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A 3-year longitudinal study of sleep disordered breathing in the elderly

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ABSTRACT: Limited and controversial data exist on the natural evolution of sleep disordered breathing (SDB) in untreated individuals. This study examines the evolution of SDB over a 3-yr period in a community-based sample of elderly subjects.

From the initial cohort of 854 healthy subjects aged mean±SD 68.4±0.8 yrs, 519 untreated subjects accepted clinical and instrumental follow-up 3.6±1.6 yrs later. SDB was defined as a respiratory disturbance index (RDI) >15 events·h^{-1}.

At baseline, 202 (39%) subjects had an RDI ⩽15 events·h^{-1} and 317 (61%) had an RDI >15 events·h^{-1}. 3 yrs later, 280 (54%) subjects were non-SDB and 239 (46%) had SDB. Between evaluations, the RDI decreased from 22.3±16.2 to 16.4±13.0 events·h^{-1}, with a greater decrease in the number of cases with an RDI >30 events·h^{-1} that in those with RDI ⩾30 events·h^{-1}. In the non-SDB group, 81% had a stable RDI and 19% increased their RDI by a mean of 13.7 events·h^{-1}. In the SDB group, the RDI decreased to values ⩽15 events·h^{-1} in 36.6% of cases, 63.4% still having SDB. The RDI changes did not depend on weight changes.

In healthy elderly subjects, the prevalence and severity of SDB did not show a tendency toward natural worsening, some cases having improvement or a remission independent of weight changes. These findings also suggest that in the elderly, natural SDB progression is still hypothetical.

KEYWORDS: Elderly, hypoxaemia, natural evolution, sleep, sleep disordered breathing, sleep fragmentation

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An article by LUGARESI *et al.* [1] was the first to theorise that snoring precedes, by a number of years, the appearance of overt obstructive sleep apnoea (sleep disordered breathing; SDB) and sleepiness, suggesting that SDB is a naturally progressive disease. Since SDB patients are at greater risk of cardiovascular diseases such as hypertension, cardiac arrhythmias, congestive heart failure, stroke and myocardial infarction [2, 3], the progressive nature of the disease would stress the need for early and effective treatment.

However, controversy arises as to whether SDB is a genuinely progressive disease and, if so, which factors contribute most to its worsening. Some studies found that upper airway resistance syndrome [4] and mild-to-moderate SDB had a tendency to worsen over time [5–7], while others found that SDB is fairly stable over time or even improves [8–12]. Longitudinal epidemiological studies on large middle-aged populations [13–15] found that over time, changes occur in SDB prevalence and severity. In the Cleveland Family Study, over a 5-yr period, the mean respiratory disturbance index (RDI) increased from 6 to 8.6 events·h^{-1}, while in the Wisconsin Sleep Cohort it rose from 4.1 to 5.5 events·h^{-1} over a 4-yr follow-up. In the above studies, weight gain was the crucial predictor of long-term changes in the prevalence and severity of SDB. However, although there is an association between increase in weight and worsening SDB, sex [14–16], severity of the disease at the first observation [7, 8, 17] and age may be critical contributors to the SDB progression. In clinical studies, snorers and those with mild-to-moderate SDB had an increase in RDI correlated with the increase in the body mass index (BMI). In contrast, patients with severe SDB had an insignificant change in RDI, suggesting a ceiling effect for SDB severity [7, 18]. Although SDB is highly prevalent in older people [19–22], few studies on its natural evolution in the elderly have been performed, these few showing that elderly patients are more likely to have stable or improved SDB [6–8, 23].

With ageing populations in Europe, the answer to the question of whether SDB progression is present in the elderly has clinical interest. A progressive nature of the disease would underline the value of frequent follow-up visits and early treatment to prevent cardiovascular and

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behavioural consequences [24], while the opposite would hold true for a stable disease. In the current study, we examined the temporal evolution of SDB defined in terms of clinical findings and instrumental assessment over a 3-yr period in a cohort of healthy elderly subjects aged ⩾68 yrs taking part in a project on ageing and cardiovascular consequences.

METHODS

Participants

Baseline and follow-up data were obtained from participants in the Prognostic Indicator of Cardiovascular and Cerebrovascular Events (PROOF) and the Autonomic Nervous System Activity, Aging and Sleep Apnea/Hypopnea (SYNAPSE) studies. The methods of the baseline assessment in the PROOF and SYNAPSE studies have been described previously [25] and are summarised in figure 1. The first step of the study was conducted among the inhabitants of the city of Saint-Etienne, France, from 2001 to 2003; subjects were eligible if they were aged 65 yrs at date of inclusion. Among 3,983 eligible participants, 11% declined participation and 67% did not reply. The final study population included 1,011 participants for whom clinical interview, neurological and cardiological examination were available. 3 yrs later, an ancillary study addressing the association between SDB, assessed by at-home polygraphic study, and cardiovascular and cerebrovascular morbidity during a 7-yr follow-up (SYNAPSE study) was proposed to the overall group but accepted by only 854 participants (58.5 % females and 41.5% males, aged 68.0±0.9 yrs at study entry). After the first polygraphic evaluation, the results of the nocturnal study and the proposition for treatment with continuous positive airway pressure therapy (CPAP) were sent to the general practitioner who established whether therapy was indicated. In the original sample, 183 subjects had a RDI >30 events·h^{-1} but only 60 started CPAP. These 60 treated subjects were followed by local pneumologists and they were excluded by our clinical and polygraphic follow-ups. The remainder of the SYNAPSE cohort were contacted for clinical and polygraphic re-evaluation ~3 yrs later (mean±SD follow-up period 3.6±1.6 yrs) and 519 (61%) subjects accepted. These 519 untreated participants constitute the sample for the present report. Table 1 provides the descriptive data at the first evaluation for subjects participating or not in the 3-yr polygraphic follow-up.

The protocols and informed-consent documents were approved by the local Ethics Committee (CCRRB Rhone-Alpes Loire) and all subjects gave written consent to study participation.

Clinical assessment

Detailed clinical assessment was focused on cardiac and cerebrovascular disease, hypertension, diabetes, and respiratory, neurological and psychiatric disorders. Current medication was analysed with regard to antihypertensive, antidiabetic, hypnotic, anxiolytic and/or antidepressant therapy. Demographic characteristics including sex, age, BMI, neck circumference, and 24-h blood pressure and heart rate measurements were obtained for all subjects at baseline and follow-up. ECG was performed

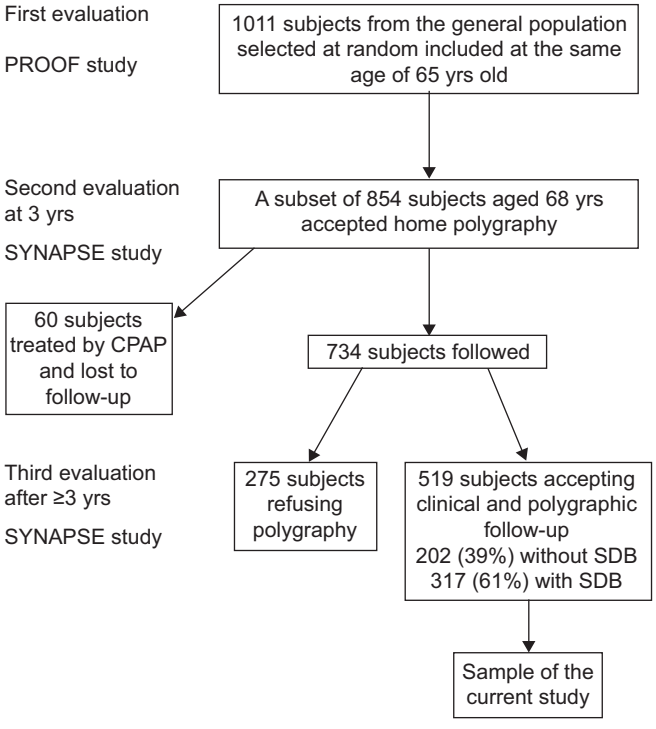

FIGURE 1. Flow chart of the Prognostic Indicator of Cardiovascular and Cerebrovascular Events (PROOF) and the Autonomic Nervous System Activity, Aging and Sleep Apnea/Hypopnea (SYNAPSE) study designs. Numbers and percentages of subjects participating in the investigation before the current study are shown. CPAP: continuous positive airway pressure.

TABLE 1 Clinical, anthropometric and polygraphic data at the first examination for the subjects refusing and accepting follow-up

	Refusing	Accepting	p-value#
Subjects n	275	519	
Age yrs	68.2±0.9	68.6±1.0	NS
Males/females %	37.7/62.3	43.2/56.8	NS
BMI kg·m^{-2}	25.9±4.0	25.2±3.6	0.02
Neck circumference cm	37.0±4.2	37.3±3.8	NS
Nocturnal SBP mmHg	107.0±16.1	107.1±14.4	NS
Nocturnal DBP mmHg	67.2±9.3	66.3±8.1	NS
Dyslipidaemia %	31.7	26.8	NS
Hypertension %	44.2	41.4	NS
Diabetes %	7.0	5.0	NS
Subjective sleep time min	456.9±84.2	464.4±71.3	NS
RDI events·h^{-1}	21.1±10.5	20.0±9.5	NS
ODI events·h^{-1}	11.1±11.0	8.3±8.2	0.001
Mean S_{p,O_2} %	95.1±2.7	95.4±1.9	NS
Minimal S_{p,O_2} %	89.3±4.7	89.9±3.7	NS
Time S_{p,O_2} <90% %	2.7±7.3	1.6±6.1	0.02
Respiratory AAI events·h^{-1}	16.4±11.3	14.9±10.2	NS
Total AAI events·h^{-1}	37.9±16.8	36.2±15.7	NS
ESS score	5.7±3.8	5.8±3.6	NS
ESS score >10 points %	8.6	9.1	NS

Data are presented as mean±SD, unless otherwise stated. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; RDI: respiratory disturbances index; ODI: oxygen desaturation index; S_{p,O_2}: arterial oxygen saturation measured by pulse oximetry; AAI: autonomic arousal index; ESS: Epworth Sleepiness Scale; NS: nonsignificant. #: unpaired t-test.

simultaneously with polygraphy and blood pressure measurements were performed 1 day after polygraphy. Subjects were defined as normotensive if they did not report a history of hypertension and antihypertensive treatment and did not have, after ambulatory blood pressure monitoring (Diasoft; Novavor, Rueil Malmaison, France), a mean systolic blood pressure >135 mmHg and a mean diastolic blood pressure >85 mmHg.

All participants were scored on the Epworth Sleepiness Scale (ESS) [26], a four-grade scale (0: non-napping; 3: high chance of napping) with a maximum score of 24 points. The presence of an excessive daytime sleepiness was defined as a score >10 points.

Sleep study

All subjects underwent full-night at-home polygraphic recording, with time in bed scheduled between 22:00–23:00 and 06:00–07:00 h, which represented their average sleep period. This nocturnal unattended home-sleep study was performed in all subjects using a polygraphic system (Tyco Healthcare HypnoPTT®; Puritan Bennett, Gosport, UK), which included sound measurement, ECG, pulse transit time, R–R timing, airflow by nasal pressure, respiratory effort and body position. Arterial oxygen saturation measured by pulse oximetry (S_{P,O_2}) was recorded. Although we did not perform a validation study, this device is similar to other validated methods used to detect the presence of SDB in middle-aged adults and the elderly [27, 28]. The HypnoPTT software package was used for downloading and analysis of tracings. All automatic analyses were visually reviewed and the polygraphic scoring was performed by the same examiner (F. Roche) at the first and second evaluations with an intrascorer reliability of 87%. To minimise potential overestimation of sleep duration, subjects completed the St Mary's Hospital questionnaire, and wakefulness before lights-off was excluded by the analyses. A subjective sleep time was calculated as the time between the reported lights-off and lights-on. A record was considered acceptable if ⩾5 h of recording of respiratory signals was obtained without missing data. A second night of monitoring was performed when subjective sleep latency exceeded 2 h on the first night, sleep duration was <5 h or the respiratory recording was considered unacceptable. Hypopnea 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 >10 s. The absence of rib cage movements associated with an apnoea defined the event as central, while progressive increase in pulse transit time allowed definition of the event as obstructive. The RDI was established as the ratio of the number of apnoeas and hypopneas per hour of subjective sleep time. The indices of nocturnal hypoxaemia measured were mean S_{P,O_2}, percentage of recording time with S_{P,O_2} <90%, minimal S_{P,O_2} value recorded during sleep and the oxygen desaturation index (ODI), *i.e.* the number of episodes of oxygen desaturation per hour of recording time during which blood oxygen fell by ⩾3%. Pulse transit time was continuously monitored, and respiratory-related, nonrespiratory-related and total autonomic arousal indices (AAIs) were calculated after visual correction according to previously defined criteria [29]. An RDI >15 events·h^{-1} with ⩾50% of events scored as obstructive was considered diagnostic of SDB [30]. Cases were stratified as mild (RDI >15 to <30 events·h^{-1}) or moderate-to-severe (RDI >30 events·h^{-1}) SDB.

Statistical analyses

The subjects' characteristics were summarised as mean±SD for continuous variables, and counts and percentages for categorical variables. Statistical significance for the groups accepting and refusing follow-up was assessed by unpaired t-tests. Differences between baseline and follow-up for the entire group of patients accepting follow-up and for the subgroups classified according to SDB severity were compared using paired t-tests. In order to investigate the determinants of SDB changes, Pearson's correlation coefficients and multiple regression analyses were performed to establish which diurnal and/or nocturnal factor affects the changes in respiratory parameters at follow-up.

All statistical analyses were conducted using the SPSS statistical software package (SPSS for Windows, version 12.0; SPSS, Chicago, IL, USA). After correction for multiple comparison, two-tailed p-values <0.05 were considered to indicate statistical significance.

RESULTS

Baseline characteristics of the 519 participants in the follow-up and of the 275 individuals refusing follow-up are indicated in table 1. Individuals accepting follow-up were more likely to have lower BMI and ODI but were otherwise comparable in terms of clinical, metabolic and cardiovascular comorbidity, as reflected by prevalence of sleepiness, hypertension, diabetes, and diurnal and nocturnal blood pressure. Importantly, there were no significant differences in the percentage of sleepy subjects, RDI, nocturnal hypoxaemia or AAI between groups.

The overall sample of participants consisted of 294 (56.6%) females and 225 (43.4%) males with a mean age of 71.9±1.2 yrs at follow-up. Tables 2 and 3 illustrate the clinical and polygraphic characteristics at baseline and 3 yrs later in the total sample. At follow-up (table 2), there was a slight increase in BMI and a significant decrease in diurnal and nocturnal blood pressure in the total sample, without changes in subjective sleepiness. In the SDB group, comparison of clinical data for mild (RDI >15 to <30 events·h^{-1}) and moderate-to-severe (RDI >30 events·h^{-1}) cases (table 4) showed a significant decrease in blood pressure values in moderate-to-severe SDB cases, in which a slight rise in ESS score and BMI occurred.

With respect to polygraphic data at baseline, 202 (39%) subjects had an RDI ⩽15 events·h^{-1} and 317 (61%) had an RDI >15 events·h^{-1}. 3 yrs later (tables 3 and 4), the RDI decreased from the baseline value of 22.3±16.0 events·h^{-1} to 16.4±13.0 events·h^{-1} ($p<0.001$), which was associated with a rise in ODI and nonrespiratory AAI. There was an increase in the number of subjects with an RDI ⩽15 events·h^{-1} (54%) and a decrease in cases with an RDI >15 events·h^{-1} (46%), their RDI decreasing from the baseline value of 31.0±14.9 events·h^{-1} to 21.1±13.7 events·h^{-1} ($p<0.001$). As shown in figure 2, the significant increase in the number of non-SDB subjects ($p<0.001$) was associated with a decrease in that of SDB cases that was significantly greater in subjects with an RDI >30 events·h^{-1} ($p=0.01$). In the group without SDB at baseline, 164 (81.2%) subjects still had an RDI ⩽15 events·h^{-1} at follow-up, while 38 (18.8%) increased their RDI by a mean of 13.7 events·h^{-1}. In the SBD group, the RDI decreased to values ⩽15 events·h^{-1} in 36.6% of the sample, the others being stable or improving.

TABLE 2 Clinical and anthropometric data for the entire group and for the sample without (respiratory disturbance index (RDI) ⩽15 events·h^{-1}) and with (RDI >15 events·h^{-1}) sleep disordered breathing at baseline and follow-up

	Total sample#			RDI ⩽15 events·h^{-1}¶			RDI >15 events·h^{-1}+		
	Baseline	Follow-up	p-value§	Baseline	Follow-up	p-value§	Baseline	Follow-up	p-value§
BMI kg·m^{-2}	25.2±3.6	25.4±3.7	0.001	24.4±3.4	24.6±3.5	NS	25.7±3.6	26.0±3.8	0.001
Neck circumference cm	37.1±3.8	36.8±3.8	<0.001	35.9±3.4	35.6±3.4	0.03	38.0±3.9	37.5±3.9	<0.001
Diurnal SBP mmHg	123.4±14.6	121.5±15.2	0.02	120.9±15.3	120.4±16.2	NS	124.8±14.0	122.2±14.4	0.006
Diurnal DBP mmHg	77.1±8.2	74.7±8.4	0.001	76.3±7.6	73.6±8.4	<0.001	77.6±8.4	75.3±8.4	<0.001
Nocturnal SBP mmHg	107.3±14.4	105.4±15.5	0.003	104.0±15.2	103.4±15.1	NS	109.3±13.5	106.8±15.6	0.009
Nocturnal DBP mmHg	66.2±8.2.	64.6±8.3	<0.001	64.7±7.7	63.2±7.4	0.03	67.1±8.3	65.5±8.7	<0.001
ESS score	5.7±3.5	5.6±3.7	NS	5.1±3.3	4.8±3.3	NS	6.1±3.5	6.2±3.9	NS

Data are presented as mean±SD, unless otherwise stated. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; ESS: Epworth Sleepiness Scale; NS: nonsignificant. #: n=529; ¶: n=202; +: n=317; §: paired t-test.

To assess which factors may affect the progression or regression of SDB, a correlation analysis of changes in RDI and ODI and clinical and polygraphic changes was performed. A significant negative correlation was found between the RDI changes and the baseline value, confirming the greater decrease in the SDB group and in severe cases (fig. 3). No correlation was found between the changes in RDI and ODI and changes in ESS (r= -0.06, nonsignificant), neck circumference (r=0.03, nonsignificant) and BMI (fig. 4). Analysis of the blood pressure and RDI changes showed a significant correlation between changes in nocturnal systolic (r=0.153, p=0.001) and diastolic (r=0.187, p=0.001) blood pressure (fig. 5) and changes in RDI, without effects on diurnal blood pressure values (nonsignificant).

To assess whether different factors were responsible for the RDI changes in non-SDB subjects and SDB cases, we performed a multiple logistic regression analysis including age, sex, tobacco smoking, RDI at baseline and BMI changes. Changes in BMI may slightly explain the RDI rise in the non-SDB group (r^2=0.02, p=0.03) but no effect was found for SDB cases (r^2=0.001, nonsignificant). A sex effect was found in the RDI changes for males (p<0.01); females, in contrast, had a tendency to be relatively stable or improve at follow-up (nonsignificant).

DISCUSSION

Studies of the evolution of SDB are important to identify the health burden of this sleep-related respiratory disorder and to improve our understanding of factors affecting the so-called natural history. The present longitudinal study in a healthy community-based elderly population showed that over the course of 3 yrs there was a small but significant decrease in SDB severity with remission or improvement in some cases. The RDI changes occurred independently of changes in weight, suggesting that in healthy elderly subjects the remission or worsening of SDB is related to factors different from those affecting middle-aged subjects. Whether this temporal evolution is specific to elderly SDB subjects needs to be elucidated.

TABLE 3 Polygraphic data for the entire group and for the sample without (respiratory disturbance index (RDI) ⩽15 events·h^{-1}) and with (RDI >15 events·h^{-1}) sleep disordered breathing at baseline and follow-up

	Total sample#			RDI ⩽15 events·h^{-1}¶			RDI >15 events·h^{-1}+		
	Baseline	Follow-up	p-value§	Baseline	Follow-up	p-value§	Baseline	Follow-up	p-value§
Subjective sleep time min	467.1±66.8	461.9±86.8	NS	469.2.± 69.5	463.6±85.9	NS	465.1± 68.7	457.9± 89.4	NS
Total AAI events·h^{-1}	36.5±15.7	41.9±26.9	<0.001	31.7±14.7	37.9±26.4	0.005	39.5±15.6	44.4±26.9	0.001
Nonrespiratory AAI events·h^{-1}	21.7±11.6	27.8±22.6	<0.001	23.8±12.6	27.8±23.5	0.04	20.4±10.8	27.7±22.0	<0.001
Respiratory AAI events·h^{-1}	14.8±10.0	14.1±10.3	NS	7.9±4.5	10.0±7.8	<0.001	19.1±10.1	16.7±10.8	0.001
RDI n·h^{-1}	22.3±16.2	16.4±13.0	<0.001	8.6±4.0	9.0±4.3	NS	31.0±14.9	21.1±13.7	0.02
ODI n·h^{-1}	8.3±8.3	9.5±9.2	<0.001	3.2±2.9	4.7±3.9	<0.001	11.5±8.9	12.6±10.2	0.04
Mean S_{p,O_2} %	95.5±1.5	95.2±1.6	0.002	95.8±1.5	95.3±1.5	<0.001	95.3±1.5	95.2±1.6	NS
Time S_{p,O_2} <90% %	1.56±6.1	2.02±6.3	NS	0.9±5.2	1.5±7.2	NS	2.0±6.6	2.4±5.6	NS
Minimal S_{a,O_2} %	89.9±3.7	89.3±4.3	<0.001	91.4±2.7	90.5±3.1	<0.001	88.9±4.0	88.6±4.8	NS

Data are presented as mean±SD, unless otherwise stated. AAI: autonomic arousal index; RDI: respiratory disturbance index; ODI: oxygen desaturation index; S_{p,O_2}: arterial oxygen saturation measured by pulse oximetry; NS: nonsignificant. #: n=529; ¶: n=202; +: n=317; §: paired t-test.

TABLE 4 Clinical, anthropometric and polygraphic data for the sleep disordered breathing subjects at the first examination and follow-up according to severity

	RDI >15 to <30 events·h^{-1} [#]			RDI >30 events·h^{-1} [¶]		
	Baseline	Follow-up	p-value [+]	Baseline	Follow-up	p-value [+]
BMI kg·m^{-2}	25.4±3.8	25.6±3.9	NS	26.1±3.3	26.5±3.6	0.002
Neck circumference cm	37.2±3.8	36.9±3.7	0.02	39.0±3.8	38.4±3.9	0.006
Diurnal SBP mmHg	123.7±14.5	122.0±15.2	NS	126.3±13.2	122.5±13.4	0.005
Diurnal DBP mmHg	77.2±8.8	75.6±8.9	0.006	78.0±8.0	75.0±7.8	<0.001
Nocturnal SBP mmHg	107.8±13.7	106.5±12.0	NS	111.2±13.1	107.1±12.3	0.005
Nocturnal DBP mmHg	66.3±8.3	65.2±9.0	NS	68.3±8.4	65.2±8.2	0.005
ESS score	6.2±3.7	6.0±4.3	NS	5.9±3.3	6.4±3.4	0.006
Subjective sleep time min	469.2±70.6	463.6±91.0	NS	459.3±76.0	450.1±99.2	NS
Total AAI events·h^{-1}	35.1±14.5	41.4±27.2	0.001	45.4±15.2	48.5±26.1	NS
Nonrespiratory AAI events·h^{-1}	21.1±11.3	28.0±23.0	<0.001	19.4±10.0	27.4±20.7	<0.001
Respiratory AAI events·h^{-1}	14.0±6.1	13.6±8.6	NS	26.0±10.4	21.1±12.1	<0.001
RDI events·h^{-1}	21.3±4.6	16.1±10.8	<0.001	44.5±13.8	28.0±14.4	<0.001
ODI events·h^{-1}	8.2±5.6	9.3±8.2	0.02	16.3±10.4	17.1±10.9	NS
Mean S_{p,O_2} %	95.2±1.7	95.2±1.7	NS	95.3±1.4	95.1±1.5	NS
Time S_{p,O_2} <90% %	1.97±8.1	2.06±5.9	NS	2.0±3.4	2.8±5.1	NS
Minimal S_{p,O_2} %	89.4±3.9	88.9±4.9	NS	88.3±4.0	88.1±4.6	NS

Data are presented as mean±SD. RDI: respiratory disturbance index; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; ESS: Epworth Sleepiness Scale; AAI: autonomic arousal index; ODI: oxygen desaturation index; S_{p,O_2}: arterial oxygen saturation measured by pulse oximetry; NS: nonsignificant. [#]: n=185; [¶]: n=132; [+]: paired t-test.

In the present study, we found that there was a general fall in the RDI that affected the overall sample, in some cases, inducing stability or improvement of the syndrome. 81% of subjects having an RDI ⩽15 events·h^{-1} at baseline remained stable and 37% of cases having an RDI >15 events·h^{-1} at the first examination had remission at follow-up. Marked increases from an RDI ⩽15 events·h^{-1} to an RDI >30 events·h^{-1} were found in only 9.7% of cases. Despite differences in the definition of SDB, *i.e.* RDI >15 events·h^{-1}, and in the method used to assess presence of SDB, *i.e.* polygraphy *versus* polysomnography, our results are similar to those reported in other older cohorts. In a 5-yr longitudinal evaluation of the Sleep Heart Health Study [31] involving 3,078 subjects aged 67 yrs at follow-up, the authors noted a modest increase in the RDI from 8.1 to 10.9 events·h^{-1} that was not associated with worsening of sleepiness or quality of life. Interestingly, as in our population, 52% of subjects with an RDI ⩽15 events·h^{-1} remained stable and <1% of the cohort developed an RDI >30 events·h^{-1}. Similar data were obtained in the Cleveland [14] and Wisconsin [13] sleep cohorts in separate 5- and 4-yr follow-ups, respectively. When we consider clinical

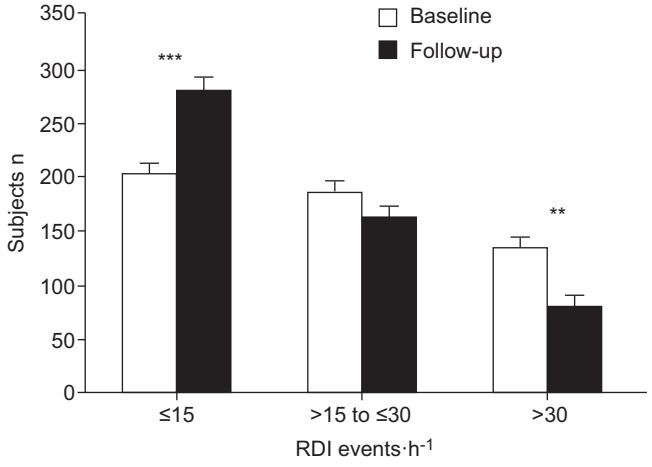

FIGURE 2. Histograms showing the number of subjects at baseline and follow-up according to their respiratory disturbance index (RDI). Data are presented as mean±SD. **: p<0.01; ***: p<0.001.

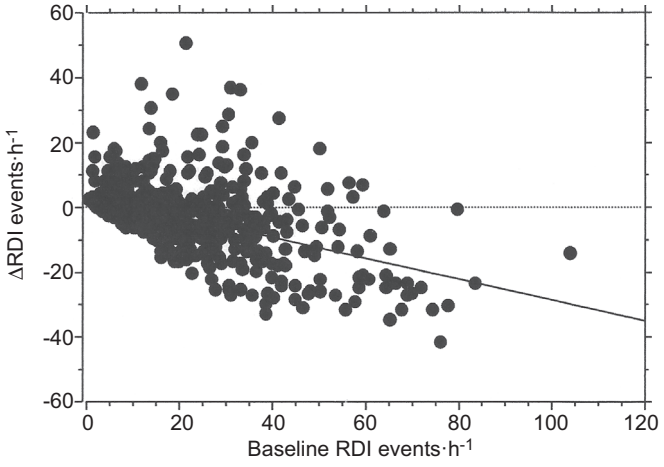

FIGURE 3. Scatterplot showing the negative correlation between change in (Δ) the respiratory disturbance index (RDI) and the RDI value at the baseline evaluation (r= -0.62, p=0.0001).

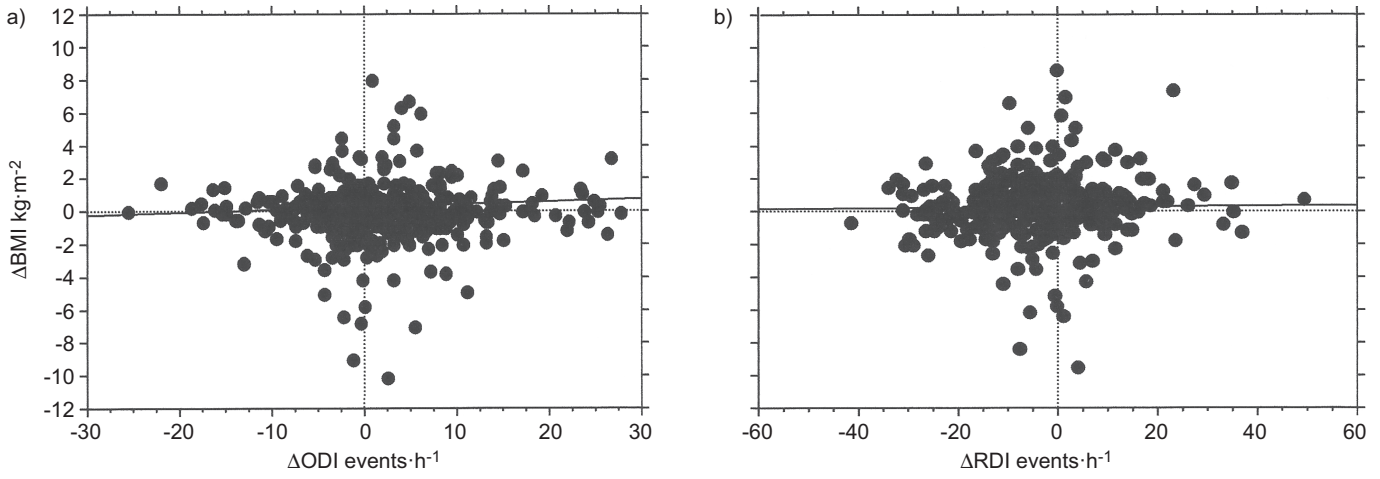

FIGURE 4. Plots representing the lack of relationship between changes (Δ) in body mass index (BMI) and change in a) oxygen desaturation index (ODI) (r=0.08, nonsignificant) and b) respiratory disturbance index (RDI) (r=0.004, nonsignificant).

data, while some studies [4, 6–8] found a significant deterioration of the RDI in 40–60-yr-old patients, others [5, 11] did not find significant changes in the RDI, suggesting that SDB does not necessarily increase over time. If these data are relatively consistent for middle-aged subjects, the progression of the disease is more controversial in the elderly. Using self-administered questionnaires, HONSBERG *et al*. [12] found that among habitual snorers, 58% snored persistently and 35% remitted over a >5-yr follow-up, age >65 yrs and lack of obesity inducing the snoring remission. In the Bay Area Sleep Cohort, BLIWISE [23] examined 103 individuals aged >64 yrs followed them for ~5 yrs to determine whether changes in RDI occurred and, if so, which factors explained these changes. In this cohort, the RDI rose from 4.5 to 8.3 events·h^{-1} with slightly higher rates of change for males. Overall, the annual median rate of change in RDI was ~0.2 events·h^{-1}, with 81 cases showing increases, 20 cases showing decreases and two cases without change. Interestingly, as in our population, the changes in BMI did not affect the changes in RDI.

Most data on SDB evolution assume that progression of the SDB is due to several factors, such as progressive neurogenic upper airways lesion [32], the ageing processes of upper airway functions [33] and increased weight. In the Wisconsin cohort study [13, 14, 34], the investigators found that a 10% weight gain predicted a 32% increase in RDI, whereas a 10% loss in weight predicted a 26% decrease in RDI. A questionnaire-based epidemiological study in 2,668 males [6] showed that over 10 yrs, snoring increased from 15% to 20%, weight gain being the most important predictor of this. Considering an elderly population [22], the temporal RDI increase occurred in subjects with higher BMI at baseline. In contrast to the BLIWISE [23] cohort, we did not find a statistically significant association between RDI changes and weight changes, or between worsening or improvement of the disease and severity of SDB at the time of enrolment. Although our study does not allow us to identify the cause of SDB improvement in our elderly subjects, some explications may be proposed. First, in our population, the degree of BMI changes from baseline to follow-up were slight

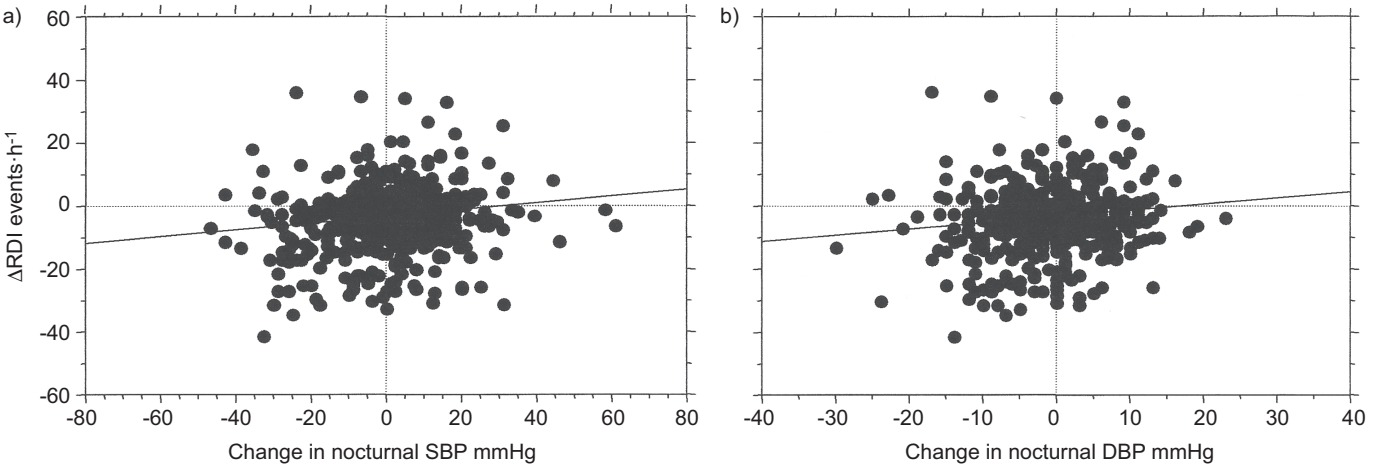

FIGURE 5. Scatterplots showing the significant positive correlation between the change in respiratory disturbance index (ΔRDI) and the changes in nocturnal a) systolic blood pressure (SBP) (r^2=0.144, p=0.002) and b) diastolic blood pressure (DBP) (r^2=0.141, p=0.002).

and even if the majority of our population (48%) was overweight, only 10.4% of our sample had a BMI >30 kg·m^{-2} at both observations. Secondly, the lack of SDB progression in elderly subjects may be related to protective mechanisms [35, 36] and to the characteristic phenotype of SDB [37, 38], which would more frequently induce stability or improvement [18]. In support of the hypothesis of protective mechanisms in elderly SDB subjects [35, 36], we found that the RDI improvement was associated with a trend toward nocturnal decline of blood pressure, independent of changes in diurnal blood pressure or changes in the antihypertensive treatment, the latter occurring only in 10% of our sample. If so, the hypothesis of reduced cardiovascular morbidity and mortality in older SDB cases could be confirmed [36].

In considering the results of our study, some limitations need to be considered. First, we must remember that our subjects were relatively ''young'' elderly and were followed for a 3-yr period, a period probably insufficient to detect longitudinal changes in SDB severity. Therefore, we cannot exclude the possibility that greater changes will occur if we consider ''older'' elderly subjects followed for >3 yrs. Secondly, in our sample, there was a slight tendency toward weight gain and only a few subjects had substantial weight changes. Therefore, the lack of association between RDI changes and weight changes in the overall population cannot be extrapolated to a more obese population. Thirdly, we used ambulatory polygraphy that does not allow assessment of sleep structure and the relation of respiratory events to sleep stages. However, ambulatory polygraphy is currently considered a useful tool for routine assessment and screening of SDB in the elderly [27, 28]. Finally, an inter-night variability is present in older SDB patients [39] and may be explained by instrumental perturbation, changes in sleep time spent in the supine position and sleep fragmentation. Since in an ambulatory setting, control of sleep position and sleep structure is not possible, the effect of disrupted sleep and sleep position on the RDI decrease cannot be excluded.

In conclusion, in a 3-yr follow-up period we found an improvement of SDB in our healthy elderly subjects, 51% of mild cases and 17% of severe cases normalising their RDI independently of weight changes. These results imply that RDI alone may not be a salient target for therapy in the elderly and other factors, such as cardiovascular morbidity and cognitive dysfunction, may be considered for appropriate therapeutic intervention.

SUPPORT STATEMENT

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CLINICAL TRIAL

This study is registered at www.clinicaltrials.gov with identifier numbers NCT00759304 and NCT00766584.

STATEMENT OF INTEREST

None declared.

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