

Aberrant DNA Methylation of the Toll-like receptors in Patients with Obstructive Sleep Apnea

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Purpose

Obstructive sleep apnea (OSA) is a syndrome characterized by repetitive upper airway collapse during sleep, leading to chronic intermittent hypoxia. The up-regulation of toll-like receptors (TLR) 2, 4 and 6 on peripheral blood cells have been found in OSA patients. Little is known about the role of DNA methylation in the pathogenesis of OSA. We hypothesized that aberrant DNA methylation in the promoter of - TLR2 and in the gene body of the - TLR6 gene may play a role in the development of OSA and its excessive daytime sleepiness (EDS) phenotype.

Method

DNA methylation over 28 cytosine-phosphate-guanine (CpG) islands of TLR2 promoter region and 3 CpG sites of the TLR6 gene body, and their protein expression were measured in 18 healthy subjects, 58 severe OSA patients (divided into 18 non-EDS and 40 EDS group), using the pyrosequencing and ELISA methods.

Results

Hypomethylated CpG#18 of TLR2 promoter region, hypermethylated CpG#1 of TLR6 gene, and the protein expression of TLR2 and TLR6 were increased significantly and independently in patients with severe OSA versus healthy subjects. CpG#2 of the TLR6 gene were hypermethylated in severe OSA with EDS versus those without EDS. Both DNA methylation level over CpG#1 of TLR6 gene and TLR6 protein expression were reduced after more than 6-month nasal CPAP treatment in 7 selected patients.

Conclusions

DNA hypermethylation of the TLR2 promoter region and TLR6 gene body may be involved in the development of severe OSA and its EDS phenotype, probably through TLR2 and TLR6 up-regulation.

中文題目：在阻塞性呼吸睡眠中止症患者 TLRs DNA 甲基化的變異表現

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