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A three-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 three-year period in a community-based elderly sample.

From the initial cohort of 854 healthy subjects aged 68.4±0.8 yr, 519 untreated subjects accepted clinical and instrumental follow-up 3.6±1.6 yr later. SDB was defined as a respiratory disturbance index (RDI)>15.

At baseline, 202 subjects (39%) had an RDI≤15 and 317 (61%) an RDI>15. Three years later, 280 subjects (54%) were non-SDB and 239 (46%) were SDB. Between evaluations, the RDI decreased from 22.3± 16.2 to 16.4 ± 13.0, with a greater fall in RDI>30 cases. In the non-SDB group, 81% had a stable RDI and 19% increased their RDI by a mean of 13.7. In the SDB group, the RDI decreased to values ≤15 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 to natural worsening, some cases having improvement or a remission independent of weight changes. These findings also suggest that in the elderly the natural SDB progression is still hypothetical.

Introduction

The study by Lugaresi and co-workers[1] was the first to theorize that snoring preceded for years the appearance of overt obstructive sleep apnea (SDB) and sleepiness, suggesting that *naturally* SDB is a 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 of an early and effective treatment.

However, controversy arises as to whether SDB is a genuinely progressive disease and, if so, which factors mostly contribute to its worsening. Some studies found that upper airway resistance syndrome[4] and mild-to-moderate SDB had a tendency to worsen over time[5,6,7] while others found that SDB is fairly stable over time, or even improves.[8,9,10,11,12] Longitudinal epidemiological studies on large middle-aged populations[13,14,15] found that over time, changes occur in SDB prevalence and severity. In the Cleveland Family Study, over a 5-year period, the mean respiratory disturbances index (RDI) increased from 6 to 8.6, while in the Wisconsin Sleep Cohort it rose from 4.1 to 5.5 over a 4-year follow-up. In the above studies, weight gain was the crucial predictor of long term changes in the prevalence and severity of sleep-disordered breathing. However, although there is an association between increase in weight and worsening in SDB, sex, [14,15,16] 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 mild-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[19,20,21,22], few studies on the natural evolution in the elderly have been done, these few showing that elderly patients are more likely to have stable or improved SDB. [6,7,8,23]

With the actual increase of an older population in our countries, the answer to the question if SDB progression is present in the elderly has clinical interest. A progressive nature of disease would underline the value of frequent follow-up visits and early treatment to prevent cardiovascular and behavioral 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 yr 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 study (PROOF study) and the Synapse study. The methods of the baseline assessment in the PROOF and Synapse studies have been described previously[25] and summarized in Fig.1. The first step of the study was conducted among the inhabitants of the city of Saint-Etienne, France, from 2001 to 2003, eligible if aged 65 yr at date of inclusion. Among 3983 eligible participants, 11% declined participation and 67% did not reply. The final study population included 1011 participants for whom clinical interview, neurological and cardiological examination were available. Three years 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 % women and 41.5% men, aged 68.0 ±0.9 yr at the study entry. After the first polygraphic evaluation, the results of the nocturnal study and the proposition for treatment with positive airway pressure therapy (CPAP) were sent to the general practitioner who established if therapy were indicated. In the original sample, 183 subjects had a respiratory disturbances index more than 30 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 approximately 3 yr later (mean follow-up period: 3.6±1.6 yr), and 519 subjects (61%) 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 and subjects declining 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 analyzed with regard to antihypertensive, antidiabetic, hypnotic, anxiolytic and/or antidepressant therapy. Demographic characteristics including sex, age, body mass index (BMI), neck circumference, and 24-h blood pressure and heart rate measurements were obtained for all subjects at baseline and follow-up. The ECG and blood pressure measurements were performed simultaneously (ECG monitoring) or 1 day after polygraphy (blood pressure measurement). Subjects were defined as normotensive if they did not report a history of hypertension and antihypertensive treatment and did not have, after the ambulatory blood pressure monitoring (ABPM) (Diasoft, Novavor, Rueil Malmaison, France), a mean systolic blood pressure >135 mmHg and a mean diastolic blood pressure>85 mmHg.

All participants filled-in the Epworth Sleepiness Scale (ESS)[26], a four grade scale (0, non napping, 3, high chance for napping) in that a maximum of 24 points could be achieved. The presence of an excessive daytime sleepiness was retained for a score>10.

Sleep study

All subjects underwent full night at-home polygraphic recording, with time in bed scheduled between 22:00h-23:00h to 06:00h-07:00h, which represented their average sleep period. Nocturnal unattended home-sleep study was performed in all subjects using a polygraphic system (HypnoPTT, Tyco Healthcare, Puritan Bennett), which included the following parameters: sound measurement, electrocardiography, pulse transit time, R-R timing, airflow by nasal pressure, respiratory effort and body position. Oxygen saturation (SaO_2) was measured by pulse oximetry. 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] A software package was used for downloading and analysis of tracings. All automatic analyses were visually reviewed and the polygraphic scoring was done by the same examiner (F.R.) at the first and second evaluations with an intrascorer reliability of 87%. To minimize 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 at least five hours of recording without missing data on respiratory signals was obtained. A second night of monitoring was performed when subjective sleep latency exceeded two hours on the first night, sleep duration was shorter than five hours or when the respiratory recording was considered as not acceptable. Hypopnea was defined as a 50% or greater reduction in airflow from baseline value lasting at least 10-s and associated with at least 3% oxygen desaturation. Apneas were defined as the absence of airflow on the nasal cannula lasting >10-s. The absence of rib cage movements associated with an apnea defined the event as central, while progressive increase in pulse transit time allowed definition of the event as obstructive. The respiratory disturbances index (RDI) was established as the ratio of the number of apneas and hypopneas per hour of subjective sleep time. Indices of nocturnal hypoxemia were the following: mean SaO_2; % of recording time below 90%; minimal SaO_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% or more. Pulse transit time was continuously monitored, and an autonomic respiratory-related (R-AAI), a non respiratory related (NR-AAI) and a total arousal index (AAI) were calculated after visual correction according to previously defined criteria.[29] An RDI >15 with at least 50% of events scored as obstructive was considered diagnostic of SDB.[30] Cases were stratified as mild form (>15RDI<30) and moderate to severe SDB cases (RDI>30).

Statistical analyses

The subjects' characteristics were summarized as means ± 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 Student's test. 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 Student's t-test for paired data. In order to investigate the determinants of SDB changes, Pearson's correlation coefficients and multiple regression analyses were done 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). 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 co-morbidity, as reflected by prevalence of sleepiness, hypertension, diabetes and diurnal and nocturnal blood pressure. Importantly, there were no significant differences in percent of sleepy subjects, RDI, nocturnal hypoxemia, and AAI between groups.

The overall sample of participants consisted of 294 (56.6%) women and 225 (43.4%) men with a mean age of 71.9$\pm$1.2 yr at follow-up. Tables 2 and 3 illustrate the clinical and polygraphic characteristics at baseline and 3-yr after 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 (>15RDI<30) and moderate to severe (RDI>30) cases (Table 4) showed a significant decrease in blood pressure values in moderate-severe SDB cases, in which a slight rise in ESS score and BMI occurred.

With respect to polygraphic data at baseline, 202 (39%) had an RDI$\leq$15 and 317 (61%) had an RDI>15. Three years later (Tables 3 and 4), the RDI decreased from the baseline value of 22.3$\pm$16 to 16.4$\pm$13 (p<0.001) associated with a rise in ODI and in non respiratory AAI. There was an increase in the number of subjects with an RDI$\leq$15 (54%) and a decrease in cases with an RDI>15 (46%), their RDI decreasing from the baseline value of 31$\pm$15 to 21$\pm$14 (p<0.001). As shown in Fig.2, the significant increase of non-SDB cases (p<0.001) was associated with a decrease of SDB cases, significantly greater in subjects with an RDI >30 (p=0.01). In the group without SDB at baseline, 164 subjects (81.2%) still had an RDI $\leq$ 15 at follow-up, while 38 (18.8%) increased their RDI by a mean of 13.7. In the SBD group, the

RDI decreased to values equal or less than 15 in 36.6% of the sample, the others being stable or improving.

To assess which factor may affect the progression or regression of SDB, a correlation analysis was constructed with changes in RDI and ODI and clinical and polygraphic changes. 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 (-0.06, *p*=ns), neck circumference (0.03, *p*=ns) 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 (*p*=ns).

To assess if different factors were responsible for the RDI changes in non-SDB and SDB cases, we performed a multiple logistic regression analysis including age, sex, tobacco smoking, RDI at baseline and BMI changes. If changes in BMI slightly explain the RDI rise in the non-SDB group (R^2=0.02, *p*=0.03), no effect was found for SDB cases (R^2=0.001, *p*=ns). A gender effect was found in the RDI changes for men (*p*<0.01); women, in contrast, having a tendency to be relatively stable or improving at follow-up (p=ns).

Discussion

Studies on the evolution of SDB are important to identify the health burden of the sleep-related respiratory disorder and to improve our understanding of factors inducing the so called *natural history*. The present longitudinal study in a healthy community-based elderly population showed that over the course of 3 yr there was a small but significant decrease in SDB severity with remission or improvement in some cases. The RDI changes occurred independently from 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.

In the present study we found that there was a general fall in the RDI affecting the overall sample inducing in some cases stability or improvement of the syndrome. 81% of subjects having an RDI≤15 at baseline remained stable and 37% of cases having an RDI>15 at the first examination had remission at follow-up. Marked increases from an RDI≤15 to an RDI greater than 30 were found in only 9.7% of cases. Despite differences in the definition of SDB, i.e., RDI>15, and in the method used to assess presence of SDB, i.e., polygraphy vs polysomnography, our results are similar to those reported in other older cohorts. In a 5 year longitudinal evaluation of the Sleep Heart Health Study[31] involving 3078 subjects aged 67 yr at follow-up, the authors noted a modest increase in the RDI from 8.1 to 10.9, not associated with worsening in sleepiness or quality of life. Interestingly, as in our population, 52% of subjects with an RDI≤15 remained stable and less than 1% of the cohort developed an RDI>30. Similar data were obtained in the Cleveland[14] and Wisconsin[13] sleep cohorts in separate 5 and 4 yr follow-ups. When we consider clinical data, while some studies[4,6,7,8] 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 yr and lack of obesity inducing the snoring remission. In the Bay area sleep cohort, Bliwise[23] examined 103 individuals aged >64 yr followed for about 5 yr to determine if changes in RDI occurred and, if so, which factors explained these changes. In this cohort the RDI rose from 4.5 to 8.3 with slightly higher rates of change for men. Overall, the annual median rate of change in RDI was about 0.2 events per hour of sleep, with 81 cases showing increases, 20 cases showing decreases and 2 without change. Interestingly, as in our population, the changes in BMI did not affect the changes in RDI.

Most data on the SDB evolution assume that progression of the SDB is due to several factors such as progressive neurogenic upper airways lesion[32], the ageing processes on 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 2668 men[6] showed that over 10 yr, snoring increased from 15% to 20%, weight gain being the most

important predictor. Considering an elderly population[22], the temporal RDI rise occurred in subjects with higher BMI at the baseline. In contrast to the Bliwise cohort[23], 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 enrollment. Although our study does not allow us to identify the cause of SDB improvement in our elderly subjects, some explications may be proposed. Firstly, in our population the degree of BMI changes from baseline to follow-up were slight and even if the majority of our population (48%) was over-weight only 10.4% of our sample had a BMI>30 at both observations. Secondly, the lack of an SDB progression in elderly subjects may be related to protecting mechanisms[35,36] and to the characteristic phenotype of SDB [37,38] that would more frequently induce stability or improvement.[18] In support of the hypothesis of protecting mechanisms in elderly SDB subjects[35,36,] we found that the RDI improvement was associated with a trend to nocturnal decline of blood pressure, independent of changes in diurnal blood pressure or changes in the anti-hypertensive 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. Firstly, we must remember that our subjects were relatively "young" elderly followed for a three-year 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 more than three years. Secondly, in our sample there was a slight tendency to 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 use an 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 as 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] explained by instrumental perturbation, changes in sleep time spent in the supine position and sleep fragmentation. Since in an ambulatory setting the control of sleep position and sleep structure is not available, 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 normalizing 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.

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Table 1. Clinical, anthropometric and polygraphic data at the first examination for the subjects refusing and accepting follow-up (mean ± SD).

	Refusing	**Accepting**	**p**
	n=275	**n=519**	
Age (yr)	68.2 (0.9)	68.6 (1.0)	ns
Sexe (M/F) (%)	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
Dyslipidemia (%)	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 (n/h)	21.1(10.5)	20.0(9.5)	ns
ODI (n/h)	11.1(11.0)	8.3(8.2)	0.001
Mean SaO_2 (%)	95.1(2.7)	95.4(1.9)	ns
Minimal SaO_2 (%)	89.3(4.7)	89.9(3.7)	ns
SaO_2<90% (%)	2.7(7.3)	1.6(6.1)	0.02
$AA_{resp}I$ (n/h)	16.4(11.3)	14.9(10.2)	ns
AAI (n/h)	37.9(16.8)	36.2(15.7)	ns
ESS	5.7(3.8)	5.8(3.6)	ns
% subjects with ESS>10	8.6	9.1	ns

Legend:
BMI: body mass index; **SBP**: systolic blood pressure; **DBP**: diastolic blood pressure; **RDI**: respiratory disturbances index; **ODI**: oxygen desaturation index; **$AA_{resp}I$:** autonomic arousal related to respiratory events index**; AAI:** total autonomic arousal index; **ESS:** Epworth Sleepiness Scale;
***p*=** *Student's test*

Table 2. Clinical and anthropometric data for the entire group and for the sample without (RDI≤15) and with (RDI>>15) SDB at baseline and follow-up. (mean ±SD).

	Total sample **(n=519)**			***RDI≤15*** **(n=202)**			***RDI>15*** **(n=317)**		
	Baseline	***Follow-up***	***p***	***Baseline***	***Follow-up***	***p***	***Baseline***	***Follow-up***	***p***
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	0.000	35.9 ± 3.4	35.6 ± 3.4	0.03	38.0 ± 3.9	37.5 ± 3.9	0.000
Diurnal SBP mm Hg	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 mm Hg	77.1 ±8.2	74.7 ± 8.4	0.001	76.3 ±7.6	73.6± 8.4	0.000	77.6 ± 8.4	75.3 ± 8.4	0.000
Nocturnal SBP mm Hg	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 mm Hg	66.2 ± 8.2.	64.6 ± 8.3	0.000	64.7± 7.7	63.2 ±7.4	0.03	67.1 ± 8.3	65.5 ± 8.7	0.000
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

Legend: BMI: body mass index; **ESS**: Epworth Sleepiness Scale; **SBP**: systolic blood pressure; **DBP**: diastolic blood pressure.
p=paired Student's t-test

Table 3. Polygraphic data for the entire group and for the sample without (RDI≤15) and with (RDI>15) SDB at baseline and follow-up. (means ± SD)

	Total sample **(n=519)**			***RDI≤15*** **(n=202)**			***RDI>15*** **(n=317)**		
	Baseline	***Follow-up***	***p***	***Baseline***	***Follow-up***	***p***	***Baseline***	***Follow-up***	***p***
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 n/h	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
Non respiratory AAI n/h	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 n/h	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	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	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 SaO_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 SaO_2 % <90% min	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 SaO_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

Legend: see Table 1.
p=paired Student's *t*-test

Table 4. Clinical, anthropometric and polygraphic data for the SDB subjects at the first examination and follow-up according to severity (mean ± SD).

	>15RDI<30 **(n=185)**			***RDI>30*** **(n=132)**		
	Baseline	*Follow-up*	*p*	*Baseline*	*Follow-up*	*p*
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 mm Hg	123.7 ±14.5	122.0 ±15.2	ns	126.3 ±13.2	122.5 ±13.4	0.005
Diurnal DBP mm Hg	77.2 ± 8.8	75.6 ±8.9	0.006	78.0 ± 8.0	75.0± 7.8	<0.001
Nocturnal SBP mm Hg	107.8± 13.7	106.5±12.0	ns	111.2± 13.1	107.1± 12.3	0.005
Nocturnal DBP mm Hg	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 n/h	35.1± 14.5	41.4 ± 27.2	0.001	45.4 ± 15.2	48.5 ± 26.1	ns
Non respiratory AAI n/h	21.1± 11.3	28.0 ± 23.0	0.000	19.4 ± 10.0	27.4 ± 20.7	<0.001
Respiratory AAI n/h	14.0± 6.1	13.6 ± 8.6	ns	26.0± 10.4	21.1± 12.1	<0.001
RDI n/h	21.3 ± 4.6	16.1 ± 10.8	0.000	44.5 ±13.8	28.0 ± 14.4	<0.001
ODI n/h	8.2 ± 5.6	9.3 ± 8.2	0.02	16.3 ± 10.4	17.1 ± 10.9	ns
Mean SaO_2 %	95.2 ±1.7	95.2 ± 1.7	ns	95.3 ± 1.4	95.1 ± 1.5	ns
Time SaO_2 % <90% min	1.97 ±8.1	2.06 ± 5.9	ns	2.0 ± 3.4	2.8 ± 5.1	ns
Minimal SaO_2 %	89.4 ±3.9	88.9 ± 4.9	ns	88.3± 4.0	88.1 ± 4.6	ns

Legend: see previous Tables.
p= paired Student t-test

Figure legends

Figure 1. Flow chart of the PROOF and Synapse designs. Numbers and percentage of subjects participating in the investigation before the current study are displayed.

First evaluation
Proof Study
1011 subjects from the general population selected at random and included at the same age of 65 years old
Second evaluation at three years
Synapse study
A subset of 854 subjects 68 years old accepted home polygraphy
60 subjects treated by CPAP and lost by follow-up
734 subjects followed
Third evaluation after at least three years
Synapse study
275 subjects refusing polygraphy
519 subjects accepting clinical and polygraphic follow-up
202 (39%) without SDB,
317 61%) with SDB
Sample of the current study

Fig.1

Figure 2. Histograms showing the number of subjects at baseline and follow-up according to the respiratory disturbances index.

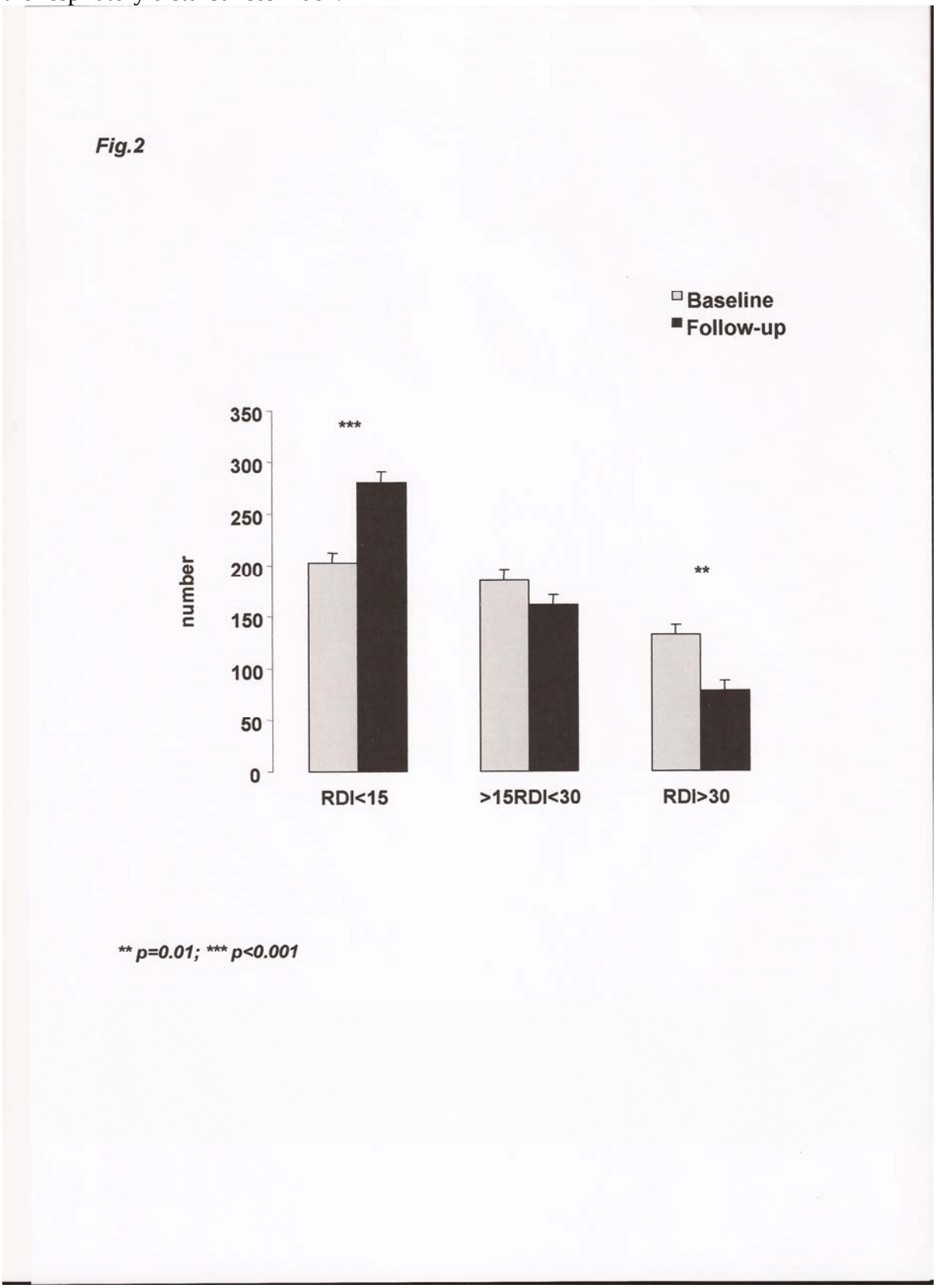


Figure 3. Scatterplot showing the negative correlation between changes in the RDI and the RDI value at the baseline evaluation.

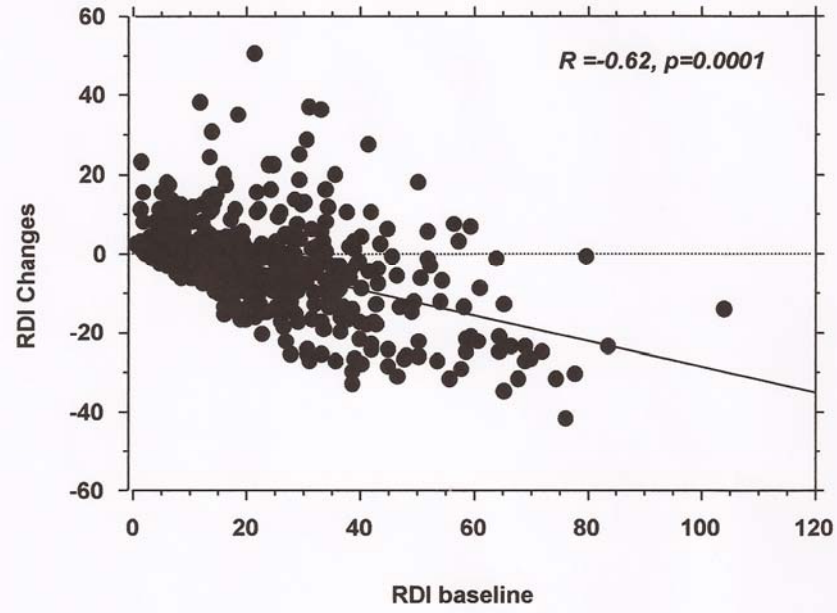


Fig.3

Figure 4. Plots representing the lack of relationship between changes in BMI and changes in oxygen saturation (ODI) (upper panel) and respiratory disturbances (RDI) (lower panel) indices.

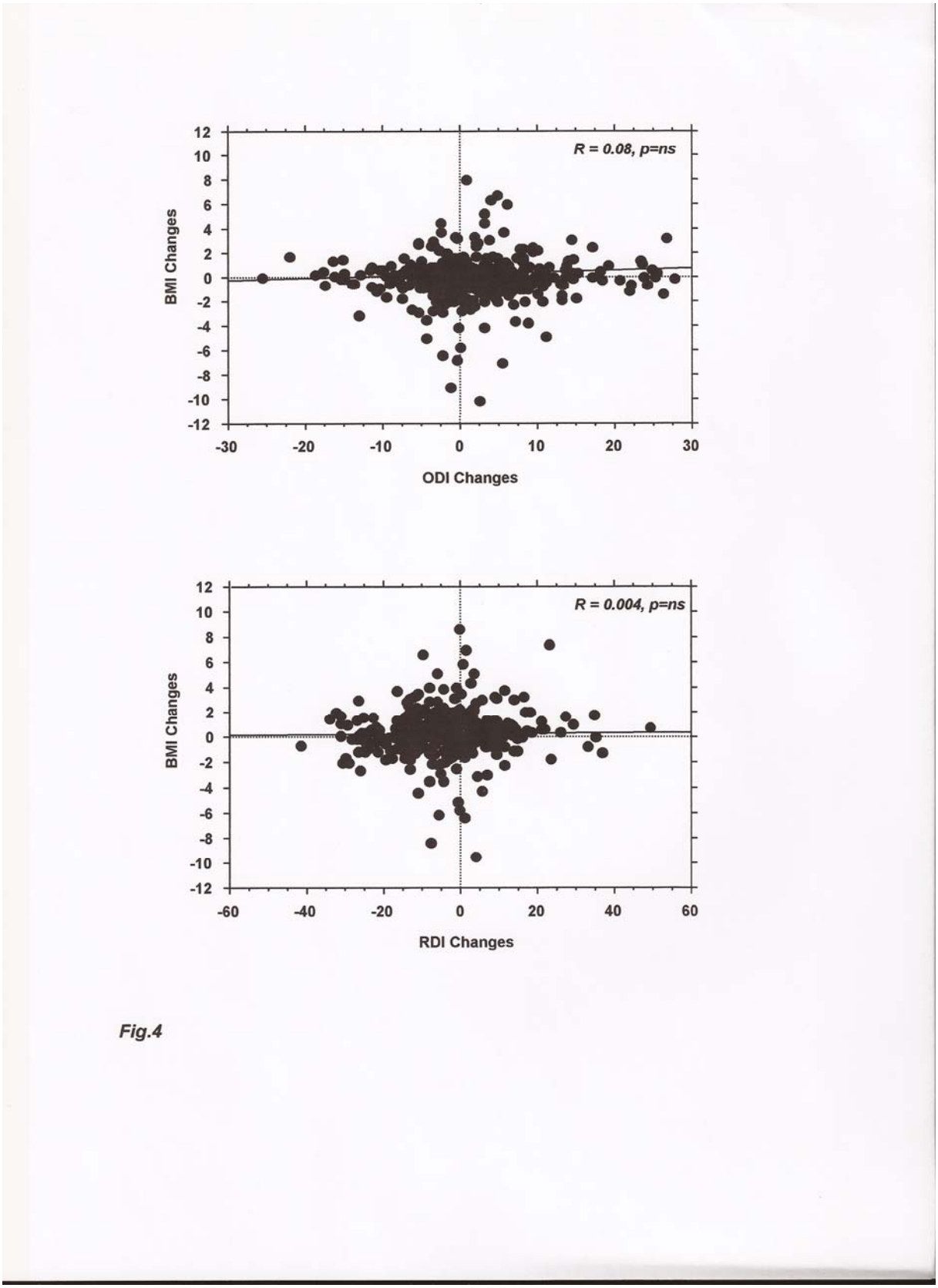
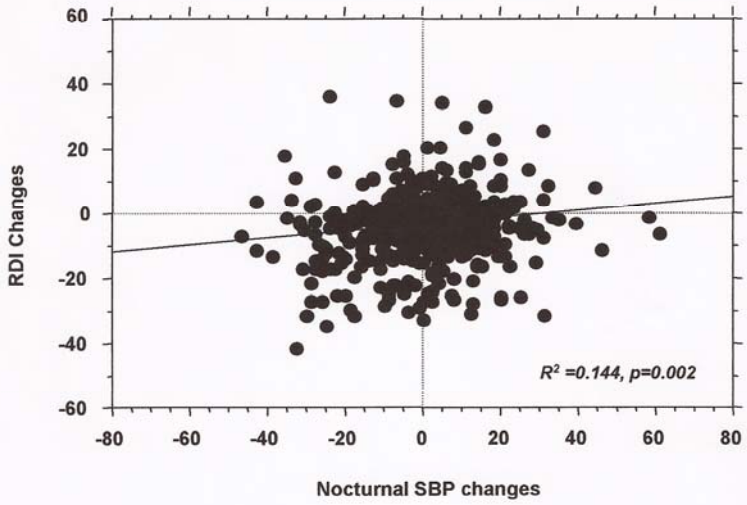


Fig.4

Figure 5. Scatterplots showing the positive significant correlation between the changes in RDI and the changes in systolic and diastolic nocturnal blood pressures.



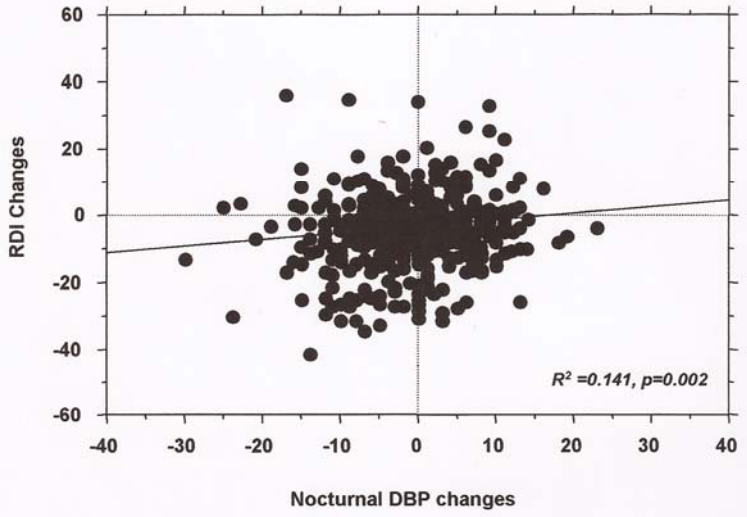


Fig.5

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