Introduction: Obstructive sleep apnea (OSA) subjects show multiple autonomic and neuropsychologic abnormalities (1, 2), together with other physiological issues. Both structural injury and functional deficits appear in multiple brain sites of OSA subjects (2, 3), and are especially prominent in the insular cortices that assist regulation of autonomic and neuropsychologic functions. The right anterior insular cortex is involved in sympathetic action, and the left, principally parasympathetic influences; both the left and right cortices play roles in mood, attention, and anxiety modulation, and have reciprocal projections to the hypothalamus, a structure significantly involved in autonomic and affective regulation. Since the functional and structural alterations that appear in the anterior insula in OSA have a unique potential to exert major effects on autonomic and multiple neuropsychologic symptoms, we examined metabolite levels to provide indications of the nature of tissue changes, which are necessary to determine mechanisms for neuroprotection in the condition. Proton magnetic resonance spectroscopy (PMRS) procedures are widely used to evaluate non-invasively regional metabolic changes in various clinical and research environments, and to suggest remedial interventions, and may be useful to examine insular metabolites in OSA subjects. Our aim was to evaluate anterior insular metabolites in OSA compared to controls to determine the nature of changes using PMRS procedures. Since the extent of earlier-demonstrated structural and functional alterations in the insular cortices was so substantial, we hypothesized that bilateral anterior insular metabolites would be modified in OSA.

Materials and methods: Thirty six OSA (age, 48±9.3 years; body-mass-index (BMI), 30.6±5.9 kg/m²; 28 male; apnea-hypopnea-index (AHI), 31.8±20.4 events/hour) and 53 healthy control subjects (age, 46.8±8.1 years; BMI, 24.7±3.8 kg/m²; 32 male) were studied. All OSA subjects were recently-diagnosed via overnight polysomnography (AHI averages=144, voxel size=10×10×10 mm³). Signal quantification of metabolites was performed using curve-fitting with standard software available (Fig. 1), using point-resolved spectroscopy pulse sequence (TR=3000 ms, TE=30 ms, spectral points=2048, spectral bandwidth=1500 Hz, ppm, and MI at 3.56 ppm (Fig. 1), and automatic curve-fitting procedures were used to obtain signal integrals. Using NAA, Cr, Cho and MI in the MRI scanner, provided by the manufacturer. After baseline correction, the NAA peak was assigned at 2.02 ppm, Cr at 3.02 ppm, Cho at 3.2 ppm, and MI at 3.56 ppm (Fig. 1), and automatic curve-fitting procedures were used to obtain signal integrals. Using NAA, Cr, Cho and MI metabolite amplitudes, metabolite ratios, including NAA/Cr, Cho/Cr, and MI/Cr were calculated. The IBM statistical package for the social sciences (v20) was used for data analyses. Demographic, biophysical, metabolite ratios, sleep variables, and neuropsychologic scores were assessed between groups by independent samples t-tests and Chi-square. Pearson’s correlation procedures were used to determine association between metabolite ratios and biophysical, sleep variables, and neuropsychologic scores in OSA.

Results: No significant differences in age or gender appeared between groups. BMI (p<0.001), BAI (p<0.001), BDI-II (p<0.001), PSQI (p<0.001), and ESS (p<0.001) significantly increased in OSA over controls. NAA/Cr ratios were significantly decreased bilaterally in OSA over control (Table 1). Significantly increased MI/Cr ratios appeared only on the left side in OSA over control subjects, while the right side showed no significant difference (Table 1). No significant differences in Cho/Cr ratios were observed (Table 1). Significant positive correlations emerged between the left insular MI/Cr ratios and AHI values (r=0.45, p<0.02), right insular Cho/Cr ratios and BDI-II scores (r=0.43, p=0.01), and right insular Cho/Cr ratios and BAI values (r=0.4, p = 0.02 in OSA subjects. Negative correlations emerged between left insular NAA/Cr ratios and PSQI scores (r=0.4, p=0.046) in OSA.

Discussion: OSA subjects show bilaterally reduced insular NAA metabolite ratios, indicating neuronal damage/loss of function, and left-sided increased MI, suggesting increased glial activation in those sites. The abnormal insular metabolites may contribute to altered insular functions that result in autonomic and neuropsychologic deficits in the condition, including the enhanced sympathetic discharge, reduced respiratory-related arrhythmia, and depression and anxiety symptoms. These findings of abnormal metabolites in OSA may result from intermittent hypoxia, failure of adequate perfusion, or impaired micronutrient support accompanying the condition. The activated glial status suggests increased inflammatory action, which may lead to more neuronal injury, and suggests that glial support may require additional or separate means for protection different from that required for neurons alone in the syndrome.

References:

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