Reduced Cerebral Blood Flow During Wakefulness In Obstructive Sleep Apnea-Hypopnea Syndrome

Eun Yeon Joo, MD; Woo Suk Tae, PhD; Sun Jung Han, MD; Jae-Wook Cho, MD; Seung Bong Hong, MD, PhD

1Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; 2Department of Neurology and Inam Neuroscience Research Center, Sanbon Medical Center, Wonkwang University School of Medicine, Korea

Study Objectives: To investigate changes in regional cerebral blood flow (rCBF) in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS).

Design: We compared the 99mTc-ethylcysteinate dimer (ECD) single photon emission computed tomography (SPECT) images of patients with OSAHS with those of age- and sex-matched healthy volunteers.

Setting: University hospital.

Patients and Participants: Twenty-seven patients with severe OSAHS and 27 healthy volunteers underwent 99mTc-ECD SPECT studies.

Intervention: For statistical parametric mapping analysis, all SPECT images were spatially normalized to the standard SPECT template and then smoothed using a 14-mm full-width at half-maximum Gaussian kernel. The Student’s t-test was used for the statistical analysis.

Measurements and Results: The mean age of patients and subjects was 44.3 years (range 31-58). All patients underwent overnight polysomnography. The mean apnea-hypopnea index of patients was 60.4 ± 17.6 per hour (range 33-104), indicating severe OSAHS. All patients snored heavily and had daytime sleepiness (mean Epworth Sleepiness Scale score, 10.7 ± 3.7, range 6-12). Statistical parametric mapping analysis showed that rCBF in patients with OSAHS was significantly reduced in bilateral parahippocampal gyri and in the right lingual gyrus, as compared with that of healthy volunteers (P < 0.05 with false discovery rate correction). Moreover, apnea-hypopnea indexes of patients were negatively correlated with rCBF in the right pericentral gyrus and right cuneus at uncorrected P < 0.001.

Conclusions: Our results show the altered rCBF pattern in bilateral parahippocampal gyri, right lingual gyrus, pericentral gyrus, and cuneus in patients with severe OSAHS. These findings may partly explain the deficit in memory, spatial learning, executive function, and attention, which are frequently found in patients with OSAHS.

Keywords: Obstructive sleep apnea syndrome, SPECT, cerebral blood flow

Citation: Joo EY; Tae WS; Han SJ; Cho JW; Hong SB. Reduced cerebral blood flow during wakefulness in obstructive sleep apnea-hypopnea syndrome. SLEEP 2007;30(11):1515-1520.

Disclosure Statement
This is not an industry supported study. The authors have indicated no financial conflicts of interest.

Submitted for publication February, 2007
Accepted for publication June, 2007
Address correspondence to: Seung Bong Hong, MD, PhD, Professor, Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Inwon-dong, Gangnam-gu, Seoul, 135-710, Korea (South); Tel: 82 2 3410 3929; Fax: 82 2 3410 0052; E-mail: sbhong@skku.edu, sbhongsrmc@gmail.com

SLEEP, Vol. 30, No. 11, 2007

1515 Reduced rCBF in Sleep Apnea Syndrome—Joo et al

OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME (OSAHS) IS CHARACTERIZED BY REPEATED EPISODES OF UPPER AIRWAY OBSTRUCTION DURING SLEEP, with disturbances in arterial blood gases and increasing inspiratory effort until the upper airway obstruction discontinues due to arousal. OSAHS has a relatively high prevalence and occurs in 5% of the adult population. OSAHS may cause daytime sleepiness, reduced work performance, increase the risk of a traffic accident, and diminish quality of life. Neurocognitive problems, such as, deficits in memory, attention, and visuoconstructive abilities, are frequently found in patients with OSAHS.

The pathophysiology of these deficits remains controversial, though the main contributory factors are presumed to be sleep fragmentation and intermittent nocturnal hypoxemia during sleep apneas. A deterioration of cognitive performance has been significantly correlated with the degree of nocturnal hypoxemia and with the severity of nocturnal breathing irregularities.

The visual inspection of a 99mTc-(d.l)-hexamethylpropyleneamine-oxime (HMPAO) single photon emission tomography (SPECT) study during repeated obstructive apneas has shown marked frontal hyperperfusion in 5 patients and left parietal hypoperfusion by the analysis of 32 regions of interests. Routine transcranial Doppler is a technique primarily used for measuring relative changes in cerebral blood flow. It has been reported that, during obstructive sleep apneas, profound changes in cerebral blood flow occur and that apnea-induced hypoxemia combined with reduced cerebral perfusion may predispose patients with OSAHS to nocturnal cerebral ischemia. Because patients with OSAHS frequently report neurocognitive problems as well as excessive daytime sleepiness, we postulated that these daytime symptoms are associated with rCBF changes during the daytime awake state as a consequence of increased hemodynamic changes during night sleep due to frequent sleep apneas. CBF changes during wakefulness have not been previously studied in patients with OSAHS.

Statistical parametric mapping (SPM) is a proven and effective method for the voxel-by-voxel analysis of functional images. The advantage of this approach lies in its promise of fully automated neurophysiologic imaging analysis throughout the whole brain using various statistical approaches. rCBF has been considered to be a marker of neuronal activity, and SPM analysis for detecting rCBF changes has allowed the exploration of regional cerebral hemodynamics with a good localizing power.

The aim of this study was to investigate the effect of frequent nocturnal obstructive sleep apneas on rCBF during the waking state in patients with OSAHS. To achieve it, we performed 99mTc-ethylcysteinate dimer (ECD) brain SPECT in severe patients with OSAHS and healthy volunteers during the waking state and then analyzed rCBF differences between the 2 groups.
METHODS

Patients and Healthy Volunteers

Twenty-eight men aged 31 to 58 years with previously untreated severe OSAHS were consecutively recruited into this study. Excessive daytime sleepiness, snoring, and witnessed apneas were the most common symptoms. Most were middle-aged (mean age 44.3 years) and overweight (mean body mass index = 26.8 kg/m²). In overnight polysomnography, the mean apnea-hypopnea index (AHI) was 60.5 per hour (range 33-104). Patients with other diseases (e.g., asthma, hypothyroidism, and periodic leg movement disorder) were excluded, as were patients on antihypertensive medication. Routine diagnostic work-ups included blood tests, electrocardiogram, and chest radiographs. No patients took regular medication, including central nervous system stimulants.

Healthy volunteers were recruited randomly and consecutively by advertisement in a local community. Each candidate had a detailed clinical interview, sleep questionnaire, and overnight polysomnography, and the results were evaluated and interpreted by 2 sleep medicine specialists (Hong SB, Joo EY). Exclusion criteria for healthy volunteers were (1) mean daily sleep time less than 7 hours, (2) abnormal sleep-wake rhythm, (3) sleep disorders, (4) heart disease, (5) cerebrovascular disease, (6) other neurologic or psychiatric diseases, (7) drug addiction or frequent alcohol drinking, and (6) a structural lesion on brain magnetic resonance imaging (MRI). If a normal volunteer had an AHI greater than 4, an arousal index greater than 10, or evidence of another sleep disorder such as periodic limb movement disorder, he was excluded.

All patients and healthy volunteers underwent brain MRI studies, which revealed no abnormal findings on visual inspection. We excluded 1 patient who showed multiple lacunar infarcts in bilateral hemispheres on his brain MRI. Finally, 27 patients with severe OSAHS and 27 normal age- and sex-matched control subjects (mean age 43.0 years, range 30-55) were enrolled. No patient or healthy volunteer had any neurologic or psychiatric condition or another sleep disorder symptom, and no patient had a history of using a central nervous system stimulant or antidepressant medication. The mean age at witnessed sleep apnea was 29 years (range 19-40), and the mean duration of presumed OSAHS was 12.9 years (range 5-29).

Overnight Polysomnography

The day before sleep studies, patients were asked to not drink alcohol or caffeinated beverages. Sleep studies were recorded using an Alice-3 system (Healthdyne, Cleveland, Ohio) or a Somnologica (Embla, Amsterdam, Netherlands). Overnight polysomnography was performed using a 4-channel electroencephalogram (C3/A2; C4/A1; O1/A2; O2/A1), a 4-channel electrooculogram, an electromyogram (of submental, intercostal, and anterior tibialis muscles), and an electrocardiogram with surface electrodes. A thermistor (for monitoring oronasal airflow), a nasal air pressure monitor, an oximeter (for measuring oxygen saturation), piezoelectric bands (for determining thoracic and abdominal wall motion), and a body-position sensor were also attached to patients. Patients were recorded on videotape, using an infrared video camera, and were continuously observed by a polysomnography technician. Patients went to bed at 23:00 and were awakened at 07:00.

Sleep architecture was scored in 30-second epochs, and sleep staging was interpreted according to the standard criteria of Rechtschaffen and Kales. Apneas and hypopneas were defined by standard criteria.11 An obstructive apnea was defined as a reduction in airflow greater than 90% lasting at least 10 seconds, in which there was evidence of persistent respiratory effort. A central apnea was defined as a reduction in airflow of more than 90% lasting at least 10 seconds, in which there was no evidence of respiratory effort. A hypopnea was defined as a reduction in airflow by 50% with a duration of at least 10 seconds or a reduction of airflow or respiratory effort by 30% for more than 10 seconds, accompanied by an electroencephalogram arousal, a 3% or greater oxygen desaturation, or both. According to the American Sleep Disorders Association Task Force criteria,12 arousals were classified as breathing-related arousals (occurring within 3 seconds following apnea, hypopnea, or snoring) and other type of arousals (spontaneous arousal or periodic limb movements-associated arousals).

Assessment of EDS

Subjective sleepiness was assessed of the Epworth Sleepiness Scale (ESS), a simple self-administered questionnaire with 8-item and 4-point scales that evaluate daytime somnolence among patients suffering from sleep-awake disorders. Objective sleepiness was evaluated by the Multiple Sleep Latency Test (MSLT). In brief, the MSLT consists of a series of five 20-minute naps at 2-hour intervals. Patients are asked to try to sleep in a dark room with a recorded montage similar to that used during polysomnography the preceding night. The MSLT recording was continued for 20 min after the first 30-second epoch of any sleep stage or after 20 min of continuous wake had occurred. Sleep latency was scored as the minutes from light-off to the first epoch of sleep, and the mean sleep latency of the five nap tests was calculated.

A final diagnosis of OSAHS was based on overnight polysomnography findings and associated clinical symptoms.

Tc-ECD Brain SPECT During Daytime Wakefulness

All participants refrained from consuming caffeinated beverages but were allowed to drink water from 07:00 until the end of the SPECT study. 99mTc-ECD (925.9 MBq) was administered at 10:00, and SPECT scans were performed 30 minutes after injecting the radiisotope using a 3-headed Triad XLT system equipped with low-energy, high-resolution collimators (Trionix Research Laboratory, Twinsburg, OH). This camera had a transaxial system resolution of 6.9 mm full width at half maximum. Images were reconstructed using a filtered back projection and a Butterworth filter. Attenuation correction was performed using the Chang’s method (attenuation coefficient = 0.12 cm−1).13 The reconstructed voxel size of SPECT was 3.56 × 3.56 × 3.56 mm (x, y, and z, respectively).

Patients and controls were instructed to not fall asleep after ECD injection. Wakefulness after an ECD injection was monitored using a 4-channel electroencephalogram, a 2-channel electrooculogram, and 1-channel electromyogram. Informed consent was obtained from all study subjects after the study protocol, the SPECT procedure, and the potential hazards of radioisotope injection had been explained. The Institutional Review Board at Samsung Medical Center authorized the informed consent form used and the study protocol, which included the administration of a radioactive substance and SPECT scanning.
SPM Analysis of SPECT Studies

SPM2 (Wellcome Department of Imaging Neuroscience, Institute of Neurology, University College London, UK) and MATLAB 7.0 (The MathWorks, Natick, MA) were used for image processing. The SPECT images of healthy volunteers and patients with OSAHS were spatially normalized to the standard SPECT template in SPM2 (with default options). To suppress noise and effects due to residual differences in functional and gyral anatomy during intersubject averaging, all subjects’ normalized SPECT images were smoothed using a 14-mm full width at half maximum Gaussian kernel. The count of each voxel was normalized to the total count of cerebral white matter to remove differences in the global CBF between individuals. Because white matter is known to be unaffected by the experimental effect or disease condition, the intensity was normalized with mean count of white matter. We confirmed that there were no silent white matter lesions on brain MRI images of patients with OSAHS, which may affect the normalization process.

First, the independent t test was used for group comparisons between controls and patients with OSAHS. The height threshold was considered to be significant at the level of FDR corrected \( P < 0.05 \); the extent threshold for whole brain was set to \( k > 50 \). The results were superimposed on the 2-dimensional planes of a single-subject MRI template of SPM2. Second, correlations of rCBF with the AHI, arousal index, and ESS scores were tested with the nuisance variable of age in patients with OSAHS. The height threshold was considered to be significant at the level of uncorrected \( P < 0.001 \); the extent threshold for whole brain was set to \( k > 50 \). The results were superimposed on the 2-dimensional planes of a single-subject MRI template of SPM2.

RESULTS

Overnight Polysomnography

All patients underwent overnight polysomnography. The mean sleep latency was 22.7 ± 43.8 minutes (range, 1.5-216, median, 8.0; interquartile range, 4.5, 16.0). The mean AHI was 60.4 ± 17.6 per hour (range 33 -104), which indicated severe OSAHS. The mean arousal index was 56.2 ± 18.8 per hour (range 29.8 - 105.8). Most of these arousals were breathing-related arousals following apnea, hypopnea, or snoring (mean 85.8% ± 9.5%, range 71.7%-100%), and the remaining occurred spontaneously. Seven patients underwent MSLT on the day following overnight polysomnography because they complained of very severe EDS. Mean sleep latency for MSLT was 9.2 ± 3.0 minutes (6.1-16.0). No sleep-onset rapid eye movement periods (SOREMP) were observed.

Wakefulness Monitoring During SPECT Studies

Electroencephalograms, electrooculograms, and electromyograms were monitored during SPECT studies to measure the duration of wakefulness after an ECD injection in all patients. Mean sleep latency after an ECD injection was 7.6 ± 4.2 minutes, (range 4.5-20). No normal control fell asleep within 10 minutes after an ECD injection. Thus, we confirmed that all subjects underwent brain SPECT during the waking state because brain uptake of the radiotracer was completed within 1 to 2 minutes after the injection.

SPM Analysis of 99mTc-ECD SPECT

In patients with severe OSAHS, rCBF was significantly reduced in bilateral parahippocampal gyri and the left lingual gyrus at the FDR level of corrected \( P < 0.05 \) (Figure 1A). However, rCBF was not found to increase in any brain region of patients with OSAHS. Among the AHI, arousal index, and ESS scores, only AHI was significantly correlated with rCBF decrease in right pericentral gyrus and right cuneus (lower row) at the level of uncorrected \( P < 0.001 \), which was depicted in Figure 1B. The arousal index and ESS scores were not correlated with rCBF.

DISCUSSION

In this study, rCBF differences in patients with OSAHS and healthy volunteers were mapped to identify rCBF abnormalities in patients with severe OSAHS.
Decreased rCBF in the Parahippocampal and Lingual Gyri of Patients with OSAHS

The parahippocampal gyrus plays an important role in the formation and retrieval of topographic memory and memories of scenes, rather than memories of faces or objects. Longitudinal analysis of the brain MRIs of elderly individuals declining to dementia have shown progressive atrophy in medial occipitotemporal regions. They suggested that medial occipitotemporal regions are the first neocortical sites affected in Alzheimer disease and that atrophy in these areas might herald the development of Alzheimer disease among nondemented individuals. Significant activation of the left parahippocampal gyrus were observed in the episodic autobiographic images of normal volunteers in a functional MRI study. During place encoding and during memory tasks, parahippocampal gyrus has been shown to be activated in normal subjects. In an adult rodent model, intermittent hypoxia, which may be observed in patients with OSAHS, has been found to be associated with neurodegenerative changes in the hippocampus and neocortex. Rats exposed to chronic hypoxia display significant spatial-learning impairment in the Morris water maze. The network connecting the parahippocampus and the hippocampus is known to be important for spatial navigation and memory.

In the present study, the rCBF of patients with OSAHS was reduced in the right lingual gyrus. The lingual gyrus of the occipital lobe lies between the calcarine sulcus and the posterior portion of the collateral sulcus. It then continues to the tentorial surface of the temporal lobe and joins the hippocampal gyrus. Bilateral occipital infarction damaging inferior lingual gyrus causes a loss of dreaming, which suggests that the lingual gyrus plays a key role in generating or recalling dreams. It has been noted that many patients with OSAHS report having never experienced recalling a dream. Investigators have insisted that the memory dysfunction of patients with OSAHS may play a significant role in the individual’s lack of dream recall. The lingual gyrus represents the contralateral upper quadrant of the binocular field of vision. It has been reported that patients with moderate to severe OSAHS show a higher incidence of visual-field defects, as compared with age-matched controls without OSAHS. Thus, a reduced rCBF in parahippocampal and lingual gyri in our results may partly explain memory impairment and spatial-learning deficits in patients with severe OSAHS.

<table>
<thead>
<tr>
<th>Brain regions showing significantly reduced rCBF</th>
<th>Location</th>
<th>Side</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Peak Z</th>
<th>*uncorrected P</th>
<th>*FDR corrected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parahippocampal gyrus</td>
<td>R</td>
<td>28</td>
<td>-6</td>
<td>-34</td>
<td></td>
<td>4.60</td>
<td>0.0000022</td>
<td>0.037</td>
</tr>
<tr>
<td>Lingual gyrus</td>
<td>L</td>
<td>-32</td>
<td>-8</td>
<td>-36</td>
<td></td>
<td>4.43</td>
<td>0.0000047</td>
<td>0.037</td>
</tr>
<tr>
<td>Cuneus</td>
<td>R</td>
<td>24</td>
<td>-52</td>
<td>18</td>
<td></td>
<td>3.70</td>
<td>0.000083</td>
<td>0.037</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Brain regions showing negative correlations of rCBF with apnea-hypopnea indexes</th>
<th>Location</th>
<th>Side</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Peak Z</th>
<th>*uncorrected P</th>
<th>*FDR corrected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericentral gyrus</td>
<td>R</td>
<td>8</td>
<td>-30</td>
<td>76</td>
<td></td>
<td>3.77</td>
<td>0.000083</td>
<td>0.037</td>
</tr>
<tr>
<td>Cuneus</td>
<td>R</td>
<td>24</td>
<td>-52</td>
<td>18</td>
<td></td>
<td>3.70</td>
<td>0.000011</td>
<td>0.037</td>
</tr>
</tbody>
</table>

MNI refers to Montreal Neurological Institute; L, left; R, right.
* Height threshold: uncorrected $P < 0.001$, Extent threshold $k_e > 50$.
* Significant at the false discovery rate corrected $P < 0.05$.

Negative Correlation of rCBF in Right Pericentral Gyrus and Cuneus with AHI in Patients with Severe OSAHS

Several lines of studies have demonstrated an impaired motor function in patients with OSAHS. In 1 study, when patients with time spent at an oxygen saturation level of less than 85% were dichotomized into the first 3 quartiles and the fourth quartile, motor speed was found to be significantly impaired in those who were more hypoxic. Although no significant differences were found in this study between patients with severe OSAHS and normal controls in routine neuropsychologic test variables, a poorer motor speed in summed grooved pegboard and processing speed performance scores in patients was associated with more severe oxygen desaturation even after controlling for degree of daytime sleepiness, age, sex, and education level.

Intermittent nocturnal hypoxemia by OSAHS may contribute to deficits in executive and motor functions, which are presumed to be related to the prefrontal lobe. Most of these deficits are corrected by the use of nasal continuous positive airway pressure therapy. Another study also found that neuropsychologic performance was significantly reduced in patients with severe OSAHS, such as in Symbol Digit Modality and digit span forward tasks, the number of errors on the basic 2-choice reaction time subtest of the attentional flexibility task, and mean reaction time on the actual attentional flexibility subtest. However, these authors reported that cognitive problems observed in patients with OSAHS appear to be remarkably similar to cognitive decline after sleep loss and, thus, suggested that sleepiness rather than prefrontal brain damage may be predominantly responsible for attention deficits in sleep apnea. The reason for such conflicting results in patients with OSAHS may be a lack of standardized neuropsychologic test battery.

The cuneus participates in attention processing and visuospatial analysis. Visual attention is significantly lower in children with sleep-disordered breathing, although within the average range, and a similar finding has been reported in children without OSAHS who snore.

A previous study measured rCBF during sleep and wakefulness in normal humans by $^{15}$O positron emission tomography. In this study, during light non-REM (NREM) sleep (stage 1 and 2), the rCBF in the midbrain, temporal lobe, and occipital lobe did not decrease when compared with that during wakefulness, whereas rCBF decreased in the left medial frontal gyrus, left inferior frontal gyrus, and left inferior parietal gyrus of the neocortex. During deep NREM sleep (stage 3 and 4), the rCBF in the midbrain teg-
mentum decreased, and there was a marked and bilateral decrease in the rCBF in all neocortical regions except for the perirolandic areas and the occipital lobe. These results mean that these primary motor or somatosensory and the visual cortices, which serve only as obligatory relays for the transfer of information to other regions of the brain, may remain functional throughout NREM sleep. Most patients with severe OSAHS in our study had a lack of deep sleep due to frequent sleep fragmentations.

In the present study, there was a daytime rCBF decrease in parahippocampal gyri and right lingual gyrus and there was a negative correlation of rCBF in the pericentral gyrus and cuneus with AHI, suggesting that frequent hemodynamic changes, including increased fluctuations of cerebral blood flow velocity and associated hypoxemia during sleep apneas, may be more detrimental to those brain regions that require the maintenance of blood flow during light sleep. Subsequent functional derangement of these regions may result in the executive impairment and attention deficit observed in patients with a long history and great severity of obstructive sleep apneas.

**CBF Patterns of Patients with OSAHS**

Some of the clinical features of patients with OSAHS are suggestive of impaired cerebral blood flow. High frequencies of ischemic cerebral complications in patients with OSAHS may be caused, in part, by sleep apnea-associated cerebral perfusion impairment.35

In a previous HMPAO SPECT study on 14 patients with moderate to severe OSAHS, SPECT images were obtained during repeated episodes of obstructive apnea detected by overnight polysomnography during stage 2 sleep.6 The visual analysis showed frontal hyperperfusion in 5 patients, and, when regional perfusion indexes were calculated for 32 regions of interest (ROI), statistical analysis showed reduced cerebral perfusion in the left parietal region. The observed parietal hypoperfusion may be, in part, a finding similar to the pericentral hypoperfusion in the present study. Sleep apneas cause hypoxemia, hypercapnia, exaggerated negative intrathoracic pressure, and arousals. Arousals during sleep are different from those during daytime wakefulness. Arousals during sleep in patients with OSAHS are induced by sleep-disordered breathing and are associated with frequency shift on the electroencephalogram, increase of sympathetic activation and consequent vasoconstriction, increased heart rate, and blood pressure surges, whereas these are not found during normal wakefulness. The observed frontal hyperperfusion in the previous study was suggested to be caused by activation of the frontal lobe by repetitive cortical arousals, and it could reflect the autonomic hyperactivity associated with arousals.

On the contrary, 99mTc-ECD was administered during wakefulness without sleep apneas in both our patients and our healthy controls. Thus, hypoperfusion in basal temporoparietal areas in our SPM results indicates the underlying CBF abnormalities during daytime wakefulness in patients with OSAHS occur as a consequence of repetitive sleep apneas during night sleep, not hemodynamic changes during sleep with frequent apneas. Furthermore, SPM analysis investigated all brain regions by voxel-to-voxel comparison, whereas the result of the ROI method may be dependent on the size, number, and covering brain areas of ROI. Therefore, the sensitivities of ROI and SPM analyses may be different. The number of subjects is also different (14 in a previous study versus 27 in our study), which may affect statistical significance.

1519

**CONCLUSIONS**

We recruited patients with severe OSAHS and excluded those with a brain lesion on MRI or who were taking a central nervous system stimulant or antidepressant to avoid the potentially confusing effects of these factors on CBF. Our patients showed reduced rCBF in the parahippocampal and lingual gyri and a negative correlation between AHI and the CBF in the pericentral gyri and cuneus during the daytime awake state. These findings may partly explain the deficit in memory, spatial learning, executive function, and attention that are frequently found in patients with severe OSAHS.

**ACKNOWLEDGMENTS**

This study was supported by a grant (M103KV010017-07K2201-01710) from the Brain Research Center of the 21st Century Frontier Research Program funded by the Ministry of Science and Technology of the Republic of Korea; by the Samsung Medical Center Clinical Research Development Program grant, #CRS106-55-2; and by a grant (No. A050462) from the Good Health R&D Project, Ministry of Health & Welfare, Republic of Korea.
REFERENCES


28. Tsang CS, Chong SL, Ho CK, Li MF. Moderate to severe obstructive sleep apnoea patients is associated with a higher incidence of visual field defect. Eye 2006;20:38-42.


