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Baroreflex Sensitivity in Relation to Clinical Characteristics in Subject Aged 40 to 80 Years

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Abstract

Baroreflex function measured as baroreflex sensitivity (BRS) mirrors an integrated capacity of the autonomic nervous system. We aimed to assess the relationship between measures of BRS and age and relevant clinical characteristics.

80 subjects participating in the Copenhagen City Heart study (43 women) with a mean age of 59 ± 11 years (range 41-79 years) were included. Baroreceptor activity was quantified through the Valsalva manoeuvre (VM) and as a spontaneous function. BRS was tested against age, gender, smoking status, body size and predicted risk of coronary heart disease based on the Framingham score.

BRS was found to decline with age, but this change disappeared when correcting for the age related increase in systolic blood pressure. We found that the VM-derived indices of sympathetic vascular control declined with age as did the vagally controlled heart rate changes in response to deep breathing and VM. We could not demonstrate any correlation between BRS, smoking status, and body size when adjusting for age and gender, whereas spontaneous BRS was reduced with increasing Framingham risk score. Principal component analysis revealed three component explaining 69% of the total variance in our population comprising one component reflecting the sympathetic activity, the parasympathetic system, and the integrated spontaneous BRS, respectively. The parasympathetic component was the only one correlating with clinical characteristics of declining age, smoking habits, systolic blood pressure and Framingham score.

It is concluded that the parasympathetic and sympathetic parts of the baroreflex arch behave differently with respect to aging and cardiovascular risk factors. The most prominent changes are seen in cardiovagal control whereas the effects of age related changes in sympathetic vascular control are less noticeable. Our study supports the use of the cardiovagal part of the baroreflex arch as an indicator of cardiovascular risk.

Keywords: Baroreflex sensitivity; Aging; Cardiovascular risk; Autonomic nervous system

Introduction

Baroreflex function measured as baroreflex sensitivity (BRS) mirrors an integrated capacity of the autonomic nervous system and is an established tool for the assessment of autonomic control of the cardiovascular system. Changes in blood pressure will lead to changes in the impulse frequency of the afferent nerves from the baroreceptors terminating in the nucleus of the solitary tract and central relaying of the signal leads to changes in the sympathetic and parasympathetic outflow. In the original study by Hering [1], it was demonstrated that stimulation of the nerves from the carotid sinus induced cardiac slowing and vasodilatation with the latter being independent on the bradycardia. This distinction between the effect on heart rate and the vascular system is reflected in the division of baroreflex sensitivity in a part that causes a change in the interbeat interval (cardiovagal BRS) and a part that changes sympathetic nerve activity or vascular tone (adrenergic BRS). Both cardiovagal and adrenergic BRS has been shown to be blunted with increasing age in a mutual independent manner [2].

Cardiovagal BRS may be quantified by the heart rate response to blood pressure changes induced by vasoactive drugs with minimal effect on the sinus node. Non-interventional alternatives are mainly represented by forced changes in cardiac filling by the Valsalva manoeuver, by direct changes in external carotid pressures through the neck chamber technique, or by analysis of spontaneous variations of blood pressure and RR interval. A linearly and invers association between cardiovagal BRS and age has been demonstrated in a number of studies [3,4] and decreased cardiovagal BRS has consistently been found in several age-related disease states such as ischemic heart disease, hypertension, heart failure, and diabetes [5-7]. Cardiovagal BRS has also been shown to be a strong, independent prognostic factor in patients with ischemic heart disease or congestive heart failure [8]. Lifestyle factors are known to influence cardiovascular health and cardiovagal BRS. Smoking increases sympathetic activity [9] and a number of studies have demonstrated that - compared to non-smokers - smokers have higher heart rates, diminished heart rate variability,

and reduced cardiovagal BRS [10] with similar or lower blood pressures [11]. Changes in body composition towards a higher relative fat content are associated with an impaired cardiovagal BRS [12] and leptin, released from adipocytes, could be a central factor through its sympathoexcitatory activity [13].

Age related changes in adrenergic BRS are less clearly defined. Aging is associated with increased sympathetic nerve activity mirrored both by increasing plasma catecholamine concentrations [14] and in measures of resting muscle sympathetic nerve activity [15] and these changes seem to be a function not just of age but also by age-related differences in ischemic heart disease, obesity, chronic physical activity, or arterial blood pressure [15].

We primarily aimed to assess the relationship between measures of baroreflex sensitivity and age. We set out to quantify both spontaneous cardiovagal BRS and forced cardiovagal and adrenergic BRS indices using the Valsalva maneuver (VM) as well as the purely parasympathetic heart rate responses to VM and deep breathing. Secondly we wanted to assess the relationship between these indices and relevant clinical characteristics of the patients included.

Subjects and Methods

We included 80 subjects without overt cardiovascular disease aged 40-80 years recruited through The Copenhagen City Heart study. The participants were equally distributed with respect to age, smoking status, and gender. Subjects were enrolled in the study between May and December 2011. The Danish Data Protection Agency and the Danish Scientific Ethical Committee approved the study and written informed consent was obtained from all participants.

Clinical characteristics registered in the study included: Age, gender, smoking status, number of pack-years (number of packs per day multiplied by the number of smoking years), height, weight, and waist circumference (measured to the nearest cm). Body mass index (BMI) and waist-to-height ratio (WHR) were calculated [16] as was the 10-year risk of coronary heart disease from the Framingham score [17].

All tests were performed between 8 a.m. and 10 a.m. in the fasting state at standard room temperature. RR-intervals and blood pressure were measured continuously from one precordial ECG-lead and by Finometer equipment (FinaPress Medical Systems BV, Amsterdam, The Netherlands), respectively. Data were sampled at 1.0 kHz and analysed using commercial software (Chart 5.59, AD Instruments Inc, Colorado Springs, USA). Data were acquired during 10 min of supine rest, where the subjects were asked to refrain from speaking and moving unnecessarily during the test. The subjects were loosely strapped to an electrically driven tilt table and tilted to the upright position within 3-4 s with the inclination of the table set at 60 degrees and held in this position for 10 minutes unless the participant asked for the test to be aborted due to orthostatic symptoms (Head-up tilt test, HUT). Following this the subjects performed a Valsalva maneuver (VM) in the sitting position as we wanted the Phase IV to reflect peripheral vasomotor adrenergic function and not cardiac function [18]. We used a mouthpiece connected to a mercury manometer by a rubber hose with a small air leak to prevent closing of the glottis and the subjects were asked to take a deep inspiration and then blow into the mouthpiece trying to maintain an expiratory pressure of 40 mmHg in 15 seconds. The procedure was repeated until two matching responses were obtained.

Following this the subjects were asked to breath at a rate of 6 min-1 during two minutes in the seated position (Deep breathing, DB).

Data analysis

Clinical blood pressure levels were obtained by the oscillometric method on the upper arm after 5 minutes in the sitting position and calculated as the mean value of three consecutive measurements for systolic and diastolic blood pressure.

The ECG was band-pass filtered with cut-off frequencies at 0.6 and 40.0 Hz and the blood pressure data were low-pass filtered with a cut-off frequency of 40.0 Hz. RR-intervals were converted to instantaneous heart rate and systolic and diastolic blood pressures were derived from the maximum and minimum values on the continuous blood pressure recording on a beat-by-beat basis

The hemodynamic response to the VM is divided in to four phases: Phase I is the early increase in blood pressure, being followed by an initial fall and subsequent rise in blood pressure during Phase II. Heart rate increases throughout these phases. Phase III is the short decrease in blood pressure at the release of strain and is followed in Phase IV by a rapid increase in blood pressure above baseline and a fast reduction in heart rate (Figure 1). The index of cardiovagal BRS (BRSv) was calculated as the slope of the regression line of RR-intervals plotted against mean blood pressure in the early Phase II [19,20]. Pressure recovery time (PRT) was calculated as the interval between trough values of systolic blood pressure in Phase III and time for return to baseline values given as the mean value from 30 s before the maneuver. Phase III was not calculated if the SBP did not decrease below baseline [20]. The adrenergic BRS was calculated as the difference in SBP between baseline and trough value in Phase III divided by the PRT (BRSa) [20] and as the fall in SBP from baseline in Phase II with the addition of 75 per cent of the drop in SBP in Phase III and then divided by PRT BRSa1 [20]. Neither BRSa nor BRSa1 were calculated if PRT could not be obtained.

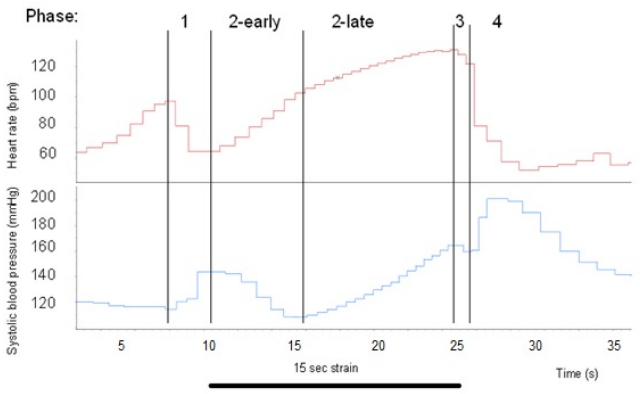

Figure 1: The Valsalva manoeuver. Heart rate (red line) and systolic blood pressure (blue line) changes in response to the Valsalva manoeuvre with 15 s strain at 40 mmHg. The various phase of the manoeuvre are given at the top.

Heart rate response to the Valsalva manoeuvre was expressed by the Valsalva ratio (VR) and calculated by dividing the longest RR-interval after the manoeuver by the shortest RR-interval during the manoeuver [21]. Heart rate response to deep breathing session was quantified by

the difference between the mean value of the lowest and highest heart rates during six consecutive breathing cycles (E-I) [21].

The sequence technique for analysing the spontaneous BRS was used [22]. Ectopic-free segments of 5 min of continuous RR-intervals (RRI) and systolic blood pressure (SBP) readings were analysed in the supine position and between the 5th and the 10th minute of HUT. Changes of at least 1 mmHg (SBP) and 6 ms (RRI) were required for the calculation using a lag between SBP and RRI of one beat. The linear correlation between RRI and SBP was computed for each of the detected sequences. A regression slope was calculated for those sequences having a correlation coefficient of 0.8 or more. We pooled the slopes for both increasing and decreasing values in SBP and RRI and the average of these regression slopes are given for the supine position (BRS-supine) and the tilted position (BRS-HUT). We calculated the change in BRS from the supine to the tilted position and expressed this as a percentage of the supine value (BRS%).

Statistical analysis was done using SPPS 19 (SPSS inc. Chicago, Illinois). Log normal transformation was used for non-normally distributed parameters (BRS-supine, BRS-HUT, BRSv, VR, PRT, BRSa, BRSa1).

Results are expressed as mean values ± standard deviations (SD) for non-transformed data and as mean values with 95% confidence intervals (CI) for transformed variables. Linear regressions were made relating measures of BRS to age. Correlations are given by Pearson's correlation coefficient r. A two-sided significance level of 0.05 was used.

A principal component analysis (PCA) was performed with respect to the BRS measures. The suitability of PCA was assessed prior to analysis using an overall Kaiser-Meyer-Olkin (KMO) measure greater than 0.60 and a Barttlett's test of sphericity with a significance level of less than 0.01.

Results

A total of 80 participants (43 women) with a mean age of 59 ± 11 years (range 41-79 years) were included in the study. Clinical characteristics of the subjects included are given in Table 1. BRS measured by the sequence method could not be calculated in 13 patients in the supine and in 10 subjects in the tilted position due to multiple ectopy or errors in blood pressure measurement. Adrenergic indices (PRT, BRSa and BRSa1) could not be calculated in 12 patients as the SBP in Phase III did not decrease below baseline values.

	Mean	SD
Age (years)	59.1	11.3
Weight (kg)	74.4	12.9
Height (cm)	173	9.2
Waist circumference (cm)	89.6	12.0
Current smoker (n)	25	
Package years (years)	14.0	16.3
BMI (kg/m2)	24.7	3.0
WHR	0.52	0.06
SBP (mmHg)	138.6	21.0
DBP (mmHg)	86.5	10.7
HR (bpm)	61.6	8.4

Table 1: Baseline characteristics of the included subjects, Clinical characteristics of the 80 subjects given as mean ± SD except from current smoking status which is reported as the number of current smokers.

Mean values for the BRS parameters in each decade are given in Table 2. Most of the BRS parameters decreased with age. There seemed to be a tendency for spontaneous BRS-values and adrenergic indices to decrease from the 4th to the 6th decade and then increase in the 7th decade, whereas the vagal indices exhibit a more linear decline with age. BRS decreased from the supine to the tilted position and the relative change elicited by orthostatic stress was diminished with age with a decrease in BRS% from 50,4% in the 4th decade to 21,8% in the 7th decade.

	Age group (y)	N	Mean	SD
BRS-supine (ms/mmHg)	40-49	19	20.4	8.73
	50-59	18	16.6	6.86
	60-69	15	12.5	5.96
	70+	15	13.4	6.46
BRS-HUT (ms/mmHg)	40-49	19	8.5	3.17
	50-59	19	8.1	2.15
	60-69	15	7.8	4.14
	70+	17	10.4	10.93
BRSv (ms/mmHg)	40-49	20	9.9	7.47
	50-59	17	7.2	3.77
	60-69	16	5.5	3.87
	70+	16	7.1	7.18
VR	40-49	22	1.6	0.33
	50-59	19	1.4	0.21
	60-69	18	1.4	0.27
	70+	19	1.3	0.17
E/I-difference (bpm)	40-49	22	14.4	3.88
	50-59	19	12.3	5.86
	60-69	19	11.2	7.45
	70+	20	6.8	2.76
Phase IV (mmHg)	40-49	21	32.1	14.70
	50-59	16	22.9	15.71
	60-69	18	11.6	21.83
	70+	17	19.5	22.17
PRT (s)	40-49	20	2.44	1.63

	50-59	15	3.09	1.90
	60-69	17	4.58	1.55
	70+	16	6.34	6.25
BRSa (mmHg/s)	40-49	18	16.0	15.84
	50-59	16	8.8	5.33
	60-69	17	9.3	3.46
	70+	16	11.5	6.92
BRSa1 (mmHg/s)	40-49	18	20.4	12.12
	50-59	16	15.4	9.93
	60-69	17	13.6	7.28
	70+	16	13.2	7.91
%BRS	40-49	17	-50.4	24.87
	50-59	18	-48.0	14.99
	60-69	13	-29.4	38.46
	70+	15	-21.8	39.84

Table 2: Measures of baroreceptor sensitivity by age-group, Mean values for BRS parameters shown by age groups.

BRS-supine and BRS-HUT are measures of spontaneous BRS in the supine and head up tilted positions respectively and BRS% is the relative ratio between these. BRSv is the cardiovagal BRS, BRSa and BRSa1 are the adrenergic BRS, PRT and Phase IV are measured adrenergic indices and the VR is the Valsalva ratio.

Data for the correlation between baseline hemodynamics, BRS-measures and age are given in Table 3. SBP showed a weak, albeit significant increase with increasing age whereas neither HR nor DBP showed significant age-related changes. Except for data obtained during HUT, cardiovagal BRS parameters tended to decline with age reaching significance in the spontaneous supine BRS and in BRS%. The overshoot in SBP during Phase IV of the Valsalva maneuvre showed a weak, but significant negative correlation with age and PRT was positively correlated to increasing age. Both the heart rate changes in response to the Valsalva manoeuvre (VR) and to deep breathing (E-I) declined significantly with age.

	Intercept	Slope	SE	r^2	p-value
SBP	93.3	0.768	0.193	0.169	<0.0005
DBP	85.5	0.018	0.107	0.000	0.868
HR	55.9	0.097	0.086	0.017	0.262
lnBRS-supine	3.43	-0.013	0.005	0.089	0.014
lnBRS-HUT	1.78	0.005	0.006	0.011	0.396
lnBRSv	2.92	-0.020	0.012	0.039	0.104
lnVR	0.67	-0.670	0.002	0.127	0.001
E-I	25.3	-0.238	0.052	0.209	<0.0005
Phase IV	52.0	-0.513	0.203	0.084	0.014
lnPRT	-1.06	0.037	0.007	0.299	<0.0005
lnBRSa	2.57	-0.006	0.008	0.008	0.480
lnBRSa1	3.446	-0.015	0.007	0.058	0.052
BRS%	-92.411	0.92	0.352	0.102	0.011

Table 3: Correlations between baro reflex sensitivity and age

As SBP increased significantly with age we adjusted the abovementioned correlations for changes in SBP. The adjustment abolished the significance of the correlation between age and BRS-supine ($p_{adjusted}$=0.147) whereas the correlations were still significant for BRS% ($p_{adjusted}$=0.040), phase IV overshoot ($p_{adjusted}$ =0.028), PRT ($p_{adjusted}$=0.001), VR ($p_{adjusted}$=0.039), and E-I ($p_{adjusted}$<0.0005). We could not demonstrate any correlations between gender and the measured or calculated variables.

Correlations between baseline hemodynamic measures and the derived parameters for autonomic cardiovascular control are given in Table 4. SBP was negatively correlated to BRS-supine and VR and positively correlated to PRT. HR correlated negatively with BRS-supine, BRS-HUT, and BRSv. HR correlated positively with BRSa and BRSa1. Neither weight, height, BMI, WH, nor smoking were significantly correlated to baseline values of HR, SBP, or DBP. When adjusted for age and gender, correlations between measures of body size, smoking and BRS lost statistical significance except for a positive correlations between weight and BRSa1 (p-value=0,026).

	SBP		HR		Gender	
	r	p	r	p	r	p
BRS-supine (ms/mmHg)	-0.331	0.006	-0.337	0.005	-0.024	0.845
BRS-HUT (ms/mmHg)	-0.111	0.360	-0.279	0.019	-0.104	0.390
BRSv (ms/mmHg)	-0.217	0.074	-0.318	0.008	0.107	0.382
VR	-0.368	0.001	-0.193	0.092	0.191	0.093
E/I-difference (bpm)	0.121	0.283	-0.109	0.342	-0.022	0.845
Phase IV (mmHg)	0.135	0.257	0.161	0.183	0.081	0.497
PRT (s)	0.284	0.019	0.078	0.530	0.197	0.107
BRSa (mmHg/s)	0.139	0.263	0.264	0.032	-0.019	0.880
BRSa1 (mmHg/s)	0.223	0.070	0.291	0.018	0.098	0.429
%BRS	0.183	0.150	-0.062	0.629	-0.071	0.578

Table 4: Correlations between gender, baseline values of systolic blood pressure and heart rate and measures of baroreflex sensitivity

Correlations between measures of cardiovascular autonomic control and baseline values for systolic blood pressure, heart rate, and gender given by the Pearson's correlation coefficient with p-values

Neither weight nor BMI was significantly correlated to age although BMI tended to increase with age (r=0,194, p=0,085) but both waist circumference (r=0,255, p=0,024), and WHR (r=0,371, p=0,001) increased with advancing age.

Framingham risk score was positively correlated to SBP (r=0,532, p=<0.0005), DBP (r=0,271, p=0,015), HR (r=0,225, p=0,048), and PRT (r=0,398, p=0,001 and negatively correlated to BRS-supine (r=-0,378, p=0,002).

In the principal component analysis, the overall Kaiser-Meyer-Olkin (KMO) measure vas 0.66 and individual KMO measures were all greater than 0.50 except for BRS-supine (KMO=0.43) and BRS-HUT (KMO=0.44). We chose to keep these two variables in the model as they were considered important BRS-indices. Removing them from the model did not change the loading of the remaining variables on the three components. Barttlett's test of sphericity was statistically significant (p<0.0005) indicating that our data were usable in a factor analysis. Inspection of the correlation matrix showed that all variables had at least one correlation coefficient greater than 0.3. Visual inspection of the scree plot indicated that three components should be retained – all had eigenvalues greater than one and explained 34.2%, 20.8% and 14.0% of the total variance, respectively. This three-component solution explained 68.9% of the total variance and exhibited a simple structure with each variable having only one component that loaded strongly upon it (Table 5). Component 1 loaded on BRSa, BRSa1, PRT, SBP and Phase IV – all indices derived from the VM and all described as adrenergic indices and is therefore denoted the adrenergic component (C_adren). Component 2 loaded on spontaneous BRS in the supine and tilted position and this component is denoted the baroreflex component (C_BRS). Component 3 loaded on BRSv, VR and the E/I-difference and as these are all indices of vagal function this component is denoted the vagal component (C_vagal).

	Component		
	C_adren	C_BRS	C_vagal
BRSa (mmHg/s)	0.958	-0.009	0.126
BRSa1 (mmHg/s)	0.944	-0.056	0.158
PRT (s)	-0.779	-0.061	0.231
Phase IV (mmHg)	-0.542	0.046	0.299
BRS-HUT(ms/mmHg)	-0.031	0.835	0.011
BRS-supine(ms/mmHg)	-0.016	0.899	-0.004
BRSv (ms/mmHg)	-0.116	-0.200	-0.887
VR	-0.024	0.246	-0.631
E/Idifference (bpm)	-0.154	-0.089	0.570

Table 5: Principal component analysis, Rotated structure matrix for PCA with a three component model

We tested our new components against basal clinical characteristics (Table 6) and found C_adren and C_BRS to be independent upon all of the basal clinical characteristics except from C_BRS being inversely correlated to heart rate. C-vagal decreased significantly with age, package years, SBP and Framingham risk score.

		C_adren	C_BRS	C_vagal
Age (years)	r	-0.220	-0.147	-0.421
	p	0.117	0.299	0.002
Gender *	r	-0.051	0.005	0.147
	p	0.720	0.975	0.303
Current smoker	r	-0.160	0.095	-0.181
	p	0.257	0.502	0.199
Package years (years)	r	-0.205	-0.149	-0.347
	p	0.145	0.291	0.012
SBP (mmHg)	r	0.054	-0.260	-0.308
	p	0.704	0.063	0.026
DBP (mmHg)	r	0.029	-0.142	0.049
	p	0.837	0.317	0.728
HR (bpm)	r	0.236	-0.300	-0.239
	p	0.092	0.031	0.088
Framingham risk %	r	-0.097	-0.245	-0.283
	p	0.492	0.080	0.042
Height (cm)	r	0.144	0.024	0.182
	p	0.309	0.868	0.197
Weight (Kg)	r	0.124	0.071	0.149
	p	0.380	0.617	0.292
BMI (kg/m2)	r	0.058	0.085	0.037
	p	0.684	0.551	0.794
Waist circumference (cm)	r	0.078	-0.106	0.106
	p	0.581	0.454	0.453
WHR	r	0.011	-0.145	0.024
	p	0.939	0.311	0.868

Table 6: Correlations between baseline characteristics and components baroreceptor function

Zero order correlations between baseline clinical characteristics and the three components of cardiovascular control derived through principal component analysis. Correlations given by Pearsons coefficient (r) with p-values (p).

Discussion

Our goal was to study the effect of aging in the different measures of baroreflex sensitivity and to assess the relationship between these measures and other important clinical characteristics. We found age-related decrease in baroreceptor sensitivity (BRS) and in the ability to adjust this sensitivity on assumption of the upright posture (BRS%). We also found a blunting in the peripheral vascular adaptation to the Valsalva maneuver and a decrease in forced changes in heart rate. We confirmed that systolic blood pressure (SBP) increased with age [23] and when corrected for this, the age related changes in BRS disappeared.

Previous studies have shown a negative, linear correlation between age and cardiovagal BRS [3,4], between age and BRS parameters derived from the VM [2], and between age and spontaneous cardiovagal BRS measured by the sequence method [24]. Our findings are more in line with a previous study showing a non-linear changes in cardiovagal BRS with the steepest decline in the 4th or 5th decade and a leveling out in older age groups [25]. This non-linearity could be due to a "survival bias" as impaired BRS has been shown to be a significant marker for cardiovascular mortality and morbidity [2,6,7].

Sympathetic nerve activity at rest has been found to increase with aging which is mirrored in increased plasma noradrenaline concentrations [26] and increased burst activity in muscle sympathetic nerve fibres measured by microneurography [27]. The correlation between age and plasma noradrenaline levels seems to be abolished when adjusted for cardiovagal BRS suggesting that decreasing cardiovagal BRS with age contributes to the relative sympathoexcitation seen with age [28]. Others have found the efferent sympathetic nerve activity during pharmacologically induced transient hypertension or hypotension to be unaffected by aging in both healthy subjects [29] and in rodents [30] and interpreted this as evidence for an intact baroreflex function during normal aging. In our study, the adrenergic vasomotor activity measured as PRT and the Phase IV overshoot revealed significantly diminished vascular reactivity with increasing age [31] suggesting that a higher sympathetic activity could be necessary to adjust for blood pressure deviations. This would explain the apparent normal baroreceptor sensitivity in older age groups with increased plasma noradrenaline and sympathetic nerve activity. Reductions in adrenergic receptor sensitivity in the target organs [32] could explain why heart rate is unaffected by age despite an increased sympathetic activity. Age related alterations in the adrenergic responsiveness in the arterial system could be the result of increased activity in G-protein-linked kinase 2 as suggested by Santulli et al. [33].

Measures of heart rate variability primarily reflect vagal control of heart rate and have been shown to be inversely related to age [34]. Vagal control is primarily transmitted through large myelinated nerve fibers and these are thought to degenerate with increasing age [35] which would result in decreasing conduction velocities and ultimately in loss of control. Our findings of age related decline in heart rate responses to deep breathing and VM are thus in accordance with the literature.

We decided to make use of principal component analysis as the number of possible measures of baroreceptor function and related parameters autonomic function is large. The PCA revealed three components that - in our minds - described the primary aspects of baroreceptor control namely the sympathetic nervous activity, the parasympathetic nervous activity and their integrated function and through these components we were able to account for more than two-thirds of the total variation encountered. The sympathetic component of baroreflex control was independent upon age, gender and clinical characteristics of our subjects - findings that are in accordance with previous studies in humans and rodents [29,30]. The parasympathetic component - on the other hand - decreased significantly with age, smoking habits, SBP and calculated cardiovascular risk. Our findings confirm the notion that it is the parameters primarily dependent on vagal activity that expresses the most pronounced relation to age, smoking and cardiovascular risk. Our findings are thus in line with studies showing the prognostic importance of changes in vagal control of heart rate [8].

Body size and composition changes with age [36] and most of our measures of changes in baroreceptor and autonomic nervous function were not correlated to changes in these parameters when corrected for age. However, the adrenergic baroreceptor parameter BRSa1 increased with increasing weight which is in concordance with several studies showing obesity to be characterized by heightened activity in the sympathetic nervous system coupled with impaired cardiovagal BRS [37,38]. Neither current smoking status nor number of package years had any significant influence on measures of BRS when adjusted for age.

Impairment of baroreflex function is not only related to cardiovascular morbidity and mortality but also contributes to the age-related increase in the incidence of orthostatic hypotension, syncope, and falls [39]. Measurement of BRS is therefore of important both in research and in the clinical setting and future studies are warranted in order to establish standardized, age corrected measures of BRS to be used in a diagnostic and prognostic set–up.

Conclusion

Our study has demonstrated that cardiovagal and adrenergic baroreceptor sensitivity behave differently with respect to aging and cardiovascular risk factors. The most prominent age related changes are seen in vagal control of heart rate whereas the effects of age related changes in sympathetic vascular control are less noticeable. We have also confirmed the correlation between reduced cardiovagal baroreceptor sensitivity and risk of cardiovascular disease and our findings support the use of measures of cardiovagal rather than adrenergic baroreceptor sensitivity as a prognostic measure in patients at risk for cardiovascular diseases.

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