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Hypercapnia is a Key Correlate of EEG Activation and Daytime Sleepiness in Hypercapnic Sleep Disordered Breathing Patients

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Background: The key determinants of daytime drowsiness in sleep disordered breathing (SDB) are unclear. Hypercapnia has not been examined as a potential contributor due to the lack of reliable measurement during sleep. To overcome this limitation, we studied predominantly hypercapnic SDB patients to investigate the role of hypercapnia on EEG activation and daytime sleepiness.

Methods: We measured overnight polysomnography (PSG), arterial blood gases, and Epworth Sleepiness Scale in 55 severe SDB patients with obesity hypoventilation syndrome or overlap syndrome (COPD+ obstructive sleep apnea) before and ~3 months after positive airway pressure (PAP) treatment. Quantitative EEG analyses were performed, and the Delta/Alpha ratio was used as an indicator of EEG activation.

Results: After the PAP treatment, these patients showed a significant decrease in their waking pCO_2, daytime sleepiness, as well as all key breathing/oxygenation parameters during sleep. Overnight Delta/Alpha ratio of EEG was significantly reduced. There is a significant cross-correlation between a reduced wake pCO_2, a faster (more activated) sleep EEG (reduced Delta/Alpha ratio) and reduced daytime sleepiness (all $p < 0.05$) with PAP treatment. Multiple regression analyses showed the degree of change in hypercapnia to be the only significant predictor for both ESS and Delta/Alpha ratio.

Conclusions: Hypercapnia is a key correlate of EEG activation and daytime sleepiness in hypercapnic SDB patients. The relationship between hypercapnia and sleepiness may be mediated by reduced neuro-electrical brain activity.

Keywords: CO_2, O_2, EEG Spectra, daytime drowsiness, hypersomnolence, hypoxia, cortical depression.

Commentary: A commentary on this article appears in this issue on page 523.

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SCIENTIFIC INVESTIGATIONS

The key determinants of general sleep disordered breathing (SDB) related daytime drowsiness are unclear. Many candidate factors such as intermittent hypoxia, apnea-hypopnea index (AHI), sleep fragmentation, BMI, sleep time, and metabolic factors have been studied, but none show a strong correlation with daytime sleepiness.[1-9] Among those factors, relatively stronger evidence supports a role for oxygen desaturation index (ODI) or intermittent hypoxia in daytime sleepiness.[1,2,6] However, supplemental O_2 does not improve hypersomnolence in obstructive sleep apnea (OSA) patients despite improving oxygenation.[10-12] Similarly, O_2 therapy does not improve neurocognitive or psychosocial performances in hypoxemic chronic obstructive pulmonary disease (COPD).[13,14] In contrast, some human experimental studies suggest that hypercapnia can cause impaired mental and psychomotor function.[15-18] While SDB is characterized by recurrent episodes of both hypoxia and hypercapnia, the relationship of hypercapnia to daytime sleepiness in this patient group has not been investigated.[1-5] This omission is likely due to the lack of clinical equipment to reliably measure continuous pCO_2 during the overnight PSG. However, in hypercapnic SDB patients, particularly those with obesity hypoventilation syndrome (OHS) and overlap syndrome (COPD+OSA), a wide range of pCO_2 can be accurately measured during awake with arterial blood gas (ABG). Therefore this subtype of SDB patients could be an ideal patient group to investigate the relationship between hypoxia, hypercapnia, and daytime sleepiness.

BRIEF SUMMARY

Current Knowledge/Study Rationale: The key determinants of daytime drowsiness in sleep disordered breathing (SDB) are unclear. Hypercapnia has not been examined as a potential contributor due to the lack of reliable measurement during sleep.

Study Impact: Our study identified that hypercapnia is a key correlate of SDB -related daytime sleepiness in severe SDB population, and there is a significant cross-correlation between the changes of hypercapnia, EEG spectral activity, and daytime sleepiness.

Dose-dependent anesthesia-like effects of CO_2 have been previously reported.[19] In fact, CO_2 has long been used as a stunning agent to produce unconsciousness during porcine slaughter, while hypoxia does not produce this effect.[20] A clinical study found that untreated OSA patients have slower EEG than normal subjects, which is not related to hypoxia. CPAP treatment corrected the EEG slowing together with reduced daytime sleepiness.[21] Recently we observed that respiratory

failure patients have a paradoxically high percentage of slow wave sleep; awake pCO_2 measured by ABG is the best predictor variable for the EEG change.[22] Furthermore, progressive hypercapnia but not hypoxia decreases EEG activation measured by an increased EEG Delta/Alpha (D/A) ratio.[23]

Given these findings, we hypothesized that in hypercapnic SDB patients, the decrease in hypercapnia, but not hypoxia, is a key correlate for the improvement in daytime sleepiness, and may cross-correlate with changes in EEG spectral power—such as D/A ratio—reflecting changes in EEG activation.[21,24-26] We conducted an observational study using PAP treatment to test these hypotheses.

METHODS

The clinical study was conducted at the clinical sleep laboratory of Royal Prince Alfred Hospital (RPAH), a major teaching hospital of the University of Sydney. The study protocol was originally designed to test clinical outcomes of OHS patients receiving CPAP/BPAP treatment over a 3-month period. Data of the present study come from post hoc analyses of the original study. The study protocol was approved by Sydney South West Area Health Service Ethics Review Committee (Protocol Numbers: X03-0022). All participants provided written informed consent. The Australian & New Zealand Clinical Trial Registry number is ACTRN12605000096651.

Patients and Procedure

Study patients were consecutive patients recruited from the Sleep and Respiratory Failure Clinics of RPAH. We sampled late afternoon awake ABG in predominantly hypercapnic patients with severe SDB. Fifty-five OSA patients with either OHS or overlap syndrome (COPD+OSA) underwent 2 overnight PSGs before and after ~3 months continuous/bilevel positive airway pressure (PAP) treatment. The recruited patients had daytime hypercapnia (arterial pCO_2 > 45 mm Hg) and/or frequent hypoventilation with significant oxygen desaturations during the initial diagnostic PSG studies. Hypoventilation was defined by an awake daytime pCO_2 > 45 mm Hg or during sleep a sustained fall in SpO_2 > 4% from baseline values accompanied by a rise in $PtcCO_2$ > 8 mm Hg. COPD was defined as FEV1/FVC ratio < 70%, with severity based on percent of predicted FEV1 (GOLD criteria, www.goldcopd.com). We included both OHS and overlap syndrome patients, considering that the effect of hypercapnia/hypoxia may share a common mechanism in affecting EEG and daytime sleepiness. Quantitative EEG spectral analyses were performed on the overnight PSG recordings. A score for the Epworth Sleepiness Scale (ESS), a widely used measure of subjective daytime sleepiness, was calculated in each patient.[27]

PSG

Overnight standard in-laboratory PSG was performed (between 22:00 and 07:00) using Compumedics E series (Compumedics; Victoria, Australia) or Alice 4 & 5 (Respironics, USA) diagnostic sleep systems. Each PSG included 4 channels of electroencephalogram (EEG) (C3/A2, C4/A1, O1/A2, O2/A1), 2 channels of electrooculogram, chin electromyogram, anterior tibial electromyogram, electrocardiogram (ECG), body position, nasal pressure, chest and abdomen movements, and SpO_2. PSG recordings were scored by experienced sleep technologists using standard criteria.[28-30] Respiratory events were scored according to Chicago criteria,[29] but no respiratory effort-related arousal events were marked. Sleep arousals were scored according to the American Sleep Disorder Association task force criteria.[30] AHI was calculated by dividing the total number of apneas and hypopneas by the total sleep time (hours). ODI was calculated by dividing the total number of ≥ 3% SpO_2 dips by the total sleep time (hours).

EEG Spectral Analyses

We converted all EEG recordings to European Data Format for the spectral analyses. We analyzed the EEG power spectra for each 5-sec segment. All EEG study sampling rates were > 200 Hz. A standard fast Fourier transform with a rectangular weighting window was performed twice: first, to the largest power of 2 data points smaller than the total number of data points, selected from the beginning of the segment, and second, to the same number of data points selected from the end. This double fast Fourier transform method weights middle data points. Delta, theta, alpha, and beta bands were defined as the frequency ranges 0.5-4.5, 4.5-8, 8-12, and 12-32 Hz, respectively, appropriate for typical adults. The EEGs were then further examined by an automatic algorithm which excluded EEG segments showing excessive delta power using a standard 2 sigma rule (i.e., median + 2 standard deviations). For our statistical analysis, we focused primarily on the EEG recorded at C3/A2. However, when the C3 channel was contaminated by excessive artifact, we used C4/A1 as alternative channel.

Statistical Analyses

Descriptive data were expressed as mean ± SD, unless otherwise stated. Pair-wise comparisons were tested by paired t-test or Wilcoxon signed-rank test depending on the normality of data distribution. Unpaired t-tests and Mann-Whitney U tests were used for between group comparisons where appropriate. Associations were tested by either Pearson or Spearman tests also based on normality of distribution. Among the EEG spectral measures, Delta/Alpha ratio was the primary outcome of interest. ESS is the other primary outcome of interest. Stepwise multiple linear regression analyses were used to identify factors contributing to the variance of ESS and D/A ratio respectively. A p-value < 0.05 was considered as significant. Analyses were performed using SPSS 17 (SPSS, Chicago, USA).

RESULTS

From the 55 patients tested, we obtained satisfactory data in 41 patients (30M, 11F, aged 54.6 ± 12.8 years). Data were excluded due to either an unsatisfactory EEG quality for spectral analyses or failure to take blood for ABG in any phase of the study. Thirty-two EEG spectra data were analyzed from C3/A2 channel, and 9 were analyzed from C4/A1 channel. Of these 41 patients, 26 had OHS and 15 had overlap syndrome. Twenty-five patients received BPAP treatment and 16 received CPAP treatment. The treatment option was allocated randomly as a part of the original study protocol in comparing the therapeutic outcomes of CPAP and BPAP. Three patients were using

O_2 supplementation during taking blood samples for ABG and during the initial diagnostic PSG. No patient had central apnea index > 5/h either in baseline or after PAP treatment.

As shown in **Table 1**, after ~3 months PAP treatment, patients showed a significant decrease in their waking pCO_2, daytime sleepiness, as well as all key breathing/oxygenation parameters during sleep. BMI also decreased slightly. Similar to our previous report,[31] no difference was found between the options of CPAP and BPAP in improving awake pCO_2 ($p = 0.27$) and SpO_2 nadir during sleep ($p = 0.62$) in the present study. EEG spectral analyses showed that the D/A ratio of EEG was significantly reduced during both sleeping and waking periods, indicating a generally faster, more activated EEG spectral profile following treatment (**Table 2**). There was also a reduction in High Beta power (15-32 Hz) after the PAP treatment (**Table 2**). This reduction was correlated with the decrease in arousal index ($r = 0.33$, $p < 0.05$).

A cross-correlation was observed between a reduced wake pCO_2, a faster (more activated) EEG (reduced D/A ratio) and reduced daytime sleepiness (**Table 3**, **Figure 1**). The cross-correlation pattern was similar between OHS and overlap syndrome subtypes of patients as shown in **Figure 1**. Specifically, there was a consistent pattern of positive correlations between the change of %Delta and ESS and pCO_2; and negative correlations between the change of %Alpha and ESS and pCO_2 (**Table 3**). The ESS change also correlated significantly with waking pCO_2 change ($r = 0.42$, $p = 0.007$; **Figure 1**). This pattern of the cross-correlations existed in both waking and sleeping periods of the PSG recordings (**Table 3**).

Given that many related parameters such as hypoxia, hypercapnia, arousal index, and BMI were improved after the PAP treatment (**Table 1**), we conducted multiple linear regression analyses, using the changes in ESS and D/A ratio as dependent variables respectively. Using the change of ESS as the dependent variable, the only significant predictor was pCO_2 change, explaining 15% of the variance of ESS ($t = 2.44$, $p = 0.02$). The change in ODI was the second best predictor but was not statistically significant, explaining only 7% of the variance in ESS. Other variables such as the changes in REM%, AHI, SpO_2 nadir, BMI, D/A ratio, arousal index, and sleep efficiency, were not significantly associated with the ESS. In regression analyses using the change of D/A ratio as the dependent variable, pCO_2 change was again the only significant predictor, explaining 27% of the variance in D/A ratio ($t = 3.51$, $p = 0.001$). SpO_2 nadir was the second best predictor (not significant), explaining only 4% of variance of D/A ratio. Other nonsignificant predictor variables were the changes of BMI, arousal index, AHI, sleep efficiency, and ODI.

DISCUSSION

We have demonstrated that hypercapnia but not hypoxia is a key correlate of both daytime sleepiness and EEG activation in patients with hypercapnic SDB. The decrease in hypercapnia was the best predictor of both reduction in daytime sleepiness and increase in EEG activation (reduced D/A ratio). We speculate that hypercapnia may cause daytime sleepiness through a reduction in brain activation in a hypercapnic SDB population.

Table 1—Sleep and pCO_2 data pre- and ~3 months post-PAP in 41 patients

	Baseline	Post-PAP	p value
BMI (kg/m^2)	50.1 ± 9.3	48.5 ± 8.7	0.009
pCO_2 (mm Hg)	54.7 ± 8.6	44.7 ± 4.8	< 0.0001
ESS	14.0 ± 5.1	5.2 ± 3.9	< 0.0001
TST (min)	278.4 ± 99.7	293.8 ± 67.9	0.29
Sleep Efficiency (%)	65.0 ± 22.3	70.7 ± 16.5	0.10
REM%	12.4 ± 7.8	17.6 ± 8.8	0.004
AHI (/h)	66.8 ± 34.1	8.8 ± 11.8	< 0.0001
NREM AHI (/h)	67.6 ± 36.2	7.0 ± 12.3	< 0.0001
REM AHI (h)	52.7 ± 30.4	17.2 ± 18.2	< 0.0001
SpO_2 Low (%)	51.6 ± 16.5	82.8 ± 6.4	< 0.0001
ODI (/h)	35.9 ± 31.2	6.9 ± 8.7	< 0.0001
T90%	40.6 ± 33.4	10.9 ± 20.5	< 0.0001
Arousal Index (/h)	60.1 ± 33.7	16.3 ± 11.8	< 0.0001

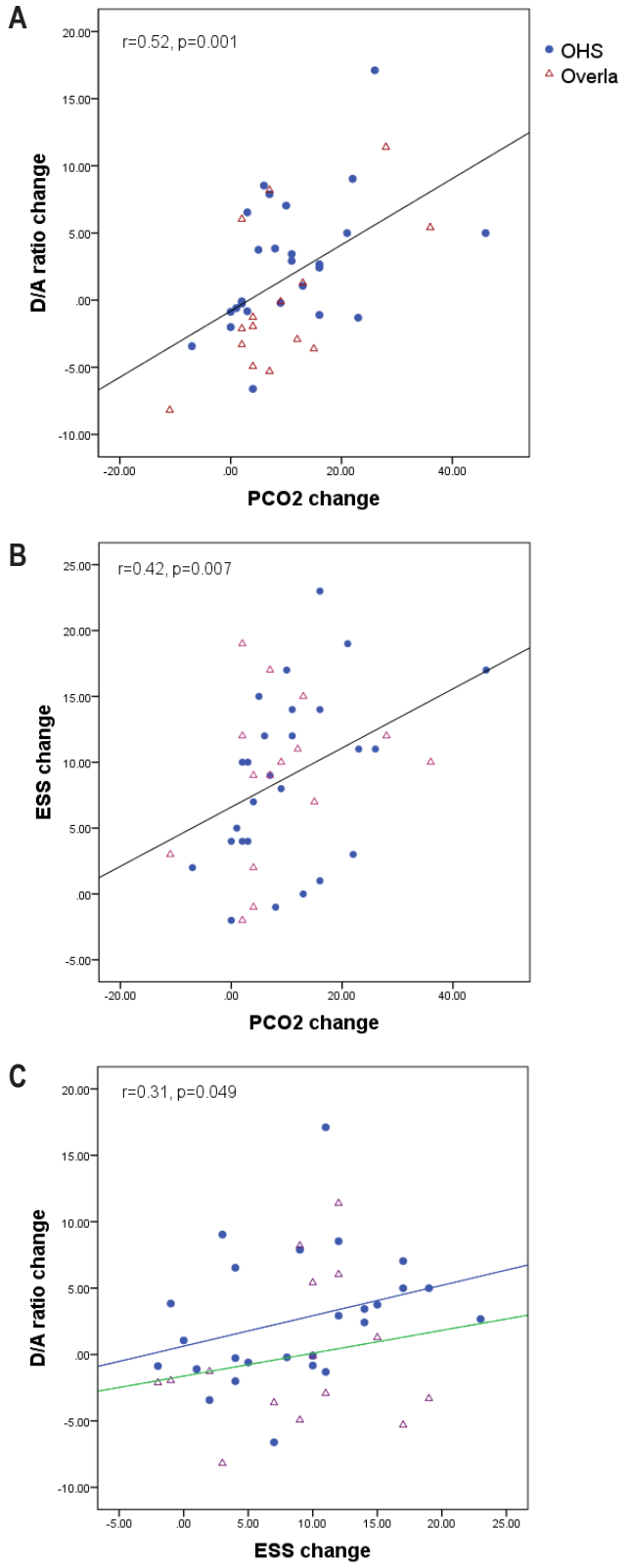
All p values lower than 0.0001 are presented as $p < 0.0001$; BMI, body mass index; ESS, Epworth Sleepiness Scale; TST, total sleep time; AHI, apnea hypopnea index; ODI, oxygen desaturation index; T90%, percentage of total sleep time with $SpO_2 < 90\%$. PAP included 25 BPAP and 16 CPAP treatments.

Table 2—Quantitative EEG spectral analyses data pre- and ~3 months post-PAP in 41 patients

	PSG (Wake+Sleep)		PSG Wake		PSG Sleep (Stage 2)	
	Pre-PAP	Post-PAP	Pre-PAP	Post-PAP	Pre-PAP	Post-PAP
Delta%	64.6 ± 12.2	62.8 ± 11.3	52.0 ± 16.3	44.1 ± 14.7†	70.5 ± 10.1	68.0 ± 9.0
Alpha%	8.7 ± 4.7	9.9 ± 4.0*	12.0 ± 7.3	15.1 ± 7.3‡	7.4 ± 3.7	9.1 ± 3.7§
D/A ratio	9.4 ± 5.2	7.8 ± 4.6*	6.4 ± 5.2	4.2 ± 4.3†	12.3 ± 6.9	9.3 ± 5.4‡
Delta, μV^2	105.5 ± 62.5	97.4 ± 67.2	92.8 ± 87.2	84.6 ± 144.7	123.9 ± 67.7	106.6 ± 51.4
Theta, μV^2	25.7 ± 23.1	24.0 ± 20.7	28.6 ± 26.6	27.1 ± 29.3	24.9 ± 23.1	24.7 ± 21.3
Alpha, μV^2	17.3 ± 18.2	17.1 ± 15.3	24.1 ± 31.4	25.9 ± 28.1	14.6 ± 14.6	16.0 ± 14.7
L-Beta, μV^2	5.8 ± 4.4	5.4 ± 3.3	7.0 ± 4.7	7.3 ± 4.9	5.4 ± 4.8	5.6 ± 3.6
H-Beta, μV^2	10.3 ± 6.6	7.9 ± 4.9†	16.9 ± 10.0	19.3 ± 15.1	7.5 ± 4.2	5.9 ± 3.1‡

Shaded cells indicate significant p values at * $p < 0.05$; † $p < 0.01$; ‡ $p < 0.005$; § $p < 0.001$. D/A ratio is the primary outcome of interest. Delta: 0.5-4.5 Hz; Theta: 4.5-8.0 Hz; Alpha: 8.0-12.0 Hz; L-Beta: 12.0-15.0 Hz; H-Beta:15.0-32.0 Hz. D/A ratio, Delta/Alpha ratio. PSGs were recorded during time in bed between 22:00-07:00. EEG spectra were compared according to the stratified PSG scoring of "Wake," "Sleep," and "Stage 2."

Figure 1—Inter-correlations between the changes of pCO_2, EEG Delta/Alpha ratio and ESS before and after PAP treatment.



The 3 panels show consistent pattern of relationships between OHS and overlap subtypes. Panel C shows that even though the overall correlation between the changes of ESS and D/A ratio is relevantly loose (p = 0.049), the OHS and overlap subgroups show a similar pattern of relationship.

Table 3—Cross-correlation between the changes of EEG spectra, ESS, and pCO_2

		ESS change		pCO_2 change	
Inter-Correlation		**r**	**p**	**r**	**p**
PSG W+S	%Delta change	0.327	0.037	0.367	0.018
	%Alpha change	-0.332	0.034	-0.356	0.023
	D/A ratio change	0.310	0.049	0.516	0.001
PSG Wake	%Delta change	0.363	0.02	0.467	0.002
	%Alpha change	-0.388	0.012	-0.514	0.001
	D/A ratio change	0.403	0.009	0.432	0.005
PSG Sleep (Stage 2)	%Delta change	0.289	0.067	0.279	0.078
	%Alpha change	-0.283	0.07	-0.308	0.05
	D/A ratio change	0.303	0.05	0.401	0.009

W+S = PSG epochs scored as "Wake" and "Sleep." ESS change significantly correlated to awake pCO_2 change, r = 0.42, p = 0.007. All changes were calculated by (Baseline – Intervention). The primary outcome of interest is D/A ratio change.

SDB is usually associated with cyclic patterns of hypoxia and hypercapnia. In the present study, we demonstrated a significant cross-correlation between a reduced waking pCO_2, a faster, more activated EEG spectral profile, and a reduced reported daytime sleepiness. Using multiple linear regression modeling, we demonstrated that hypercapnia accounted for more than double the variance of ESS compared to ODI (a measure of intermittent hypoxia frequency), and nearly 7 times the variance in EEG spectral (D/A ratio) compared to hypoxic severity. By contrast, hypoxia was not a significant predictor for the variance of ESS, although it is still a better predictor than AHI, arousal index, BMI, and sleep efficiency.

We are not aware of any previous study showing hypercapnia as covarying with hypersomnolence in any subtypes of SDB.[1-7] In the largest PAP intervention trial in sleep apnea, measures of hypoxia were only weakly associated with ESS, explaining < 2% of the variance. The degree of hypercapnia in their study patients was unknown.[6] In another large study of determinants of sleepiness in 2,882 OSA patients,[32] there was no real difference in hypoxia between those patients with or without sleepiness (only 1% difference). Interestingly, OSA patients with excess sleepiness had increased slow wave sleep compared to the non-sleepy patients, supporting a correlation between daytime sleepiness and a slower EEG spectral activity[32]; pCO_2 was not measured in this study.[32] Importantly, if hypoxia is a key factor in sleepiness, then hypersomnolence should be alleviated by giving supplemental O_2. However, this prediction is not supported by the few relevant studies.[10-13]

Our notion that hypercapnia affects cerebral neural activity is supported by a number of experimental animal and human studies. Hypercapnia, acute or chronic, leads to the slowing of EEG in eels, rats, rabbits, dogs, and monkeys.[33-37] In human experimental studies, hypercapnia led to slower EEG spectral activity with decreased alpha and beta activity[38-42] and increased delta activity.[39] A recent study tested the effects of mild hypercapnia (5% CO_2) on magnetoencephalogram, event-related potentials, auditory pattern recognition, and visual semantic

tasks in seven healthy volunteers.[41] Hypercapnia attenuated evoked and spontaneous magnetoencephalogram spectral activity. In addition, comparable decreases were observed in early sensory components in both auditory and visual modalities as well as cognitive components related to memory and language, and the depressant effects were distributed across all cortical regions.[41] Similarly, a few experimental studies reported dose-response relationship between higher CO_2 tensions and impaired cognitive and psychomotor performance.[15-17] In addition, breathing of CO_2 was reported to attenuate sensory and affective components of experimental ischemic pain and produce a dose-dependent elevation of heat pain threshold.[19] In this context, 80% CO_2 is commonly used as a porcine stunning agent to produce unconsciousness before slaughtering; hypoxia does not produce a similar anesthetic effect.[20,43] Given these data, exposure to sustained hypercapnia or possibly even brief bursts of intermittent hypercapnia in sleep disordered breathing may result in drowsiness secondary to reduced brain neuroelectrical activation and overall depression of cortical activity.

In our studies, we used the Delta/Alpha ratio obtained from EEG spectral analyses as an objective marker of EEG activation that correlated to daytime sleepiness. An important consideration is that the D/A ratio can avoid the misinterpretation of an increased Delta power purely caused by a global, frequency independent, increase in EEG power. Ratios of slow and fast EEG frequency bands are commonly used in neurological studies to indicate activation of EEG.[21,24-26] The D/A ratio has been previously identified as the best discriminator between wake, and stage 1, 2, and slow wave sleep,[26] and the best brain biomarker correlating to the clinical outcomes of subacute ischemic stroke.[24]

In the present study we only examined severe SDB patients with awake hypercapnia, so our findings may not apply to SDB patients in general, especially mild-moderate OSA patients, although the mechanism may play a role. To study the less severe SDB patients requires a fully validated and accurate continuous measure of pCO_2, fast enough to respond to the rapid changes due to respiratory events. Such a machine is currently not available. The commonly used transcutaneous pCO_2 ($PtcCO_2$) measurement are often affected by a drifting artifact, while a CO_2 analyzer connected to nasal cannula cannot sample expired air during a prolonged apnea. We speculate that in milder SDB patients, the daytime hypersomnolence would be affected by the CO_2 mechanisms of (1) cyclic hypercapnia episodes during apnea; (2) mild hypercapnia in daytime; and (3) SDB related chemoreflex changes, particularly those CO_2 related factors such as CO_2 threshold. Indeed, even in healthy individuals, average resting pCO_2 may vary largely, ranging from 32 to 44 mm Hg.[44]

There are a number of limitations to the study. This is not a prospective study originally designed to serve the purpose. The data were retrieved from post hoc analyses of an interventional clinical study. Those patients were randomly allocated to BPAP or CPAP treatment, thus the PAP treatment they were receiving might not be fully tailored to individual clinical conditions. There was still some residual SDB after PAP treatment. Three patients were using O_2 supplementation during blood sampling for ABG and during the initial diagnostic PSG, which could affect pCO_2 and SpO_2 results. In addition, most of our patients were taking different medications, and it is not possible to obtain a medication-free group of patients with severe SDB. Nevertheless, our study used patients as their own controls, so that the effect of this potential confounding factor was minimized. Furthermore, our studies relied on self-reported measures of sleepiness. A further study using multiple sleep latency test or maintenance of wakefulness test to quantify daytime sleepiness in addition to ESS and EEG spectral analyses would be more definitive. Moreover, the sampling rate of our two PSG systems was slightly different, being 256 Hz for Compumedics and 200 Hz for Alice. Nevertheless, as the primary outcome of interest of the present study is Delta/Alpha ratio (rather than an absolute spectral power) as an EEG activation marker, the potential confounding effect on our conclusion is therefore minimal. The last, it would be of interest to examine neurometabolic imaging during hypercapnia to clarify the relationship between hypercapnia, a slower EEG spectral profile and hypersomnolence.

In conclusion, we identified that in hypercapnic SDB population, hypercapnia is a key correlate of SDB-related daytime sleepiness, and there is a significant cross-correlation between the changes of hypercapnia, EEG spectral activity, and daytime sleepiness. We speculate that hypercapnia may cause drowsiness through a reduced brain neuroelectrical activation in this population. Whether similar mechanisms also apply to less severe SDB patients without daytime hypercapnia deserve further investigation.

ABBREVIATIONS

ABG, arterial blood gas
AHI, apnea-hypopnea index
BMI, body mass index
COPD, chronic obstructive pulmonary disease
CPAP, continuous positive airway pressure
D/A ratio, Delta/Alpha ratio
ECG, electrocardiogram
EEG, electroencephalography
ESS, Epworth Sleepiness Scale
ODI, oxygen desaturation index
OHS, obesity hypoventilation syndrome
OSA, obstructive sleep apnoea
PSG, polysomnography
$PtcCO_2$, transcutaneous PCO_2
REM, rapid eye movement sleep
SDB, sleep disordered breathing
SpO_2, oxygen saturation
T90, total sleep time with $SpO_2 < 90\%$
TST, total sleep time

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