Reduction in sympathetic activity after long-term CPAP treatment in sleep apnoea: cardiovascular implications

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Reduction in sympathetic activity after long-term CPAP treatment in sleep apnoea: cardiovascular implications. J. Hedner, B. Darpö, H. Ejnell, J. Carlson, K. Caidahl. ©ERS Journals Ltd 1995.

ABSTRACT: Twelve patients with severe obstructive sleep apnoea were included in an open, long-term, prospective, follow-up study addressing the effects of nasal continuous positive airway pressure (CPAP) on sympathetic activity, cardiac structure and blood pressure.

Plasma norepinephrine (P-NE) (daytime at rest), daytime and night-time urinary excretion of NE (U-NE), vanylmandelic acid and metanephrines, together with 24 h noninvasive blood pressure (BP) recording and Doppler-echocardiography, were assessed before and after a mean of 20.5 (range 14–26) months of CPAP. Average self-reported use of CPAP was 89% (range 65–100%) of time spent in bed.

Resting daytime P-NE ranged 0.35–0.83 ng·ml^{-1}, which is elevated compared to healthy controls. Only night-time U-NE, mean daytime BP and average 24 h BP were related to severity of OSA. Night-time metanephrine was related to daytime and night-time diastolic, as well as night-time systolic, BP. Left ventricular mass index (LVMI) at baseline was correlated to daytime systolic BP and P-NE. Long-term CPAP treatment reduced biochemical markers of sympathetic activity. P-NE decreased by approximately 50%, and daytime and night-time vanylmandelic acid and metanephrine by 32–54%. In contrast, there were no overall reductions in BP or LVMI.

It is concluded that obstructive sleep apnoea is associated with high sympathetic activity both during sleep and waking periods. Urinary metanephrine excretion seemed to reflect blood pressure, but neither daytime nor night-time catecholamine excretion was directly related to disease severity in patients with severe obstructive sleep apnoea. In spite of a marked reduction of catecholamine excretion at follow-up, BP and cardiac structure remained unchanged. Although increased sympathetic activity may act as a contributory trigger for cardiovascular disease in sleep apnoea, a reduction of activity after nasal CPAP is not associated with changes in blood pressure or cardiac structure.
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Obstructive sleep apnoea (OSA) has been associated with increased mortality rate [1, 2], which is possibly due to high co-existing cardiovascular morbidity [2]. Systemic hypertension is present in approximately 50% of OSA patients [3–6], and an increased incidence of myocardial infarction has recently been reported [7]. In addition, snoring and possibly OSA appear to be risk factors for development of ischaemic brain infarction [8]. The association between OSA and systemic hypertension is confounded by factors such as sex, age and excess weight [6]. Although some previous studies have identified OSA as an independent predictor for sustained hypertension [9–11], this has not been confirmed by other investigators [12, 13].

Among the several potential pathogenic links between OSA and cardiovascular complications, increased sympathetic activity [14–22], and changes in water and electrolyte metabolism [23, 24] have received the most intense scientific attention. Elevated sympathetic nerve traffic [14, 19], and circulating levels of norepinephrine [14–22] have been demonstrated not only during sleep and apnoeic events, but also during resting waking periods.

Nasal continuous positive airway pressure (CPAP) is an efficient and widely used method for treatment of OSA [25, 26]. The complete alleviation of OSA during CPAP therapy has been reported to result in a reduction or a normalization of elevated blood pressure after short- [27] and long-term [28] treatment. Clearly, this finding supports the aetiological importance of OSA in the development of some forms of hypertension. The results of short-term treatment with CPAP on plasma and urinary levels of catecholamines and metabolites is somewhat controversial. Although some investigators have found

no reduction of urinary norepineprine excretion [20], others have reported a pronounced decrease [21, 22] already during the first night on CPAP. JENNUM *et al.* [27] found a reduction of plasma epinephrine along with a normalization of elevated blood pressure after 7 days of CPAP.

The present study in patients with OSA was undertaken to investigate the relationship between severity of sleep-disordered breathing on the one hand, and circulating norepinephrine, urinary catecholamine excretion and cardiovascular changes, on the other. The effect of long-term CPAP therapy on these markers of sympathetic activity was evaluated in relation to cardiac structure and systemic blood pressure.

Material and methods

Patient population

Fourteen consecutive patients with previously diagnosed severe OSA and scheduled for nasal CPAP were included in the study. Exclusion criteria were chronic obstructive pulmonary disease, recent myocardial infarction, pharmacologically treated angina, or severe hypertension not permitting wash-out of antihypertensive medication. Two male patients were lost to follow-up; one died from myocardial infarction and one had poor compliance. All calculations were based on the remaining study material consisting of 10 male and 2 female patients, with a mean age of 54 yrs (range 37–72 yrs). Four patients had documented hypertension at the start of the study, defined as ongoing antihypertensive medication or a systolic and/or diastolic blood pressure $\geq 160/\geq 95$ mmHg in three independent measurements. Further characteristics of the study group are shown in table 1.

Table 1. – Physical and sleep study characteristics of patients studied

Patient No.	Sex	Age yrs	Hypertension	OD n	Sao_2min %
1	M	51	Y	650	60
2	M	53	N	533	62
3	M	49	N	412	66
4	M	46	N	335	65
5	M	65	Y	533	58
6	F	72	Y	366	67
7	M	46	N	356	<50
8	M	60	N	221	72
9	M	37	N	280	77
10	M	64	Y	240	73
11	F	62	N	565	<50
12	M	44	N	530	66

M: male; F: female; Y: yes; N: no; OD: total number of oxygen desaturations in overnight study; Sao_2min: lowest Sao_2 value during overnight recording. Hypertension was established according to description in Methods section.

General study procedure

All investigations except nocturnal respiratory monitoring (for details see below) were performed in an identical manner at start and termination of the study. Evaluable data were obtained from 9–11 patients in each investigation (see below). Patients with treated systemic hypertension were subjected to a 3 week complete wash-out of antihypertensive medication prior to the two investigations, but antihypertensive therapy was maintained unchanged during the follow-up period.

Investigations involved a 24 h noninvasive blood pressure recording, Doppler-echocardiography (n=10), determination of plasma norepinephrine (P-NE, n=11) (during daytime, awake and resting), as well as daytime (7 a.m. to 7 p.m.) and night-time (7 p.m. to 7 a.m.) urinary excretion of norepinephrine (U-NE, n=10/10, daytime/night-time), vanylmandelic acid (VMA, n=11/11) and metanephrines (MN, n=9/10). Mean time to follow-up investigation was 20.5 (range 14–26) months. Overnight recordings and measurements after the treatment period were performed during a night without CPAP treatment. P-NE was investigated in the morning following CPAP withdrawal.

The study protocol was reviewed by the Ethics Committee of the University of Göteborg and oral consent was obtained from each participating subject after oral and written information.

Nocturnal respiratory monitoring

All patients underwent an overnight diagnostic investigation in the sleep laboratory from 11 p.m. to 6 a.m. Arterial oxygen saturation (Sao_2) was measured continuously *via* a finger probe (Biox 3700, Ohmeda, USA). Nasal and oral airflow were monitored *via* oronasal thermistors, and respiratory movements were measured *via* a static charge-sensitive bed (PVDS motion sensor, Dourek Ltd, Raisio, Finland). An apnoea was scored when a cessation of air flow was recorded ≥ 10 s and the Sao_2 dropped $\geq 4\%$ below the immediately preceding baseline. Due to incomplete airflow and movement data at the initial recording, only the total number of oxygen desaturations (OD) and minimum overnight Sao_2 (Sao_2min) were used to express the disease severity (table 1). Re-investigations with CPAP (see below) were undertaken with recordings of Sao_2, respiratory movements, and actual mask pressure (Rescare, Sydney, Australia) in all patients. No respiratory monitoring was performed on either of the nights involving blood pressure measurements and urine sampling.

CPAP therapy

Therapeutic CPAP was determined during a full night with respiratory monitoring. The CPAP pressure resulting in complete alleviation of sleep-disordered breathing events was determined after consecutive pressure increments of 0.5 cmH_2O. The therapeutic effect of

CPAP was routinely reinvestigated at 3, 12 and 24 months after initiation of treatment, and less than 5% of the initial number of apnoea events were allowed without pressure adjustment. Compliance with prescribed CPAP therapy was based on the self-reported estimated use at the end of the study period. The use of CPAP (%) during the study period, expressed as average time with CPAP in relation to total time spent in bed, was 89% (range 65–100%).

Doppler-echocardiography

All patients were investigated with M-mode directed by two-dimensional echocardiography (Acuson-128 computed sonograph, Mountain View, California, USA). The left ventricular (LV), septal and posterior wall diastolic dimensions were measured from M-mode tracings, according to guidelines of the American Society of Echocardiography. LV mass index (LVMI) was computed as described previously [29].

Blood pressure

A noninvasive portable blood pressure recorder (Model 90207, Space Labs Inc., Redmond, Washington, USA) was used. The recording was obtained by an oscillometric method which meets the British Hypertension Society standards for ambulatory blood pressure equipment [30]. Blood pressure was recorded at 30 min intervals for 24 h before and after the CPAP treatment period. Recordings were made during the patient's usual activities using an appropriately sized cuff, and the same arm and cuff size were used for both blood pressure recordings. A detailed log was kept of the patients activities during the recording. There were two recording periods, with daytime defined as 7 a.m. to 10 p.m. and night-time 10 p.m. to 7 a.m. Ambulatory blood pressure data from two patients (Nos 4 and 11) before CPAP therapy were technically incomplete and not used for further analysis.

Biochemical assays

All blood sampling took place after a minimum of 15 min supine rest. Samples were collected in prechilled tubes and kept on ice until cold-centrifugation (+4°C). After separation, plasma was stored at -70°C until analysis. Plasma norepinephrine (P-NE) was analysed using a high performance liquid chromatography (HPLC) technique with electrochemical detection as described previously [31]. The lower detection limit for P-NE was 0.1 nmol·l^{-1}. The interassay and intra-assay coefficients of variation were 2 and 4% in the 1–2 nmol·l^{-1} concentration range.

Samples for determination of urinary NE (U-NE), VMA and MN were collected during a daytime period defined as 7 a.m. to 7 p.m. and night-time period 7 p.m. to 7 a.m. HCl (6.4 ml of 5 mol·l^{-1}) was added to a urine volume corresponding to 1,000 ml. Samples were stored at +4°C until analysis. Determination of U-NE, VMA and MN was made using a HPLC technique with electrochemical detection as described previously [32]. The interassay and intra-assay coefficients of variation were 4 and 5% in the 200 nmol·l^{-1} concentration range. The results were expressed in terms of mmol or µmol·mol^{-1} of creatinine.

Statistics

All values are given as means±SEM unless otherwise stated. Multiple regression analysis was performed by the method of least squares. Statistical comparisons were performed by Wilcoxon signed rank test. A p-value of less than 0.05 was considered significant. All calculations were performed on a Macintosh SE microcomputer, using statistical and graphical programs (Statview 512+ and MacDraw II).

Results

Severity of OSA catecholamines, blood pressure and LVMI

All patients had severe OSA (table 1) with an OD of 418±140 (mean±SD, range 221–650) and Sao_2min of 61±14% (mean±SD, range 33–77%). Urinary catecholamines and 24 h ambulatory BP were only partly related to the severity of OSA.

The only measure of urinary catecholamine excretion that was related to OSA severity (Sao_2min) was night-time U-NE (r=0.66; p<0.036). P-NE ranged 0.35–0.83 ng·ml^{-1} at the start of the study, and was unrelated to disease severity. Mean 24 h diastolic but not systolic BP was related to OD (r=0.74; p<0.023; n=10). Both systolic and diastolic BP subdivided into daytime and night-time means tended to be higher in patients with higher OD, although a significant relationship was found only for daytime diastolic BP (r=0.64; p<0.045; n=10). LVMI was unrelated to disease severity and BP.

There was a significant correlation between night-time systolic (p<0.017) but not daytime diastolic BP and P-NE. U-NE and VMA were unrelated to BP but night-time MN was related to night-time systolic (p<0.026) and diastolic (p<0.019) BP (fig. 1). LVMI at baseline was correlated to daytime systolic BP (r=0.84; p<0.017) and P-NE (r=0.69; p<0.042) (fig. 2).

Mean time to follow-up after CPAP was 20.5 (range 14–26) months. In the 12 study patients, there was a high level of self-reported compliance, 89% (range 65–100%) with prescribed CPAP therapy.

Catecholamines, blood pressure and LVMI at follow-up

At follow-up, there was a marked decrease in P-NE and urinary catecholamine metabolite excretion, but no
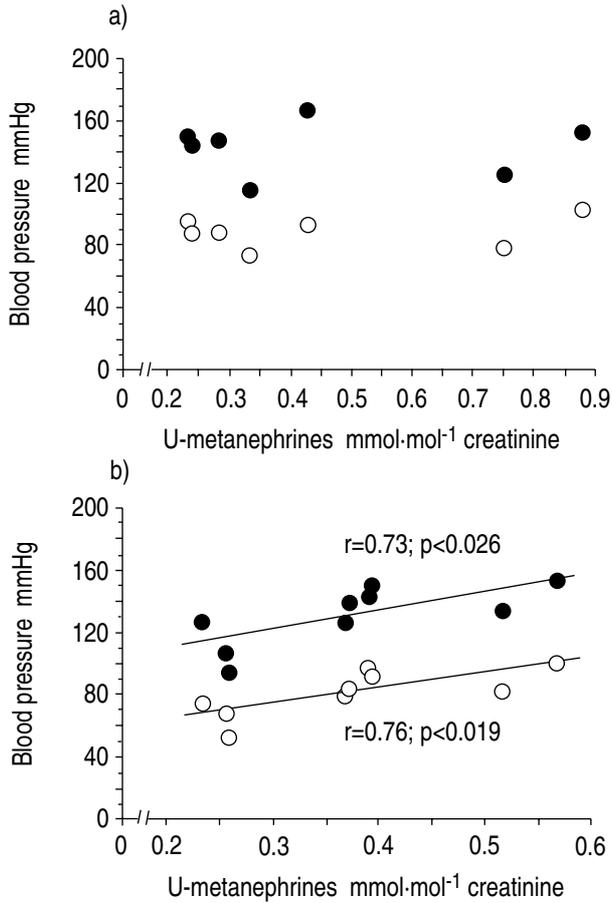
a)

b)

r=0.73; p<0.026

r=0.76; p<0.019

Fig. 1. – Systolic (●) and diastolic (○) blood pressure in relation to urinary (U) metanephrine excretion during: a) daytime (7 a.m. to 7 p.m.); and b) night-time (7 p.m. to 7 a.m.). Each point represents the value from one patient. Regression coefficients and p-values are indicated.
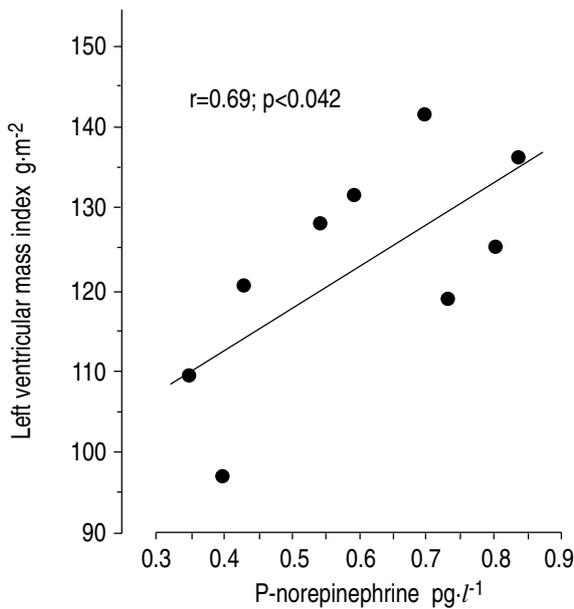

r=0.69; p<0.042

Fig. 2. – Left ventricular mass index and plasma (P) norepinephrine concentration before continuous positive airway pressure (CPAP) treatment in nine patients with obstructive sleep apnoea. Each point represents the values from one patient. The regression coefficient and the p-value are indicated.
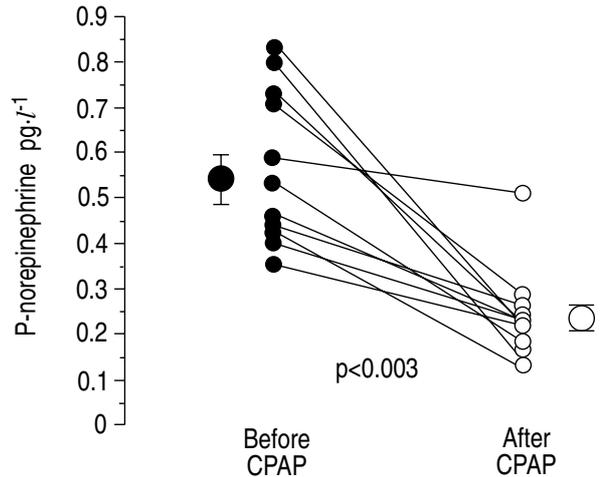

p<0.003

Fig. 3. – Individual values for plasma (P) norepinephrine concentration before (●) and after (○) nasal continuous positive airway pressure (CPAP) therapy. Each point represents the values from one patient. Mean±SEM indicated.
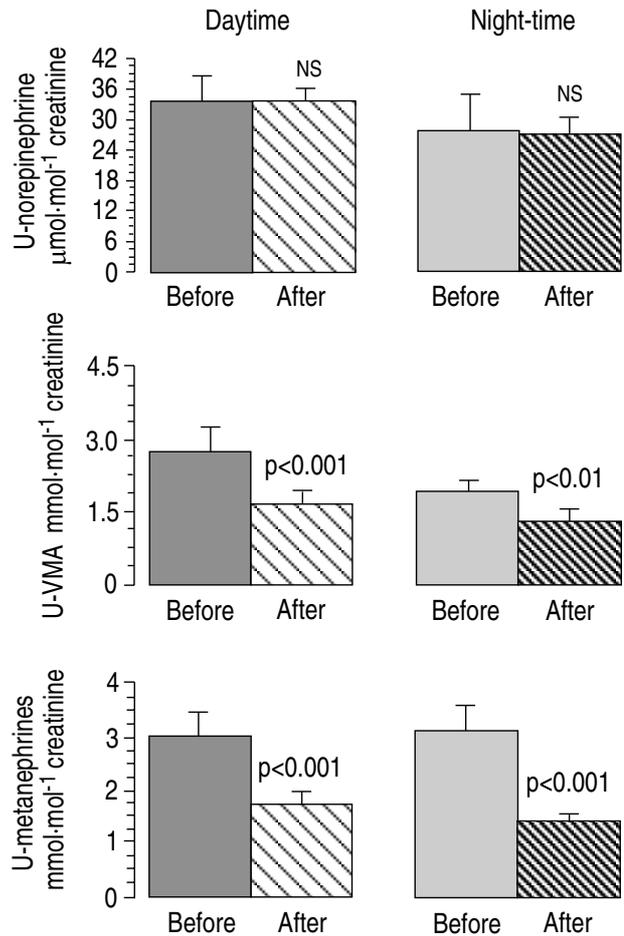

Fig. 4. – Urinary (U) catecholamine concentrations during daytime 7 a.m. to 7 p.m.; and night-time (7 p.m. to 7 a.m.) before (filled bars) and after (cross hatched) nasal continuous positive airway pressure (CPAP) therapy. Data are presented as means±SEM of 9–11 patients. Statistics by Wilcoxon rank sum test. NS: non-significant; U-VMA: urinary vanylmandelic acid.

Table 2. – CPAP treatment, haemodynamic and cardiac structural data

Pt No.	Before treatment			After treatment			
	BMI kg·m^{-2}	SBP/DBP mmHg	LVMI g·m^{-2}	CPAP cmH$_2$O	BMI kg·m^{-2}	SBP/DBP mmHg	LVMI g·m^{-2}
1	35.7	157/106	97	7.5	35.5	157/96	95
2	35.6	144/86	148	10	35.2	151/83	152
3	29.7	114/91	128	7.5	29.7	150/90	113
4	32.7	140/92*	121	10	32.4	134/90	100
5	29.0	152/103	137	10	29.0	169/106	131
6	39.7	166/94	110	10	41.1	185/97	124
7	34.5	145/88	119	10	35.2	172/99	117
8	25.6	117/72	132	7.5	25.3	124/82	121
9	17.6	115/73	-	5	17.6	112/70	72
10	30.8	147/92	142	7.5	29.9	160/91	145
11	51.9	129/88*	-	7.5	47.0	126/86	-
12	36.3	155/84	125	6	36.3	150/79	138

Pt: patient; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; LVMI: left ventricular mass index; CPAP: continuous positive airway pressure; -: missing data. Blood pressure refers to average 24 h ambulatory blood pressure. *: mean from three ambuatory blood pressure recordings.

corresponding haemodynamic changes were observed. P-NE was reduced ($p<0.003$) by approximately 50% (fig. 3). Daytime ($p<0.001$ and $p<0.001$, respectively) and night-time ($p<0.01$ and $p<0.001$, respectively) VMA and MN were reduced by 32–54%, whilst U-NE was unchanged (fig. 4).

Mean 24 h blood pressure and LVMI both remained unchanged after CPAP (table 2). The four patients with known systemic hypertension (Nos 1, 5, 6 and 10) had not reduced either daytime or night-time blood pressure at follow-up (data not shown). Mean 24 h heart rate tended to decrease from 85±3.6 to 82±2.2 beats·min^{-1} after CPAP, although this change did not reach statistical significance.

There were no significant relationships between individual changes in cardiovascular parameters and P-NE or urinary catecholamine metabolites.

Discussion

The present study demonstrates that nasal CPAP treatment is associated with a marked reduction of biochemical markers of sympathetic activity, including P-NE, MN and VMA, in patients with severe OSA. Despite these changes, CPAP therapy did not lead to a change in blood pressure or cardiac structure. Moreover, though the severity of OSA did not predict the extent of night-time urinary excretion of catecholamines, both daytime and night-time excretion of MN was related to BP during these periods. P-NE, but not urinary catecholamines, was correlated to LVMI. The findings indicate that amplifying mechanisms other than elevated sympathetic activity may play a pivotal role for the functional and structural haemodynamic changes proposed in OSA.

Several studies have suggested an increased sympathetic activity during sleep in patients with OSA. WILDSCHIÖDTZ et al. [16] reported a high urinary catecholamine excretion, and other investigators found elevated catecholamine

concentrations [15, 18, 20, 22]. Biochemical assessment of sympathetic activity has been widely used, but the information obtained by such techniques should be interpreted in the light of the high differentiation of the sympathetic system. Although NE, which is the main transmitter in the sympathetic nervous system, leaks from the synaptic cleft into plasma, where its concentration reflects its neurotransmitter function [33], circulating NE represents only 5–10% of the total amount secreted from nerve terminals [34]. Both plasma and urinary NE levels may depend on changes in secretory rate and clearance of NE, which may vary between specific organs or tissues [33]. However, the plasma concentration of endogenous NE in forearm venous blood reflects muscle nerve sympathetic activity during rest, and in different physiological states associated with elevated activity [35].

The technique for direct recording of sympathetic traffic in muscle nerve fibres has also resulted in the possibility of assessing muscle sympathetic activity at short intervals. We have previously demonstrated that obstructive apnoeas during sleep are associated with sudden and repetitive bursts of sympathetic nerve traffic in OSA patients [14]. In these studies, we have also demonstrated both increased sympathetic nerve activity and a doubling of P-NE during daytime wakefulness in OSA patients compared to controls [19]. Using the same biochemical analysis technique, we found a similar elevation of resting daytime P-NE in the present study of patients with severe OSA. Thus, although no control subjects were recruited in this study, it may be stated that sympathetic activity was elevated at baseline before CPAP treatment.

P-NE is rapidly removed from the circulation. The plasma level of NE may, therefore, fluctuate and does not necessarily reflect the mean rate of NE released over a longer time interval. In preference, urinary excretion of catecholamines, which is mainly derived from the circulation [36], provides a widely-used, integrated index

of sympathoadrenal medullary activity. The decrease in urinary catecholamine excretion normally seen during sleep in healthy subjects [37] was absent in patients with OSA. Day- and night-time excretion of catecholamines differed only marginally, suggesting a relatively more pronounced elevation of sympathetic activity during the sleeping period. This elevation may be explained by the repeated bursts of sympathetic outflow detected during apnoea recorded by microneurography [14]. As a complete sleep study was not undertaken, factors potentially influencing overall sympathetic activity, such as arousal, which increases sympathetic nerve activity during sleep in normal subjects [38], were not taken into account. However, in patients with severe OSA, as studied in this paper, it is not unlikely that the frequency of arousals may be reflected by OD. Other data have suggested that the degree of hypoxaemia may be an important predictor of sympathoadrenal medullary activity. EISENBERG et al. [18] found the highest overnight P-NE concentration in the patient with the most severe hypoxaemia during sleep. A similar correlation was found in the present study between urinary NE and Sao_2min.

Further support for elevated sympathoadrenal activity in OSA was obtained upon reinvestigation after CPAP. Nasal CPAP treatment is well-tolerated in OSA patients, especially in those with severe OSA [26, 39]. Except for one drop-out, all patients in the present study had a more than 65% compliance with prescribed CPAP therapy. This degree of self-reported compliance is similar, or slightly higher, than that reported elsewhere [40, 41], and is likely to represent an approximately 15% overestimation of true use [41]. Therefore, significant bias due to faulty assessment of CPAP use in the present study, is unlikely to have markedly influenced the results. Moreover, the effectiveness of CPAP therapy was continuously followed-up, and treatment was associated with alleviation of clinical symptoms of OSA.

P-NE as well as daytime and night-time metabolite excretion was markedly reduced after CPAP. These results are in line with those of other investigators [21, 22], who have reported a reduction as early as during the first night on CPAP, as well as data showing a reduction in P-NE along with a normalization of elevated blood pressure after 7 days of CPAP [27]. In another study [20], however, this finding was not confirmed. Clearly, there may be methodological problems involved when catecholamine excretion is monitored as early as during the first night on CPAP treatment. CPAP application may be associated with discomfort from poor mask fit or the unfamiliar sensation of breathing with positive airway pressure, which would influence catecholamine release. Potential confounders like these were avoided in the present study by reinvestigating the patients without CPAP treatment. This procedure may also have implications for the outcome of urinary catecholamine excretion at follow-up. Although sleep-disordered breathing is likely to have reappeared during this night there was still a marked reduction in VMA and MN excretion. However, the reappearance of apnoeas may have led to a rapid increase of urinary NE excretion, which would explain why only VMA and MN, but not

urinary NE, decreased after CPAP. Alternatively, it may be speculated that the stability of NE in urine was lower than that of the metabolites. Elevated VMA and MN could also have resulted from increased epinephrine secretion. Finally, the stable overnight urinary NE after CPAP may be explained by the fact that some hours of wakefulness could have been included in the "nocturnal period". Nevertheless, overall sympathetic nervous system activity was lower both during wakefulness and sleep after CPAP therapy.

The exact aetiological factor responsible for sympathoexcitation during daytime wakefulness in OSA patients is unknown. However, it may be speculated that the sustained daytime elevation represents a functional adaptation to changes occurring during sleep and obstructed breathing. Elevated sympathetic activity may have a definite pathophysiological implication for development of cardiovascular complications, such as systemic hypertension [14–22] and cardiac arrhythmias [42]; and, thereby, possibly also for increased mortality [2] in OSA. However, there were only a few relatively weak relationships between BP and severity of OSA in the present study. In addition, only night-time MN showed a direct relationship with average overnight BP. These findings should be interpreted in the light of the small study group, which was also homogeneous with respect to severity of OSA. Although OSA may represent an independent risk factor for development of hypertension, additive to obesity [9–11], it is important to point out that several studies have suggested that obesity may be a far more important predictor for hypertension than OSA [12, 13].

There was no correlation between severity of OSA and LVMI in the present study, but a higher LVMI was associated with higher P-NE. In a previous case-control study, we have demonstrated increased LVMI in OSA patients, also after correction for co-existing hypertension and/or obesity [43]. Left ventricular hypertrophy has been demonstrated after repetitive hypoxia in the rat [44], and acute increases in left ventricular afterload from intrathoracic pressure swings and blood pressure rises in sleep apnoea may increase ventricular wall stress [45]. Increased sympathetic nervous system tone may also directly promote cardiac tissue growth [46, 47]. Needless to say, these factors are all intimately linked, as more severe sleep-disordered breathing is likely to be associated with higher P-NE. Also, hypertension which was present in 4 out of the 12 patients is likely to have confounded any relationship between severity of OSA and cardiac structural changes. However, if elevated sympathetic activity acts as a mediator of tissue growth in OSA, it may have been anticipated that cardiac structural changes should have been resolved with treatment of OSA if sympathetic activity was reduced.

Somewhat unexpectedly, there were no cardiovascular or haemodynamic effects of long-term CPAP therapy. This finding contrasts with those of other investigators who have demonstrated a marked reduction of blood pressure after short-term [27], or long-term [28] CPAP treatment. The discrepancy is not readily explained, but information from the present study should be treated with

some caution, since only four patients with established hypertension participated. These four patients may also have had hypertension for other reasons than OSA. Moreover, even if there is a direct causative link between OSA and systemic hypertension, it cannot by definition be assumed that OSA-induced hypertension is reversed by treatment. Hypertension may have induced functional or structural changes which remain in spite of alleviation of a potential aetiological factor. It is also possible that other confounders play an important role in the maintenance of elevated blood pressure. RAUCHER *et al.* [40] have attributed the reduction in blood pressure after CPAP to weight loss, which was not a factor in this study.

Also LVMI remained unchanged in spite of efficient CPAP therapy over 2 yrs. This finding, as well as the absence of an overall blood pressure reduction, indicates that the potential structural and vascular amplifying mechanisms in OSA may involve factors other than increased sympathetic activity. Such obvious factors involve excess weight, elevated blood pressure, or the disturbances in volume regulating systems recently described in OSA [23, 24]. Indeed, blood pressure reduction in hypertensive patients is associated with regression of structural vascular and cardiac changes only after certain forms of antihypertensive pharmacological treatment [48]. Thus, the antitrophic effects of the renin-angiotensin-aldosterone system blockade may be a better predictor for reversal of structural vascular changes than actual blood pressure reduction [48], or a reduction of sympathoadrenal medullary activity.

In conclusion, OSA is a condition characterized by elevated sympathetic activity both during wakefulness and sleep with apnoeic events. This elevated activity was markedly reduced after therapy with nasal CPAP. Elevated activity was, in part, associated with higher blood pressure and LVMI in this small group of patients, but CPAP therapy failed to influence haemodynamics or cardiac structure. Even though elevated sympathetic activity may be involved in the pathogenesis of cardiovascular complications in OSA, other unidentified amplifying mechanisms are likely to play a crucial role for maintenance of these functional and structural changes.

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