

# BODY MASS INDEX IS RELATED TO AUTONOMIC NERVOUS SYSTEM ACTIVITY AS MEASURED BY HEART RATE VARIABILITY – A REPLICATION USING SHORT TERM MEASUREMENTS

J. KOENIG<sup>1</sup>, M.N. JARCZOK<sup>2</sup>, M. WARTH<sup>1</sup>, R.J. ELLIS<sup>3</sup>, C. BACH<sup>1</sup>, T.K. HILLECKE<sup>1</sup>, J.F. THAYER<sup>4</sup>

1. School of Therapeutic Sciences, SRH University Heidelberg, Heidelberg, Germany; 2. Mannheim Institute of Public Health, Social and Preventive Medicine, Mannheim Medical Faculty, Heidelberg University, Mannheim, Germany; 3. Department of Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA; 4. Department of Psychology, The Ohio State University, Columbus, OH, USA. Corresponding author: Julian Koenig, SRH University Heidelberg, Maaßstraße 26, 69123 Heidelberg, julian.koenig@fh-heidelberg.de, Tel. +049 151 58748926, Fax. +049 6221 884152

**Abstract:** *Objectives:* The present analysis is a replication of previous findings presenting first evidence of an association between body mass index (BMI) and autonomic nervous system (ANS) activity as measured by heart rate variability (HRV), in healthy non-obese adults. *Design:* A total of fifty-nine apparently healthy male (M) and female (F) individuals (M/F = 15/44) were included in the trial. HRV data for analysis was derived from 5 minutes of baseline recordings, while the subject was sitting on a comfortable chair. Subjects' body measures (weight and height) were taken and BMI was obtained according to common calculation (kg/m<sup>2</sup>). *Results:* BMI was inversely related to pNN50 and RMSSD components of HRV. Statistically significant differences between stratified groups (BMI < 20, BMI 20-25, BMI > 25) only occurred for analysis of pNN50 components. The pNN50 components and RMSSD are strongly associated with cardiac vagal influence, and thus represents parasympathetic activity. *Conclusions:* The present data supports previous findings, that sympatho-vagal balance is related to BMI in non-obese, healthy individuals, providing evidence for a prominent role of the vagus nerve in the modulation of the energy expenditure of the human organism. Furthermore, this relation can be observed in short term recordings of HRV of 5 minutes in length.

**Key words:** Autonomic nervous system, body mass index, vagus nerve, HRV.

## Introduction

The autonomic nervous system (ANS) contributes to the modulation of the energy expenditure of the human organism. Heart rate variability (HRV) teases out the relative contribution of the sympathetic and parasympathetic branches of the ANS in the chronotropic control (i.e., timing of the heart beats) of the heart and therefore serves as an index and measurement of ANS activity. While HRV has been extensively studied in obesity (1-3) furthermore the influence of ANS activity on body weight in healthy, non-obese subjects is of interest. A recent short communication published in the European Journal of Clinical Nutrition provided first evidence of an association between sympatho-vagal balance and body mass index (BMI) in healthy, non-obese adults (4). The authors found higher BMI scores to be correlated to higher sympathetic and lower parasympathetic activity, indexed by frequency domain measures of HRV obtained from 24-h ECG recordings in 25 healthy individuals. Within the present paper we aim to replicate these findings using HRV short term recordings (5 minutes) from 59 apparently healthy individuals, including time-domain measures (RMSSD and pNN50) of HRV.

## Materials and Methods

The study was approved by the Institutional Review Board, and all participants provided written informed consent prior to their assessment. Self-rated health (SRH) was measured using the question "How do you rate your current health status?" on a

0 "very bad" to 6 "excellent" scale. Only subjects indicating a SRH  $\geq 3$  "fair" were considered for inclusion in the present analysis. A total of fifty-nine apparently healthy male (M) and female (F) individuals (M/F = 15/44) were included in the trial. Subjects' body measures (weight and height) were taken and BMI was obtained according to common calculation (kg/m<sup>2</sup>). None of the subjects reported current medication intake or suffering from chronic or acute disease. HRV was measured for 5 minutes while the subject was sitting on a comfortable chair. A Polar RS800CX portable device was used to record inter-beat intervals (IBI) at sampling frequency of 1000 Hz, providing a temporal resolution of 1 ms for each R-R interval. The device's transmitter consists of a stable polyamide case with electrodes attached to an elastic belt fixated to the chest of the subjects. Device-specific software (Polar ProTrainer 5) was used to transfer recordings to a personal computer. IBI data were imported and analyzed with "Kubios HRV - Heart Rate Variability Analysis Software" (Biosignal Analysis and Medical Imaging Group, University Kuopio, Finland, Version 2.0, (5)) and analyzed. For the present analysis the square root of the mean squared difference of successive NN intervals (RMSSD, ms), the proportion of pairs of successive NNs that differ by more than 50 ms (pNN50, %), and absolute spectral power expressed as normalized units of high frequency (HF<sub>n.u.</sub>; 0.15–0.4 Hz), and low frequency components (LF<sub>n.u.</sub>; 0.04–0.15 Hz) were obtained. Data on HRV measures was skewed and successfully log-transformed for further analysis, in particular Pearson's correlation test and analysis of variance (ANOVA). The HF component reflects cardiac vagal (i.e.,

**Table 1**  
 HRV measures according to BMI (kg/m<sup>2</sup>)

Group	BMI (kg/m <sup>2</sup> )	Age (years)	HFn.u§	LFn.u§	RMSSD§	pNN50§
BMI<20 (n=13)	18.9 (0.9)*	22.8 (4.0)*	3.43 (0.47)	4.17 (0.22)	4.3 (0.7)	3.2 (0.8)*
BMI 20-25 (n=33)	22.2 (1.3)*	23.0 (2.6)*	3.59 (0.33)	4.11 (0.18)	4.1 (0.5)	2.9 (0.8)*
BMI >25 (n=13)	28.8 (4.6)*	26.5 (6.2)*	3.39 (0.56)	4.15 (0.31)	3.9 (0.7)	2.0 (1.2)*

All values are means and standard deviations in brackets (SD); BMI, body mass index; HF, high frequencies; LF, low frequencies; RMSSD, square root of the mean squared difference of successive NN intervals; pNN50, the proportion of pairs of successive NNs that differ by more than 50 ms; \* indicates a significant difference between the groups on the p<0.05 level; \*\*indicates a significant difference between the groups on the p<0.005 level, see text for LSD post-hoc comparisons; §=Log transformed for analysis

parasympathetic) activity, while the LF component is associated with baroreflex activity (for a discussion on common misinterpretations of LF power, see (6,7,8)). RMSSD and pNN50 are closely related to the HF component of the power spectrum, and thus are strongly associated with cardiac vagal activity, reflecting a parasympathetic influence.

**Results**

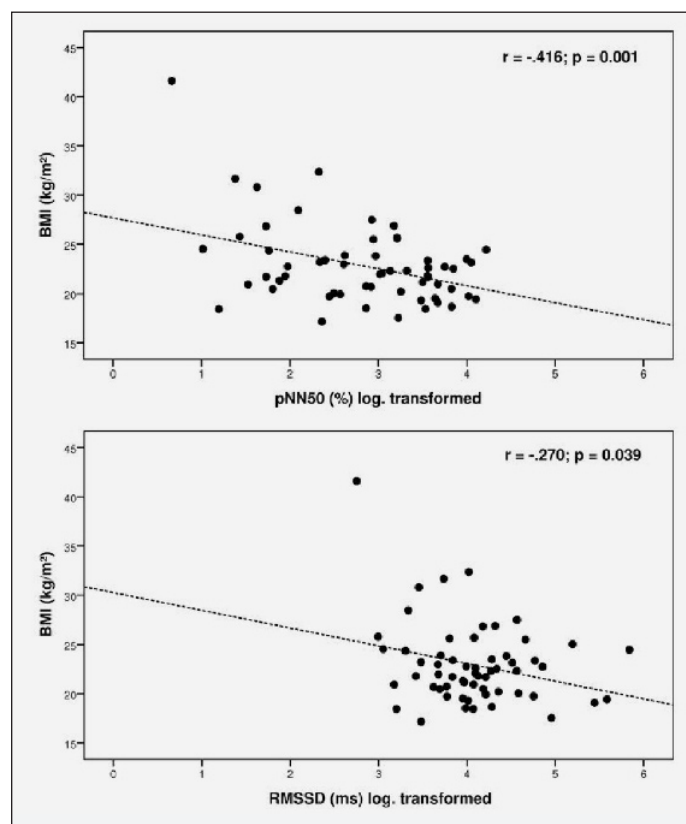
Subjects' mean age was 23.7±4.1 years, mean body weight was 67.1±14.1kg, and mean BMI was 22.93±4.1kg/m<sup>2</sup>. Age showed no significant correlation to any HRV measure (p > .05). Body weight did not correlate with LFnu, HFnu or RMSSD but was inversely related to pNN50 (r=-.284, p = 0.029). BMI correlated with pNN50 (r = -.416, p = 0.001) and RMSSD (r = -.270, p = 0.039) with higher BMI scores being associated with lower HRV measures. No significant correlation was found to any frequency domain measure of HRV. According to Molfino et al. (4), subjects were then stratified by BMI (BMI < 20, BMI 20-25, BMI > 25). Only the pNN50 showed statistical significant differences between the groups. The pNN50 was significantly lower in subjects with higher BMI (BMI > 25) than those measured in subjects with moderate (BMI 20-25) or lower BMI (BMI < 20). The pNN50 was significantly higher in subjects with moderate BMI (BMI 20-25) than in subjects with higher BMI (BMI > 25) and pNN50 was significantly higher in subjects with lower BMI (BMI < 20) than in subjects with moderate BMI (BMI 20-25). Also subjects with moderate BMI (BMI 20-25) and lower BMI (BMI < 20) showed no statistical significant differences. Subjects with higher BMI (BMI > 25) were significantly older compared to the mean age of the other two groups (Table 1).

**Discussion**

The present analysis is a replication of previous findings presenting first evidence of an association between the body mass index (BMI) and autonomic nervous system (ANS) activity as measured by heart rate variability (HRV) in healthy non-obese adults (4). While the authors of the aforementioned study found that higher BMI is correlated with increased sympathetic and lowered parasympathetic activity in a 24-h ECG recording, we aimed at investigating the relationship

between HRV and BMI using short term recordings of 5 minutes. Analysing data from 59 apparently healthy young adults revealed that BMI was inversely related to pNN50 and RMSSD components of HRV. The pNN50 components and RMSSD are strongly associated with cardiac vagal influence, and thus represent parasympathetic activity (Figure 1).

**Figure 1**



However, statistically significant differences between stratified groups (BMI<20, BMI 20-25, BMI >25) only occurred for analysis of pNN50 components. While we do not find any correlation of frequency domain measures of HRV and BMI as previously reported (4), our results support the general finding, that higher BMI is associated with lower parasympathetic activity as mirrored by a negative correlation of BMI and RMSSD and BMI and pNN50. The length of

## AUTONOMIC NERVOUS SYSTEM

recording possibly contributes to the missing of likewise correlations reflected by frequency domain measures. Recent analysis by our group showed a close correlation of 24h HRV and glycemic status in healthy employees. Here vagally mediated HRV was associated with fasting plasma glucose and HbA1c independent of other components of the metabolic syndrome (9). More important, this association was independent of sympathetic activity as measured by overnight urinary norepinephrine (10). These results furthermore provide insights to an unique association of ANS activity and energy expenditure modulation of the human organism, pointing out a prominent role of the vagus nerve. The present data supports previous findings, that sympatho-vagal balance is related to BMI in non-obese, healthy individuals. Furthermore, this relation can be observed in short term recordings of HRV of 5 minutes in length.

*Conflict of interest statement:* The authors did not receive funding for the work presented. The authors declare no conflict of interests, all authors are listed, and all have contributed substantially to the manuscript.

### References

1. Karason K, Mølgaard H, Wikstrand J, Sjöström L. Heart rate variability in obesity and the effect of weight loss. *Am J Cardiol* 1999;83:1242-1247
2. Martini G, Riva P, Rabbia F, Molini V, Ferrero GB, Cerutti F, et al. Heart rate variability in childhood obesity. *Clin Auton Res* 2001;11:87-91
3. Kim JA, Park YG, Cho KH, Hong MH, Han HC, Choi YS, et al. Heart rate variability and obesity indices: emphasis on the response to noise and standing. *J Am Board Fam Pract* 2005;18:97-103
4. Molfino A, Fiorentini A, Tubani L, Martuscelli M, Rossi Fanelli F, Laviano A. Body mass index is related to autonomic nervous system activity as measured by heart rate variability. *Eur J Clin Nutr* 2009;63:1263-1265
5. Tarvainen MP, Niskanen JP, Lipponen JA, Ranta-aho PO, Karjalainen PA. Kubios HRV – A Software for Advanced Heart Rate Variability Analysis. *IFMBE Proceedings* 2009;22:1022–1025
6. Casadei B, Cochrane S, Johnston J, Conway J, Sleight P. Pitfalls in the interpretation of spectral analysis of the heart rate variability during exercise in humans. *Acta Physiol Scand* 1995;153:125-131
7. Moak JP, Goldstein DS, Eldadah BA, Saleem A, Holmes C, Pechnik S, et al. Supine low frequency power of heart rate variability reflects baroreflex function, not cardiac sympathetic innervation. *Cleve Clin J Med* 2009;76:51-59
8. Goldstein DS, Benthó O, Park MY, Sharabi Y. Low-frequency power of heart rate variability is not a measure of cardiac sympathetic tone but may be a measure of modulation of cardiac autonomic outflows by baroreflexes. *Exp Physiol* 2011;96:1255-1261
9. Jarczok MN, Li J, Mauss D, Fischer JE, Thayer JF. Heart Rate Variability is Associated with Glycemic Status After Controlling for Components of the Metabolic Syndrome. *Int J Card* 2012;doi:10.1016/j.ijcard.2012.02.002
10. Jarczok MN, Koenig J, Schuster AK, Thayer JF, Fischer JE. Nighttime heart rate variability, overnight urinary norepinephrine, and glycemic status in apparently healthy human adults. *Int J Card* 2013;doi:10.1016/j.ijcard.2013.04.147