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ASSOCIATION STRENGTH OF THREE ADIPOSITY MEASURES WITH AUTONOMIC NERVOUS SYSTEM FUNCTION IN APPARENTLY HEALTHY EMPLOYEES

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Abstract

Objectives: To investigate the association of different measures of central (abdominal) and overall adiposity with autonomic nervous system (ANS) function, indexed by heart rate variability (HRV), in apparently healthy human adults.

Design and Measurements: Cross-sectional data of 8,538 participants (20% female, age: 41 ± 11 years, body mass index (BMI): 24 ± 4 kg/m^2, waist circumference (WC): 91 ± 12 cm, waist-to-height ratio (WHtR): 0.45 ± 0.08) were available for analysis.

Results: All measures of adiposity were inversely correlated with vagally-mediated HRV indexed by RMSSD (all $p<0.001$). Strongest associations were found with WC and RMSSD ($r = -0.29$). Associations were stronger in males (WC $r = -0.32$) than in females (WC $r = -0.23$). Partial correlations revealed the same pattern for RMSSD (WC all pcc = −0.12 $p<0.001$; WC male pcc = −0.14 $p<0.001$; WC female pcc = −0.06 $p<0.05$). Correlation strength of BMI and WHtR with RMSSD were similar and significantly weaker compared to WC ($p < .001$) in unadjusted analysis. Overall, nonparametric Kendall's τb led to the same conclusions.

Conclusion: The present data supports previous findings, that HRV is related to measures of adiposity in healthy individuals. In line with previous research, we found that WC is more strongly related to measures of HRV, indicating that WC best captures adiposity related risk.

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Conflicts of interest: The authors declare that there are no conflicts of interest.

Ethical standards: The Ethical Committee of the Mannheim Medical Faculty, Heidelberg University, approved secondary analysis of these data. All participants gave written informed consent prior to examination.

Keywords

Adiposity; autonomic nervous system; heart rate variability; body mass index; waist circumference; waist-to-height ratio

Introduction

Obesity is a risk factor for mortality and morbidity that has already reached epidemic proportions in the industrialized world (1-5). The body mass index (BMI) is commonly used as a measure of obesity. However, there is controversy as to whether BMI adequately captures the toxic elements of obesity, as it reflects overall adiposity (6-8). Central (abdominal) adiposity may be the more toxic element and other measures of adiposity have been suggested to better capture central adiposity (7, 9).

Lower vagally-mediated heart rate variability (HRV) has been shown to be a risk factor for death and disability from a host of diseases and disorders, in particular cardiovascular disease (10). Importantly, low HRV has been shown to precede clinical signs of various disorders and to predict levels of inflammation (11). While HRV has been extensively studied in obesity (12-14), the association of autonomic nervous system activity with measures of adiposity in healthy, non-obese subjects has not been fully investigated. Previous research including a recent study by our work group (15, 16) revealed a distinct association between HRV and BMI in healthy, non-obese adults. Higher BMI scores were associated with lower parasympathetic activity, as indexed by frequency domain measures of HRV. However, evidence on the relation of HRV and BMI comes from considerably smaller sample sizes ((15): n = 25; (16): n = 59). A recent study on the relationship between HRV and adiposity used different measures to discriminate central from overall adiposity (17). Based on their findings the authors proposed that central (abdominal) adiposity, not overall adiposity, accounts for obesity-related autonomic dysfunction.

Therefore in an effort to identify the measure of adiposity that best captures risk, we examined the association between HRV and three commonly used measures of obesity in a large cross-sectional sample of apparently healthy men and women. In line with previous research (17) we assumed that waist circumference (WC) might be more sensitive to reflect the toxic element of obesity, and the waist-to-height ratio (WHtR) may represent a better index of general adipose tissue distribution. Accordingly, we hypothesized that both - WC and WHtR – would show stronger negative correlations with HRV compared to BMI. Adding to the literature, we investigated day- and night-time differences in the association of measures of adiposity and HRV and report analyses stratified by gender.

Methods

Data from a large cross-sectional study was used (Mannheim Industrial Cohort Study) for secondary analysis. The Ethical Committee of the Mannheim Medical Faculty, Heidelberg University, approved secondary analysis of these data. All participants gave written informed consent prior to examination. Details on the measurements and population are published elsewhere (18, 19). The data was collected as part of a voluntary health risk assessment that was offered to all employees during working hours. An agent independent from the employer conducted the health risk assessments and data collection (HealthVision Ltd., Berlingen, Switzerland). Data collected from 2010–2012 at 13 study sites (companies from the secondary and tertiary sectors) across Germany were available.

Participants were invited to take part in the “Work Health Check” and were offered a detailed individual report containing their health status as assessed by medical examination and self reports. This sample encompassed the entire workforce aged 17 and 65 years. All participants were enrolled and examined between 10 a.m. and 5 p.m. on workdays (Monday - Friday) during work hours. Upon arrival, a medical examination was performed. Weight and height (via stadiometer) were recorded without shoes and in typical business clothes. BMI was calculated (kg/m^2) and WC was measured in cm, about 2.5 cm above the anterior superior iliac crests. WHtR was calculated in terms of waist circumference (cm) divided by height (m).

Heart rate (HR) was recorded as interbeat intervals (IBI) using a t6 Suunto Memory Belt (SuuntoVantaa, Finland), sampling at a rate of 1000 Hz. The Suunto Memory Belt is a reliable measure of electrocardiography (ECG) compared to a 5 lead ECG. IBIs were determined as the interval between two successive R-spikes. After attaching the ambulatory HR recorder, participants commenced their routine work duties followed by after work leisure and sleep activities. Participants were asked to return the HR recorder after a minimum of 22 hours of wearing or in case of any difficulties. The 24-hour IBI-data were decomposed into blocks of 5.35 minutes each and subjected to further analysis if the artifact rate was below 5%. The root mean squared successive differences (RMSSD) were averaged from 12 hour long-term HR monitoring (beat to beat) for day-time and night-time as indicators of vagal tone. RMSDD is strongly associated with cardiac vagal activity, reflecting a parasympathetic influence. Raw IBIs were analyzed by researchers at the Center for Neuropsychological Research (University of Trier, Germany) according to the “Task Force Guidelines of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology” (20). Day and night time periods were calculated based on self-reports of bedtimes and wake up times.

Only subjects with complete data on all variables of interest were included in the analysis. Bivariate (r) and partial correlations (pcc) adjusting for age, sex, smoking, sleep quality, and physical activity (both Pearson’s correlation and nonparametric Kendall’s τb) were calculated stratified by sex and recording time (day vs. night). RMSSD and WC were skewed and log transformed prior to analysis. All analyses were carried out using STATA 12.1SE. Two-sided differences between correlation coefficients were calculated using STATISTICA to compare correlation strengths between measures.

Results

Cross-sectional data of 8,538 participants (20% female, age: 41 ± 11 years, BMI: 24 ± 4 kg/m^2, waist circumference (WC): 91 ± 12 cm, WHtR: 0.45 ± 0.08) were available for analysis. All measures of adiposity were highly correlated (all $p < .0001$; BMI and WC $r = 0.876$; BMI and WHtR $r = 0.998$; WC and WHtR $r = 0.878$) and inversely correlated with

RMSSD (29 ± 13 ms; all $p<0.001$). Strongest associations were found with WC and RMSSD ($r = -0.29$) (Table 1). Associations were stronger in males (WC $r = -0.32$) than in females (WC $r = -0.23$). Partial correlations revealed the same pattern for RMSSD (WC all pcc = −0.12 $p<0.001$; WC male pcc = −0.14 $p<0.001$; WC female pcc = −0.06 $p<0.05$, see Table 2). Correlation strength of BMI and WHtR with RMSSD were similar. Overall, nonparametric Kendall's τb led to the same conclusions.

Analysis of differences between correlation coefficients revealed significant differences comparing measures of BMI and WC (all $p < .001$), WHtR and WC (all $p < .001$), but not BMI and WHtR for all participants and men in unadjusted analysis (r, Table 1), independent of the time of recording (day and night). No significant differences between correlations were found in women, and when analyzing correlation coefficients derived from adjusted analyses (Table 2).

Discussion

Recent literature (15,16) provides evidence that higher BMI in healthy, none-obese subjects is associated with lower parasympathetic activity as indexed by a negative correlation of BMI and RMSSD. However, overall adiposity indexed by BMI may not adequately reflect the toxic element of adiposity. The present paper aimed to investigate the association between BMI, WC, WHtR, and HRV in large cross-sectional sample of healthy employees to identify the measure of adiposity that best captures risk.

In line with previous research (17) we found that WC, a measure of centrally distributed adipose tissue, is more strongly correlated with HRV. Adding to the literature, we found that the association of any measure of adiposity and HRV was stronger in men than in women in this sample, and dependent on the time of HRV recording. The study has several notable strengths. First, analyses are based on a large occupational sample of employees with differing socioeconomic backgrounds rather than being limited to one particular professional group. Furthermore, all participants were from a similar cultural background, so genetic and cultural heterogeneity were likely minimized. Finally, this study accounts for many potential covariates in the statistical analyses and HRV was recorded over 24h.

However, several limitations of this study also need to be addressed. Due to the cross-sectional design of our study causal directions or temporal associations between measures of adiposity and HRV cannot be concluded. The sample size for women within the present analysis is relatively small. Future research should examine more clearly whether the present findings generalize to women to determine the origin of the gender differences presented. The present sample is Caucasian and therefore these results might not generalize to other ethnicities as a recent meta-analysis provides evidence for ethnic differences in HRV (21). In addition, we studied apparently healthy employees and health status was not measured by detailed objective assessments or medical records. Thus, unrecognized medical conditions may have influenced some findings. Consequently, findings may not be generalized to individuals of poorer health or those outside the labor force.

Conclusion

To our knowledge, this is the first study to analyze the complex interplay between ANS function at day- and night-time, gender and three comprehensive measures of adiposity. Adding to the existing literature, the results provide evidence of a stronger association of ANS activity with centrally distributed adipose tissue as indicated by WC compared to measures of overall adiposity (BMI and WHtR). Extending previous findings, we report gender and day/night differences in the correlation of HRV and measures of adiposity. Measures of adiposity and ANS function show a stronger association in men compared to women. Furthermore, the association of measures of adiposity and ANS function is stronger when analyzing day-time recordings of HRV, highlighting the prominent role of the vagus nerve in energy expenditure.

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Table 1

Bivariate Pearson's and Kendall's τb correlations

	RMSSD (night)		RMSSD (day)	
	r	**τb**	**r**	**τb**
All participants (n = 8,538)				
WC	−0.18***	−0.12***	−0.29***	−0.20***
BMI	−0.11***	−0.08***	−0.22***	−0.15***
WHtR	−0.10***	−0.07***	−0.21***	−0.14***
Female (n = 1,748)				
WC	−0.17***	−0.10***	−0.23***	−0.14***
BMI	−0.15***	−0.09***	−0.19***	−0.11***
WHtR	−0.14***	−0.08***	−0.18***	−0.11***
Male (n = 6,790)				
WC	−0.22***	−0.15***	−0.32***	−0.22***
BMI	−0.12***	−0.08***	−0.22***	−0.15***
WHtR	−0.11***	−0.08***	−0.21***	−0.15***

* $p<0.05$

** $p<0.01$

*** $p<0.001$

Table 2

Partial Pearson's and Kendall's τb correlation coefficients (PCC); PCC adjusted for age, smoking, sleep quality and physical activity

	RMSSD (night)		RMSSD (day)	
	r	**τb**	**r**	**τb**
All participants (n = 8,538)				
WC	−0.04**	−0.05***	−0.12***	−0.11***
BMI	−0.02	−0.03***	−0.11***	−0.09***
WHtR	−0.02	−0.03***	−0.11***	−0.08***
Female (n = 1,748)				
WC	−0.02	−0.03	−0.06*	−0.06***
BMI	−0.03	−0.03	−0.06**	−0.05**
WHtR	−0.03	−0.03	−0.06**	−0.05**
Male (n = 6,790)				
WC	−0.05***	−0.05***	−0.14***	−0.11***
BMI	−0.02	−0.03***	−0.12***	−0.09***
WHtR	−0.02	−0.03***	−0.12***	−0.08***

* p<0.05

** p<0.01

*** p<0.001