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Temperament, health-related behaviors, and autonomic cardiac regulation: The cardiovascular risk in young Finns study

Sampsa Puttonen [a,b,*], Marko Elovainio [c], Mika Kivimäki [d], Tuomas Koskinen [e], Laura Pulkki-Råback [a], Jorma S.A. Viikari [f], Olli T. Raitakari [g], Liisa Keltikangas-Järvinen [a]

[a] *Department of Psychology, PO Box 9, University of Helsinki, FIN-00014 Helsinki, Finland*
[b] *Finnish Institute of Occupational Health, Topeliuksenkatu 41 a A, FIN-00250 Helsinki, Finland*
[c] *National Research and Development Centre for Welfare and Health, PO Box 220, FIN-00531 Helsinki, Finland*
[d] *International Centre for Health and Society, Department of Epidemiology and Public Health, University College London, 1-19 Torrington Place, WC1E 6BT London, UK*
[e] *Cardiorespiratory Research Unit, Kiinamyllynkatu 10, University of Turku, FIN-20520 Turku, Finland*
[f] *Department of Medicine, Kiinamyllynkatu 4-8, University of Turku, FIN-20520 Turku, Finland*
[g] *Department of Clinical Physiology, Kiinamyllynkatu 4-8, University of Turku, FIN-20521 Turku, Finland*

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ABSTRACT

Temperament, as indicated by Cloninger's psychobiological model predicts coronary heart disease risk, but its association with autonomic cardiac regulation, a potential mediating mechanism, is unclear. We examined the associations between temperament traits and autonomic cardiac regulation in a resting situation in 798 women and 580 men derived from a population-based sample. After adjustment for age and sex, harm avoidance was associated with lower level of high-frequency (HF) variation, root mean square successive differences (RMSSDs), the percentage of successive R–R intervals >50 ms (pNN50) and higher heart rate (HR) (all $p \leq 0.005$), suggesting that harm avoidance is related to low parasympathetic activity. Additional adjustments for behavioral factors attenuated these associations more than the adjustment for biological risk factors. Novelty seeking was associated with higher RMSSD ($p = 0.007$) and pNN50 ($p = 0.012$) and lower heart rate ($p < 0.001$). With adjustment for behavioral risk factors, the associations with RMSSD ($p = 0.136$) and pNN50 ($p = 0.236$) attenuated to the null, but adjustment for biological risk factors had little effect. Reward dependence and persistence were unrelated to indices of cardiac regulation.

1. Introduction

Dysfunctions in autonomic cardiac control, measured by heart rate and heart rate variability (HRV), are important markers of future health risk. For example, elevated resting HR predicts the development of hypertension (Dyer et al., 1980; Garrison et al., 1987), increases the risk for progression of atherosclerosis (Beere et al., 1984; Kaplan et al., 1987), and is a risk factor for sudden myocardial ischemia (Palatini and Julius, 1997) and cardiac death in the general population (Kannel et al., 1987; Seccareccia et al., 2001). Lower HRV, in turn, has been linked with subclinical inflammation (Sajadieh et al., 2004), the development of hypertension and diabetes (Carnethon et al., 2003; Schroeder et al., 2003), increased coronary heart disease (CHD) incidence (Liao et al., 1997), and higher all cause mortality (Dekker et al., 2000).

Personality-related factors are known to contribute to the development of poor health including atherosclerosis and CHD. In prospective studies, anger (Matthews et al., 1998) (Räikkönen et al., 2004) and hostility (Julkunen et al., 1994; Pollitt et al., 2005) have been shown to predict the progression of subclinical atherosclerosis and studies have shown an association between incident CHD events and anger (Chang et al., 2002; Kawachi et al., 1996; Williams et al., 2000). Similarly, non-clinical depressive tendencies have shown to be independently associated with increased atherosclerosis (Elovainio et al., 2005) and the progression of carotid atherosclerosis (Haas et al., 2005), and to be a significant predictor of disease end points, such as myocardial infarction and mortality (Barefoot and Schroll, 1996; Wulsin et al., 2005). As regards to temperament, previous studies suggest that certain temperament dimensions are markers of increased risk of CHD (Keltikangas-Järvinen et al., 1999; Lovallo and Gerin, 2003).

* Corresponding author at: Department of Psychology, PO Box 9, University of Helsinki, FIN-00014 Helsinki, Finland. Tel.: +358 9 191 29524; fax: +358 9 191 29521.
E-mail addresses: Sampsa.Puttonen@helsinki.fi, sampsa.puttonen@ttl.fi (S. Puttonen).

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Cloninger's psychobiological model of temperament and character (Cloninger, 1987; Cloninger et al., 1993) is a leading conceptualization of temperament. The four temperament dimensions novelty seeking (NS), harm avoidance (HA), reward dependence (RD), and persistence (P), in particular, have attracted interest among researchers because they seem to be associated with clinical outcomes such as psychiatric disorders and precursors of somatic diseases. Novelty seeking is viewed as a heritable bias in the activation or initiation of behaviors such as frequent exploratory activity in response to novelty. High novelty seekers are characterized by impulsive decision making and active avoidance of frustration (Cloninger et al., 1993). Harm avoidance refers to inhibition or cessation of behaviors, and is manifest as anticipatory worry, fear of uncertainty, shyness with strangers, and rapid fatigability. Reward dependence predicts the facility in the formation of conditioned signals of reward, particularly to verbal signals of social approval. Individuals who are high in reward dependence tend to be sentimental, eager to help and please others, and warmly sympathetic. Persistence predicts resistance to the extinction of behavior despite intermittent reinforcement and it is measured in terms of perseverance despite frustration and fatigue (Cloninger et al., 1993).

The aim of the present study was to explore whether temperament dimensions assessed by the temperament and character inventory are related to resting autonomic cardiac control in a large population-based cohort of healthy men and women. Previously Cloninger's temperament dimensions have been associated with the development of metabolic syndrome (Keltikangas-Järvinen et al., 1999), an important risk factor for CHD (Lakka et al., 2002). Little is known about physiological pathways of this association, however. Considering that dysfunction in autonomic cardiac control is a precursor of CHD and related morbidity, we hypothesized that temperament may be linked with disease risk through autonomic nervous system (ANS) dysfunction indicated by elevated resting heart rate and reduced HRV. One physiological pathway that may connect temperament to cardiovascular health is the ANS. According to Cloninger's model, the neurobiological processes associated with temperament dimensions are functionally organized as independently varying brain systems which are responsible for the ANS activation related to temperament dispositions (Cloninger et al., 1994).

We used both frequency and time domain HRV indices which are among the most widely used noninvasive measures of ANS control of the heart. Short-term HRV measures are fairly stable (Sloan et al., 1995; Tarkiainen et al., 2005) and have a significant heritable component (Singh et al., 2001). Heart rate and beat-to-beat variability of the heart's rhythm are largely under the control of the ANS. Under resting conditions, vagal (parasympathetic) tone prevails (Levy, 1971) and variations in heart period are largely dependent on vagal modulation (Chess et al., 1975). Temperament dimensions are known to be associated with health risk behaviors (Cloninger et al., 1994; Ravaja and Keltikangas-Järvinen, 2001) and may also reflect biological coronary risk factors, such as blood pressure (Keltikangas-Järvinen et al., 1999). Therefore, we also studied the contribution of health behaviors and biological coronary risk factors to the association between temperament and autonomic cardiac control.

The psychobiological model does not suggest specific associations between temperament dimensions and ANS activity in a resting situation. Impulsivity, a personality factor that correlates with novelty seeking (Zuckerman and Cloninger, 1996), has been found to associate with lower levels of resting heart rate (Mathias and Stanford, 2003) and novelty seeking has been found to be inversely associated with resting stress hormone concentrations (i.e. cortisol) (Tyrka et al., 2007). Based on this knowledge, we hypothesized that novelty seeking would be associated with low HR and high vagal modulation of the HR. Studies utilizing constructs similar to harm avoidance (i.e., anxiety) suggest that harm avoidance would be related to higher HR and reduced levels vagal modulation of the HR (Kawachi et al., 1995; Watkins et al., 1998). Although reward dependence and persistence have been shown to be associated with CHD risk factors (Keltikangas-Järvinen et al., 1999), their possible associations with cardiac activity is somewhat unclear and the present analyses on reward dependence and persistence are necessary to some extent exploratory. Reward dependence includes aspects opposite to the traditional psychological CHD risk factors and it is theoretically linked with low adrenergic activity (Cloninger, 1987; Cloninger et al., 1993). Thus, reward dependence was thought to be associated with a profile of low HR and high vagal modulation of the HR and/or low sympathetic modulation of the HR. As workers, individuals scoring high on persistence are confident, hard-working, ambitious, heroic, and forceful overachievers who frequently push themselves to exhaustion (Cloninger, 1987). We hypothesized that this kind of behavioral style might induce recurrent allostatic load that expresses itself in high levels of HR and low levels of vagal modulation of the HR.

2. Methods

2.1. Subjects

The subjects were 1384 males ($n = 580$) and females ($n = 798$) aged 24–39 participating in the prospective epidemiological cardiovascular risk in young Finns study (Åkerblom et al., 1991), where the development of risk factors for CHD has repeatedly been monitored since 1980. The original sample of the young Finns study consisted of 3596 randomly selected healthy Finnish children and adolescents in the age cohorts of 3, 6, 9, 12, 15, and 18 years. In the present study, subjects were derived from the respondents of the sixth follow-up in 2001 (Juonala et al., 2004; Raitakari et al., 2003). HRV was assessed in 2054 participants and temperament in 2104 participants. Only those with complete information on all the study variables were included in the study. A total of 1574 participants had valid data on both temperament and HRV. A missing value in one of the biological factors or very high triglyceride level (>4 mmol/l) reduced the number of participants to 1537, and finally, 153 participant had a missing value in one of the health behavioral factors, resulting in the final sample of 1384 participants. It has been shown previously that those who dropped out during the 21-year follow-up period were more often male, had a lower socio-economic status, and had a more sedentary lifestyle than those who had stayed (Juonala et al., 2004; Pulkki-Råback et al., 2005; Raitakari et al., 2003). With respect to serum lipoprotein levels, blood pressure, smoking, and body mass index (BMI), there has been no systematic selection in drop-out (Juonala et al., 2004; Raitakari et al., 2003). The study was approved by local ethics committees and all subjects gave written informed consent.

2.2. Temperament

Temperament was measured by the temperament and character inventory (Cloninger et al., 1993, 1994), a self-administrated questionnaire assessing four temperament dimensions comprising 107 items. The temperament dimensions include novelty seeking (four subscales: exploratory excitability, impulsiveness, extravagance, and disorderliness), harm avoidance (four subscales: anticipatory worry and pessimism, fear of uncertainty, shyness with strangers, and fatigability and asthenia), reward dependence (three subscales: sentimentality, attachment, and dependence), and persistence. For each dimension, the mean score of all items were summed up to yield a temperament level index, which was treated as a continuous variable. The Cronbach's alpha reliabilities for the scales were 0.85, 0.92, 0.80, and 0.64, respectively.

2.3. Measures of cardiac regulation

Electrocardiogram (ECG) data were measured during a period of 3 min controlled breathing at frequency of 0.25 Hz with three Ag/AgCl electrodes placed in a configuration which closely corresponds the connection V3. During ECG measurement, participants were in supine position. The ECG signal was digitized at 200 Hz. From a stationary data period R peaks were identified and the RR time series and HR time series were formed. The mean number of analysed R-peaks was 196 (S.D. 34). We excluded data in subjects with three or more ectopic beats ($n = 87$), and manually interpolated all recordings including less than three ectopic beats. Heart rate variability indices were calculated in the time domain and the frequency domain using commercial WinCPRS program (Absolute Aliens, Turku, Finland), a program for general analysis of physiological data. To calculate the frequency domain measures the time series were detrended and resampled at 5 Hz. The power density spectra of HRV was then computed over low-frequency and high-frequency bands using a fast Fourier transform algorithm and Hanning window function. The frequency domain measures subtracted form heart rate spectra were high-frequency (HF) band (0.15–0.5 Hz), low-frequency (LF) band (0.04–0.15 Hz), and LF/HF ratio. The time domain measures calculated were root mean square successive differences (RMSSDs) and the percentage of successive R–R intervals >50 ms (pNN50). HF, RMSSD, and pNN50 reflect mainly vagally mediated influences to the myocardium, whereas LF/HF is thought to be associated with sympathetic control of the heart rhythm. Although LF has sometimes been treated as an indicator of sympathetic activity LF, as well as HR, are considered as better indicators of the joint effects of sympathetic and parasympathetic activity (Berntson et al., 1997; Camm et al., 1996).

2.4. Health behavioral and biological risk factors

Health-related behaviors were cumulative smoking (never smokers = 1, those who have ever smoked on daily basis = 2), alcohol consumption (how often beer, wine, or spirits were used at least six portions or more at a time (one portion equals to 12 g of alcohol): 1 = once a year or never, 2 = two to six times a year, 3 = once a month, 4 = two to three times a month, 5 = once a week, 6 = at least twice a week), and physical activity (Telama et al., 1997) (an index consisting of five variables describing intensity of physical activity, frequency of intensive physical activity, hours/week of intensive physical activity, average duration of physical activity, and participation in structured sports, e.g. in a sports club; $\alpha = 0.78$). In the current study, "One hour a week of intensive physical activity" was coded as one, and sports club membership was coded as follows: no = 1, yes = 2, yes—once a week = 2, yes—many hours/times a week = 3. High scores on physical activity index indicate high physical activity. Dietary fat was assessed as the type of fat most often used in daily food preparing (1 = vegetable oil, 2 = margarine, and 3 = butter) (Leino et al., 1999). Body mass index (weight (kg)/height^2 (m^2)) was categorized as follows: 1 = less than 25, 2 = 25.0–29.9, and 3 = 30 or more.

All measurements of lipid levels were taken in duplicate in the same laboratory using standardized enzymatic methods measuring levels of high-density lipoprotein (HDL-C) cholesterol and triglycerides. The low-density lipoprotein (LDL-C) cholesterol concentration was calculated by the Friedewald formula (Friedewald et al., 1972). Systolic blood pressure (SBP) was measured with a random zero sphygmomanometer and the average of three blood pressure measurements were used in the statistical analysis. Details of the methods have been reported elsewhere (Raitakari et al., 2003).

2.5. Statistical analysis

HF, LF, LF/HF, RMSSD, and triglyceride values were log transformed to correct for skewness. The associations between autonomic cardiac control and temperament dimensions were assessed using multiple linear regressions. We formed four different hierarchical regression models. The first model was adjusted for age and sex. The second model included, in addition to age and sex, health behavior factors (BMI, dietary fat, smoking, physical activity, and alcohol consumption). The third model included age, sex, and biological factors (triglycerides, HDL-cholesterol, LDL-cholesterol, and SBP). The fourth was a fully adjusted model including all covariates. The analyses were performed with the SAS software, Version 9.0 (SAS Institute, Cary, NC).

3. Results

The characteristics of the respondents are presented in Table 1. The mean age of the subjects was 31.6 years and 58% were women. In the present sample participants who were excluded were more often males ($p < 0.001$), were more often smokers ($p < 0.001$), used more often butter in food making ($p = 0.001$), and had somewhat lower level of HDL-C ($p = 0.046$).

3.1. Univariate associations of temperament and cardiac regulation with covariates

Harm avoidance showed a direct association with HDL-C and was inversely associated with physical activity and alcohol use. Novelty seeking was directly associated with smoking, alcohol use, BMI, and triglycerides and inversely with SBP. Reward dependence showed a pattern of associations characterized by favorable physiology (low levels of SBP, triglycerides, and LDL-C and a high level of HDL-C) and health-related behaviors (low levels of BMI, dietary fat, and alcohol use). Persistence was directly associated with physical activity (Table 2).

Table 1
Characteristics of respondents ($n = 1384$)

Variable	*n*	%	Mean (S.D.)	Range
Age	1384		31.6 (5.1)	24.0–39.0
Sex				
Males	581	42.0		
Females	803	58.0		
Temperament				
Novelty seeking	1384		2.98 (0.41)	1.48–4.58
Harm avoidance	1384		2.59 (0.52)	1.00–4.86
Reward dependence	1384		3.36 (0.43)	1.71–4.46
Persistence	1384		3.21 (0.55)	1.50–4.75
Body mass index				
<25	799	57.7		
25.0–29.9	421	30.4		
30 or more	164	11.9		
Dietary fat				
Vegetable oil	678	49.0		
Margarine	367	26.5		
Butter	339	24.5		
Smoking (cumulative)				
Never smoker	823	59.5		
Ever smoker	561	40.5		
Physical activity	1384		9.6 (2.3)	5.0–16.0
Heavy alcohol use[a]	1384		1.5 (1.4)	1.0–6.0
Triglycerides (mmol/l)[b]	1384		1.26 (0.64)	0.30–3.90
HDL-cholesterol (mmol/l)	1384		1.31 (0.32)	0.31–2.82
LDL-cholesterol (mmol/l)	1384		3.27 (0.84)	1.10–7.90
Systolic blood pressure (mmHg)	1384		116.2 (13.1)	84.0–166.7
HF (log)	1384		6.31 (1.16)	1.95–9.80
RMSSD (log)	1384		3.70 (0.61)	1.61–5.60
pNN50	1384		25.4 (23.8)	0–88.6
LF (log)	1384		5.68 (0.96)	1.10–8.80
LF/HF (log)	1384		3.98 (1.03)	1.06–8.31
HR	1384		66.1 (10.4)	39.3–112.8

[a] How often alcohol were used at least six portions or more at a time 1 = once a year or never, 2 = two to six times a year, 3 = once a month, 4 = two to three times a month, 5 = once a week, and 6 = at least twice a week.
[b] Log-transformed values for triglycerides were used in the analyses.

Age, sex, physical activity, and SBP were most strongly associated with cardiac measures. HDL-cholesterol was unrelated to variables of parasympathetic control (HF, pNN50, and RMSSD) but was significantly associated with LF, LF/HF, and HR ($p < 0.05$ for all). Dietary fat was unrelated to cardiac regulation (Table 3).

3.2. Multivariate associations of temperament and cardiac regulation

In the age and sex adjusted regression models harm avoidance was associated with a profile of reduced vagal modulation of the heart rate (Table 4). This was indicated by negative relations to HF, RMSSD, pNN50 and a positive relation to HR ($p \leq 0.005$ for all). Further adjustments for health-related behaviors and biological risk factors did not attenuate the associations significantly. However, in the fully adjusted model only the direct association between harm avoidance and HR was significant ($p = 0.011$). High level of HA was also associated with reduced LF band variability ($p = 0.032$), but this association attenuated after controlling for health-related behaviors ($p = 0.121$). In the age and sex adjusted model, NS was positively associated with RMSSD ($p = 0.007$), pNN50 ($p = 0.012$) and negatively with HR ($p < 0.001$) (Table 5). Taking into account the effects of health-related behaviors dropped the associations of RMSSD and pNN50, suggesting that the association between NS and cardiac control is partly mediated by health behavioral factors. In the fully adjusted models none of the associations of novelty seeking was significant. The tempera-

Table 2
Standardized univariate regression coefficients (β) of demographics and risk factors on temperament in men and women (n = 1384)

Variable	NS		HA		RD		P	
	β	p-Value	β	p-Value	β	p-Value	β	p-Value
Age	−0.04	0.164	0.01	0.656	−0.08	0.002	−0.07	0.013
Sex[a]	−0.10	<0.001	−0.19	<0.001	−0.42	<0.001	0.03	0.309
Body mass index	0.06	0.023	0.03	0.321	−0.09	<0.001	−0.04	0.144
Dietary fat	−0.04	0.105	−0.00	0.869	−0.10	<0.001	−0.00	0.881
Smoking	0.21	<0.001	−0.01	0.794	−0.03	0.214	−0.04	0.172
Physical activity	0.05	0.059	−0.19	<0.001	0.03	0.263	0.08	0.003
Heavy alcohol use	0.22	<0.001	−0.12	<0.001	−0.12	<0.001	0.02	0.511
Triglycerides (mmol/l)	0.06	0.026	0.01	0.578	−0.08	0.003	−0.01	0.787
HDL-C (mmol/l)	−0.04	0.146	0.07	0.013	0.14	<0.001	0.02	0.420
LDL-C (mmol/l)	−0.04	0.129	−0.01	0.825	−0.10	<0.001	−0.05	0.068
Systolic BP (mmHg)	−0.08	0.002	−0.01	0.647	−0.19	<0.001	−0.00	0.996

Note. NS = novelty seeking, HA = harm avoidance, RD = reward dependence, P = persistence.
[a] 1 = women, 2 = men.

Table 3
Standardized univariate regression coefficients (β) of risk factors on HR and HRV measures in men and women (n = 1384)

Variable	HF		RMSSD		pNN50		LF		LF/HF		HR	
	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value
Age	−0.27	<0.001	−0.23	<0.001	−0.23	<0.001	−0.13	<0.001	0.18	<0.001	−0.01	0.731
Sex[a]	−0.11	<0.001	−0.03	0.274	−0.05	0.077	0.24	<0.001	0.34	<0.001	−0.21	<0.001
Body mass index	−0.14	<0.001	−0.12	<0.001	−0.10	<0.001	−0.04	0.193	0.12	<0.001	0.04	0.093
Dietary fat	−0.02	0.524	−0.01	0.689	−0.02	0.514	0.00	0.957	0.02	0.051	−0.00	0.983
Smoking	0.06	0.023	0.09	<0.001	0.09	<0.001	0.03	0.276	−0.04	0.012	−0.14	<0.001
Physical activity	0.12	<0.001	0.15	<0.001	0.15	<0.001	0.10	<0.001	−0.04	0.130	−0.20	<0.001
Heavy alcohol use	0.02	0.500	0.07	0.011	0.08	0.005	0.10	<0.001	0.07	0.007	−0.17	<0.001
Triglycerides (mmol/l)	−0.14	<0.001	−0.14	<0.001	−0.13	<0.001	−0.04	0.117	0.12	<0.001	0.10	<0.001
HDL-C (mmol/l)	0.03	0.250	−0.00	0.994	−0.01	0.693	−0.06	0.038	−0.09	0.001	0.11	<0.001
LDL-C (mmol/l)	−0.15	<0.001	−0.14	<0.001	−0.14	<0.001	−0.06	0.029	0.11	<0.001	0.05	0.078
Systolic BP (mmHg)	−0.24	<0.001	−0.25	<0.001	−0.23	<0.001	−0.00	0.721	0.26	<0.001	0.19	<0.001

[a] 1 = women, 2 = men.

ment dimensions reward dependence and persistence did not show any associations with cardiac control variables.

In the preceding analyses, sex and age were used as covariates. This procedure does not allow us to make inference about the moderating effects of these variables. To answer this, we tested the temperament × sex and temperament × dichotomized age (young = 24–30 years of age and old = 33–39 years of age) interactions in predicting HRV and HR. The results of the regression analyses showed no significant interactions between sex and temperament (all p-values >0.05), whereas all the novelty seeking × age interactions were significant (p-values from <0.001 to 0.028): The association between novelty seeking and cardiac autonomic control was stronger in the group of younger participants. Finally, we calculated the sex and age adjusted associations between NS subscales and HRV and HA subscales and HRV. This was done to test for possible differences in the effect of subscales in the significant associations. To maintain an error rate of 0.05, we adjusted the critical p-value to 0.0125 (=0.05/4).

The harm avoidance subscale fear of uncertainty was associated with RMSSD, pNN50, and HR (p-values ≤0.008) and similarly, shyness with strangers was related to RMSSD, pNN50, and HR (p-values ≤0.006). Fatigability and asthenia subscale of HA was significantly associated with HF, RMSSD, pNN50, and HR (p-values from 0.005 to 0.008), while anticipatory worry and pessimism scale was significantly associated only with HR (p = 0.005). None of the subscales showed a significant association with LF (p-values ranged from 0.019 to 0.395). None of the NS subscales was significantly associated with RMSSD (p-values from 0.028 for impulsiveness to 0.267 for disorderliness), or pNN50 (p-values from 0.0019 for extravagance to 0.359 for disorderliness). Exploratory excitability (p < 0.001) and impulsiveness (p = 0.001), were significantly associated with HR, while extravagance and disorderliness were not (p-values 0.025 and 0.019). In sum, the subscale differences were not large, although the NS exploratory excitability and impulsiveness and HA fatigability and asthenia scales tended to have strongest associations with autonomic cardiac activity.

Table 4
Standardized regression coefficients (β) of harm avoidance on cardiac measures in men and women (n = 1384)

	HF		RMSSD		pNN50		LF		LF/HF		HR	
	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value
Step 1	−0.07	0.005	−0.09	<0.001	−0.09	<0.001	−0.06	0.032	0.03	0.208	0.13	<0.001
Step 2	−0.06	0.037	−0.07	0.012	−0.07	0.012	−0.04	0.121	0.02	0.362	0.09	<0.001
Step 3	−0.06	0.019	−0.08	0.003	−0.08	0.003	−0.05	0.063	0.02	0.367	0.11	<0.001
Step 4	−0.04	0.121	−0.05	0.058	−0.05	0.055	−0.04	0.185	0.01	0.621	0.06	0.011

Note. Step 1: model adjusted for age and sex; step 2: model adjusted for age, sex, body mass index, dietary fat, smoking, physical activity, and alcohol consumption; step 3: model adjusted for age, sex, triglycerides, HDL-cholesterol, LDL-cholesterol, and systolic blood pressure; step 4: model adjusted for age, sex, body mass index, dietary fat, smoking, physical activity, alcohol consumption, triglycerides, HDL-cholesterol, LDL-cholesterol, and systolic blood pressure.

Table 5
Standardized regression coefficients (β) of novelty seeking on cardiac measures in men and women (n = 1384)

	HF		RMSSD		pNN50		LF		LF/HF		HR	
	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value
Step 1	0.04	0.097	0.07	0.007	0.07	0.012	0.01	0.687	−0.04	0.120	−0.11	<0.001
Step 2	0.02	0.393	0.04	0.136	0.03	0.263	0.01	0.828	−0.02	0.418	−0.06	0.017
Step 3	0.04	0.127	0.07	0.011	0.06	0.022	0.01	0.624	−0.03	0.198	−0.10	<0.001
Step 4	0.01	0.770	0.02	0.432	0.01	0.708	0.00	0.932	−0.01	0.800	−0.04	0.148

Note. Step 1: model adjusted for age and sex; step 2: model adjusted for age, sex, body mass index, dietary fat, smoking, physical activity, and alcohol consumption; step 3: model adjusted for age, sex, triglycerides, HDL-cholesterol, LDL-cholesterol, and systolic blood pressure; step 4: model adjusted for age, sex, body mass index, dietary fat, smoking, physical activity, alcohol consumption, triglycerides, HDL-cholesterol, LDL-cholesterol, and systolic blood pressure.

4. Discussion

Our results showed that adulthood temperament, as defined by Cloninger's model, contributes to autonomic cardiac control. To our knowledge this is the first study examining these relations in a large population-based sample. We found that increased levels of harm avoidance were associated with lower vagal control and higher resting heart rate, an ANS profile reflecting higher CHD risk. In contrast, novelty seeking showed positive associations with indices of parasympathetic control activity (excluding HF, which was only marginally significant) and lower heart rate, reflecting a lower CHD risk. Other temperament dimensions in Cloninger's psychobiological model were unrelated to resting cardiac activity.

Present findings suggest that a high level of harm avoidance may be linked to the development of ill health through alterations in ANS function (Dekker et al., 2000; Dyer et al., 1980; Kaplan et al., 1987; Schroeder et al., 2003). In the age and sex adjusted model, harm avoidance was inversely associated with parasympathetic control (HF, pNN50, RMSSD) and directly with HR. Individuals scoring high on harm avoidance were also prone to a sedentary lifestyle, lower alcohol use, and higher HDL-cholesterol. However, adjustment for the health behaviors attenuated the relationship between harm avoidance and cardiac control only slightly, suggesting that the behavioral association may not be an important pathogenic mechanism. In the full model, adjusted for health-related behaviors and biological factors, only the association for HR remained significant, implying that HR may be most strongly directly associated with harm avoidance. Our findings of harm avoidance are in line with previous studies of anxiety, a construct similar to harm avoidance (Ball et al., 2002; Giancola et al., 1994). These studies have revealed that trait anxiety is associated with lower parasympathetic modulation of the heart rate (Kawachi et al., 1995; Thayer et al., 1996; Watkins et al., 1998), although contradicting results also exist (Virtanen et al., 2003). The associations for harm avoidance were somewhat mixed in regard to possible health risk factors. The strongest association was found with sedentary life-style, but it was also associated with higher HDL-cholesterol and lower alcohol use.

The relation between novelty seeking and high parasympathetic cardiac control was mostly explained by health-related behaviors and attenuation in the strength of association was likely to be attributable to differences in smoking habits and heavy alcohol use. This was confirmed by the analyses of individual health behavioral factors. Adjustment for smoking (in addition to sex and age) attenuated the associations for pNN50 and RMSSD to null (βs 0.04 and 0.05 and p-values 0.124 and 0.092). Adjustment for heavy alcohol use resulted in comparable changes in the associations between novelty seeking and pNN50 and RMSSD (βs 0.04 and 0.05 and p-values 0.118 and 0.065). The univariate analyses indicated that novelty seeking was associated with smoking and heavy alcohol use, and that smoking and heavy alcohol use were associated with higher parasympathetic control, that is, with indicators of lower cardiac risk (pNN50 and RMSSD). These findings seem contradictory at first glance, because traditionally smoking and heavy alcohol use have been associated with adverse cardiovascular outcomes. It is, however, possible that novelty seeking may explain both associations and no true mediation would exist. In other words, novelty seekers may have naturally high levels of parasympathetic activity, and they are also likely to be stimulant users but the co-existence of these factors may explain also the attenuation of associations. In addition, the subjects were relatively young and the deleterious effects may have influenced their naturally higher parasympathetic activity. In line with reasoning was the finding that the associations of NS and HRV were stronger in younger subjects. However, longitudinal studies are needed in order to get firm answers to these questions. As for HA, adjustment for biological risk factors (lipids and blood pressure) had little effect on the results, suggesting that the relations of temperament and cardiac control are relatively independent of the lipid metabolism and blood pressure.

Our finding of an association between novelty seeking and lower heart rate is in agreement with a previous study on impulsiveness (Mathias and Stanford, 2003), which is a partially overlapping construct (Zuckerman and Cloninger, 1996). Novelty seeking was related to health-related and biological factors known to associate with adverse health outcomes with the exception of an inverse association with SBP. In our study, novelty seeking was directly associated with triglycerides and BMI, and in agreement with previous studies (e.g. Wills et al., 1994), with smoking and alcohol use. The psychobiological model of temperament (Cloninger, 1987) proposes that temperament may have both direct influences on ANS functioning and that temperament also modifies the behavioral choices of an individual. In congruence with previous observations, temperament was associated with several risk factors for CHD and the multivariate analyses suggested that especially health behaviors may influence the health effects of novelty seeking and harm avoidance. Thus, it may be possible to reduce health risks of temperament by interventions targeted to health behaviors. Temperament factors are generally viewed as stable predispositions and the health behaviors related them are also likely to be persistent (Cloninger et al., 1994). Therefore, an intervention program focusing on temperament-related health habits might not be as successful as an intervention targeted to health behaviors as well as psychological correlates that are viewed as more transient or malleable than temperamental factors. The present study focused on relatively young adults with ages from 24 to 39, and already at this age the temperament-related living habits appeared to be associated with ANS function. Therefore, possible interventions could be targeted to these age groups or preferably to even younger individuals.

Reward dependence was to resting autonomic cardiac control. However, reward dependence showed coherent and favorable associations with health behavioral and biological risk factors with the exceptions of being unrelated to smoking and physical activity.

One explanation for this comes from Cloninger's theory which proposes that persons high in RD are sensitive to clues of social rewards (Cloninger et al., 1993), and may therefore be prone to follow social norms regulating health-related behaviors. Persistence did not show any associations with autonomic cardiac control. In addition, our results suggest that persistence is relatively independent of risk factors, as it was only associated with physical activity.

The sample was restricted to men and women aged 24–39 and therefore further studies are warranted to confirm these findings in the general population. Although the present subjects were derived from a population-based sample some selection bias has occurred during the 21-year follow-up period. Those who have dropped have been more often male, had a lower socio-economic status, and had a more sedentary lifestyle than those who had stayed. With respect to serum lipoprotein levels, blood pressure, smoking, and BMI, there has been no systematic selection in drop-out, however. In the present study temperament and autonomic cardiac control were measured only once. The cross-sectional nature of the study does not allow us to infer causality and therefore additional studies with repeated measures of cardiac activity are needed to determine whether temperament predicts changes in the cardiovascular risk. Although we were able to include several potential risk factors as covariates in the analyses, there may be residual confounding by unmeasured variables or some of the measured variables, also. For example, the measures of dietary fat, smoking, and alcohol use were relatively crude.

Loss of participants was due to the large number of variables included in the study. In the present sample the excluded participants were more often men and there appeared to be some health selection in the sample, that is, those having worse health habits tended to drop-out (smoked more often, tended to use butter in food making, and had lower level of HDL-cholesterol). Health-related attrition may have led to restricted variance which, in turn, may lead to under-estimations rather than over-estimations of real effects (Harald et al., 2007; Matthews et al., 2006).

Our main finding was that harm avoidance is associated with a reduced vagal cardiac control, previously shown to predispose to impaired cardiovascular health, whereas novelty seeking was suggested to associate with higher level of vagal modulation of the heart rhythm. The associations between temperament and autonomic cardiac control reduced with adjustments for health behaviors, suggesting that the associations found for HA and, especially for NS, are influenced by health behavioral factors.

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