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A longitudinal study in youth of heart rate variability at rest and in response to stress

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Abstract

Background—Few longitudinal studies have examined ethnic and sex differences, predictors and tracking stabilities of heart rate variability (HRV) at rest and in response to stress in youths and young adults.

Methods—Two evaluations were performed approximately 1.5 years apart on 399 youths and young adults (189 European Americans [EAs] and 210 African Americans [AAs]; 190 males and 209 females). HRV was measured at rest and during a video game challenge.

Results—AAs showed significantly higher resting root mean square of successive differences (RMSSD) of normal R-R intervals and high-frequency (HF) power than EAs (Ps< 0.01). Females displayed larger decrease of RMSSD and HF during video game challenge than males (Ps< 0.05). These ethnic and sex differences were consistent across 1.5 years. No significant sex difference of resting HRV or ethnic difference of HRV response to stress was observed. In addition to age, ethnicity or sex, baseline resting HRV or HRV response to stress are predictors of the corresponding variables 1.5 years later (Ps< 0.01). Furthermore, weight gain indexed by either body mass index or waist circumference predicts declined resting HRV levels during follow up (Ps < 0.05). Tracking stabilities were high (>0.5) for resting HRV, but relatively low (<0.3) for HRV in response to stress.

Conclusion—AAs show higher resting HRV than EAs, and females display greater HRV response to stress than males; and these ethnic and sex differences are consistent across 1.5 years. Resting HRV declines with weight gain.

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None

Keywords

heart rate variability; longitudinal study; sex; ethnicity

1. Introduction

Heart rate variability (HRV) is a measure of cardiac autonomic regulation. It can be indexed by time- and frequency-domain parameters, of which root mean square of successive differences (RMSSD) of normal RR intervals and high-frequency power (HF) specifically reflect vagal activity (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Reduced HRV, mainly reflecting a decreased vagal control of the heart rhythm, is a predictor of all-cause mortality, arrhythmic events and sudden death after acute myocardial infarction as well as in the general population (Reinhardt *et al*., 1996; Dekker *et al.*, 1997; Thayer and Lane, 2007).

Ethnic and sex differences in resting HRV levels have been reported in the literature. Most of the available evidence(Liao *et al.*, 1995; Urbina *et al.*, 1998; Wang *et al.*, 2005) indicates that African Americans (AAs) have higher HRV than European Americans (EAs). The evidence on sex differences is more controversial with some studies showing higher HRV in females (Evans *et al*., 2001; Koskinen *et al.*, 2009) than in males or vice versa (Umetani *et al.*, 1998; Bonnemeier *et al.*, 2003). There are also studies reporting absence of any sex difference (Fagard *et al*., 1999; Sloan *et al*., 2008).

Physiological reactivity to behavioral or psychological stressors has long been regarded as a potential contributor to individual differences in cardiovascular risk (Treiber *et al*., 2003). Although ethnic and sex differences have been documented in sympathetic reactivity with AAs and males having a higher response than EAs and females (Light *et al*., 1994), only one study explored ethnic differences in cardiac vagal reactivity (Arthur *et al.*, 2004) and no study to date has looked at sex differences.

Above mentioned evidence on ethnic and sex differences in HRV at rest or in response to stress is based on cross-sectional studies. For ethnic and sex differences in HRV to be meaningful the differences must be reliable. We are not aware of any study that has addressed this question. Therefore, in the present study which includes a large number of EA and AA youth and young adults followed for 1.5 years, our first aim was to examine the ethnic and sex differences in HRV at rest and in response to stress and the reliability of these differences over time.

Besides ethnicity and sex, cross-sectional studies have shown that several other factors including aging (Liao *et al*., 1995), obesity (Gutin *et al.*, 2005) and chronic stress (Lucini *et al.*, 2005) are associated with decreased HRV. However, all of the existing evidence stems from cross-sectional studies. Therefore, the second purpose of this study was to longitudinally examine the effect of these factors on HRV at rest and in response to stress 1.5 years later. Furthermore, although HRV has been increasingly used as a predictor of cardiovascular health, few studies have investigated the stability of HRV over time (i.e., tracking), especially for HRV in response to stress. Accordingly, the third purpose was to examine the tracking stabilities of HRV at rest and in response to stress.

2. Methods

The present study comprised subjects from a longitudinal cohort which was established in 1989 to study the development of cardiovascular risk factors. It included almost equal number of AA and EA youths with evaluations conducted annually. All the subjects were recruited from

the southeastern United States and were overtly healthy and free of any acute or chronic illness based on parental report. Study design, selection criteria and the criteria to classify subjects as AAs or EAs for the longitudinal study have been described previously (Dekkers *et al.*, 2002). A total of 399 subjects including 189 EAs (105 males and 84 females) and 210 AAs (85 males and 125 females) who had beat-to-beat heart rate recorded both in 2003 and 2005 during two routine scheduled examinations were available for this study. These two visits were approximately 1.5 years apart and subjects' mean age at the first assessment (visit 1) was 23.1 with a range of 14.8–30.9. The Institutional Review Board at the Medical College of Georgia had given approval for the study. Informed consent was provided by all subjects and by parents if subjects were <18 years.

At both visits, height, weight and waist circumference were measured as described elsewhere (Dekkers et al., 2002). Body mass index (BMI) was calculated as a measure of general obesity, and waist circumference (WC) was used as an index of central obesity. Blood pressure (BP) was measured with the Dinamap Vital Signs Monitor (model 1864 SX; Criticon Incorporated, Tampa, FL). BP measurements were taken at the 11th, 13th, and 15th minutes during a 15-minute supine relaxation period. The average of the last 2 readings was used to represent systolic BP (SBP) and diastolic BP (DBP) values. Socioeconomic status (SES) was used as a proxy for environmental stress exposure and indexed by the number of years of father's education attainment. Its level as measured at the midpoint of the study was taken as a representative for the whole study period, because it remained highly stable across the years of the study.

Continuous RR intervals were recorded by BioZ (CardioDynamics, San Diego, CA) impedance monitors. Four dual sensors connected to the BioZ were placed on the subject's neck and thorax, which formed 4 ECG vectors. These ECG vectors can be detected by the BioZ. The BioZ then converted the RR interval into beat-to-beat heart rate with precision of 2 decimal places, including a record of the real time of each beat. The instrument and recording procedure were used both at rest and during stress. Subjects rested quietly in a supine position for 15 minutes. At the 11th, 13th, and 15th minute, a 30-second continuous period of RR intervals was recorded. Subjects also performed a modified version of the video game protocol of Murphy et al (Murphy *et al.*, 1992). Instructions for the video game task "Breakout" have been standardized via videotape in which an adult female of the same ethnicity provides instructions and a demonstration without regard to sex. The subject will lie supine on a hospital bed. A 25 inch color television monitor will be positioned two meters away and at a height and angle comfortable for viewing. The 10 min session of Breakout was played under the condition of challenge (i.e., money incentive) without harassment. During the 10-minute stress task, a 30-second continuous period of RR intervals was recorded once every 2 minutes. A total of 37 subjects also had continuous RR intervals recorded for the entire resting and stress period.

Prior to calculation of HRV parameters, the raw RR interval data were processed for artifacts using the following two criteria: (1) RR intervals were between 300 and 2000 ms; (2) successive RR interval ratios were between 0.8 and 1.2 (Timonen *et al.*, 2006). Software developed by Tarvainen et al (Kubios HRV analysis, version 2.0 beta; Tarvainen and Niskanen) was used to generate the HRV parameters from the recorded RR intervals. One time-domain measure, RMSSD, and one frequency-domain measure, HF (the power between the 0.15 and 0.40 Hz band, using Fast Fourier Transformation), were used in the present study. Both measures specifically reflect vagal activity and have been recommended by the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996).

HRV parameters at rest and during stress were calculated based on the combination of the three 30-second segments of continuous RR intervals at rest and five 30-second segments of RR intervals during the video game challenge. Based on the data from the 37 subjects who also had continuous RR intervals recorded for the entire resting and stress period, we observed that HRV parameters calculated from the combination of these 30-second segments were highly correlated ($r>0.95$) with the HRV parameters calculated from the entire resting and stress period. The responses of RMSSD and HF to stress were indexed by the (stress-rest)/rest ratio.

To examine whether there was an ethnic/sex difference in HRV at rest or in response to stress and whether the difference was consistent across the two visits, repeated measures analysis of variances (ANOVAs) were used to compare RMSSD and HF at rest and in response to stress across the two visits. The potential interactions of ethnicity*sex, ethnicity*visit, sex*visit, and ethnicity*sex*visit were also tested. Multiple regression analyses were performed to examine the potential predictors of HRV at rest and in response to stress at visit 2. First, in the base model the effects of age, sex and ethnicity were examined. Second, HRV at rest or in response to stress, SES, BMI and waist circumference at visit 1 as well as BMI and waist circumferences changes from visit 1 to visit 2 were entered into the base model separately, along with their interactions with ethnicity and sex. Partial correlation coefficients were used to examine the tracking stabilities of HRV at rest and in response to stress across the two visits adjusting for age, ethnicity and sex.

Prior to analysis, RMSSD and HF at rest were log-transformed to obtain a better approximation of the normal distribution. In regression analyses, BMI and waist circumference were centered on their means. Repeated measures ANOVA were performed using SPSS 15.0 (Chicago, IL) and all the other statistical analyses were done using STATA 8.0 (StataCorp, College Station, TX).

3. Results

Descriptive statistics of demographics, anthropometric measures, blood pressure, SES and HRV at rest and in response to stress by visit, ethnicity and sex are shown in Table 1.

Ethnic and sex differences in HRV at rest and in response to stress are shown in Table 2. For HRV at rest, AAs showed significantly higher RMSSD and HF levels compared to EAs ($p= 0.009$ and 0.004, respectively). For HRV response to stress, females showed significantly larger decreases of both RMSSD and HF during stress than males ($p= 0.018$ and 0.020, respectively). No significant effect of visit was observed for HRV levels at rest or in response to stress. No significant sex difference on RMSSD and HF at rest or ethnic difference on their response to stress was observed. Furthermore, no significant ethnicity by visit interaction on RMSSD and HF levels at rest or significant sex by visit interaction on their responses to stress was observed, which indicates that the ethnic difference of HRV at rest and the sex difference of HRV in response to stress are consistent across the two visits.

Predictors of RMSSD and HF at rest at visit 2 were similar and results were presented in Table 3. In model 1, age was negatively related to RMSSD ($p= 0.049$) and HF ($p=0.037$) and AAs showed higher levels of RMSSD ($p= 0.001$) and HF ($p=0.001$) at visit 2. In model 2, both RMSSD ($p < 0.001$) and HF ($p < 0.001$) at rest at visit 1 were positively related to their levels at visit 2. Neither BMI nor WC at visit 1 was significantly related to HRV at rest at visit 2 (model 3 and model 5, respectively). However, the change of BMI ($p= 0.032$ and 0.042) and WC ($p= 0.017$ and 0.021 for RMSSD and HF, respectively) from visit 1 to visit 2 were negatively related to HRV levels at visit 2. That is, subjects who increased their BMI or WC during follow up showed decreased HRV levels at rest at visit 2 (model 4 and model 6,

respectively). Father's educational level was not a significant predictor of HRV level (model 7). No significant interactions with sex and ethnicity were observed.

As shown in Table 4, females showed larger decreases in response to stress than males for both RMSSD and HF (p= 0.015 and 0.010, respectively, model 1). RMSSD and HF responses to stress at visit 1 were also significantly associated with their response to stress at visit 2 (p< 0.001 and 0.002, respectively). That is, subjects with larger HRV response at visit 1 had larger response at visit 2. Resting levels of RMSSD and HF at visit 1 were not associated with their respective responses at visit 2 (p= 0.443 and 0.333, model 3). Obesity measures at visit 1 (either BMI or WC, model 4 or model 6, respectively) and the changes of obesity measures during follow up (model 5 or model 7, respectively) were not significantly associated with RMSSD and HF response to stress at visit 2. No significant effect of father's educational level on HRV response to stress at visit 2 was found (model 8). Furthermore, no significant interactions with sex and ethnicity were observed.

Partial correlation coefficients of HRV at rest and in response to stress across 1.5 years after adjusting for age, sex and ethnicity were shown in Table 5. Both the levels of RMSSD and HF at rest showed high tracking stabilities, with partial correlation coefficients of 0.62 and 0.58, respectively. However, the HRV response to stress showed low tracking correlations of 0.24 and 0.16 for RMSSD and HF, respectively.

4. Discussion

The present study is the first longitudinal study to estimate ethnic and sex differences, predictors and tracking stabilities of HRV at rest and in response to stress in youths and young adults. The important findings are that AAs show higher HRV at rest than EAs, and females show a greater HRV decrease in response to stress than males. These ethnic or sex differences are consistent across 1.5 years. In addition to age, ethnicity or sex, baseline resting HRV level or HRV response to stress are predictors of the same variable 1.5 years later. Furthermore, resting HRV levels during follow-up declined with weight gain. Our data also indicated that the tracking stability of resting HRV level was high (>0.5), but it was low (<0.3) for HRV in response to stress.

Previously, there were 3 studies in adults (Guzzetti *et al.*, 2000; Lampert *et al.*, 2005; Liao *et al.*, 1995) and 5 studies in youths (Franke *et al.*, 2004; Gutin *et al.*, 2005; Urbina *et al.*, 1998; Wang *et al.*, 2005; Zion *et al.*, 2003) having explored ethnic difference in resting HRV levels, with 5 studies showing that AAs have higher HRV than EAs.(Gutin *et al.*, 2005; Guzzetti *et al.*, 2000; Liao *et al.*, 1995; Urbina *et al.*, 1998; Wang *et al.*, 2005) The 3 studies that reported other findings either reported ethnic differences in HRV parameters not representing parasympathetic activity (Lampert *et al.*, 2005) or involved small sample sizes (Franke *et al.*, 2004; Zion *et al.*, 2003). For example, in a study involving 360 adult outpatients, Lampert et al (Lampert *et al.*, 2005) found that AAs had lower ultralow frequency (ULF) power than EAs. However, ULF is associated with the range of physical activity engaged in by the patients and is not an index of the vagal control of the heart (Thayer *et al.*, 2006). In two studies involving small sample size in youth, Zion et al (Zion *et al.*, 2003) found that AAs (n=32) had lower HF than non-AAs (n=29) and Franke et al (Franke *et al.*, 2004) did not observe any ethnic differences (n=18). The present study extends the previous findings in at least two important ways. First, this is the largest study involving youth to explore ethnic differences in resting HRV. Our results confirm the majority of previous findings that AAs show higher levels of parasympathetic control of the heart. Second, as a longitudinal study on ethnic difference in HRV, this study shows that the ethnic difference is consistent across 1.5 years.

Ethnic differences in autonomic tone have been implicated in the etiology of essential hypertension (EH) and a greater sympathetic drive in AAs has been hypothesized as a possible explanation for the higher prevalence of EH in AAs than in EAs (Lang *et al.*, 1997). The result of the present and previous studies on HRV indicate that compared to EAs, AAs are also characterized by an increased parasympathetic influence on the heart. As lower HRV has been found in patients with EH (Liao *et al.*, 1996; Singh *et al.*, 1998; Schroeder *et al.*, 2003) and prospective studies show that lower HRV may actually precede the onset of EH (Liao *et al.*, 1996; Singh *et al.*, 1998), future studies exploring the potential causes of ethnic difference in EH should consider both the sympathetic and parasympathetic part of the autonomic system.

Sex differences in HRV have also been reported. In adults, several studies have found that women have higher HRV than men (Evans *et al.*, 2001; Snieder *et al.*, 2007). It has been hypothesized that the sex difference reflects a possible role of estrogens on vagal activity, which is supported by evidence from a study in rats (McCabe *et al.*, 1981). A higher vagal tone in women may protect them against fatal arrhythmias and sudden cardiac death and potentially explains their lower risk for these conditions compared to men (Kannel *et al.*, 1998). However, there are also studies showing conflicting results (Umetani *et al.*, 1998; Bonnemeier *et al.*, 2003) or absence of any sex difference (Liao *et al.*, 1995). For example, in a large population based adult sample, Liao et al found that HF was similar between men and women (Liao *et al.*, 1995). To the best of our knowledge, only two studies explored sex differences in HRV in youth (Wang *et al.*, 2005; De Geus *et al.*, 2003) and neither study observed sex differences in RMSSD, HF or respiratory sinus arrhythmia (another index of parasympathetic activity). Our study confirmed the absence of sex differences in resting HF and RMSSD levels in youth at two visits across 1.5 years. Continued follow up of this cohort into adulthood will tell us at which age sex differences in HRV may appear and how they change over time.

Cardiovascular reactivity to behavioral or psychological stressors has long been regarded as a potential contributor to individual differences in cardiovascular risk (Treiber *et al.*, 2003). So far, only one study explored ethnic differences in cardiac vagal reactivity (Arthur *et al.*, 2004) and no study has looked at sex differences. Arthur et al did not find differences in RMSSD response to a mental arithmetic task between AAs and EAs in a sample of 60 adults (Arthur *et al.*, 2004). Our study not only confirmed the absence of ethnic differences in HRV reactivity in a much larger sample of youth at two visits across 1.5 years but also, for the first time, explored the potential sex difference in HRV response to stress. Females displayed a larger HRV decrease during video game challenge than males. Porges and colleagues proposed that vagal response to stress functions as a “brake” to quickly regulate responses to environmental demands and individuals with higher resting vagal control should exhibit greater vagal withdraw during stress (Porges, 1995). Further studies are needed to evaluate whether the higher vagal response in females is cardioprotective.

Our study is the first longitudinal study to examine predictors of future resting HRV levels and future HRV response to stress. As expected, baseline HRV levels or HRV response to stress contribute significantly to the variance of the corresponding variables at follow up. In addition, we observed that increased levels of obesity (indexed by both BMI and WC) was inversely related to resting HRV at follow up, which indicates cardiac vagal regulation declines with weight gain. This is consistent with previous intervention studies which showed HRV profiles were improved by weight loss (Rissanen et al., 2001; Poirier *et al.*, 2003). The mechanism underlying the relationship between vagally mediated cardiac autonomic regulation and obesity is not clear, although some hormonal signals, such as insulin (Vollenweider *et al.*, 1994), free fatty acids (Grekin *et al.*, 1997) and leptin (Haynes *et al.*, 1997) have been postulated.

Although HRV has been increasingly used as a predictor of cardiovascular health, available evidence on tracking stability of HRV over time is scant and limitated by small sample size or short follow up periods (Sandercock *et al.*, 2005; Schroeder *et al.*, 2004). Schroeder et al reported the repeatability of HRV measures in 63 healthy adults across 1 week; and found that correlation coefficients were greater than 0.7 for time-domain measures and greater than 0.5 for frequency domain measures (Schroeder *et al.*, 2004). Based on 3 years of follow up on 64 subjects, Goedhart et al observed very high correlation coefficients of sitting HRV (0.7 and 0.8 for RMSSD and HF, respectively) (Goedhart *et al.*, 2007). In the present study, based on data from a large sample with 2 measurements of HRV taken 1.5 years apart, we found partial correlation coefficients of HRV at rest were greater than 0.5, which is consistent with abovementioned studies (Goedhart *et al.*, 2007; Sandercock *et al.*, 2005; Schroeder *et al.*, 2004).

We are aware of only one study that reported tracking of HRV in response to stress. Salomon (2005) examined the stability of HRV reactivity to two stress tasks repeated 3 years later in adolescents and reported a correlation of 0.21 for a reaction time task and 0.18 for a mirror tracing task. Similarly, we found low tracking stability for HRV in response to a video game challenge (partial correlation coefficients were less than 0.3). This is not unexpected because change scores were used, which contain potential measurement errors of both the baseline measure and of the response measure. As several studies (Kamarck and Lovallo, 2003; Kamarck et al, 1994) have shown that aggregating cardiovascular responses to comparable stressors increase the stability of change scores, future studies on the stability of HRV response to stress should include multiple stressors and use aggregate reactivity scores.

Different from most of the previous studies in which HRV was measured using long recordings (from 2 to 24 hours) or short recordings (from 2–15 minutes), in the current study, HRV parameters were calculated based on 3 30-second segments of continuous RR intervals at rest and 5 30-second segments of continuous RR intervals during stress. It has been documented that HRV from short recordings can assess cardiac autonomic activity and predict all-cause mortality and cardiac death as accurately as long recordings (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). There has also been interest in using ultra-short recordings (from 10 seconds to 1 minute) (Bigger *et al.*, 1993) similar to our study. Correlations between time domain HRV parameters derived from 10-seconds and 6 minutes recording procedures were quite high and reproducibility of measures from the 10-second records was as good as the reproducibility of measures from the 6-minutes if the mean from 2 or 3 10-second records was used (Schroeder *et al.*, 2004). For the frequency domain HRV parameters, the study by De Rivecourt et al (2008) also observed high correlations between HF calculated from 240 second-segments with those from 30, 60 and 120 second-segments. Thus, HRV parameters in our data set, which were calculated based on the combination of 3 30-second segments of RR intervals at rest or 5 30-second segments of RR intervals during stress, should be accurate enough to assess cardiac autonomic activity.

An important strength of the present study is the longitudinal design which enabled us to evaluate the effect of weight gain on prediction of HRV at follow up. It also provides more confidence that the effects of the investigated predictors are truly causal. However, some caution is warranted because our follow-up period of 1.5 years was relatively short.

In summary, the present study suggests that ethnic and sex difference in HRV at rest and in response to stress exist in youth and young adults with AAs showing higher resting HRV levels than EAs and females showing larger HRV decreases in response to stress than males. These ethnic and sex differences are consistent across 1.5 years. The finding that resting HRV declines with weight gain confirms the results of previous intervention studies.

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References

Arthur CM, Katkin ES, Mezzacappa ES. Cardiovascular reactivity to mental arithmetic and cold pressorin African Americans, Caribbean Americans, and white Americans. Ann Behav Med 2004;27(1):31–37. [PubMed: 14979861]

Bigger JT, Fleiss JL, Rolnitzky LM, Steinman RC. The ability of several short-term measures of RR variability to predict mortality after myocardial infarction. Circulation 1993;88(3):927–934. [PubMed: 8353919]

Bonnemeier H, Richardt G, Potratz J, Wiegand UK, Brandes A, Kluge N, Katus HA. Circadian profile of cardiac autonomic nervous modulation in healthy subjects: differing effects of aging and gender on heart rate variability. J Cardiovasc Electrophysiol 2003;14(8):791–799. [PubMed: 12890036]

De Geus EJ, Boomsma DI, Snieder H. Genetic correlation of exercise with heart rate and respiratory sinus arrhythmia. Med Sci Sports Exerc 2003;35(8):1287–1295. [PubMed: 12900680]

De Rivecourt M, Kuperus MN, Post WJ, Mulder LJ. Cardiovascular and eye activity measures as indices for momentary changes in mental effort during simulated flight. Ergonomics 2008;51(9):1295–1319. [PubMed: 18802817]

Dekkers JC, Snieder H, Van Den Oord EJ, Treiber FA. Moderators of blood pressure development from childhood to adulthood: a 10-year longitudinal study. J Pediatr 2002;141(6):770–779. [PubMed: 12461492]

Dekker JM, Schouten EG, Klootwijk P, Pool J, Swenne CA, Kromhout D. Heart rate variability from short electrocardiographic recordings predicts mortality from all causes in middle-aged and elderly men. The Zutphen Study Am J Epidemiol 1997;145(10):899–908.

Evans JM, Ziegler MG, Patwardhan AR, Ott JB, Kim CS, Leonelli FM, Knapp CF. Gender differences in autonomic cardiovascular regulation: spectral, hormonal, and hemodynamic indexes. J Appl Physiol 2001;91(6):2611–2618. [PubMed: 11717226]

Fagard RH, Pardaens K, Staessen JA. Influence of demographic, anthropometric and lifestyle characteristics on heart rate and its variability in the population. J Hypertens 1999;17(11):1589–1599. [PubMed: 10608473]

Franke WD, Lee K, Buchanan DB, Hernandez JP. Blacks and whites differ in responses, but not tolerance, to orthostatic stress. Clin Auton Res 2004;14(1):19–25. [PubMed: 15045596]

Goedhart AD, van der Sluis S, Houtveen JH, Willemsen G, de Geus EJ. Comparison of time and frequency domain measures of RSA in ambulatory recordings. Psychophysiology 2007;44(2):203–215. [PubMed: 17343704]

Grekin RJ, Dumont CJ, Vollmer AP, Watts SW, Webb RC. Mechanisms in the pressor effects of hepatic portal venous fatty acid infusion. Am J Physiol 1997;273(1):R324–330. [PubMed: 9249567]

Gutin B, Howe C, Johnson MH, Humphries MC, Snieder H, Barbeau P. Heart rate variability in adolescents: relations to physical activity, fitness, and adiposity. Med Sci Sports Exerc 2005;37(11): 1856–1863. [PubMed: 16286853]

Guzzetti S, Mayet J, Shahi M, Mezzetti S, Foale RA, Sever PS, Poulter NR, Porta A, Malliani A, Thom SA. Absence of sympathetic overactivity in Afro-Caribbean hypertensive subjects studied by heart rate variability. J Hum Hypertens 2000;14(5):337–342. [PubMed: 10822322]

Haynes WG, Morgan DA, Walsh SA, Mark AL, Sivitz WI. Receptor-mediated regional sympathetic nerve activation by leptin. J Clin Invest 1997;100(2):270–278. [PubMed: 9218503]

Kamarck TW, Jennings JR, Pogue-Geile M, Manuck SB. A multidimensional measurement model for cardiovascular reactivity: stability and cross-validation in two adult samples. Health Psychol 1994;13 (6):471–478. [PubMed: 7889901]

Kamarck TW, Lovallo WR. Cardiovascular reactivity to psychological challenge: conceptual and measurement considerations. Psychosom Med 2003;65(1):9–21. [PubMed: 12554812]

Kannel WB, Wilson PW, D'Agostino RB, Cobb J. Sudden coronary death in women. Am Heart J 1998;136 (2):205–212. [PubMed: 9704680]

Koskinen T, Kahonen M, Jula A, Laitinen T, Keltikangas-Jarvinen L, Viikari J, Valimaki I, Raitakari OT. Short-term heart rate variability in healthy young adults: the Cardiovascular Risk in Young Finns Study. Auton Neurosci 2009;145(1–2):81–88. [PubMed: 19019739]

Lampert R, Ickovics J, Horwitz R, Lee F. Depressed autonomic nervous system function in African Americans and individuals of lower social class: a potential mechanism of race- and class-related disparities in health outcomes. Am Heart J 2005;150(1):153–160. [PubMed: 16084163]

Lang CC, Stein CM, He HB, Belas FJ, Blair IA, Wood M, Wood AJ. Blunted blood pressure response to central sympathoinhibition in normotensive blacks: increased importance of nonsympathetic factors in blood pressure maintenance in blacks. Hypertension 1997;30(2):157–162. [PubMed: 9260974]

Liao D, Barnes RW, Chambless LE, Simpson RJ Jr, Sorlie P, Heiss G. Age, race, and sex differences in autonomic cardiac function measured by spectral analysis of heart rate variability--the ARIC study. Atherosclerosis Risk in Communities. Am J Cardiol 1995;76(12):906–912. [PubMed: 7484830]

Liao D, Cai J, Barnes RW, Tyroler HA, Rautaharju P, Holme I, Heiss G. Association of cardiac autonomic function and the development of hypertension: the ARIC study. Am J Hypertens 1996;9(12):1147–1156. [PubMed: 8972884]

Light KC, Turner JR, Hinderliter AL, Girdler SS, Sherwood A. Comparison of cardiac versus vascular reactors and ethnic groups in plasma epinephrine and norepinephrine responses to stress. Int J Behav Med 1994;1(3):229–246. [PubMed: 16250799]

Lucini D, Di Fede G, Parati G, Pagani M. Impact of chronic psychosocial stress on autonomic cardiovascular regulation in otherwise healthy subjects. Hypertension 2005;46(5):1201–1206. [PubMed: 16203875]

McCabe PM, Porges SW, Carter CS. Heart period variability during estrogen exposure and withdrawal in female rats. Physiol Behav 1981;26(3):535–538. [PubMed: 7195595]

Murphy JK, Alpert BS, Walker SS. Ethnicity, pressor reactivity, and children's blood pressure. Five years of observations. Hypertension 1992;20(3):327–332. [PubMed: 1516952]

Poirier P, Hernandez TL, Weil KM, Shepard TJ, Eckel RH. Impact of diet-induced weight loss on the cardiac autonomic nervous system in severe obesity. Obes Res 2003;11(9):1040–1047. [PubMed: 12972673]

Porges SW. Orienting in a defensive world: mammalian modifications of our evolutionary heritage. A Polyvagal Theory. Psychophysiology 1995;32(4):301–318. [PubMed: 7652107]

Reinhardt L, Mäkijärvi M, Fetsch T, Martinez-Rubio A, Böcker D, Block M, Borggrefe M, Breithardt G. Reduced beat-to-beat changes of heart rate: an important risk factor after acute myocardial infarction. Cardiology 1996;87(2):104–111. [PubMed: 8653725]

Rissanen P, Franssila-Kallunki A, Rissanen A. Cardiac parasympathetic activity is increased by weight loss in healthy obese women. Obes Res 2001;9(10):637–643. [PubMed: 11595781]

Salomon K. Respiratory sinus arrhythmia during stress predicts resting respiratory sinus arrhythmia 3 years later in a pediatric sample. Health Psychol 2005;24(1):68–76. [PubMed: 15631564]

Sandercock GR, Bromley PD, Brodie DA. The reliability of short-term measurements of heart rate variability. Int J Cardiol 2005;103(3):238–247. [PubMed: 16098384]

Schroeder EB, Liao D, Chambless LE, Prineas RJ, Evans GW, Heiss G. Hypertension, blood pressure, and heart rate variability: the Atherosclerosis Risk in Communities (ARIC) study. Hypertension 2003;42(6):1106–1111. [PubMed: 14581296]

Schroeder EB, Whitsel EA, Evans GW, Prineas RJ, Chambless LE, Heiss G. Repeatability of heart rate variability measures. J Electrocardiol 2004;37(3):163–172. [PubMed: 15286929]

Singh JP, Larson MG, Tsuji H, Evans JC, O'Donnell CJ, Levy D. Reduced heart rate variability and new-onset hypertension: insights into pathogenesis of hypertension: the Framingham Heart Study. Hypertension 1998;32(2):293–297. [PubMed: 9719057]

Sloan RP, Huang MH, McCreath H, Sidney S, Liu K, Dale Williams O, Seeman T. Cardiac autonomic control and the effects of age, race, and sex: the CARDIA study. Auton Neurosci 2008;139(1–2):78–85. [PubMed: 18304893]

Snieder, HMA. Twin methodology. In: Cooper, DN., editor. Encyclopedia of the Human Genome. London: Nature Publishing Group; 2003.

Snieder H, van Doornen LJ, Boomsma DI, Thayer JF. Sex differences and heritability of two indices of heart rate dynamics: a twin study. Twin Res Hum Genet 2007;10(2):364–372. [PubMed: 17564526]

Tarvainen, MP.; Niskanen, JP. Kubios HRV analysis (version 2.0 beta) user's guide. http://kubios.uku.fi/

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. Circulation 1996;93(5):1043–1065. [PubMed: 8598068]

Thayer JF, Lane RD. The role of vagal function in the risk for cardiovascular disease and mortality. Biol Psychol 2007;74(2):224–242. [PubMed: 17182165]

Thayer JF, Wang X, Snieder H. Ethnic differences in heart rate variability: does ultralow-frequency heart rate variability really measure autonomic tone? Am Heart J 2006;152(3):e27. [PubMed: 16923401]

Timonen KL, Vanninen E, de Hartog J, Ibald-Mulli A, Brunekreef B, Gold DR, Heinrich J, Hoek G, Lanki T, Peters A, Tarkiainen T, Tiittanen P, Kreyling W, Pekkanen J. Effects of ultrafine and fine particulate and gaseous air pollution on cardiac autonomic control in subjects with coronary artery disease: the ULTRA study. J Expo Sci Environ Epidemiol 2006;16(4):332–341. [PubMed: 16205787]

Treiber FA, Kamarck T, Schneiderman N, Sheffield D, Kapuku G, Taylor T. Cardiovascular reactivity and development of preclinical and clinical disease states. Psychosom Med 2003;65(1):46–62. [PubMed: 12554815]

Umetani K, Singer DH, McCraty R, Atkinson M. Twenty-four hour time domain heart rate variability and heart rate: relations to age and gender over nine decades. J Am Coll Cardiol 1998;31(3):593–601. [PubMed: 9502641]

Urbina EM, Bao W, Pickoff AS, Berenson GS. Ethnic (black-white) contrasts in heart rate variability during cardiovascular reactivity testing in male adolescents with high and low blood pressure: the Bogalusa Heart Study. Am J Hypertens 1998;11(2):196–202. [PubMed: 9524048]

Vollenweider P, Randin D, Tappy L, Jequier E, Nicod P, Scherrer U. Impaired insulin-induced sympathetic neural activation and vasodilation in skeletal muscle in obese humans. J Clin Invest 1994;93(6):2365–2371. [PubMed: 8200969]

Wang X, Thayer JF, Treiber F, Snieder H. Ethnic differences and heritability of heart rate variability in African- and European American youth. Am J Cardiol 2005;96(8):1166–1172. [PubMed: 16214458]

Winsley RJ, Armstrong N, Bywater K, Fawkner SG. Reliability of heart rate variability measures at rest and during light exercise in children. Br J Sports Med 2003;37(6):550–552. [PubMed: 14665601]

Zion AS, Bond V, Adams RG, Williams D, Fullilove RE, Sloan RP, Bartels MN, Downey JA, De Meersman RE. Low arterial compliance in young African-American males. Am J Physiol Heart Circ Physiol 2003;285(2):H457–462. [PubMed: 12738618]

Table 1

General characteristics and HRV parameters (mean±SD) by visit, ethnicity and sex.

	Visit 1				Visit 2			
	EA		AA		EA		AA	
Characteristics	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
n	105	84	85	125	105	84	85	125
Age, year	22.6±3.0	22.9±2.7	23.4±2.8	23.6±2.7	24.2±3.1	24.6±2.7	25.0±2.9	25.2±2.7
Height,cm	178.4±7.5	164.8±5.8	176.4±6.1	164.6±6.8	178.6±7.2	164.7±5.9	176.3±6.0	164.7±6.7
Weight,kg	82.9±17.9	79.1±23.7	87.5±22.4	85.6±27.3	84.7±18.2	79.3±25.9	88.2±23.0	87.6±27.7
BMI, kg/m^2	26.0±5.0	29.2±8.9	28.2±7.2	31.5±9.7	26.6±4.9	29.7±9.3	28.9±7.2	32.3±9.9
WC,cm	90.0±13.0	91.1±19.1	90.4±17.7	93.2±19.6	91.5±12.6	92.4±19.9	92.8±17.6	95.3±20.3
Father's education level, year	14.3±2.5	13.7±2.1	12.5±2.6	13.0±2.1	…	…	…	…
SBP,mm Hg	116.8±11.1	105.5±10.0	121.0±12.1	112.8±11.8	116.2±11.7	106.8±8.9	123.7±13.8	116.3±15.3
DBP,mm Hg	61.2±6.8	60.9±6.6	64.8±8.6	65.9±8.4	62.7±6.9	62.5±5.8	68.0±8.9	67.9±8.4
HRV at rest								
RMSSD,ms	68.4±37.7	74.2±44.9	75.0±32.9	71.3±35.0	66.9±32.6	63.9±36.0	76.8±35.3	73.6±36.8
HF,ms^2	1676.5±1750.6	2001.0±2068.5	1944.2±1675.3	1890.0±1640.3	1641.8±1449.4	1564.9±1824.8	2101.5±2462.5	1951.7±1782.7
HRV during stress								
RMSSD,ms	55.5±29.6	57.2±36.9	66.6±30.4	56.7±30.5	58.4±30.0	51.9±33.2	67.9±34.1	58.9±28.9
HF,ms^2	1072.3±1057.8	1200.0±1454.4	1433.5±1291.4	1108.8±1243.8	1180.1±1325.7	992.7±1211.9	1592.2±1662.2	1190.5±1419.2
HRV response to stress ((stress-rest)/rest)								
RMSSD	−0.16±0.22	−0.21±0.21	−0.12±0.29	−0.19±0.25	−0.09±0.30	−0.16±0.24	−0.08±0.38	−0.16±0.24
HF	−0.21±0.55	−0.22±0.73	−0.07±0.80	−0.34±0.46	−0.16±0.70	−0.22±0.73	−0.09±1.33	−0.29±0.53

AA= African American; BMI= body mass index; DBP= diastolic blood pressure; EA= European American; HF= high frequency power; HRV= heart rate RMSSD= root mean square of successive differences of normal RR intervals; SBP= systolic blood pressure; SD= standard deviation; WC= waist circumference

Table 2

Repeated measures ANOVA for HRV at rest and in response to stress across visits.

HRV parameters	Source of variance	F	p-value
HRV at rest			
1. RMSSD	Visit	0.259	0.611
	Sex	0.517	0.472
	Ethnicity	6.994	0.009
	Visit*sex	1.094	0.296
	Visit*ethnicity	2.205	0.138
	Ethnicity*sex	0.101	0.751
	Visit*ethnicity*sex	1.997	0.158
2. HF	Visit	0.129	0.720
	Sex	0.033	0.855
	Ethnicity	8.422	0.004
	Visit*sex	1.240	0.266
	Visit*ethnicity	1.421	0.234
	Ethnicity*sex	0.008	0.930
	Visit*ethnicity*sex	1.396	0.238
HRV in response to stress			
1. Response of RMSSD	Visit	0.409	0.523
	Sex	5.690	0.018
	Ethnicity	0.032	0.858
	Visit*sex	0.000	0.983
	Visit*ethnicity	0.551	0.458
	Ethnicity*sex	0.117	0.732
	Visit*ethnicity*sex	0.604	0.438
2. Response of HF	Visit	0.015	0.902
	Sex	5.450	0.020
	Ethnicity	0.026	0.872
	Visit*sex	0.039	0.844
	Visit*ethnicity	0.152	0.697
	Ethnicity*sex	2.623	0.106
	Visit*ethnicity*sex	0.168	0.682

Age at visit 1 was adjusted for in all the models.

Responses of RMSSD and HF to stress were indexed by the (stress-rest)/rest ratio.

ANOVA= analysis of variance; HRV= heart rate variability; HF= high frequency power; RMSSD= root mean square of successive differences of normal RR intervals.

Table 3

Linear regression results for HRV at rest at visit 2

HRV	Model	Variables	B	p-value	adjusted R^2
RMSSD	1	Age + sex + ethnicity			0.030
		Age	−0.108	0.049	
		Sex	−0.066	0.212	
		Ethnicity	0.185	0.001	
	2	Model 1 + visit 1 RMSSD at rest			0.339
		Visit 1 RMSSD at rest	0.571	< 0.001	
	3	Model 1 + BMI at visit 1			0.030
		BMI at visit 1	−0.003	0.309	
	4	Model 1 + BMI change			0.043
		BMI change*	−0.027	0.032	
	5	Model 1 + WC at visit 1			0.031
		WC at visit 1	−0.005	0.246	
	6	Model 1 + WC change			0.042
		WC change†	−0.025	0.017	
	7	Model 1 + Father's education level			0.032
		Father's education level	0.017	0.150	
HF	1	Age + sex + ethnicity			0.029
		Age	−0.110	0.037	
		Sex	−0.091	0.387	
		Ethnicity	0.173	0.001	
	2	Model 1 + visit 1 HF at rest			0.251
		Visit 1 HF at rest	0.481	< 0.001	
	3	Model 1 + BMI at visit 1			0.033
		BMI at visit 1	−0.011	0.107	
	4	Model 1 + BMI change			0.041
		BMI change*	−0.051	0.042	
	5	Model 1 + WC at visit 1			0.033
		WC at visit 1	−0.013	0.097	
	6	Model 1 + WC change			0.040

HRV	Model	Variables	B	p-value	adjusted R^2
		WC change†	−0.049	0.021	
	7	Model 1 + Father's education level			0.024
		Father's education level	0.030	0.182	

*BMI change= BMI at visit 2 – BMI at visit 1;

†WC change= WC at visit 2 – WC at visit 1

BMI= body mass index; HF= high frequency power; HRV= heart rate variability; RMSSD= root mean square of successive differences of normal RR intervals; WC= waist circumference.

Table 4

Linear regression results for HRV response at visit 2.

HRV	Model	Variables	B	p-value	adjusted R^2
RMSSD	1	Age + sex + ethnicity			0.008
		Age	−0.001	0.922	
		Sex	−0.130	0.015	
		Ethnicity	0.009	0.765	
	2	Model 1 + visit 1 RMSSD response			0.064
		Visit 1 RMSSD response	0.262	< 0.001	
	3	Model 1 + visit 1 RMSSD resting level			0.003
		Visit 1 RMSSD resting level	−0.0003	0.443	
	4	Model 1 + BMI at visit 1			0.005
		BMI at visit 1	−0.0001	0.943	
	5	Model 1 + BMI change			0.009
		BMI change*	−0.006	0.372	
	6	Model 1 + WC at visit 1			0.005
		WC at visit 1	−0.001	0.733	
	7	Model 1 + WC change			0.004
		WC change†	−0.001	0.882	
	8	Model 1 + Father's education level			0.006
		Father's education level	−0.002	0.712	
HF	1	Age + sex + ethnicity			0.011
		Age	0.006	0.703	
		Sex	−0.13	0.010	
		Ethnicity	0.080	0.362	
	2	Model 1 + visit 1 HF response			0.024
		Visit 1 HF response	0.16	0.002	
	3	Model 1 + visit 1 HF resting level			0.005
		Visit 1 HF resting level	−0.0002	0.333	
	4	Model 1 + BMI at visit 1			0.008
		BMI at visit 1*	−0.0008	0.886	
	5	Model 1 + BMI change			0.012

HRV	Model	Variables	B	p-value	adjusted R^2
		BMI change	−0.022	0.286	
	6	Model 1 + WC at visit 1			0.009
		WC at visit 1	−0.003	0.649	
	7	Model 1 + WC change			0.008
		WC change†	−0.002	0.919	
	8	Model 1 + Father's education level			0.014
		Father's education level	−0.027	0.156	

*BMI change= BMI at visit 2 – BMI at visit 1

†WC change= WC at visit 2 - WC at visit 1

Responses of RMSSD and HF to stress were indexed by the (stress-rest)/rest ratio.

BMI= body mass index; HF= high frequency power; HRV= heart rate variability; RMSSD= root mean square of successive differences of normal RR intervals; WC= waist circumference.

Table 5

Partial correlation coefficients of HRV parameters between visit 1 and visit 2.*

	HRV	N	r	p-value
Resting	RMSSD	391	0.62	< 0.001
	HF	391	0.58	< 0.001
Response	RMSSD	371	0.24	< 0.001
	HF	375	0.16	< 0.001

*All the partial correlation coefficients were adjusted for sex, ethnicity and age at visit 1.

Responses of RMSSD and HF to stress were indexed by the (stress-rest)/rest ratio.

HF= high frequency power; HRV= heart rate variability; RMSSD= root mean square of successive differences of normal RR intervals.