Is there an association between altered baroreceptor sensitivity and obstructive sleep apnoea in the healthy elderly?

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ABSTRACT Obstructive sleep apnoea (OSA) is associated with a rise in cardiovascular risk in which increased sympathetic activity and depressed baroreceptor reflex sensitivity (BRS) have been proposed. We examined this association in a sample of healthy elderly subjects with unrecognised OSA.

801 healthy elderly (aged ⩾65 years) subjects undergoing clinical, respiratory polygraphy and vascular assessment were examined. According to the apnoea–hypopnoea index (AHI), the subjects were stratified into no OSA, mild–moderate OSA and severe OSA cases.

OSA was present in 62% of the sample, 62% being mild–moderate and 38% severe. No differences were found for BRS value according to sex and OSA severity. 54% of the group had normal BRS value, 36% mild impairment and 10% severe dysfunction. BRS was negatively associated with body mass index (p=0.006), 24-h systolic (p=0.001) and diastolic pressure (p=0.001), and oxygen desaturation index (ODI) (p=0.03). Regression analyses revealed that subjects with lower BRS were those with hypertension (OR 0.41, 95% CI 0.24–0.81; p=0.002) and overweight (OR 0.42, 95% CI 0.25–0.81; p=0.008), without the effect of AHI and ODI.

In the healthy elderly, the presence of a severe BRS dysfunction affects a small amount of severe cases without effect on snorers and mild OSA. Hypertension and obesity seem to play a great role in BRS impairment.

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Introduction

Obstructive sleep apnoea (OSA) is a common disease affecting 9% of women and 24% of men aged 30–60 years [1], with an even higher prevalence reported in the elderly population (aged >65 years). In the latter group, 24–62% suffered from a mild form and 19–44% represented moderate–severe cases [2–4]. Epidemiological studies demonstrated a strong link between OSA and cardiovascular diseases such as hypertension [5–7], coronary arterial disease, arrhythmias and heart failure [8]. Several mechanisms have been proposed to play a key role in the association between OSA and cardiovascular disease, including oxidative stress, inflammation and in particular the rise of sympathetic tonus in response to chemoreceptor stimulation by apnoea-related intermittent hypoxia [8–11]. A controversial point on the pathophysiology of vascular OSA consequence is the influence of a more complex dysregulation of the autonomic nervous system including both an increase of sympathetic activity and an impaired and/or suppressed spontaneous cardiac baroreflex sensitivity (BRS), a marker of parasympathetic activity that prevents the reflex rise of arterial blood pressure along the obstructive apnoea [12]. In the study of HESSE et al. [13] considering healthy subjects, BRS was inversely correlated with mean 24-h blood pressure values. Few studies are present in the literature that consider the link between BRS and OSA severity. In middle-aged adult patients, a BRS dysfunction has been found in some OSA cases [14, 15], frequently in severe cases [16, 17], but not in mild OSA patients [18] or in snorers [19, 20].

To our knowledge, no data are presented in the literature concerning a possible association between altered BRS and OSA in the healthy elderly. Reduced BRS has been reported in older subjects due to the age-related reduction in cardiac parasympathetic tone [21, 22] and increased basal sympathetic nerve activity [23]. Since age in itself may blunt the BRS response, we would expect a greater association between BRS and OSA in an older population. The purpose of the present study was two-fold in order to assess the following: 1) if there was an independent association between BRS and OSA in a homogenous large group of healthy elderly with unrecognised OSA; and 2) the potential contribution of other factors, such as overweight, smoking habit [24] and alcohol consumption [25], which are known to affect autonomic system regulation.

Materials and methods

Participants

Subjects were selected from the participants of a population-based cohort of 1011 volunteers aged ⩾65 years residing in the city of Saint-Etienne (France). The cases were enrolled in the PROOF (PROgnostic indicator OF cardiovascular and cerebrovascular events) [26] survey, an ongoing study on the prognostic value of autonomic nervous system activity indicators on cerebrovascular and cardiovascular morbidity and mortality. Exclusion criteria were defined as follows: age <65 years, previous reported myocardial infarction, arrhythmia, cardiac pacemaker, stroke, previous diagnosis of neurological or psychiatric disease, insulin-dependent diabetes, chronic obstructive pulmonary, renal or liver disease, cerebral magnetic resonance imaging suggesting neurological disease or initial dementia and currently living in an institution. Of the 3983 eligible participants, the final PROOF study included 1011 volunteers (609 females and 402 males). An ancillary study (Autonomic Nervous System Activity, Aging and Sleep Apnea/Hypopnea (SYNAPSE)) focusing on the association between OSA, as assessed by home-based polygraphy and cardiovascular consequences, was proposed to the participants, and the final sample was of 825 subjects. After exclusion of subjects who refused BRS measurement or home polygraphy, the final sample of 801 subjects aged 66.9±0.9 years underwent a complete evaluation, including clinical interview, anthropometric measurements, 24-h blood pressure measurement, BRS assessment and ambulatory respiratory polygraphy.

The PROOF and the SYNAPSE studies were approved by the university hospital and the local ethics committee (CCPRB, Rhone-Alpes Loire, France). The French National Committee for Information and Liberty gave consent for data collection. All subjects gave their written consent prior to participation in the study.

Clinical and instrumental assessments

Clinical assessment

Clinical evaluation was assessed by a structured interview, which included history of cardiac and cerebrovascular diseases, arterial hypertension, diabetes and neurological and psychiatric disorders. Subjects were defined as normotensive if they did not report a history of hypertension and antihypertensive treatment and did not have a clinical measurement of systolic blood pressure (SBP) >135 mmHg and a diastolic blood pressure (DBP) >85 mmHg [27]. Habitual and past smoking, alcohol consumption (>2 glasses of wine and/or spirit per day) and medications were analysed, with the latter focusing on antihypertensive, antidiabetic and antihypercholerolaemic medications by analysing medical prescriptions.

Anthropometric measurements

Anthropometric measurements included body mass index (BMI) and neck circumference, measured for all subjects. BMI was calculated as body weight divided by the square of height (kg·m^{-2}). We classified the

subjects into three groups on the basis of BMI value: normal weight for BMI <25 kg·m^{-2}; overweight for BMI >25 kg·m^{-2} and <30 kg·m^{-2}; and obese for BMI >30 kg·m^{-2}. neck circumference was measured at the middle of the neck between the mid-cervical spine and the mid-anterior neck 0.5 cm below the laryngeal prominence.

Blood pressure assessment

Diurnal SBP and DBP were measured by a physician using a standard mercury sphygmomanometer on the right arm while the subject was in the supine position following a 5-min period of rest. Ambulatory blood pressure monitoring was assessed over a 24-h period by an ambulatory recording device using an auscultatory method (Diasys Integra; Novacor, Rueil-Malmaison, France); the measurements were taken at 15-min intervals during the day and every 30 min during the night, with cuff placement on the nondominant arm. Diurnal and nocturnal periods were defined on the basis of the reported time when participants were lying down with the lights switched off. Subjects were defined as normotensive if no history of hypertension or antihypertensive treatment was reported, and if the 24-h ambulatory blood pressure monitoring did not show a diurnal mean SBP ⩾135 mmHg and a mean DBP ⩾85 mmHg [28].

Measurement of BRS

Spontaneous cardiac BRS was calculated over 15 min at rest in the supine position under the control of a doctor checking that the subjects did not move during the examination. Although the vasoactive drug bolus technique is widely used, the spontaneous method provides a reliable low stress and painless assessment of human vagal cardiac baroreflex activity. Finger arterial blood pressure was measured by the volume-clamp method by means of a noninvasive continuous blood pressure monitor (Finapres 2300; Ohmeda, Amsterdam, The Netherlands). For the calculation of BRS using the sequence method, the software listed all sequences of at least three or more successive heart beats in which there were concordant increases and decreases in SBP, and the R–R interval. For each sequence, linear regression slope was calculated. Then the BRS (expressed in ms·mmHg^{-1}) was calculated as the mean of the slopes of all the sequences. Such a sequence method has been already used in our laboratory in post-myocardial infarction patients as well as in chronic obstructive pulmonary disease. For the last study [28], we determined normal range values of BRS in healthy 67-year-old volunteers (7.8±4.9 ms·mmHg^{-1}). In chronic obstructive pulmonary disease patients as well as in high-risk post-myocardial infarction patients, the mean value of BRS was 3.4±2.6 and 3.1±2.1 ms·mmHg^{-1}, respectively. In accordance with thresholds of BRS proposed in the Autonomic Tone and Reflexes After Myocardial Infarction (ATRAMI) study, we classified our sample according to a mean slope <3 ms·mmHg^{-1} as a severe alteration of the cardiac baroreflex, a mean slope between 3–6 ms·mmHg^{-1} as a moderate alteration and a mean slope >6 ms·mmHg^{-1} as a normal BRS range.

Ambulatory home polygraphy

All subjects underwent a full night ambulatory polygraphic recording using a polygraphic system (HypnoPTT; Medtronic, Dublin, Ireland). The following parameters were included: sound measurement, electrocardiography, pulse transit time, R–R timing, nasal pressure, respiratory effort and body position. Oxygen saturation was measured by pulse oximetry (S_{pO_2}). To minimise potential overestimation of sleep duration, subjects completed the St. Mary's Hospital questionnaire, while wakefulness before lights off was excluded by the analysis. All examinations were visually validated and manually scored for respiratory events and nocturnal S_{pO_2} by a single scorer (F. Roche), with an intrascorer reliability of 87%. Hypopnoea was defined as a ⩾50% reduction in airflow from the baseline value lasting ⩾10 s and associated with ⩾3% oxygen desaturation. Apnoea was defined as the absence of airflow in the nasal cannula lasting for ⩾10 s. The absence of rib cage movements associated with apnoea defined the event as central, while a progressive increase in pulse transit time and respiratory efforts allowed definition of the episode as obstructive. Apnoea–hypopnoea index (AHI) was defined as the ratio of the number of obstructive apnoeas and hypopnoeas per hour of reported sleeping time. The indices of nocturnal hypoxaemia were as follows: mean S_{pO_2}; percentage of recording time with a S_{pO_2} ⩽ 90%; minimum S_{pO_2} value recorded during sleep (minimum S_{pO_2}); and oxygen desaturation index (ODI), *i.e.*, the number of episodes of oxyhaemoglobin desaturation per hour of reported sleep time during which blood oxygen level fell ⩾3%. Pulse transit time was continuously monitored, and autonomic respiratory-related and total autonomic arousal indices were calculated after visual correction [29]. According to recent data in elderly subjects [30], an AHI ⩾15 events·h^{-1} with at least 50% of events scored as obstructive was considered diagnostic of OSA. Cases were subsequently stratified as mild-to-moderate (AHI ⩾15 events·h^{-1} and <30 events·h^{-1}) and severe OSA cases (AHI ⩾30 events·h^{-1}).

Statistical analyses

Study population characteristics were reported as mean±SD for continuous variables, and counts and percentages for categorical variables. Differences between men and women were assessed with the

Chi-squared test for categorical variables and t-test for continuous variables. ANOVA with Bonferroni's correction for multiple comparisons was used to estimate differences between groups stratified according to AHI and type of BRS. Pearson's correlation analysis was done to evaluate the link between BRS value and clinical and polygraphic data. Multivariate regression analysis was performed where the type of BRS dysfunction was the dependent variable and polygraphic data were the independent variables, with adjustment for potential confounding factors such as sex, BMI, smoking and alcohol, diabetes, dyslipidaemia and hypertension.

Data were analysed using the Statistical Package for the Social Sciences version 17 for Windows (SPSS Inc., Chicago, IL, USA). All reported p-values are two-tailed, with the threshold of statistical significance set at p<0.05.

Results

Table 1 shows the clinical, anthropometric, vascular and polygraphic data for the total sample and for women and men. Overall, participants had an average age of 66.9±0.9 years with a female prevalence of 59% and a mean BMI of 25.5±3.8 kg·m^{-2}. About 3% of the population had type 2 diabetes, 35% dyslipidaemia and 45% hypertension. Comparison analysis between sexes (table 1) revealed that women had lower values of BMI, neck circumference, SBP and DBP, and they were less frequently smokers or taking alcohol. In contrast, they had significantly lower values of AHI and indices of nocturnal hypoxaemia. Considering BRS, the mean values were in the normal range without sex differences. Table 2 reports the clinical, anthropometric and polygraphic data for subjects stratified according to AHI. Subjects without OSA (AHI <15 events·h^{-1}) represented 44% of the total population, with 35% labelled as mild–moderate (AHI ⩾15 events·h^{-1} and <30 events·h^{-1}) and 21% as severe cases (AHI ⩾30 events·h^{-1}). Comparison analysis between groups revealed a tendency to progressive and significant increases in BMI, neck circumference, the number of subjects taking alcohol, prevalence of hypertension and high values of blood pressure paralleling the severity of AHI, and indices of nocturnal hypoxaemia with significant differences both in moderate (p=0.001) and severe (p<0.001) cases. Interestingly, no differences in BRS value were found between the three groups. Table 3 shows the clinical, anthropometric and polygraphic data according to BRS value. The majority of subjects had normal BRS (54%), 36% had mild impairment and 10% had severe blunted BRS. Subjects with severe BRS alteration (BRS <3) were those having a significant rise on the percentage of hypertension and all values of blood pressure examined (p<0.001), associated with an

TABLE 1 Clinical, anthropometric and polygraphic data for the whole group and for women and men

	Total	Women	Men	p-value
Subjects n	801	462	339	
BMI kg·cm^{-2}	25.5±3.8	25.2±4.2	26.0±3.0	0.006
Neck circumference cm	37.1±3.9	34.6±2.6	40.5±2.8	<0.001
Hypertension %	45.1	42.2	44.9	0.05
Diabetes %	2.5	1.3	4.3	0.008
Dyslipidaemia %	35	38	30	<0.001
Alcohol %	46	32	61	<0.001
Smoking %	26	12	66	<0.001
SBP 24-h mmHg	119.1±14.3	116.6±13.7	122.3±14.3	<0.001
DBP 24-h mmHg	76.0±7.9	74.2±7.6	78.6±7.8	<0.001
SBP diurnal mmHg	123.1±14.8	121.3±14.8	125.6 ±14.5	<0.001
DBP diurnal mmHg	77.1±8.2	75.6±8.2	79.1±7.8	<0.001
SBP nocturnal mmHg	106.9±15.5	105.6±16.3	108.8±14.2	0.003
DBP nocturnal mmHg	66.4±9.2	64.6±9.1	68.7±8.8	<0.001
BRS ms·mmHg^{-1}	6.9±3.5	7.0±3.5	6.7±3.6	NS
AHI events·h^{-1}	20.4±14.7	16.7±12.4	25.6±16.4	<0.001
ODI events·h^{-1}	9.3±9.4	7.4±7.7	12.1±10.8	<0.001
Mean S_{pO_2} %	95.3±1.7	95.5±1.6	95.1±1.9	0.002
Minimal S_{pO_2} %	89.7±4.1	90.3±3.6	89.0±4.0	<0.001
Time with S_{pO_2} <90% %	1.9±5.7	1.4±5.0	2.6±6.6	0.01
Respiratory AAI events·h^{-1}	15.6±10.5	13.7±8.0	18.3±12.2	<0.001

Data are presented as mean±SD, unless otherwise stated. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; BRS: baroreceptor sensitivity; AHI: apnoea–hypopnoea index; ODI: oxygen desaturation index; S_{pO_2}: oxygen saturation measured by pulse oximetry; AAI: autonomic arousal index; NS: nonsignificant. Significance was determined by t-test or Chi-squared difference between women and men.

TABLE 2 Clinical, anthropometric and polygraphic data for the three groups of subjects stratified according to obstructive sleep apnoea severity

	AHI <15 events·h^{-1}	AHI ≥15 events·h^{-1} and <30 events·h^{-1}	AHI ≥30 events·h^{-1}	p-value
Subjects n	354	277	170	
BMI kg·cm^{-2}	24.7±3.5	25.8±3.9	26.9±3.6	<0.001
Neck circumference cm	35.7±3.6	37.3±3.9	39.5±3.7	<0.001
Hypertension %	38	51	54	0.001
Diabetes %	1	2	4	NS
Dyslipidaemia %	37	35	30	NS
Alcohol %	40	49	53	0.009
Smoking %	23	27	28	NS
SBP 24-h mmHg	116.1±13.7	121.0±14.1	122.2±14.6	<0.001
DBP 24-h mmHg	74.5±7.1	76.1±8.2	78.0±8.6	<0.001
SBP diurnal mmHg	120.8±14.8	124.5±14.4	125.8±14.9	<0.001
DBP diurnal mmHg	76.0±7.7	77.6±8.6	78.3±8.4	0.001
SBP nocturnal mmHg	103.9±14.9	108.7±16.4	105.3±14.1	<0.001
DBP nocturnal mmHg	64.6±8.5	67.1±10.0	68.8±8.6	<0.001
BRS ms·mmHg^{-1}	7.0±3.3	6.7± 3.4	7.0±4.1	NS
AHI events·h^{-1}	8.4±3.9	21.9±4.5	43.1±12.0	0.001
ODI events·h^{-1}	3.7±3.4	9.3±5.8	20.9±11.8	<0.001
Mean S_{pO_2} %	95.5±1.8	95.2±1.6	95.1±1.5	0.003
Minimal S_{pO_2} %	91.1±2.9	89.0±4.2	87.6±4.6	<0.001
Time with S_{pO_2} <90% %	1.2±5.8	1.9±4.6	3.3±6.6	<0.001
Respiratory AAI events·h^{-1}	8.9±5.2	15.9±6.5	28.9±11.3	<0.001

Data are presented as mean±SD, unless otherwise stated. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; BRS: baroreceptor sensitivity; AHI: apnoea–hypopnoea index; ODI: oxygen desaturation index; S_{pO_2}: oxygen saturation measured by pulse oximetry; AAI: autonomic arousal index; NS: non-significant. Significance was determined by ANOVA.

TABLE 3 Clinical, anthropometric and polygraphic data for the three groups of subjects stratified according to the baroreflex sensitivity threshold

	BRS <3 ms·mmHg^{-1}	BRS >3 ms·mmHg^{-1} and <6 ms·mmHg^{-1}	BRS >6 ms·mmHg^{-1}	p-value
Subjects n	76	292	433	
BMI kg·cm^{-2}	27.3±3.7	25.5±3.8	25.1±3.7	<0.001
Neck circumference cm	39.2±3.7	37.0±3.8	36.7±4.0	<0.001
Hypertension %	68	48	40	<0.001
Diabetes %	4	4	1	0.03
Dyslipidaemia %	47	35	33	NS
Alcohol %	41	25	23	0.009
Smoking %	26	12	66	<0.001
SBP 24-h mmHg	127.6±16.8	120.0±13.9	117.1±13.5	<0.001
DBP 24-h mmHg	81.2±9.2	76.1±7.6	75.1±7.6	<0.001
SBP diurnal mmHg	130.1±16.9	123.5±15.7	121.7±13.4	<0.001
DBP diurnal mmHg	80.5±9.1	76.8±8.7	76.6±7.5	0.001
SBP nocturnal mmHg	115.1±13.7	107.2±15.8	105.3±15.2	<0.001
DBP nocturnal mmHg	71.0±8.2	66.1±9.7	65.7±8.9	<0.001
BRS ms·mmHg^{-1}	2.9±0.5	4.6±0.9	9.2±3.2	<0.001
AHI events·h^{-1}	23.5±15.2	20.1±14.2	20.0±15.0	0.001
ODI events·h^{-1}	13.2±10.5	9.4±9.1	8.6±9.3	<0.001
Mean S_{pO_2} %	94.6±1.7	95.3±1.6	95.4±1.8	0.001
Minimal S_{pO_2} %	87.9±4.4	89.7±3.9	90.0±4.0	<0.001
Time with S_{pO_2} <90% %	3.7±6.9	2.0±6.4	1.5±5.0	0.006
Respiratory AAI events·h^{-1}	18.2±12.4	15.4±10.3	15.2±10.3	<0.001

Data are presented as mean±SD, unless otherwise stated. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; BRS: baroreceptor sensitivity; AHI: apnoea–hypopnoea index; ODI: oxygen desaturation index; S_{pO_2}: oxygen saturation measured by pulse oximetry; AAI: autonomic arousal index; NS: nonsignificant. Significance was determined by ANOVA.

increase in alcohol intake and indices of hypoxaemia. No significant differences were found for all considered factors in subjects with normal or mild BRS impairment.With correlation analysis, the BRS value was negatively associated with BMI (r=−0.98; p=0.006), 24-h systolic (r=−0.180; p=0.001) and diastolic (r=−0.142; p=0.001) blood pressures and with ODI (r=−0.08; p=0.03). Multiple logistic regression analyses (table 4) adjusted for sex, BMI, diabetes, dyslipidaemia, hypertension, alcohol, smoking, AHI and ODI revealed that subjects with a BRS <3 were those with hypertension (OR 0.41; 95% CI 0.24–0.81; p=0.002) and overweight (OR 0.42; 95%CI: 0.25–0.81; p=0.008) without contribution of AHI and ODI.

Discussion

To the best of our knowledge, the present study is the first to evaluate the potential independent association between dysfunction of baroreceptor sensitivity and the presence of OSA in a large group of healthy elderly subjects. The main finding of our study was that severe BRS dysfunction was present in only 10% of the group, the majority having normal values (54%). Moreover, the altered BRS affected mostly the severe OSA cases, without effect on snorers and mild–moderate subjects. A second interesting result is that neither smoking habit and alcohol consumption nor AHI and indices of hypoxaemia contributed to BRS dysregulation, with hypertension and obesity being the most important factors. Although speculative, we can suggest that BRS dysfunction in healthy elderly OSA reflects more of an autonomic dysfunction of the sympathetic–parasympathetic balance predisposing to hypertension rather than as a contributing factor of OSA vascular consequences.

It is known that, apart from the acute activation of sympathetic activation related to apnoea and arousal, persistent sleep fragmentation and repeated episodes of intermittent hypoxia–hypercapnia might induce not only a rise in the chemoreceptor sympathetic tone but also a downwards resetting of baroreceptor sensitivity [31] and its set-points, both reducing the cardio-protective effects of parasympathetic activity on the heart [32]. Despite an association between blunted BRS and hypertensive risk [17, 18] in OSA patients, controversial data are reported in the literature and are probably related to differences in methodology, sample size, definition of abnormal BRS and different study design. In initial studies performed during sleep [18, 33], BRS was depressed during daytime and night-time, but only in severe OSA cases. Moreover, despite studies performed after positive continuous positive pressure [20, 34] and surgery [35] showing a BRS improvement, there was not a complete normalisation. Furthermore, if RYAN et al. [15] observed that the frequency of oxygen desaturation >4% predicts decreased nocturnal BRS, this was not the case in children after adenotonsillectomy [41] and in our cases in whom any significant link was found between severity of hypoxaemia and BRS level. Overall, these data might suggest a threshold level of frequency and severity of hypoxaemia dips to induce a depressed BRS.

Another mechanism acting on cardiovascular risk in OSA patients is apnoea-related sleep fragmentation translated by arousals occurring at the end of apnoea, known to contribute to the dysfunction of the autonomic nervous system in OSA patients. Since our subjects had a polygraphic study that did not allow a correct estimation of sleep fragmentation, respiratory autonomic activations were analysed as surrogate markers of sleep disruption [36], and they were not associated with BRS. These results are supported by two

Explicative variables[#]	BRS >3 ms·mmHg^{-1} and <6 ms·mmHg^{-1}		BRS <3 ms·mmHg^{-1}	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Sex (women)	0.63 (0.34–1.21)	0.16	0.70 (0.39–1.31)	0.26
Hypertension (yes)	0.61 (0.35–1.05)	0.09	**0.41 (0.24–0.81)**	**0.002**
Dyslipidaemia (yes)	0.61 (0.35–1.08)	0.07	0.63 (0.37–1.1)	0.09
Diabetes (yes)	2.37 (0.61–9.20)	0.21	0.78 (0.17–3.55)	0.75
Alcohol (yes)	1.23 (0.47–1.47)	0.22	0.83 (0.47–1.48)	0.54
Smoking (yes)	0.84 (0.39–1.27)	0.42	0.71 (0.39–1.27)	0.25
BMI[¶] (>25 kg·m^{-2} and <30 kg·m^{-2})	0.59 (0.21–1.00)	0.08	**0.45 (0.25–0.81)**	**0.008**
BMI[¶] (>30 kg·m^{-2})	**0.60 (0.35–1.25)**	**0.045**	**0.38 (0.17–0.82)**	**0.01**
AHI (>15 events·h^{-1})	0.71 (0.90–2.09)	0.71	0.90 (0.52–1.57)	0.71
ODI (>15 events·h^{-1})	0.88 (0.52–1.57)	0.49	1.05 (0.52–2.10)	0.88

TABLE 4 Mutivariate stepwise regression models and p-value for the two type of baroreceptor sensitivity dysfunction

BMI: body mass index; AHI: apnoea-hypopnoea index; ODI: oxygen desaturation index. [#]: the stable condition is defined as BRS >6 ms·mmHg^{-1}; [¶]: the stable condition is defined as BMI <25 kg·m^{-2}. A p-value <0.05 was considered significant and is indicated in bold.

previous studies considering the vascular response to arousals during flow limitation [37] and apnoea [38] in healthy older subjects showing a blunted and delayed arousal response to respiratory events. Therefore, we can suggest that in healthy elderly the long duration of the disease may be considered as an ischaemic "preconditioning" [39] reducing the autonomic response to apnoea, hypoxic dip and arousals and contributing to lower mortality in older OSA.

Little attention has been given to the influence of ageing on BRS and few studies have demonstrated that cardiovagal BRS is blunted in normal ageing [14–16, 40], related to an age-related increase in basal sympathetic activity and the consequent reduction in tonic baroreflex suppression of the central sympathetic outflow. Taking into account that with ageing the prevalence of OSA increased [2–4] and BRS declined, we would expect a greater BRS dysfunction in our OSA elderly. Contrary to this expectation, no significant association was found between the level of BRS dysfunction and OSA, a blunted BRS present only in 10% of cases and without significant differences between subjects with normal BRS and those with a small impairment. An interesting finding is that subjects with greater BRS dysfunction were those having a slight rise in AHI and ODI but a stronger increase in BMI, hypertension, alcohol intake and dyslipidaemia, all factors [18, 24–26] known to affect BRS. These findings were confirmed by multivariate regression analysis showing the key role of obesity and hypertension on BRS dysfunction.

Strengths and limitations

The strengths of this study include the relatively large sample size with a near equal number of men and women, and an extensive evaluation including not only an objective estimation of BRS, AHI and hypoxaemia but also an analysis of confounder factors such as self-reported alcohol, smoking, diabetes, dyslipidaemia and hypertension, all known to affect BRS. However, we have to underline that our population is a very selective sample in which several exclusion criteria on reported cardiac, vascular and cerebral disease were applied. Thus, we have to recognise that the results obtained in our population may differ from those which would be obtained for elderly patients referred to sleep clinics, and underline the need to be replicated in large patient samples. Finally, as previously described, we did not perform polysomnography that would better estimate the role of sleep fragmentation and age-related sleep disturbances on BRS dysfunction.

Conclusions

This study has demonstrated that in healthy elderly with unrecognised OSA, the risk of blunted baroreceptor sensitivity was low, affecting only 10% of the sample and essentially in severe cases. In our population, neither the severity of hypoxaemic dips nor the OSA severity as defined by AHI explained the presence of an altered baroreceptor sensitivity, with obesity and hypertension playing key roles. These results need to be taken into account in longitudinal studies and in large populations in order to better define the link between OSA and the cardiovascular outcome in older people.

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