Sleep Breath
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SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

Nocturnal blood pressure fluctuations measured by using pulse transit time in patients with severe obstructive sleep apnea syndrome

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Abstract
Background Obstructive sleep apnea syndrome (OSAS) is related to arterial hypertension. In the present study, we test the hypothesis that patients with severe OSAS have excessive apnea induced blood pressure (BP).
Methods We investigated 97 patients with an apnea/hypopnea index (AHI) greater than 30. Systolic BP (SBP) was continuously determined by using the pulse transit time (PTT). Apnea/hypopnea induced nocturnal BP fluctuations (NBPFs) were detected and showed phenomena of continuous increases of the SBP baseline. Such periods of SBP baseline elevations ≥ 10 mmHg were called superposition. Respiratory and cardiac parameters were obtained from the polysomnographic investigation.
Results Eighty-four periods of superposition were detected in 48 patients. They occurred mainly during REM sleep (76%). Apnea duration was increased and the time in respiration was reduced in periods of superposition compared to non-superposition periods. In superposition periods mean oxygen saturation (SpO_2) and the minimal SpO_2 were lower, desaturations were more pronounced, and the mean heart rate (HR) was increased. The maximum SBP during superposition was significantly increased (204 ± 32 vs.171 ± 28 mmHg). The clinic BP was higher in patients with superposition (SBP 149.2 ± 17.5 vs. 140 ± 19.1, DBP 91.5 ± 11.5 vs. 86.3 ± 11.8).
Conclusions The study reveals that patients with severe OSAS can have periods of BP superposition during night with extremely high SBP and very low oxygen saturation, which may add to a high risk for cardiovascular events during the night.

Keywords Obstructive sleep apnea · Blood pressure · Nocturnal blood pressure fluctuations · Pulse transit time · Hypertension

Introduction

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by a complete or partial collapse of the upper airway, which results in cessation of the airflow (apnea) or significant reduction (hypopnea). Based on cohort studies conducted in the USA, Europe, Australia, and Asia, the prevalence of OSA was estimated [1]. Approximately, one in five adults has at least mild OSA (AHI 5–14), while one in 15 adults has moderate (AHI 15–29) or even severe OSA (AHI ≥ 30). OSA is accompanied by fragmented sleep, which may induce daytime sleepiness. It is associated with hypertension and systolic non-dipping blood pressure (BP) during sleep [2, 3]. The term OSA syndrome (OSAS) is used if OSA is accompanied with daytime symptoms, Cheyne-Stokes breathing, and sleep hypoventilation syndrome [4]. OSA also correlates with drug-resistant hypertension [5, 6]. Moreover, OSA(S) has been associated with cardiovascular events such as myocardial infarction, stroke, arrhythmia, and congestive heart failure [1, 7].

Apnea/hypopneas induce hypoxemia and hypercapnia, which cause an arousal reaction along with the activation of

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the sympathetic nervous system. As a result, BP and HR increase [8]. In addition, the intermittent hypoxia in OSA may also cause oxidative stress, endothelial dysfunction, and systemic inflammation [9–12]. These factors contribute to the risk of vascular diseases and life-threatening cardiovascular events. In the present study, we hypothesize that patients with severe OSAS show excessive apnea induced elevations of the systolic BP (SBP), which may increase the chance for cardiovascular events during the night.

A better knowledge of nighttime BP behavior does not only help for better understanding of the pathophysiology of hypertension in OSA patients, but may support diagnosis and therapy of hypertension in this high-risk group. We therefore investigated the nighttime SBP beat-to-beat by using a recently established method based on pulse transit time (PTT, [13]). Validation studies showed a clinically acceptable accuracy of this method under physiological and pathophysiological conditions [13–15]. It was also shown that NBPFs measured by the PTT-based method and by the Portapres™ system correlated significantly in patients with OSA [16]. In the present study, we investigate NBPFs, which go along with increases of the SBP baseline, called superposition of SBP. The rise of the SPB baseline in combination with increased amplitudes of NBPFs causes extremely high SBP, which implies a high risk for nocturnal cardiovascular events in OSA patients.

Methods

Subjects

We investigated 97 patients with the diagnosis of OSAS (AHI ≥ 30) based on polysomnographic measurements in the context of clinical investigations. In total, 48 patients showing superposition phenomena were included in this retrospective study. For this type of study, formal consent is not required. Tables S1 and S2 in the supplemental material show the morphometric parameters, comorbidities, medications, and parameters of sleep of the 97 patients. All procedures performed in study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Measurement equipment and polysomnographic parameters

Polysomnography was performed by using the SOMNOscreen™ polysomnography device (SOMNOmedics GmbH, Randersacker, Germany) configured to record electroencephalogram (leads C4, C3, A2, A1), electrooculogram, chin electromyogram, electrocardiogram (after Nehb), nasal flow (cannula), snoring sounds, respiratory effort signals (thoracic and abdominal), oxygen saturation (SpO_2), pulse rate, EMG of the anterior tibial muscle, finger plethysmogram, ambient light, and body position. The determination of the PTT and calculation of SBP were performed with the DOMINO software (version 2.7.) as described before [13]. The data were manually scored by a qualified sleep practitioner in accordance to the AASM Manual for the Scoring of Sleep and Associated Events [17]. Sleep stage and percentages, arousal index, PLM associated arousal index, and oxygen desaturation index (ODI, 4% drop in blood oxygen levels) were analyzed.

Each apnea/hypopnea was terminated by cortical arousals and reestablishment of breathing. The general activation of the central nervous system was accompanied by transient increases in SBP and HR. There were two scenarios for the SBP behavior at the end of a respiratory event: (i) SBP completely recovered and reached the value before the arousal correlated rise or (ii) SBP did not recover to the baseline but remained somewhat elevated, which corresponds to an increase in the basal SBP. Thus, the basal SPB is the SBP before and after an apneic event, respectively (see Fig. 1). With the aim to characterize these periods, the change in HR, basal SBP, and the maximum SBP were analyzed. The relation of superposition phenomena to the respiration was studied by determining the time in apnea and hypopnea, respectively (%), mean apnea/hypopnea duration (s), time in respiration (%), mean oxygen saturation during a period (SpO_2), change in the baseline of oxygen saturation during a period (ΔSpO_2), and minimum of oxygen saturation during a period; (min SpO_2, see Fig. 1). Increases of basal SBP ≥ 10 mmHg during apneic breathing characterizes the superposition of BP. To get information about possible mechanisms of the increase in the baseline of the SBP, all these parameters were studied in periods of superposition of the SBP and compared to adjacent periods of apneas without superposition of the SBP (non-superposition).

Calibration protocol

Calibration of the PTT-based SBP was performed immediately after starting the polysomnographic device in each patient: The patient's BP was measured simultaneously by a cuff-based method manually at the contralateral upper arm under resting conditions and upright sitting. The time point of this single BP measurement was marked manually in the protocol and digitally in the software. These cuff derived BP values served for calibration of the PTT-based BP determination.

Detection of SBP by using the PTT

The PTT was defined as the time between the R-wave of the ECG and the arrival of the pulse wave at the site of the finger

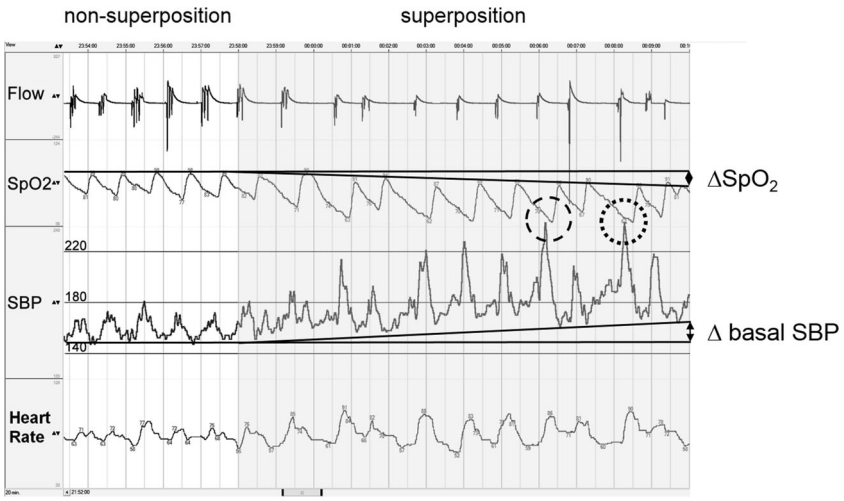

Fig. 1 Original data showing flow, oxygen saturation (SpO_2), systolic blood pressure (SBP), and instantaneous heart rate for a period of non-superposition and superposition during obstructive apneic breathing. Maximum SBP (dotted circle), the change in the baseline of the SBP (Δbasal SBP), decrease in SpO_2 baseline (ΔSpO_2), and min SpO_2 (broken circle) are indicated for the period of superposition. The same parameters have been obtained for non-superposition periods (not displayed)

measured by plethysmography. The arrival was defined as the steepest part of leading edge of the pulse wave. The pulse wave velocity was calculated as the quotient of the travel distance (from the midline of breast bone to the finger, determined by using the body correlation factor [18] and the PTT. SBP values were determined automatically beat-to-beat with the DOMINO software based on a non-linear pulse wave velocity-SBP function in combination with an initial BP calibration (see *protocol* and [13]). The algorithm is matter of a patent (11/364174 US 2006/0217616 A1, 7374542).

Clinic BP

Clinic BP was measured in every patient before sleep examinations (2–3 per patient) under resting condition by using the Riva Rocci method between 6 p.m. and 8 p.m. We averaged these measurements for each patient.

Statistics

Data are presented as bars and whiskers (mean and standard deviation). Student's *t* test served for testing the differences between parameters measured in the superposition period compared to the non-superposition period in patients with superposition. The *t* test was also used to test differences between the groups with superposition vs. without superposition. $P < 0.05$ was considered significant.

Results

Periods of obstructive apnea were accompanied with NBPFs in all patients, i.e., the BP transiently increased at the end of each apneic period (Fig. 1). In some periods, the amplitude of the apnea related BP fluctuations and the baseline of the SBP increased (Fig. 1). Both, the increase of apnea related NBPFs as well as the increase in the baseline SPB add to the phenomenon of very high BP in under these conditions (superposition). We found 84 periods of superposition in 48 patients, while 49 patients did not show superposition. Patients with superposition vs. without superposition did not significantly differ regarding the age, height, body mass, and BMI (see Tables S1 and S2 in the supplement). N1, N2, N3, and N1 + N2 (all in percentage of time in bed (TIB)) did not differ comparing patients with and without superposition. However, patients with superposition showed a larger proportion of REM (15.5 ± 12.2 vs. 6.2 ± 6.0%, Fig. 2). The percentages of awake (5.3 ± 6.7 vs. 10.2 ± 7.3%) and of N1 + N2 + awake (81.6 ± 13.4 vs. 90.3 ± 8.6%) were smaller in patients with superposition (Fig. 2). The ODI was slightly, but significantly increased in patients with superposition (81.5 ± 15.4 vs. 74.6 ± 15.8%). No differences were found for arousal index, PLM arousal index, and AHI (Fig. 3). There were more females in the group without superposition (14/49 vs. 7/48). We obtained higher values for the clinic systolic and diastolic BP in the group of patients with superposition (SBP 149.2 ± 17.5 vs. 140 ± 19.1, $p < 0.05$, DBP 91.5 ± 11.5 vs. 86.3 ± 11.8, $p < 0.05$). The BP differences remain when the groups were reduced to male patients. Patients of the superposition group received less antihypertensive drugs than non-superposition patients did (71 vs. 122). Detailed information about individual medication is available in Tables S1 and S2 in the supplement to this article. In the superposition group, 10 out of 39 patients (25.6%) with the diagnosis of hypertension met the criteria of resistant hypertension. There were 15 out of 42 (35.7%) patients with resistant hypertension in the group of patients without superposition.

Superposition group: The mean duration of superposition periods was 17 ± 7 min. The mean change of basal SBP was + 16.7 ± 6.7 and + 0.6 ± 2.9 mmHg during the periods of superposition and non-superposition, respectively. The maximum systolic pressure during superposition periods was higher

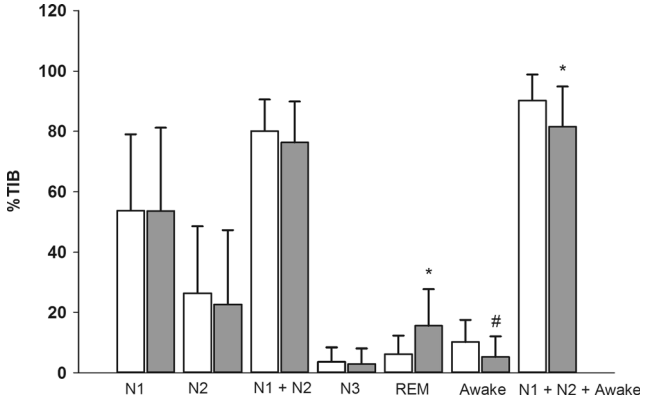

Fig. 2 Sleep characteristics for patients with (gray bars) and without superposition phenomena of SBP (open bars, *%TIB* % to the time in bed, N1 to N3—sleep stages according to the ASSM (see method section), *REM* rapid eye movement sleep, $^{*}p < 0.0001$, $^{\#}p < 0.01$)

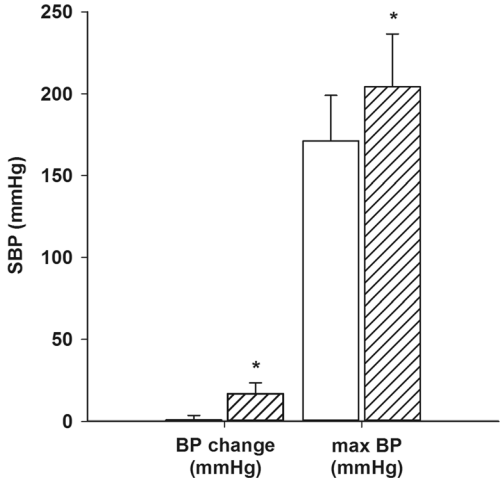

Fig. 4 Change of the basal SBP (BP change) and maximum SBP (max BP) in periods of non-superposition (open bars) vs. periods of superposition (hatched bars, $^{*}p < 0.0001$)

(204.4 ± 32.1 mmHg) than during non-superposition (171.2 ± 27.9 mmHg, Fig. 4). Superposition occurred mainly during REM sleep (76% of all superposition periods) and in the last third of the night (40%). The AHI was lower in superposition (73.7 ± 20.0) compared to non-superposition periods (84.8 ± 26.7). The mean apnea duration and the time in apnea were prolonged (25.0 ± 13.7 vs. 15.4 ± 10.4 s and 50.8 ± 24.7 vs. 37.4 ± 24.4%, respectively). The time in respiration was shortened (49.2 ± 24.7 vs. 62.6 ± 24.7%) in periods of superposition compared to non-superposition periods (Fig. 5). The mean SpO_2 (85.1 ± 5.8 vs. 90.2 ± 3.2%) and the minimal SpO_2 (70.5 ± 89 vs. 80.4 ± 9.7%) were lower during superposition. The desaturation was pronounced during superposition periods (9.2 ± 6.3 vs. 1.7 ± 3.1%, Fig. 6). The mean HR during superposition was slightly, but significantly, increased (71.4 ± 8.2 vs. 69.0 ± 8.7 bpm) and there was a rise of HR over the time of superposition compared to non- superposition (4.5 ± 7.6 bpm vs. 0.6 ± 4.1 bpm, Fig. 7).

Discussion

Several studies showed that nighttime SBP and ambulatory blood pressures, respectively, have the highest ability to predict all cause of mortality or cardiovascular mortality compared to office BP and home BP. It was also shown that night time BP predicts cardiovascular events better then daytime BP [19, 20]. In addition, increased nighttime SBP or the night-day BP-ratio independently predicted higher incidence of cardiovascular events [21, 22]. The present study demonstrates that patients with severe OSAS can develop very high SBP values during superposition periods. These extreme apnea related SBP values occur mainly in REM sleep phases and are characterized by a successive increase of the basal SBP as well as an increase of the apnea induced NBPF. This high SBP may increase the risk for cardiovascular events during night.

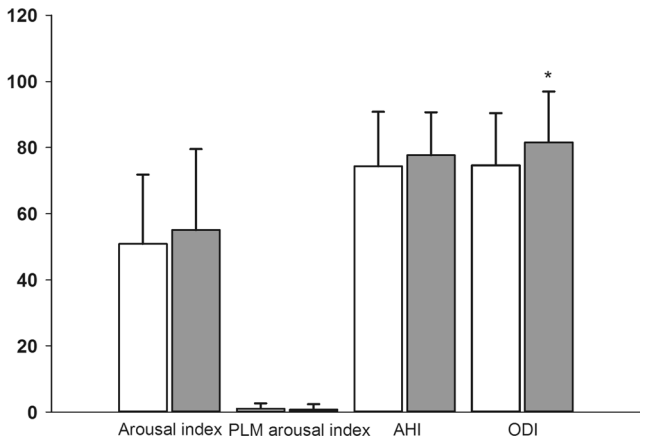

Fig. 3 Sleep characteristics for patients with (gray bars) and without superposition phenomena of SBP (open bars, *AHI* apnea hypopnea index, *ODI* oxygen desaturation index, $^{*}p < 0.05$)

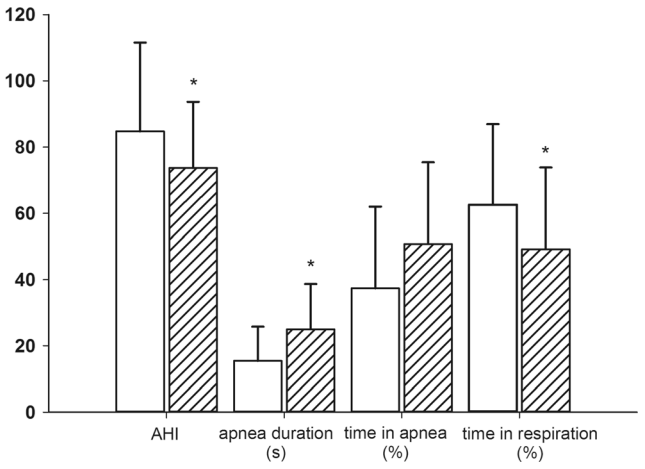

Fig. 5 The respiratory parameters AHI (apnea/hypopnea index), apnea/hypopnea duration (apnea duration), time in apnea/hypopnea (time in apnea), and time in respiration for periods of non-superposition (open bars) and superposition (hatched bars, $^{*}p < 0.0001$)

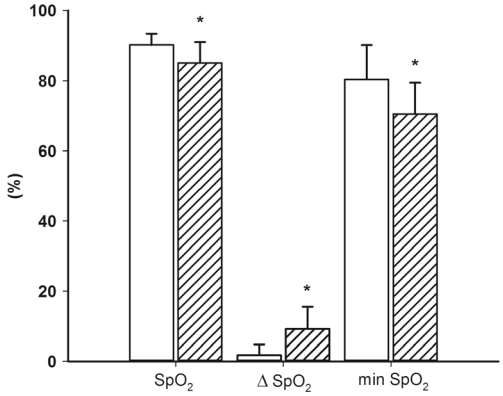

Fig. 6 Oxygen saturation parameters during periods of non-superposition (open bars) and superposition (hatched bars). SpO_2—mean oxygen saturation during a period, ΔSpO_2—change in baseline oxygen saturation during a period (desaturation. See Fig. 1), min SpO_2—minimum of oxygen saturation during a period (*$p < 0.0001$)

Furthermore, these BP elevations lead directly to non-dipping and or reverse dipping behavior and nocturnal hypertension.

Patients with superposition phenomenon also showed increased clinic BP compared to the patients without superposition in the present study. This observation is in line with the assumption of a causative relation between OSA and hypertension [6, 23]. Anthropometric parameters such as age, height, body mass, or BMI of patients with and without superposition did not differ significantly. There is a relatively smaller number of women in the superposition group. Remarkably, differences in the number of women do not influence the SBP differences between both groups. The incidence of the metabolic syndrome (definition after WHO) is higher in patients with superposition. They had less prescription of medication including antihypertensive drugs. Latter may bias the BP data; however, it is difficult to estimate the potential influence of the medication on BP. The proportion of patients with resistant hypertension was higher in the non-superposition group, which reflects the higher number of antihypertensive medication in this group.

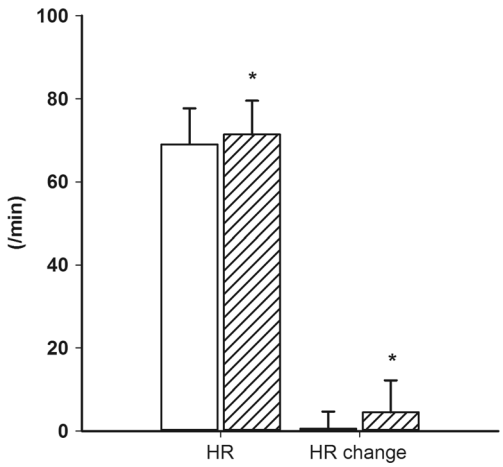

Fig. 7 Mean heart rate (HR) and change in HR (HR change) during periods of non-superposition (open bars) and superposition (hatched bars, *$p < 0.0001$)

Hypertension and particularly resistant hypertension are strongly represented in patients with sleep apnea. Although the relation between OSA and hypertension has been revealed in numerous studies, the pathomechanism is still poorly understood. Sympathetic activation during the apneic periods and increased activation during daytime as shown in several studies suggest a contribution of the sympathetic nervous system [24]. The intermittent hypoxia during phase of apnea seems to be an important factor for the genesis of hypertension and cardiovascular diseases [25, 26]. A further elucidation of the underlying pathophysiological mechanism of the OSA-hypertension relation requires BP measurements during sleep. The ambulatory BP measurement using cuff-based methods provides only few BP values during the night and is unable to measure dynamic changes. Continuously working methods, for example, that after Penaz, are not established in daily clinical work and are not very common in clinical or experimental research. Therefore, measurements of BP fluctuations during sleep in patients are rare. Here, we applied an indirect beat-to-beat measurement of SBP based on the PTT, which enables us to detect dynamic changes of the SBP [13, 27]. Compared to cuff-based methods, the PTT method has several benefits, such as its continuous and non-reactive measurement principle. This allows for undisturbed detection of superposition periods with a mean duration of 17 ± 7 min as shown in this study. Due to the discontinuous nature of ABPM, these episodes cannot be detected with this cuff-based measurement. By application of the continuous and non-reactive PTT method, we observed novel patterns of SBP behavior during apneic periods. The so-called superposition phenomenon is associated with changes in respiratory patterns. The time in apnea was increased and the time in respiration was shorter when comparing superposition vs. non-superposition periods. The AHI was smaller during periods of superposition. This suggests that the increased time in apnea induces stronger autonomic reactions, i.e., strong activation of the sympathetic nervous system along with a decreased vagal tone. Further, desaturations were more pronounced during superposition, which indicates lower pO_2 and higher pCO_2 in these phases, and consequently enhanced activity of chemoreceptors activating the autonomic nervous system. Elevations of basal HR in superposition periods support the assumption of a sympathetic activation.

The study has limitations. We provide clinic BP values but are aware that ambulatory BP would allow a more comprehensive interpretation of the observed apnea induced BP phenomena. Another constraint is related to the method of BP measurement. The determination of BP by using the PTT as performed in the present study has some inherent limitations. They are related to incomplete knowledge about effects of vasoactive substances on the PTT and the variability of pre-

ejection period under certain conditions. However, despite of these and other potential sources of error, a recent validation study showed identical apnea induced BP transients when comparing mean values obtained from the PTT- and the Penaz-method during the night. Moreover, BP values obtained by these methods correlated very well [16]. These findings indicate that the PTT method is similar effective to the Penaz-method for nighttime BP measurement. Other limitations might be due to the retrospective character of the study and the fact that the patients were recruited from the patient population of one sleep laboratory. Although, the selection of patients included in the study based on the screening for sleep apnea and not for hypertension, bias due to the selection cannot be excluded.

The superposition occurred mainly during REM sleep and in the last third of the night. BP has a circadian pattern showing low BP during the night, but with a trend to higher values in the early morning hours. In patients with severe OSA, sympathetic activation in the last third of the night leads to much higher BP and this may contribute to the increased cardiovascular risk observed in the morning hours [28]. Several studies showed that the morning rise of BP poses an independent risk factor for example for stroke (for review see Giles [29]). It has also been demonstrated that patients with OSA have myocardial infarction in the morning hours [30]. Therefore, the detailed investigation of nocturnal BP fluctuations using continuous and non-reactive measuring methods is of serious clinical interest.

In conclusion, patients with severe obstructive apnea demonstrate periods in which the basal SBP rises and the amplitude of SPB fluctuations increases, both leading to extreme high SBP peaks. This may be due to prolonged apneas and shortened breathing periods resulting also in very low oxygen saturation. Activation of the sympathetic nervous system along with reduction in vagal tone during the apneic events very likely mediates the cardiovascular reactions.

The further elucidation of BP behavior during night by routinely application of a non-invasively and continuously working method may potentially improve prognosis, diagnosis, therapy, and follow-up of patients with hypertension.

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Compliance with ethical standards

Conflict of interest J.G. is an employee and G.K. is the CEO of SOMNOmedics GmbH. A.P. advices SOMNOmedics in methods of BP measurement and received travel support. The authors certify that they have no other affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, nor other equity interest; and expert testimony or patent-licensing arrangements) or no non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

1. Somers VK, White DP, Amin R, Abraham WT, Costa F, Culebras A et al (2008) Sleep apnea and cardiovascular disease: an American Heart Association/american College Of Cardiology Foundation Scientific Statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council On Cardiovascular Nursing. In collaboration with the National Heart, Lung, and Blood Institute National Center on Sleep Disorders Research (National Institutes of Health). Circulation 118(10):1080–1111
2. Jenner R, Fatureto-Borges F, Costa-Hong V, Lopes HF, Teixeira SH, Marum E, et al. (2017) Association of obstructive sleep apnea with arterial stiffness and nondipping blood pressure in patients with hypertension. J Clin Hypertens (Greenwich). https://doi.org/10.1111/jch.13008
3. Crinion SJ, Ryan S, McNicholas WT (2017) Obstructive sleep apnoea as a cause of nocturnal nondipping blood pressure: recent evidence regarding clinical importance and underlying mechanisms. Eur Respir J:49(1). https://doi.org/10.1183/13993003.01818-2016
4. Parati G, Lombardi C, Hedner J, Bonsignore MR, Grote L, Tkacova R et al (2012) Position paper on the management of patients with obstructive sleep apnea and hypertension: joint recommendations by the European Society of Hypertension, by the European Respiratory Society and by the members of European COST (COoperation in Scientific and Technological research) ACTION B26 on obstructive sleep apnea. J Hypertens 30(4):633–646
5. Peppard PE, Young T, Palta M, Skatrud J (2000) Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 342(19):1378–1384
6. Logan AG, Perlikowski SM, Mente A, Tisler A, Tkacova R, Niroumand M et al (2001) High prevalence of unrecognized sleep apnoea in drug-resistant hypertension. J Hypertens 19(12):2271–2277
7. Tilkian AG, Guilleminault C, Schroeder JS, Lehrman KL, Simmons FB, Dement WC (1977) Sleep-induced apnea syndrome. Prevalence of cardiac arrhythmias and their reversal after tracheostomy. Am J Med 63(3):348–358
8. Somers VK, Dyken ME, Clary MP, Abboud FM (1995) Sympathetic neural mechanisms in obstructive sleep apnea. J Clin Invest 96(4):1897–1904
9. Loffredo L, Zicari AM, Occasi F, Perri L, Carnevale R, Angelico F et al (2015) Endothelial dysfunction and oxidative stress in children with sleep disordered breathing: role of NADPH oxidase. Atherosclerosis 240(1):222–227
10. Carpagnano GE, Kharitonov SA, Resta O, Foschino-Barbaro MP, Gramiccioni E, Barnes PJ (2003) 8-Isoprostane, a marker of oxidative stress, is increased in exhaled breath condensate of patients with obstructive sleep apnea after night and is reduced by continuous positive airway pressure therapy. Chest 124(4):1386–1392
11. Sanchez-de-la-Torre M, Campos-Rodriguez F, Barbe F (2013) Obstructive sleep apnoea and cardiovascular disease. Lancet Respir Med 1(1):61–72
12. Jelic S, Lederer DJ, Adams T, Padeletti M, Colombo PC, Factor PH et al (2010) Vascular inflammation in obesity and sleep apnea. Circulation 121(8):1014–1021

13. Gesche H, Grosskurth D, Kuchler G, Patzak A (2012) Continuous blood pressure measurement by using the pulse transit time: comparison to a cuff-based method. Eur J Appl Physiol 112(1):309–315
14. Patzak A, Mendoza Y, Gesche H, Konermann M (2015) Continuous blood pressure measurement using the pulse transit time: comparison to intra-arterial measurement. Blood Press 24(4):217–221
15. Bartsch S, Ostojic D, Schmalgemeier H, Bitter T, Westerheide N, Eckert S et al (2010) Validation of continuous blood pressure measurements by pulse transit time: a comparison with invasive measurements in a cardiac intensive care unit. Dtsch Med Wochenschr 135(48):2406–2412
16. Hennig A, Gesche H, Fietze I, Penzel T, Glos M, Patzak A (2012) Measurement of sleep apnoea-related changes in blood pressure using the pulse transit time and the Penaz principle. Article in German. Atemwegs- und Lungenkrankheiten 38:1–8
17. The AASM manual for the scoring of sleep and associated events: rules, terminology, and technical specification. 1st ed. ed. Westchester, IL: American Academy of Sleep Medicine; 2007
18. Nygaard HA (2008) Measuring body mass index (BMI) in nursing home residents: the usefulness of measurement of arm span. Scand J Prim Health Care 26(1):46–49
19. Fagard RH, Van Den Broeke C, De CP (2005) Prognostic significance of blood pressure measured in the office, at home and during ambulatory monitoring in older patients in general practice. J Hum Hypertens 19(10):801–807
20. Sega R, Facchetti R, Bombelli M, Cesana G, Corrao G, Grassi G et al (2005) Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow-up results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study. Circulation 111(14):1777–1783
21. Roush GC, Fagard RH, Salles GF, Pierdomenico SD, Reboldi G, Verdecchia P et al (2014) Prognostic impact from clinic, daytime, and night-time systolic blood pressure in nine cohorts of 13,844 patients with hypertension. J Hypertens 32(12):2332–2340
22. Fagard RH, Thijs L, Staessen JA, Clement DL, De Buyzere ML, De Bacquer DA (2009) Night-day blood pressure ratio and dipping pattern as predictors of death and cardiovascular events in hypertension. J Hum Hypertens 23(10):645–653
23. Hla KM, Young T, Finn L, Peppard PE, Szklo-Coxe M, Stubbs M (2008) Longitudinal association of sleep-disordered breathing and nondipping of nocturnal blood pressure in the Wisconsin Sleep Cohort Study. Sleep 31(6):795–800
24. Linz D, Mahfoud F, Linz B, Hohl M, Schirmer SH, Wirth KJ et al (2014) Effect of obstructive respiratory events on blood pressure and renal perfusion in a pig model for sleep apnea. Am J Hypertens 27(10):1293–1300
25. Ryan S, Taylor CT, McNicholas WT (2005) Selective activation of inflammatory pathways by intermittent hypoxia in obstructive sleep apnea syndrome. Circulation 112(17):2660–2667
26. Troncoso Brindeiro CM, da Silva AQ, Allahdadi KJ, Youngblood V, Kanagy NL (2007) Reactive oxygen species contribute to sleep apnea-induced hypertension in rats. Am J Physiol Heart Circ Physiol 293(5):H2971–H2976
27. Bilo G, Zorzi C, Ochoa Munera JE, Torlasco C, Giuli V, Parati G (2015) Validation of the Somnotouch-NIBP noninvasive continuous blood pressure monitor according to the European Society of Hypertension International Protocol revision 2010. Blood Press Monit 20(5):291–294
28. Neutel JM, Smith DH (1997) The circadian pattern of blood pressure: cardiovascular risk and therapeutic opportunities. Curr Opin Nephrol Hypertens 6(3):250–256
29. Giles T (2005) Relevance of blood pressure variation in the circadian onset of cardiovascular events. J Hypertens Suppl 23(1):S35–S39
30. Aboyans V, Cassat C, Lacroix P, Tapie P, Tabaraud F, Pesteil F et al (2000) Is the morning peak of acute myocardial infarction's onset due to sleep-related breathing disorders? A prospective study. Cardiology 94(3):188–192