Evaluation of cerebral microstructural changes in adult patients with obstructive sleep apnea by MR diffusion kurtosis imaging using a whole-brain atlas

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Abstract

Purpose: The association between obstructive sleep apnea (OSA) and cognitive impairment is well-recognized, but little is known about neural derangements that underlie this phenomenon. The purpose of this study was to evaluate the utility of diffusion kurtosis imaging (DKI) using a whole-brain atlas to comprehensively assess microstructural tissue changes in the brain of patients with OSA.

Methods: This prospective study was conducted in 20 patients with moderate-to-severe OSA and 20 age- and gender-matched controls. MRI data acquisition was performed with 3 Tesla and data was analyzed using a whole-brain atlas. DKI data were processed and transformed into a brain template space to obtain various kurtosis parameters including axial kurtosis (AK), radial kurtosis (RK), mean kurtosis (MK), and kurtosis fractional anisotropy (KFA) using a 189-region brain atlas in the same template space. These kurtosis measurements were further analyzed using a student t-test in order to determine kurtosis measurements that present significant differences between the OSA patient set and the control set. Results: Significant differences ($P < 0.05$) were found in AK (54 regions), RK (10 regions), MK (6 regions) and KFA (41 regions) values in patients with OSA as compared to controls. DKI indices, using an atlas-based whole-brain analysis approach used in our study, showed widespread involvement of the anatomical regions in patients with OSA. Conclusion: The kurtosis parameters are more sensitive in demonstrating abnormalities in brain tissue structural organization at the microstructural level before any detectable changes appear in conventional MRI or other imaging modalities.

Key words: Kurtosis imaging; MRI; obstructive sleep apnea

Introduction

Obstructive sleep apnea (OSA) is a common yet under-diagnosed sleep-related breathing disorder. OSA
is clinically characterized by chronically fragmented sleep as well as intermittent hypoxemia. Well-recognized clinical manifestations or associations of OSA include cardiovascular disease, neurocognitive impairment, and impaired metabolic functions.\cite{1,2} Despite substantial evidence of an association between OSA and cognitive impairment, little is known about the tissue structural alterations in brain anatomical regions underlying the impairment.\cite{3,4} Functional MRI studies in OSA patients have shown changes in neural activation that are related to cognitive impairment and autonomic dysfunction; it is likely that these functional changes are due to deficits in tissue structural deficits.\cite{5,6} Neuroimaging studies have given insight into the brain anatomical structures and functions affected in individuals with OSA.\cite{7,8} The neuroimaging methods used in these studies complement more traditional sleep-assessment techniques such as polysomnography or neuropsychological tests. Patients with OSA show brain abnormalities in white matter (WM) and gray matter (GM) using advanced MR imaging techniques such as diffusion tensor imaging (DTI), functional MRI, and magnetic resonance (MR) spectroscopy.\cite{9,10} Diffusion kurtosis imaging (DKI) is an extension of the DTI technique, which allows estimation of the more commonly used diffusion tensor metrics as well as diffusion kurtosis metrics.\cite{9,10}

It is established that water molecular diffusion displacement behavior in a tissue of human organ deviates from a strict Gaussian model that is assumed in DTI, due to the presence of cellular structural barriers and intracellular organelles that hinder free diffusion. In contrast, DKI uses a non-Gaussian model for characterizing water diffusion, thereby providing a more accurate representation of restricted diffusion, which may give additional biomarkers in disease conditions. In contrast to DTI, DKI uses higher b-values and provides additional metrics that are complementary to DTI metrics.\cite{9,10} Few studies have assessed the brain tissue microstructural changes using DTI\cite{11-16} or DKI\cite{17,18} in the patients of OSA. These studies had shown that there are significant microstructural changes in patients of OSA as compared to controls. Previous studies of OSA patients by DKI had been done by using region of interest (ROI)-based analysis with Matlab; however in our study, we used whole-brain atlas analysis with four commonly used DKI parameters (axial kurtosis [AK], radial kurtosis [RK], mean kurtosis [MK], and kurtosis fractional anisotropy [KFA]) in 189 brain ROIs. There is no definitive and clinically useful neuropathologic correlates available for cerebral changes in patients with OSA using conventional brain imaging modalities. Therefore, we evaluated tissue microstructural changes within the brain of patients with OSA using DKI.

**Materials and Methods**

This was a prospective case-control study, conducted from July 2015 to November 2016, after approval from the institutional ethical committee. Inclusion criteria for the patients included in the study were: recently diagnosed OSA patient via polysomnography, apnea-hypopnea index (AHI) ≥15, treatment native, and without any medications, such as β-blockers, α-agonists. Exclusion criteria included the history of stroke or heart failure, uncooperative patients and those having contraindications to MR examination such as metallic implants. The inclusion criteria for the controls included in the study were: no history of stroke or heart failure and no focal structural lesions on routine MRI. Twenty newly diagnosed patients (age range 22–60 years, 17 males) with moderate to severe OSA and 20 age- and gender-matched healthy controls were included in the study. All participants or their relatives provided informed and written consent before participation.

All subjects were scanned using a 3 Tesla MRI scanner (Verio; Siemens Healthcare, Erlangen, Germany), equipped with a 12-channel head coil. A 35-minute protocol included conventional MRI sequences, 3D-T1, and DKI acquisitions. The MRI sequences include fluid-attenuated inversion recovery (FLAIR, TE/TR: 94/9000 ms, 25 slices, 4-mm slice thickness), T2 (spin-echo; TE/TR: 96/6000 ms, 25 slices, 4-mm slice thickness) and T1 (MPRAGE; TE/TR: 3.77/1800 ms, 1 mm isotropic). DKI data were obtained using a single-shot twice-refocused 2D spin-echo echo-planar imaging sequence with TE/TR: 98/8600, contiguous slices with 3 mm thickness, 3 mm isotropic resolution, one signal average, 30 noncollinear diffusion-weighted gradient directions, 3 diffusion weightings (b = 0, 1000, 2000 s/mm²), generalized autocalibrating partially parallel acquisition (GRAPPA) acceleration factor of 2.0, and an acquisition time of ~9.1 minutes. Both diffusion-weighted (b = 1000, 2000 s/mm²) and non-diffusion-weighted (b = 0 s/mm²) data were processed using diffusion kurtosis estimator (DKE)\cite{19} and DiffeoMap\cite{20} and analyzed using ROIEditor\cite{21} [Figure 1].Briefly, after processing with DKE, we obtained four DKI-based metrics, that is, AK, RK, MK, and KFA. Second, the subject-space FA and b0 images of each subject were registered to a single-subject FA and b0 images (i.e., Ele template in Montreal Neurological Institute, i.e., MNI space) using DiffeoMap. Third, we transformed the 189-region brain atlas in MNI space to an individual subject space using DiffeoMap. Fourth, we used the atlas in each subject’s space in ROIEditor to obtain data for statistical analyses from 189 ROIs for the four DKI matrices (AK, KFA, RK, and MK).

**Statistical analysis**

Comparisons of DKI metrics and demographic data between the control group and OSA patients groups were performed using the student’s t-test. All statistical tests were two-sided and a P < 0.05 was considered for significance. The statistical analysis was carried out using SPSS (SPSS Inc., Chicago, IL, version 21.0 for Windows).
Results

The mean age of the patients and controls was 47.3 years and 44.9 years, respectively. Five patients had moderate sleep apnea (15 ≤ AHI < 30) and 15 patients had severe sleep apnea (AHI ≥ 30). The majority of the patients showed unremarkable findings on conventional MRI. Multifocal nonspecific periventricular T2 and FLAIR hyperintensities were seen in three patients. One patient showed mild diffuse cerebral cortical atrophy.

AK, RK, KFA, and MK mean values were calculated in 189 brain ROIs in both patients and the control group. Significant differences ($P < 0.05$) in the patient group were found and these include: AK in 54 ROIs [Table 1], KFA in 41 ROIs [Table 2], MK in 6 ROIs [Table 3], and RK in 10 ROIs [Table 4]. Bar diagram of areas from the Eve template in Montreal Neurological Institute (MNI) space showing significant difference between patient and control groups in AK [Figure 2], KFA[Figure 3], MK [Figures 4 and 5].
Table 1: Showing AK values which showed a significant difference between patients and control

| Area               | Patients       | Control       | P       |
|--------------------|----------------|---------------|---------|
| SFG_PFC_L          | 0.746          | 0.678         | 0.031   | 0.000 |
| SFG_PFC_R          | 0.753          | 0.675         | 0.041   | 0.005 |
| SFG_pole_L         | 0.688          | 0.563         | 0.070   | 0.000 |
| SFG_pole_R         | 0.758          | 0.617         | 0.049   | 0.000 |
| MFG_DPC_L          | 0.744          | 0.646         | 0.036   | 0.000 |
| MFG_DPC_R          | 0.781          | 0.667         | 0.033   | 0.001 |
| IFG_orbitals_L     | 0.770          | 0.673         | 0.037   | 0.002 |
| IFG_orbitals_R     | 0.822          | 0.737         | 0.030   | 0.012 |
| IFG_triangularis_L | 0.791          | 0.748         | 0.043   | 0.008 |
| LFOG_L             | 0.823          | 0.753         | 0.046   | 0.002 |
| LFOG_R             | 0.868          | 0.755         | 0.054   | 0.001 |
| MFOG_L             | 0.938          | 0.820         | 0.084   | 0.000 |
| MFOG_R             | 1.037          | 0.821         | 0.107   | 0.000 |
| RG_L               | 0.857          | 0.799         | 0.072   | 0.002 |
| RG_R               | 0.847          | 0.750         | 0.071   | 0.001 |
| PeCG_R             | 0.668          | 0.696         | 0.039   | 0.030 |
| MTG_L_pole         | 0.787          | 0.734         | 0.046   | 0.007 |
| ITG_L              | 0.839          | 0.797         | 0.040   | 0.029 |
| rostral_ACC_L      | 0.742          | 0.702         | 0.031   | 0.001 |
| rostral_ACC_R      | 0.727          | 0.699         | 0.040   | 0.029 |
| Amyg_L             | 0.733          | 0.705         | 0.048   | 0.047 |
| Amyg_R             | 0.747          | 0.718         | 0.043   | 0.040 |
| Caud_L             | 0.676          | 0.646         | 0.041   | 0.035 |
| Put_L              | 0.844          | 0.777         | 0.069   | 0.002 |
| GP_L               | 0.945          | 0.887         | 0.079   | 0.021 |
| GP_R               | 0.980          | 0.917         | 0.088   | 0.010 |
| Mynert_L           | 0.864          | 0.783         | 0.078   | 0.001 |
| Mynert_R           | 0.829          | 0.768         | 0.075   | 0.018 |
| NucAccumbens_L     | 0.934          | 0.771         | 0.071   | 0.003 |
| NucAccumbens_R     | 0.783          | 0.735         | 0.079   | 0.038 |
| Snigra_L           | 1.015          | 0.934         | 0.069   | 0.001 |
| Snigra_R           | 0.968          | 0.900         | 0.111   | 0.041 |
| CP_L               | 0.734          | 0.700         | 0.034   | 0.002 |
| Medbrain_R         | 0.779          | 0.747         | 0.036   | 0.038 |
| SCP_L              | 0.759          | 0.726         | 0.049   | 0.045 |
| MCP_L              | 0.911          | 0.880         | 0.036   | 0.040 |
| ICP_L              | 0.924          | 0.875         | 0.057   | 0.036 |
| ICP_R              | 0.903          | 0.891         | 0.060   | 0.036 |
| PonS_R             | 0.912          | 0.857         | 0.052   | 0.028 |
| Medulla_L          | 0.853          | 0.198         | 0.735   | 0.094 |
| ACR_L              | 0.889          | 0.823         | 0.057   | 0.000 |
| ACR_R              | 0.901          | 0.826         | 0.044   | 0.007 |
| GGC_L              | 0.703          | 0.645         | 0.046   | 0.000 |
| GGC_R              | 0.730          | 0.674         | 0.055   | 0.003 |
| ALIC_L             | 0.858          | 0.814         | 0.050   | 0.004 |
| ALIC_R             | 0.844          | 0.804         | 0.042   | 0.005 |
| PLIC_L             | 0.819          | 0.771         | 0.039   | 0.000 |
| PLIC_R             | 0.796          | 0.772         | 0.026   | 0.024 |
| RIC_L              | 0.796          | 0.765         | 0.038   | 0.040 |
| CCC_L              | 0.881          | 0.853         | 0.032   | 0.013 |

Table 1: Contd...

| Area               | Patients       | Control       | P       |
|--------------------|----------------|---------------|---------|
| IFO_L              | 0.787          | 0.767         | 0.053   | 0.002 |
| AnteriorCom_R      | 0.685          | 0.728         | 0.058   | 0.046 |
| LenticularFasc_R   | 0.828          | 0.775         | 0.074   | 0.016 |

Discussion

This prospective study showed that there were significant alterations in many brain anatomical regions for four DKI metrics (i.e., AK, RK, MK, and KFA) in OSA patients. This study was done by using whole-brain atlas analysis template in Montreal Neurological Institute (i.e., MNI space) using DiffeoMap to have more objectivity and uniformity rather than ROI-based analysis done in the previous studies. These findings indicate that microstructural changes occur in specific cerebral regions in the patient group. The observed associations between the regional changes observed by brain imaging metrics and neurocognitive outcomes indicate the anatomical regions with significant structural alterations. Changes in brain morphology of OSA patients have been described in literature. However, there is no specific correlation of these nonspecific cerebral changes with OSA, though the complex disease process in OSA may accentuate these cerebral changes. Though conventional MRI may show apparent cerebrovascular changes and cerebral atrophy, it cannot detect subtle vascular and microstructural damages.

We found altered AK values in 54 brain ROIs in the patient group that includes the insula, internal capsule, cingulum, hippocampus, amygdala, dorsolateral pons, and cerebellar peduncles. Our results in the above mentioned anatomical regions agree with the findings of Tummala et al. in a group of OSA patients. Moreover, our study found increased AK values in additional anatomical regions in the patient group. We speculate that the higher number of regions with significant AK values in the patient group may be due to either the severity of the patient group enrolled in our study or the data analysis method we used or both. Though most of the areas are bilaterally involved, unilateral involvement is also seen in some of the WM tracts and brainstem. AK values are indicative of the microstructural
Our study showed that all DKI indices (i.e., AK, RK, KFA, and MK) were altered in the brain of OSA patients as compared to controls. We performed atlas-based whole-brain analysis that includes GM and WM regions of the brain. Our findings agree well with the results of studies. The fact that our study found several altered GM regions in OSA patients illustrates the advantages of using DKI to assess changes in GM regions, too.

Table 2: KFA values which showed a significant difference between patients and control

| Area            | Patients Mean | Patients SD | Control Mean | Control SD | P    |
|-----------------|---------------|-------------|--------------|------------|------|
| SFG_PFC_L       | 0.325         | 0.046       | 0.282        | 0.045      | 0.004|
| SFG_PFC_R       | 0.336         | 0.059       | 0.291        | 0.051      | 0.013|
| SFG_pole_R      | 0.309         | 0.076       | 0.247        | 0.057      | 0.006|
| MFG_DPC_L       | 0.310         | 0.056       | 0.252        | 0.048      | 0.001|
| MFG_DPC_R       | 0.333         | 0.070       | 0.263        | 0.044      | 0.001|
| IFG_orbitalis_R | 0.334         | 0.059       | 0.283        | 0.050      | 0.006|
| IFG_triangularis_L | 0.313      | 0.047       | 0.283        | 0.045      | 0.048|
| IFG_triangularis_R | 0.297       | 0.045       | 0.262        | 0.046      | 0.020|
| RG_L            | 0.317         | 0.043       | 0.286        | 0.045      | 0.031|
| rostral_ACC_L   | 0.286         | 0.054       | 0.249        | 0.057      | 0.043|
| rostral_ACC_R   | 0.274         | 0.056       | 0.236        | 0.050      | 0.031|
| Ins_L           | 0.221         | 0.027       | 0.182        | 0.040      | 0.001|
| Hippo_R         | 0.262         | 0.036       | 0.234        | 0.039      | 0.028|
| Put_L           | 0.451         | 0.044       | 0.381        | 0.051      | 0.000|
| Put_R           | 0.429         | 0.060       | 0.363        | 0.065      | 0.002|
| GP_L            | 0.423         | 0.062       | 0.360        | 0.058      | 0.002|
| GP_R            | 0.420         | 0.069       | 0.364        | 0.064      | 0.011|
| Mynert_L        | 0.432         | 0.050       | 0.385        | 0.044      | 0.003|
| Mynert_R        | 0.419         | 0.064       | 0.369        | 0.044      | 0.007|
| NucAccumbens_L  | 0.400         | 0.068       | 0.357        | 0.058      | 0.038|
| Snigra_L        | 0.413         | 0.063       | 0.357        | 0.059      | 0.007|
| Snigra_R        | 0.408         | 0.067       | 0.361        | 0.063      | 0.030|
| Midbrain_L      | 0.282         | 0.035       | 0.252        | 0.032      | 0.006|
| Midbrain_R      | 0.272         | 0.043       | 0.243        | 0.035      | 0.024|
| MCP_L           | 0.380         | 0.050       | 0.344        | 0.031      | 0.009|
| MCP_R           | 0.358         | 0.044       | 0.324        | 0.029      | 0.007|
| ICP_L           | 0.358         | 0.067       | 0.306        | 0.042      | 0.006|
| ICP_R           | 0.328         | 0.056       | 0.290        | 0.043      | 0.021|
| Medulla_L       | 0.295         | 0.059       | 0.259        | 0.048      | 0.041|
| Medulla_R       | 0.348         | 0.054       | 0.303        | 0.056      | 0.013|
| ACR_R           | 0.477         | 0.050       | 0.439        | 0.046      | 0.016|
| EC_L            | 0.443         | 0.053       | 0.393        | 0.052      | 0.005|
| EC_R            | 0.420         | 0.059       | 0.378        | 0.067      | 0.046|
| CGH_L           | 0.377         | 0.049       | 0.334        | 0.049      | 0.008|
| FxST_L          | 0.316         | 0.045       | 0.276        | 0.046      | 0.010|
| IFO_L           | 0.457         | 0.041       | 0.419        | 0.049      | 0.011|
| SS_L            | 0.384         | 0.046       | 0.355        | 0.035      | 0.035|
| Mammillary_L    | 0.071         | 0.020       | 0.088        | 0.025      | 0.020|
| Mammillary_R    | 0.064         | 0.019       | 0.082        | 0.019      | 0.006|
| LV_frontal_L    | 0.118         | 0.024       | 0.150        | 0.038      | 0.003|
| LV_frontal_R    | 0.124         | 0.022       | 0.149        | 0.043      | 0.029|

The anatomical regions include mostly GM-rich ROIs such as frontal gyrus, fronto-orbital gyrus, gyrus rectus, and entorhinal area. Our results overlap with the findings of Tummala et al.[17] in which significantly increased RK values in the hippocampus, amygdala, temporal and frontal lobes, insula, midline pons, and cerebellar peduncles of their patient group were reported. Higher RK values are usually indicative of demyelination or dysmyelination. Changes in the axonal diameter or density (number of axons in a bundle) may also influence RK values.

Akkyounlu et al. (2012) found a significant increase in the ADC values in the hippocampus, amygdala, and putamen in OSA patients and concluded that these were likely indicative of hypoxia and vasogenic edema in specific regions of the brain. [13] We found increased MK values in six ROIs including frontal gyrus, fronto-orbital gyrus right, entorhinal region right, and anterior commissure right. Tummala et al. have reported significantly increased MK values in the basal forebrain, extending to the hypothalamus, thalamic, insular cortices, basal ganglia, ventral temporal lobe, hippocampus, limbic regions, cerebellar areas, parietal cortices, ventrolateral medulla, and midline pons. [13] Our findings agree well with the results of their study in many regions.

KFA is a summary measure of microstructural complexity in both the axial and radial directions of the WM in the brain. Though it is highly sensitive to microstructural complexity changes, it is less specific to whether the change occurred in axial or radial or both directions of axons. We found altered KFA in multiple brain ROIs including regions in the frontal lobe, cingulate, putamen, globus pallidus, substantia nigra, cerebellar peduncle, and insula. Macey et al.[13] studied FA derived from DTI in patients with untreated OSA with AHI more than 15. They found multiple brain regions with lower FA in the OSA group such as the anterior corpus callosum, right column of the fornix, anterior and posterior cingulate cortex and cingulum bundle, portions of the frontal, ventral prefrontal, parietal and insular cortices, bilateral internal capsule, middle cerebellar peduncle, left cerebral peduncle and corticospinal tract, and deep cerebellar nuclei. Though there is no one-to-one agreement between the brain regions shown by their study and our findings, there is a general trend of some brain regions that are common in both the studies. The fact that our study found several altered GM regions in OSA patients illustrates the advantages of using DKI to assess changes in GM regions, too.

Chen et al. have calculated various DTI indices and found significantly low FA, increased RD, and no significant difference in AD and MD in the brain of patients with OSA. [12] Our study showed that all DKI indices (i.e., AK, RK, KFA, and MK) were altered in the brain of OSA patients as compared to controls. We performed atlas-based whole-brain analysis that includes GM and WM regions.

organization of the WM (axons) bundles in the brain. Its direction of change (i.e., increased or decreased compared to AK values in healthy brains) tends to depend on the type of microstructural changes that occur in pathological conditions. For example, it decreases in axonal injury but increases with brain maturation.

We found significantly altered RK values in 10 ROIs of the patient group as compared to that of the control group.
whereas the above study assessed only WM regions. Castronovo et al. have reported decreased FA and MD by DTI analysis in the WM of OSA patients.\textsuperscript{14} We found significantly increased KFA and MK in a relatively higher number of anatomical regions of the brain in OSA patients. Our results indicate that the brain tissue structural alterations are more widespread than reported by previous studies. But contrary to above study\textsuperscript{12} we found that changes in MK were more localized to frontal lobes as compared to medullary respiratory regulatory sites. Our results were also similar to Kumar et al.\textsuperscript{6} who found significant differences in RD and AD in recently diagnosed patients with OSA by using DTI. We found significant changes in 54 and 10 brain ROIs for AK and RK, respectively.

Our results of significant changes in MK in many ROIs of the brain of patients with OSA agrees with the findings of Kumar et al.\textsuperscript{7} who found altered MD in the brain of certain anatomical regions in patients with OSA as compared to controls. Furthermore, we found additional anatomical regions with altered MK values that suggest tissue structural alterations due to OSA are more widespread within the brain than reported by other studies using DTI and other MRI techniques. Thus, the brain of patients with OSA can be better evaluated using DKI data.

There are a few limitations to our study. First, we have not compared the DKI parameters of patients with OSA with the DTI parameters of them in this study. Thus, the relative sensitivity of the DKI parameters over the DTI parameters for the evaluation of tissue structural alterations in the brain of patients with OSA could not be ascertained in this study. Second, we could not establish correlation with the neurocognitive impairments in the domains of memory, visual memory, and execution functions with the DKI parameters of the brain of patients with OSA. Since any neurocognitive function is thought to originate or localize in more than one brain anatomical regions and also execution of it requires a coordination between the regions, a different type of advanced data analysis method (e.g., brain network or circuit level and brain connectome-wide analyses) is necessary for the evaluation of the associations between the neurocognitive deficits found in this group of patients and their neuroimaging findings. Large sample size and morphological brain imaging data are also needed for such an analysis, and therefore no attempt was made to do such an analysis in this study.

Conclusions

This prospective study in OSA patients demonstrated significant abnormalities for various DKI parameters using a whole-brain atlas in several brain anatomical regions as compared to controls. Furthermore, DKI data showed significantly more subtle tissue structural abnormalities than other routinely used clinical MRI techniques. Thus, the

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
Area & Patients & Control & \textbf{P} \\
\hline
SFG_pole_L & 0.651 & 0.122 & 0.560 & 0.075 & 0.007 \\
SFG_pole_R & 0.703 & 0.150 & 0.666 & 0.049 & 0.12 \\
MFG_DPFC_R & 0.746 & 0.150 & 0.673 & 0.036 & 0.045 \\
LFOG_R & 1.064 & 0.304 & 0.843 & 0.128 & 0.006 \\
ENT_R & 0.699 & 0.098 & 0.746 & 0.032 & 0.046 \\
AnteriorCom_R & 0.717 & 0.156 & 0.802 & 0.078 & 0.036 \\
\hline
\end{tabular}
\caption{MK values which showed a significant difference between patients and control}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
Area & Patients & Control & \textbf{P} \\
\hline
SFG_pole_L & 0.655 & 0.085 & 0.559 & 0.079 & 0.001 \\
SFG_pole_R & 0.689 & 0.128 & 0.603 & 0.056 & 0.009 \\
MFG_DPFC_R & 0.709 & 0.073 & 0.657 & 0.039 & 0.007 \\
MFG_DPFC_R & 0.756 & 0.125 & 0.688 & 0.041 & 0.030 \\
LFOG_R & 0.853 & 0.175 & 0.764 & 0.059 & 0.043 \\
MFOG_L & 0.942 & 0.101 & 0.855 & 0.114 & 0.016 \\
MFOG_R & 1.094 & 0.267 & 0.855 & 0.143 & 0.001 \\
RG_R & 0.725 & 0.043 & 0.754 & 0.037 & 0.034 \\
AnteriorCom_R & 0.778 & 0.082 & 0.867 & 0.112 & 0.007 \\
\hline
\end{tabular}
\caption{RK values which showed a significant difference between patients and control}
\end{table}
kurtosis parameters are more sensitive in demonstrating tissue structural organization abnormalities at the microstructural level before any detectable changes appear in conventional MRI or other imaging modalities. In addition, DKI showed tissue structural alterations in multiple brain regions, which may be the underlying pathology for the neurocognitive impairments observed in OSA patients. These findings indicate the importance of using DKI for future in-depth studies to evaluate the brain tissue microstructural changes in patients with OSA and associate the changes with their clinical signs or symptoms and cognitive functions.

Ethical approval
All procedures performed in the studies involving human participants 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.

Declaration of patient consent
Informed consent was obtained from all individual participants included in the study.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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