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258. Cardiometabolic and neurocognitive changes in obstructive sleep apnoea

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Structural brain changes related to disease duration in patients with asthma
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Dyspnea is the impairing, cardinal symptom patients with asthma repeatedly experience over the course of the disease. However, its accurate perception is also crucial for timely initiation of treatment. Reduced perception of dyspnea is associated with negative treatment outcome, but the underlying brain mechanisms of perceived dyspnea in patients with asthma remain poorly understood. We examined, whether increasing disease duration of asthma is related to structural brain changes and studied the associations between structural brain changes and perceived dyspnea.

By using magnetic resonance imaging in combination with voxel-based morphometry, gray matter volumes of the insular cortex and brainstem periaqueductal grey (PAG) were examined in fourteen patients with mild-to-moderate asthma and correlated with asthma duration and perceived affective unpleasantness of resistive load induced dyspnea.

Whereas no associations were observed for the insular cortex, longer duration of asthma was associated with increased gray matter volume in the PAG. Moreover, increased PAG gray matter volume was related to reduced ratings of dyspnea unpleasantness.

The present results demonstrate that increasing disease duration is associated with increased PAG gray matter volume in patients with mild-to-moderate asthma. This structural brain change might contribute to reduced perception of dyspnea in some patients with asthma and, thus, negatively impact treatment outcome.

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The impact of obstructive sleep apnea on glucose regulation and liver injury in nondiabetic men

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Objective: We explored the effect of Obstructive sleep apnea syndrome (OSAS) on glucose regulation and liver injury in nondiabetic men.

Research design and methods: We enrolled 49 non diabetic men of the OSAS patients without concomitant diseases/medications based on overnight polysomnography and blood tests. We measured fasting serum glucose (FPG), fasting insulin (FIS), C-reactive protein (CRP), liver enzymes such as alanine aminotransferase (ALT) and lactate dehydrogenase (LDH) and calculated new homeostasis model assessment estimates of insulin resistance (HOMA2-IR), insulin sensitivity (HOMA2-IS) and pancreatic beta-cell function (HOMA2-B).

Results: Median fasting insulin level, HOMA2-IS, and HOMA2-IR of the severe OSAS group were significantly higher than those of the other OSAS subgroups and controls. No significant differences were observed for FPG and HOMA2-B. CRP levels were significantly correlated with BMI, with AHI, with minimum SpO₂, with HOMA2-IR and with LDH during sleep. Both levels of ALT and LDH were significantly positively correlated with insulin and HOMA2-IR ($p=0.001$ respectively). Significant elevations in HOMA2-IR ($p=0.001$), fasting serum insulin ($p=0.001$), levels of CRP ($p=0.024$) levels of ALT ($p=0.040$) and levels of LDH ($p=0.047$) and significant reductions in HOMA2-IS ($p=0.002$) were found in subjects with AHI>15/h compared to those with AHI<15/h matched by BMI, sex and age.

Conclusions: We demonstrated that OSAS contribute to the development of insulin resistance and liver injury. Insulin resistance may be the first key effect of OSAS on glucose regulation. Insulin resistance may be the pathophysiologic basis of liver injury in OSAS.

P2225

Importance of controlled blood pressure values in a population with obstructive sleep apnea syndrome (OSA) and arterial hypertension (HT)
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Rationale: OSA and HT are associated through cause-effect relationship, but few data in literature studies the effect of blood pressure (BP) control medication on OSA.

Methods: We analysed 162 OSA patients with treated HT, 46.9% with controlled BP (cBP), 53.1% with uncontrolled BP (uBP), and studied differences between groups regarding demographics, anthropometric data, symptoms, comorbidities, sleep study's reports, therapy. We use SPSS (T, chi tests) ListenRead phonetically.

Results: 76 cBP patients: 22 (28.9%) women, 54 (71.1%) men, mean age 55.7±10.8 years, average apnea-hipopnea index (AHI) 49.5±36.5/h; 86 uBP patients: 20 (%) women, 66 (%) men, mean age 55.3±8.9 years, average AHI 58.1±38.7/h. Statistically significant differences ($p < 0.05$): Epworth sleepiness score (9.70±5.61 in cBP group vs 11.65±5.61), snoring, morning headache, nocturnal dyspnea - more common in uBP group, nocturia - more common in cBP group, period elapsed since diagnosis (higher for uBP), AHI postCPAP (13.5±13.3 vs 21.5±19.9 cm H₂O for uBP), explained by the higher proportion of CPAP failure among uBP (12.8% vs 5.2%). The hypothesis regarding existing differences related to the cardiovascular comorbidities is not supported.

Conclusions: Controlled blood pressure deletes sleepiness and reduces some other symptoms. The results is that OSA is more difficult to suspect in these patients, who, according to the results of this study, would benefit more from CPAP therapy. OSA may coexist in patients with HT controlled by medication in the absence of symptoms or signs and the patient, mostly young or middle-aged adult, cannot receive adequate treatment.

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Severity of sleep-disordered breathing is an independent predictor of metabolic dysfunction in a population with obstructive sleep apnoea

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People with obstructive sleep apnoea syndrome (OSAS) are at increased risk of insulin resistance, dyslipidaemia, and adverse cardiovascular outcomes. However, obesity is a major confounding factor in studies examining the impact of OSAS on the development of these sequelae. It remains uncertain if sleep-disordered breathing is an independent driver of metabolic dysfunction.

We sought to assess the influence of OSAS severity on metabolic health by prospectively studying the fasting lipid & glycaemic profiles of newly diagnosed OSAS patients. Subjects were stratified according to OSAS severity, and lipid profiles were compared between groups. The relationship between OSAS severity and metabolic health was examined using a hierarchical multivariate linear regression model.

239 subjects were studied. Those with severe OSAS were more obese, more likely to be male, and younger than those with mild-moderate disease. No significant difference was seen to occur in total cholesterol, LDL-cholesterol, or serum triglycerides with OSAS severity. HDL-cholesterol was lower in subjects with severe OSAS (mild-moderate 1.18 mmol/l vs. severe 1.01 mmol/l; $p < 0.001$). In univariate analysis, HDL level correlated inversely with apnoea/hypopnoea index (AHI) ($r = -0.323$; $p < 0.001$). This relationship persisted following adjustment for demographic, anthropometric, and other metabolic variables ($\beta = -0.152$; $p = 0.043$). Interestingly, this relationship was stronger for AHI than for markers of nocturnal oxygenation.

OSAS severity is independently associated with dyslipidaemia. Mechanistic studies examining the interaction of OSAS with obesity and adipose tissue function are required.

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Effect of CPAP treatment on endothelial function, inflammatory markers, blood pressure and glucose control in patients with OSAS with emphasis on gender differences

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Introduction: Research evidence suggests the presence of endothelial dysfunction

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and systemic inflammation in patients with obstructive sleep apnea syndrome (OSAS). The effects of CPAP on the aforementioned pathophysiological pathways, as well as on the systemic disease that result or coexist with the OSAS remain elusive.

Aim: To assess the effect of CPAP therapy on endothelial-dependent dilation, plasma levels of inflammatory markers, blood pressure and glucose control in male and female patients with OSAS.

Methods: Our study group consisted of 40 patients with no prior history of cardiovascular disease, with an Apnea-Hypopnea Index (AHI) >15 who were assigned to receive CPAP treatment. Measurement of Flow Mediated Dilation (FMD), 24-hour ambulatory blood pressure (BP) and blood analysis were performed at baseline and 3 months after CPAP therapy.

Results: Baseline FMD values were negatively correlated the AHI ($r=-0.55$, $p=0.001$). After 3 months of CPAP there was a significant increase in the FMD values and a significant reduction in the patients' 24hr systolic BP, diastolic BP and Pulse Pressure (PP), daytime systolic and diastolic BP, nighttime systolic BP and PP, the C-reactive protein (CRP) and HbA1c levels. When divided by gender, only male patients produced similar statistically significant results.

Conclusion: Our results suggest that CPAP therapy improves the endothelial function, the blood pressure and glucose control in male patients with OSAS. Further research is warranted in order to further elucidate the impact of CPAP on the cardiovascular risk of male and female patients with OSAS.

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Endothelial function in obstructive sleep apnea syndrome

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Introduction: Obstructive sleep apnea (OSA) is an independent risk factor for myocardial infarction and stroke. Endothelial dysfunction could be one of the pathogenetic mechanisms linked to OSAS related risk for cardiovascular diseases.

Methods: We studied 38 patients by polysomnography in the laboratory, 27-86 years with newly diagnosed OSAS (AHI \geq 15), free of known chronic diseases. Endothelial functioning assessed by the reactive hyperemia peripheral arterial tone index (RH-PAT index) and the levels of urine albumin/creatinine ratio (ACR) testing for microalbuminuria.

Results: 24 out of 38 patients who had abnormally low RH-PAT defined as an index < 1.65 were compared with 13 OSAS subjects with normal RH-PAT (1.41 \pm 0.1 vs. 2.11 \pm 0.5, $p=0.01$). They were slightly older (51 \pm 14 years vs. 43 \pm 1 years, $p=0.09$), with similar BMI (33.6 \pm 8.1 kg/m² vs. 38.1 \pm 9.1 kg/m², $p=0.13$), lower AHI (28.1 \pm 23.4 vs. 49.4 \pm 29.4, $p=0.02$) and higher minimal SaO₂ (80.3% \pm 9.1% vs. 71.8% \pm 14.7%, $p=0.03$). There was no correlation between RH-PAT with Epworth Sleepiness Scale. ACR was higher in patients with low RH-PAT index (7.92 \pm 2.7 mg/g vs. 4.7 \pm 2.5 mg/g, $p=0.02$) but without microalbuminuria per se (defined as 30-299mg/g). ACR was significantly correlated with BMI ($r=0.362$, $p=0.04$). Multiple regression analysis showed that the value of ACR was the most significant factor for RH-PAT variance (adjusted R²=0.23, $p=0.008$, $\beta=-0.450$, $p=0.04$). The morning RH-PAT index was lower in patients over the age of 50 years (1.55 \pm 0.3 vs. 1.76 \pm 0.6, $p<0.05$).

Conclusion: Our findings suggest that the AHI is not related with markers of endothelial dysfunction. The harmful consequences of OSAS might be more prominent in the elderly and obese patients.

P2229

The lack of evidence based knowledge of metabolic syndrome in obesity hypoventilation syndrome

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Introduction: The obesity hypoventilation syndrome (OHS) is a severe sleep related breathing disorder, with obstructive sleep apnea syndrome (OSAS) as the predominant sleeping pattern. It is often accompanied by multiple organ tract involvement. In OSAS, the interaction with metabolic syndrome is well studied. In OHS however, it is unclear whether the severity of disease has consequences for the occurrence and severity of metabolic syndrome. We evaluated the presence of evidence based knowledge.

Methods: A systematic Pubmed and Cochrane search was performed, final check 24th February 2011, for metabolic syndrome in concurrence with OSAS and OHS, and related terms and synonyms in title and abstract (exclusion criterion: duplicates). The final data set was achieved by elimination of studies that contained predefined criteria: animal studies, studies < 1990, age < 18 years, genetic diseases, case reports, and studies without original data. Outcome parameters were total number of studies and randomized controlled trials (RCT), before and after the elimination strategy, for OSAS versus OHS.

Results: 767 initial hits were found in OSAS, versus 273 for OHS. After the predefined elimination strategy, 171 remained, containing 5 RCT's for OSAS, versus 6 studies, without any RCT, for OHS (Fischer exact $p<0.0001$ for final total number and $p<0.05$ for RCT's).

Conclusion: A markedly lower number of hits was found for metabolic syndrome in OHS, as compared to OSAS. Within the complexity of clinical features in OHS, the metabolic syndrome seems to be an unexplored area in research.

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C-reactive protein (CRP) levels in obstructive sleep apnea (OSA) patients and relation to severity of OSA

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Introduction: CRP has been proposed as a cardiovascular risk marker. OSA is associated to metabolic syndrome and major cardiovascular events.

Objectives: To study CRP levels in OSA patients in comparison to healthy people, and the relationship between severity of OSA and CRP levels.

Method: Case-control study including 100 consecutive diagnosed OSA patients and 113 healthy people randomly selected from general population. Age, sex, hypertension, diabetes, dyslipidemia, body mass index (BMI), smoking, Epworth scale, spirometry, respiratory disturbance index (RDI) and high sensitivity CRP (hsCRP) were recorded.

Results: Cases and controls characteristics are shown in Table 1.

Table 1. Case and control characteristics

	OSA patients	Healthy people	P value
Age (years) [mean (standard deviation)]	54 (13.7)	49 (14.8)	0.01
Male (%)	71	52	0.003
BMI (kg/m ²)	33.1 (7.1)	28.7 (5.7)	<0.01
Hypertension (%)	37	28	0.174
Diabetes (%)	22	10	0.02
Hyperlipidaemia (%)	39	34.5	0.46
Smoker or ex-smoker (%)	51	34.5	0.015
hsCRP (mg/dl)	0.47(0.5)	0.44(0.75)	0.032

Multiple regression model analysis coefficients of CRP levels in OSA patients are shown in Table 2.

Table 2. Multiple linear regression model coefficients for hsCRP levels in OSA patients

	Coefficient	P value
Sex	-0.08	0.86
Age	-0.004	0.34
RDI	0.006	0.62
BMI	0.01	0.31
Smoker or ex-smoker	0.03	0.73
Hypertension	0.28	0.02
Diabetes	0.18	0.21
Hyperlipidaemia	0.04	0.69
RDI*BMI	0	0.62

TDI*BMI: interaction variable.

Conclusion: Although OSA patients shows slightly higher levels of hsCRP than healthy people in our sample, other factors rather than severity of OSA measured by the RDI influence that issue.

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Efficacy of BiPAP AutoSV advanced in subjects with congestive heart failure and central apnea

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Introduction: Auto-Servo Ventilation effectively suppresses Sleep Disordered Breathing (SDB) in patients with Congestive Heart Failure (CHF). This study compared the efficacy of a new mode of ASV that incorporates an automatic EPAP (ASV-Advanced), with and without its Bi-Flex comfort feature, to manually titrated ASV (ASV) in patients with central SDB and CHF.

Methods: Following diagnostic PSG and titration, patients underwent 3 consecutive treatment nights in a random order: ASV, ASV-Advanced and ASV-Advanced with Bi-Flex. For the ASV night, EPAP was set to the level determined during the titration night and IPAP set at EPAP+20cmH₂O. For the ASV-Advanced nights, the

Table 1

	Diagnosis	ASV3 Bi-Flex	ASV3	ASV2
RDI (/h)	41.6 \pm 14.5	7.3 \pm 7.2*	7.0 \pm 8.8*	10.6 \pm 13.3*
AHI REM (/h)	19.3 \pm 18.2	6.9 \pm 13.3	6.0 \pm 10.7	6.0 \pm 11.7
AHI NREM (/h)	44.3 \pm 14.8	7.5 \pm 6.8*	7.7 \pm 9.2*	11.8 \pm 15.1*
cAI (/h)	18.1 \pm 16.0	0.6 \pm 0.9*	0.6 \pm 0.9*	1.4 \pm 2.6*
HI (/h)	15.8 \pm 10.4	6.5 \pm 6.6	5.7 \pm 7.5	7.9 \pm 9.5
CSRI (/h)	23.7 \pm 16.0	0.9 \pm 2.6*	1.5 \pm 2.0*	4.4 \pm 8.5*
RAI (/h)	18.6 \pm 12.2	3.5 \pm 5.9*	3.7 \pm 6.0*	3.9 \pm 6.5*

RDI, Respiratory Disturbance Index; AHI, Apnoea Hypopnoea Index; cAI, Central Apnoea Index; HI, Hypopnoea Index; CSRI, Cheyne Stokes Respiration Index; RAI, Respiratory Arousal Index. * $p<0.001$ vs. diagnosis

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device was set to automatically determine EPAP and IPAP pressures with a maximum pressure support of 20cmH₂O. When activated, Bi-Flex was set to its maximum expiratory pressure relief. Data were analyzed with ANOVA and Bonferroni. **Results:** 10 males participated (mean \pm SD: age 67.4 \pm 11.7 y, BMI 28.4 \pm 5.5 kg/m², LVEF 25.7 \pm 5.7%). Sleep time and efficiency were similar. **Conclusion:** ASV-Advanced treats central SDB as effectively as ASV in patients with CHF.

P2232**Metabolic and inflammatory profile in obese and non obese children with obstructive breathing disorders**

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Introduction: Adult OSA is a known risk factor for metabolic diseases, but still unexplored in children. Obesity, an important cofactor, is increasing in the pediatric population.

Aim: To study the metabolic profile and the levels of TNF- α in obese and non obese children with obstructive breathing disorders.

Methods: Children of both genders, aged 6 to 12 years, with obstructive breathing disorders were included. Children were divided in 2 groups, non obese and obese (Z score > +2), diodespiratory sleep study. In the morning after the sleep study, blood samples were taken for analysis. The lipids, glucose, insulin, tyroxin and TNF- α levels were determined. Results were compared for the 2 groups.

Results: 17 children, median age of 6.5 years, 10 obese- and 7 non obese, were included. There glucose level was 85 mg/dL in both groups. Insulin level was higher in the obese group (10.7 \pm 2.36 mU/L X 6.7 \pm 3.29 mU/L, p<0.01). There were no difference in total cholesterol (168.4 \pm 37 mg/dL X 181.5 \pm 33, p>0.05), HDL (56.8 \pm 14.5 mg/dL X 49.5 \pm 17.8 mg/dL, p>0.05) and LDL (98.6 \pm 27.7 mg/dL X 110.7 \pm 28 mg/dL) in the non obese and obese group, respectively. TGL levels were higher in the obese group (106.5 \pm 37 mg/dL X 64.3 \pm 23 mg/dL). Thyroxin and TSH levels did not differ in both groups. The average TNF- α was 0.36 \pm 0.09 pg/ml, but differed in obese 0.56 \pm 0.53 pg/ml and 0.10 \pm 0.07 pg/ml (p<0.05).

Conclusion: Obesity may cause additional metabolic changes (increased insulin resistance and TGL levels) in children with obstructive breathing disorders. The metabolic inflammatory profile must be investigated for a better understanding of OBD in childhood.

P2233**Cognition, quality of life and adherence to CPAP after 18-months treatment in obstructive sleep apnea patients**

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Obstructive Sleep Apnea (OSA) determines cognitive dysfunctions and diminished quality of life (QoL). Adherence to PAP treatment although effective, still remains a challenge for patients.

Aims: To evaluate neurocognitive functions, adherence to PAP and QoL in a consecutive group of OSA patients at baseline (BL) compared to age and education-matched normal controls and to assess changes after 18-months of fixed PAP treatment (FU) with C-flex (Philips/Respironics).

Methods: 67 males (mean age 50.3 \pm 10.4) with severe OSA (mean AHI=55.1 \pm 22.8) and 15 controls. Neurocognitive functions (attention, vigilance, memory, executive functions, visuo-constructional abilities), sleepiness, mood and QoL (SF36 and FOSQ) were evaluated at BL and at FU. At FU objective compliance to PAP (hours of use per night and % of days of use) was assessed by EncorePro software.

Results: 10 patients were excluded for low compliance to PAP within the 18-months observation period. At BL patients showed significantly lower scores than controls in all neurocognitive domains (p<.001) as well as in FOSQ (p<.001) and in the general health subscale of SF36. At FU an overall significant improvement of cognition (all domains), QoL, sleepiness and mood was observed. At FU mean compliance to PAP was 6.1 \pm 1.1 hrs and % of days of use 88.5 \pm 15.1.

Conclusion: Our data showed that cognitive functions and QoL, all impaired when compared to controls at BL, significantly improved at FU when patients, if adherent to the device, were able to reach the same scores of controls. Adherence to PAP can be considered the trigger of improvement both in QoL and cognition but still remains a challenge for both patients and physicians.

P2234**Association between arterial hypertension and impaired glucose tolerance (IGT) in obstructive sleep apnoea (OSA) patients**

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Obstructive sleep apnoea is a risk factor of cardiovascular and metabolic distur-

bances. The aim of this study was to assess relationship between IGT and AHI, obesity and cardiovascular diseases in OSA subjects. We studied 255 OSA pts [195 males (76.5%) and 60 females (23.5%), mean: age - 56.8 \pm 10.7 years, AHI - 42.3 \pm 20.5, BMI - 33.1 \pm 5.5 kg/m², SaO₂ - 91.7 \pm 4.7%, T90-19.1 \pm 25.4%]. Impaired glucose tolerance (IGT) [plasma level \geq 140 mg% after 2 hours of administration 75 g glucose in oral glucose tolerance test (OGTT)] was found in 69 subjects (27.1%). In 11 patients (4.3%) OGTT confirmed diabetes (glucose \geq 200 mg%). Comparison of OSA patients with- and without IGT is shown in the table.

Variable	Normal OGTT (186pts)	IGT (69 pts)	p
AHI (n/h)	41.4 \pm 20.5	44.8 \pm 20.7	NS
BMI (kg/m ²)	32.7 \pm 5.8	34 \pm 4.7	NS
Age (years)	55.9 \pm 11.1	59.3 \pm 9.2	NS
Mean SaO ₂ (%)	91.9 \pm 4.7	91.3 \pm 4.6	NS
T90 (%)	18.3 \pm 25.3	21.2 \pm 25.9	NS
Fasting glucose (mg%)	89.1 \pm 9.2	100.8 \pm 17.8	<0.0001
HbA1c (%)	5.9 \pm 0.6	6.3 \pm 0.5	0.0008
Arterial Hypertension (n/%)	127 (68.3%)	59 (85.5%)	0.006
COPD (n/%)	18 (9.7%)	4 (5.8%)	NS
Heart failure (n/%)	11 (5.9%)	3 (4.3%)	NS
Atrial fibrillation (n/%)	13 (7%)	5 (7.2%)	NS
Coronary artery disease (n/%)	31 (16.7%)	12 (17.4%)	NS

Conclusions: Prevalence of impaired glucose tolerance in OSA subjects was high (more than 25%). IGT in OSA pts was related to higher incidence of arterial hypertension, elevated plasma fasting glucose and HbA1c concentration. There were no any significant correlations between AHI, BMI, overnight desaturation or other diseases and results of OGTT.

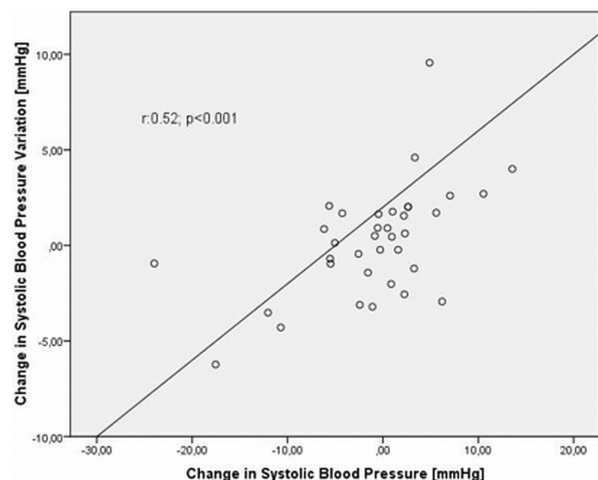
P2235**Impact of obstructive sleep apneas/hypopneas on blood pressure during a short period of stable sleep. A relevance for blood pressure variation?**

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Introduction: There is evidence that obstructive sleep apneas (OSA) are involved in the development of hypertension. However, the precise mechanism is still under discussion.

Methods: We analysed 34 patients via polysomnography and simultaneous beat to beat measurement of systolic (Sys) and diastolic (Dia) blood pressure (BP) (NexfinHD). Group1: apnea/hypopnea index (AHI) 0-15/h, n=16; Group2: AHI >15/h n=18. All results during 10 min. stable N2 sleep were calculated after data export using the SPSS software. A p<0.05 was considered significant.

Results: In group1 BP decreased during N2 sleep (Sys -1.9 \pm 1.8 mmHg; Dia -1.3mmHg \pm 1.36 mmHg) while in group2 Sys showed no change (-0.05 \pm 1.6 mmHg) and Dia increased (+0.41 mmHg \pm 1.1 mmHg). However, these results did not reach significance. BP changes did not correlate with the AHI, desaturation-index, percent of oxygen<90%, cyclic alternating patterns or the Arousal-index but with the variation in Sys (Fig1) and Dia (R:0.50, P=0.002) BP.



Discussion: We could show, that in OSAS patients during a short period of sleep the changes of BP are not directly correlated with the expected sleep or respiratory parameters but with the variation of blood pressure values. The relevance of this result for the development of hypertension remains to be proven.

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P2236**Perception of problems driving and driving simulator performance in obstructive sleep apnoea syndrome (OSAS)**

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Introduction: Advising patients with OSAS about driving is difficult. In the absence of an objective test reliance has to be given to a patient's account of their driving ability. In simulated driving, OSAS patients perform worse than controls but an individual's performance does not correlate with severity or symptoms of OSAS. Patients' account is also likely to be influenced by worry of losing licence. The relationship between patients' perception & driving simulator performance was explored as part of development of an advanced office based driving simulator (MiniSim) for patients with OSAS.

Methods: 72 patients (ESS 12±6, ODI 39±21) completed a questionnaire pertaining to their driving behaviour & completed 50 minutes of simulated motorway driving. Two events were programmed that required evasive action to avoid a crash; minor & major. A "fail" was defined by an unprovoked crash or crash at the minor event. A crash at the major event was deemed as "indeterminate", the rest were deemed to have "passed". Chi squared test was performed to see whether patients admitted to problem driving were more likely to "fail". Logistic regression analysis was performed to predict a "fail" from the questionnaire.

Results: 54% subjects admitted to problem driving. Only the ESS was higher in these patients (p=0.0001). A "fail" could not be predicted from the questionnaire. Subjects who reported problem driving were not significantly more likely to fail than others. This highlights that patients' perceptions are not a reliable indicator of driving ability in OSAS. An objective test that is credible, reliable and practicable for everyday clinical use is needed to inform decision making.

P2237**Effects of non-surgical therapeutic program on the metabolic syndrome (MetS) in morbidly obese patients**

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Objective: The aim of this study was to assess the effects of non-surgical therapeutic program on the metabolic syndrome (MetS) in morbidly obese patients.

Design: This is a prospective study. Sixty-four extremely obese patients were involved in the therapeutic program, which consisted of two alternating phases: the three-week therapeutic fasting or semi-fasting in hospital conditions and the low calorie diet (LCD) with dosed physical activity in outpatient conditions. At the baseline we measured: anthropometric parameters, blood pressure and lipid profile. Subjects underwent an oral glucose tolerance test (OGTT) and insulin resistance/sensitivity was evaluated by the homeostasis model assessment (HOMA) and the oral glucose insulin sensitivity (OGIS). After weight reduction by at least 10%, all mentioned assessments were repeated.

Results: None of the patients had significant adverse effects. Forty-one patients aged 43.0±11.5 years completed the study. The mean weight loss was 27 kg or 18% of the initial weight (p<0.01), which was followed by a significant decrease of the insulin resistance, the overall prevalence of MetS (32%) and all MetS parameters, without the significant change in high-density lipoprotein (HDL). In the subgroup of 15 patients weight reduction of 20% of the initial weight (p<0.01) resulted in AHI reduction of 31%.

Conclusions: This weight loss program substantially improves the MetS in extremely obese patients. The tailored alternating either fasting or semi fasting should be considered as an optional approach to manage extreme obesity and related metabolic adverse effects and reduce severity of sleep breathing disorders.

P2238**A study of insulin resistance in moderate to severe obstructive sleep apnea in non diabetics and its response to nasal CPAP treatment**

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Background: The effects of nasal continuous positive airway pressure (nCPAP) for obstructive sleep apnoea (OSA) on insulin resistance (IR) are not clear and have found conflicting results.

Aims and objectives: To evaluate IR in non diabetic patients with moderate to severe OSA and the effect of treatment with nCPAP on IR in these patients.

Method: 30 consecutively newly diagnosed patients with moderate to severe OSA were enrolled in the study. Samples of peripheral venous blood for measurement of glucose and insulin were collected after overnight fasting and IR was calculated by HOMA (Homeostasis model assessment) method. Patients were treated with nCPAP for 1 month and HOMA IR was again measured.

Results: 30 OSA subjects, with a mean apnoea-hypopnoea index (AHI) of 80.46 [57.24] were included in the study. The HOMA IR (5.78) was significantly higher compared to normal south indian population. There was no positive correlation of

HOMA IR with AHI. This may be due to the small sample size and IR attributable to OSA may be small and constant and not related to the severity. The HOMA IR was measured 1 month after use of CPAP. The HOMA IR significantly improved from 5.78 to 4.82 (p=0.024) after 1 month of treatment with nCPAP in OSA patients. There was also significant improvement in insulin levels from 21.75 to 19.39 (p=0.009).

Characteristics	Before-CPAP	After-CPAP	P-value
Fasting-Insulin(microU/ml)	21.75[19.48]	19.39[17.54]	0.009
Fasting-Glucose(mg/dl)	100.36[19.24]	98.76[19.45]	0.714
HOMA-IR	5.78[6.01]	4.82[4.39]	0.024

Results are presented as mean{SD}

Conclusion: OSA is associated with an increase in IR which may be one of the reasons that OSA is a risk factor for coronary artery disease (CAD). Treatment with CPAP rapidly improves the insulin sensitivity in patients with OSA and thus may contribute to a reduction of cardiovascular risk in patients with moderate to severe OSA.

P2239**Relationships between obstructive sleep apnea and oxidant/antioxidant status**

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Introduction: In Sleep Apnea Syndrome (SAS) the episodes of hypoxia/reoxygenation can generate reactive oxygen species and promote oxidative stress.

Aim of the study: Evaluation of possible relationships between obstructive sleep apnea and biomarkers of oxidative stress in patients with SAS.

Methods: Two Romanian groups, consisting of 29 patients diagnosed with SAS and 17 healthy controls, were recruited. All subjects underwent cardiorespiratory polygraphy. Plasma levels of homocysteine (Hcy), glutathione reductase (GSSG-Red), glutathione peroxidase, endothelin-1, low density lipoprotein (LDL), high density lipoprotein (HDL) and uric acid were assessed. Statistical analysis was performed using Spearman and Pearson correlations tests, two tailed t-test and one-way ANOVA test.

Results: The mean values of LDL were statistically significant higher in SAS patients (p=0.05), while GSSG-Red was higher in controls (p=0.01). In the SAS group, correlations were found as follows: GSSG-Red and snoring (r=0.34; p=0.05); GSSG-Red and apneas number (r= -0.36; p=0.05); body mass index (BMI) and uric acid (r=0.43; p=0.01); ratio Hcy/BMI and HDL (r=0.52; p=0.003). With regard to the smoking status, the Hcy values were statistically significant higher in SAS smokers than SAS non-smokers (p=0.03).

Conclusions: Plasma GSSG-Red and Hcy levels may be used as possible markers to provide information related to oxidant/antioxidant status in SAS patients, making them more prone to developing proatherosclerotic disease.

P2240**Road traffic collisions caused by sleepiness in UAE**

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Introduction: Road traffic collision RTC is a major health problem in UAE. Sleep as a contributing factor to RTC is not well-studied in the Middle East.

Objective: We aimed to study to the proportion of RTC caused by sleep behind the wheel and the factors contributing to sleep related collisions SRC.

Methods: All data of hospitalized drivers who were involved in RTC in Al-Ain city were prospectively collected during the period of April 2006-October 2007. Variables studied included, driver's demographic data, time, date, location, mechanism of collision, speed at collision and whether sleepiness was a contributing factor reported by the divers. A direct logistic regression model was performed to define factors related to sleep while driving.

Results: 444 drivers (92% males) were involved in RTC's during the study period. Sleepiness of drivers was a contributing factor in 5%. Most of the drivers with SRC (79%) reported to speed 100 Km/hr or more during the collision. Rollover was the most frequent mechanism of SRC (58%). SRC was strongly over-represented during the month of Ramadan (42%), in driving in highway (83%) and in driving during the day time (67%). A logistic regression analysis model has shown that driving during the month of Ramadan (OR = 7.58) and on highways (OR =

Logistic regression analysis

Variables	OR	P value
Age	0.98	0.46
Gender	0.784	0.767
Ramadan	7.58	<0.001
Daytime	1.458	0.42
Day	0.94	0.445
Highway	3.99	0.032
Speed	1.01	0.192

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3.99) were the most significant independent contributors to increasing the odds of sleep-related collisions.

Conclusion: Sleep is an important contributing factor to RTC's in UAE. Drivers should be advised to discontinue driving when feeling sleepy especially during the month of Ramadan.

P2241

WITHDRAWN

P2242

Relationship between obstructive sleep apnoea syndrome (OSAS) and the levels of endothelial progenitor cells (EPC) in patients with acute stroke

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OSAS is a cardiovascular risk factor that has a high prevalence in patients with stroke. Endothelial progenitor cells (EPC) are an endogenous repair mechanism of endothelium, which could be altered in OSA and contribute to endothelial dysfunction. The aim of this prospective study is to assess the relationship of OSAS and circulating EPC levels in acute stroke patients. The patients underwent a respiratory polygraphic (RP) evaluation on the 7th day of stroke (acute phase). EPC were measured by flow cytometry at inclusion and were repeated at the 7th day. EPC were considered those that were positive for three markers: CD34, CD133 and KDR (VEGF receptor). 42 of 52 patients were included (age 69±12.5 years, 54.8% male, BMI 27±4 kg/m², Epworth 7±3.6). OSA prevalence in the acute phase of stroke was 54.76% (AHI>20) and 35.71% (AHI>30) with a predominant hypopnoea pattern. Significant differences between EPC levels on inclusion and on the 7th day (0.0004762% ± 0.00175636 vs 0.0034857% ± 0.0061183 (p=0.005) were found. There were no differences between non-OSAS patients and the group with AHI>10, except for age 59,73±15,58 vs 72,61±9,41 (p = 0,013). Patients with AHI>10 had lower EPC baseline levels but the analysis showed no significant differences compared to non-OSA patients. Neither AIH nor EPC values were significantly associated with neurological variables in acute stroke. The results suggest that EPC show a peak on the 7th day of acute stroke, which can express the endothelial repair capacity of the organism. OSA patients showed a lower baseline EPC values but failed to demonstrate significant differences regarding non-OSA population.