is associated with increased fatigue. The study also found that the R-R interval significantly decreased, meaning that heart rate increased during the fatiguing task, and increased heart rate usually accompanies increased autonomic nervous system (ANS) sympathetic activity. Similar HRV findings were found in adolescents with chronic fatigue syndrome. Compared to control participants, chronic fatigue adolescents were found to have increased absolute and normalized LF and decreased absolute and normalized HF activity during mild orthostatic stress (Wyller, Barbeiri, Thaulow, & Saul, 2008; Wyller, Saul, Amlie, & Thaulow, 2007). Another study examined 59 indicators for unexplained fatigue in patients including multiple symptoms, gene and clinical variables, and found oxidative stress, immune system dysfunction, and potassium imbalance were common in chronic fatigue patients. They concluded that this leads to an impaired sympatho-vagal balance and reflects strongly in abnormal HRV (Broderick et al., 2006).

As argued above, fatigue is a prevalent problem in society that is known to present serious risks in society such as road- and work-related accidents, and evidence also suggests fatigue can increase chances of complications in diseases such as depression and heart disease (Fuher & Wessely, 1995). Nevertheless, it is also recognized that, as a condition, fatigue is not well understood and therefore needs further research in order to clarify its nature in order to effectively manage associated complications (Bultmann et al., 2002). Fatigue states have been found to be associated with distressing feelings, depressive mood, and anxiety (Bultmann et al., 2002; Craig et al., 2006; Pawlikowska et al., 1994). Latest research suggests that fatigue and psychological distress are highly correlated with shared symptoms (Bultmann et al., 2002). However, research that employed principal components analysis found the constructs "distress" and "fatigue" to be distinctly independent factors (Bultmann et al., 2002). In addition, prior research has found preliminary evidence that fatigue is associated with increased levels of sympathetic activity (Egelund, 1982). The research presented in this paper provides evidence that fatigue occurring as a result of a monotonous task in healthy individuals is associated with increased levels of sympathetic activity. Autonomic nervous system sympathetic activity is known to play a prominent role in the human stress response (Black & Garbutt, 2002). Therefore, it is quite possible that many of the subjects were experiencing unpleasant or distressing feelings when fatiguing. For example, we know from the data that, as the subjects experienced increased levels of both mental and physical fatigue, they experienced increased heart rate, and the frequency of their eyeblinks increased as they struggled to keep their eyes open. Because of the demands of participating in the simulated driving task, they would have mentally and physically struggled to remain alert. This could well be the reason why people become aroused sympathetically. While it has been thought that fatigue experienced during a demanding task is a condition resulting in a more relaxed or pleasantly sleepy state (Lal & Craig, 2001), the findings of this study suggest quite the reverse.

This study addressed a further question focusing on the demographic and psychological determinants of the change in the LF/HF ratio associated with the increased levels of fatigue. A number of factors were found to contribute: The personality trait social boldness was found to contribute the most (18.6%) to change in LF/HF ratio associated with fatigue. This finding suggests that a person more likely to be sympathetically aroused when they fatigue is low in social boldness - an introversion factor. Therefore, introversion is a potential risk factor for experiencing higher levels of distress during fatigue. Interestingly, in prior papers we reported findings that suggest that extroverted persons are more at risk of experiencing fatigue (Craig et al., 2006; Wijesuriya et al., 2007). This raises the possibility that, while extroverted people may have a greater risk of becoming *fatigued* during monotonous tasks, introverted people are more likely to become distressed as a result of becoming fatigued. Emotional stability also significantly contributed to the change in LF/HF ratio with higher emotional stability scores associated with greater changes in LF/HF ratio. This finding will need replication, as Liu and colleagues (2004) found that people scoring higher in emotional stability had lower normalized LF and HF activity during a reaction time task, but a raised normalized LF and HF during an actual flying task. Although not significant (p = .07), 16PF tension factor and POMS Vigor contributed 5.3% and 5.1%, respectively, to change in LF/HF ratio, suggesting that people with higher tension and lower vigor scores are also more likely to show greater LF/HF change from pre- to posttask. This is supported by our previous finding that fatigue is associated with a predisposition to be anxious with lower vigor levels (Wijesuriya et al., 2007). However, it must be noted that these findings need to be treated with some caution as recent evidence questions the relationship of the LF/HF ratio as a marker for sympathetic control (Goedhart, Willemsen, Houtveen, Boomsma, & Geus, 2008).

Clearly, the association of fatigue and HRV needs further investigation. The results of this study suggest fatigue is associated with increased sympathetic activity in a healthy population, and that psychological factors contribute to this process. One feature that may need attention in future studies is controlling circadian rhythm influences by assessing fatigue in the same period during the day. While we did not control for this factor in the present study, there were no significant differences in the HRV variables between the morning and afternoon experimental sessions. Additionally, future studies should control for the influence of factors that may affect autonomic regulation and circulatory physiology, including medications such as antihypertensive drugs and pharmaceuticals such as the contraceptive pill. Given the risk of morbidity and mortality as a consequence of fatigue-related accidents and the negative involvement of fatigue in serious disease, it is imperative that we better understand its complex nature and its association with a person's psychophysiology.

#### Acknowledgments

This project was supported by the Australian Research Council (LP0560590). We thank the 50 nonprofessional drivers who participated, allowing us to explore the fatigue process further.

## References

- Ahsberg, E., Gamberale, F., & Gustafsson, K. (2000). Perceived fatigue after mental work: An experimental evaluation of a fatigue inventory. *Ergonomics*, 43, 252–268.
- Åkerstedt, T., & Folkard, S. (1995). Validation of the S and C components of the Three-Process Model of alertness regulation. *Sleep*, 18, 1–6.
- Åkerstedt, T., Knutsson, A., Westerholm, P., Theorell, T., Alfredsson, L., & Kecklund, G. (2004). Mental fatigue, work and sleep. *Journal of Psychosomatic Research*, 57, 427–433.
- Apparies, R.J., Riniolo, T.C., & Porges, S.W. (1998). A psychophysiological investigation of the effects of driving longercombination vehicles. *Ergonomics*, 41, 581–592.
- Arnedt, J.T., Geddes, M.A.C., & Maclean, A.W. (2005). Comparative sensitivity of a simulated driving task to self-report, physiological, and other performance measures during prolonged wakefulness. *Journal of Psychosomatic Research*, 58, 61–71.
- Bear, M.F., Connors, B.W., & Paradiso, M.A. (2006). *Neuroscience. Exploring the brain*. Baltimore: Lippincott Williams & Wilkins.
- Black, P.H., & Garbutt, L.D. (2002). Stress, inflammation and cardiovascular disease. *Journal Psychosomatic Research*, 52, 1–23.
- Boneva, R.S., Decker, M.J., Maloney, E.M., Lin, J.M., Jones, J.F., Helgason, H.G. et al. (2007). Higher heart rate and reduced heart rate variability persist during sleep in chronic fatigue syndrome: A population-based study. *Autonomic Neuroscience*, 137, 94–101.
- Broderick, Craddock, R.C., Whistler, T., Taylor, R., Klimas, N., & Unger, E.R. (2006). Identifying illness parameters in fatiguing syndromes using classical projection methods. *Pharmaco*genomics, 7, 407–419.
- Bultmann, U., Kant, I., Kasl, S., Beurskens, A.J.H.M., & van den Brandt, P.A. (2002). Fatigue and psychological distress in the working population. Psychometrics, prevalence and correlates. *Journal of Psychosomatic Research*, 52, 445–452.
- Caffier, P.P., Erdmann, U., & Ullsperger, P. (2003). Experimental evaluation of eye-blink parameters as a drowsiness measure. *European Journal Applied Physiology*, *89*, 319–325.
- Campagne, A., Pebayle, T., & Muzet, A. (2004). Correlation be-

tween driving errors and vigilance level: Influence of the driver's age. *Physiology Behavior*, *80*, 515–524.

- Cattell, R.B., Eber, H., & Tatsuoka, T. (1986). *The 16 PF handbook*. Champaign, IL: IPAT.
- Chalder, T., Berelowitz, G., Pawlikowska, T., Watts, L., Wessely, S., Wright, D. et al. (1993). Development of a fatigue scale. *Journal of Psychosomatic Research*, 37, 147–153.
- Connor, J., Norton, R., Ameratunga, S., Robinson, E., Civil, I., Dunn, R. et al. (2002). Driver sleepiness and risk of serious injury to car occupants: Population based case control study. *British Medical Journal*, 324, 1125.
- Craig, A., Hancock, K., & Craig, M. (1996). The lifestyle appraisal questionnaire: A comprehensive assessment of health and stress. *Psychology and Health*, *11*, 331–343.
- Craig, A., Tran, Y., Wijesuriya, N., & Boord, P. (2006). A controlled investigation into the psychological determinants of fatigue. *Biological Psychology*, 72, 78–87.
- Dinges, D.F. (1995). An overview of sleepiness and accidents. *Journal of Sleep Research*, *4*, 4–14.
- Dinges, D.F., Pack, F., Williams, K., Gillen, K.A., Powell, J.W., Ott, G.E. et al. (1997). Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. *Sleep*, 20, 267–277.
- Dishman, R.K., Nakamura1, Y., Garcia, M.E., Thompson, R.W., Dunn, A.L., & Blair, S.N. (2000). Heart rate variability, trait anxiety, and perceived stress among physically fit men and women. *International Journal of Psychophysiology*, 37, 121–133.
- Egelund, N. (1982). Spectral analysis of heart rate variability as an indicator of driver fatigue. *Ergonomics*, 25, 663–672.
- Flachenecker, P., Rufer, A., Bihler, I., Hippel, C., Reiners, K., Toyka, K.V. et al. (2003). Fatigue in MS is related to sympathetic vasomotor dysfunction. *Neurology*, *61*, 851–853.
- Friedman, B.H., & Thayer, J.F. (1998). Autonomic balance revisited: Panic and heart rate variability. *Journal of Psychosomatic Research*, 44, 33–151.
- Fuhrer, R., & Wessely, S. (1995). The epidemiology of fatigue and depression: A French primary-care study. *Psychological Medicine*, 25, 895–905.
- George, C.F.P. (2004). Sleep 5: Driving and automobile crashes in patients with obstructive sleep apnoea/hypopnoea syndrome. *Thorax*, *59*, 804–807.
- Goedhart, A.D., Willemsen, G., Houtveen, J.H., Boomsma, D.I., & De Geus, E.J.C. (2008). Comparing low frequency heart rate variability and preejection period: Two sides of a different coin. *Psychophysiology*, 45, 1086–1090.
- Jaffe, R.S., Fung, D.L., & Behrman, K.H. (1994). Optimal frequency ranges for extracting information on autonomic activity from the heart rate spectrogram. *Journal Autonomic Nervous System, 46*, 37–46.
- Johns, M.W. (1991). A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep*, 15, 376–381.
- Kawachi, I., Sparrow, D., Vokonas, P.S., & Weiss, S.T. (1995). Decreased heart rate variability in men with phobic anxiety. *American Journal of Cardiology*, 75, 882–885.
- Lal, S., & Craig, A. (2001). Electroencephalography activity associated with driver fatigue: Implications for a fatigue countermeasure device. *Journal of Psychophysiology*, 15, 183–189.
- Lamond, N., & Dawson, D. (1999). Quantifying the performance impairment associated with fatigue. *Journal of Sleep Research*, 8, 255–262.

- Liu, X.F, Miao, D.M., Xiao, W., Huang, W.F., Liu, F., Liu, P. et al. (2004). Comparison of heart rate variability and heart rate between individuals with different emotional stability in two situations. *Space Medicine and Medical Engineering*, 17, 85–88.
- Lucini, D., Norbiato, G., Clerici, M., & Pagani, M. (2002). Hemodynamic and autonomic adjustments to real life stress conditions in humans. *Hypertension*, 39, 184–188.
- Malik, M. (1996). Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *European Heart Journal*, 17, 354–381.
- Marple, S.L. (1987). *Digital spectral analysis with applications*. New York: Prentice-Hall.
- McNair, D.M., Lorr, M., & Droppleman, L.F. (1971). *Profile of mood states manual*. San Diego: Educational and Industrial Testing Service.
- Mills, P.J., Parker, B., Dimsdale, J.E., Sadler, G.R., & Ancoli-Israel, S. (2005). The relationship between fatigue and quality of life and inflammation during anthracycline-based chemotherapy in breast cancer. *Biological Psychology*, 69, 85–96.
- Mitchell, R., Driscoll, T., & Healey, S. (2004). Work-related road fatalities in Australia. *Accident Analysis Prevention, 36*, 851–860.
- Nilsson, T., Nelson, T.M., & Carlson, D. (1997). Development of fatigue symptoms during simulated driving. Accident Analysis Prevention, 29, 479–488.
- Pawlikowska, T., Chalder, T., Hirsch, S.R., Wallace, P., Wright, D.J., & Wessley, S.C. (1994). Population-based study of fatigue and psychological distress. *British Medical Journal*, 308, 763–766.
- Phillip, P. (2005). Sleepiness in occupational drivers. *Industrial Health*, 43, 30–33.
- Philip, P., Taillard, J., Klein, E., Sagaspe, P., Charles, A., Davies, W.L. et al. (2003). Effect of fatigue on performance measured by a driving simulator in automobile drivers. *Journal of Psychosomatic Research*, 55, 197–200.
- Rottenberg, J., Wilhelm, F.H., Gross, J.J., & Gotlib, I.H. (2002). Respiratory sinus arrhythmia as a predictor of outcome in major depressive disorder. *Journal of Affective Disorders*, 71, 265–272.
- Tabachnick, B.G., & Fidell, L.S. (1996). Using multivariate statistics. New York: Harper Collins College Publishers.
- Tarvainen, M.P., Ranta-aho, P.O., & Karjalainen, P.A. (2002). An advanced detrending method with application to HRV analysis. *IEEE Transactions Biomedical Engineering*, 49, 172–175.
- Turkington, P.M., Sircar, M., Allgar, V., & Elliott, M.W. (2001). Relationship between obstructive sleep apnoea, driving simulator performance and risk of road traffic accidents. *Thorax*, 56, 800–805.
- Verwey, W.B., & Zaidel, D.M. (1999). Preventing drowsiness accidents by an alertness maintenance device. Accident Analysis Prevention, 31, 199–211.
- Wijesuriya, N., Tran, Y., & Craig, A. (2007). The psychophysiological determinants of fatigue. *International Journal of Psychophysiology*, 63, 77–86.
- Wyller, V.P., Barbeiri, R., Thaulow, E., & Saul, J.P. (2008). Enhanced vagal withdrawal during mild orthostatic stress in adolescents with chronic fatigue. *Annals of Noninvasive Electrocardiology*, 13, 67–73.
- Wyller, V.P., Saul, J.P., Amlie, J.P., & Thaulow, E. (2007). Sym-

pathetic predominance of cardiac regulation during mild orthostatic stress in adolescents with chronic fatigue. *Clinical Physiology and Functional Imaging*, 27, 231–238.

- Yeragani, V.K., Pohl, R., Berger, R., Balon, R., Ramesh, C., Glitz, D. et al. (1993). Decreased heart rate variability in panic disorder patients: A study of power-spectral analysis of heart rate. *Psychiatry Research*, 46, 89–103.
- Yoshiuchi, K., Quigley, K.S., Ohashi, K., Yamamoto, Y., & Natelson, B.H. (2004). Use of time-frequency analysis to investigate temporal patterns of cardiac autonomic response during head-up tilt in chronic fatigue syndrome. *Autonomic Neuroscience-Basic and Clinical*, 113, 55–62.

#### Accepted for publication: August 28, 2009

Yvonne Tran

Centre in Health Technologies University of Technology PO Box 123 Broadway Sydney, NSW 2007 Australia Tel. +61 2 9514-1357 Fax +61 2 9514-1359 E-mail yvonne.tran@uts.edu.au