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Title: Increased toll-like receptor 4 expression in mice lung tissue under intermittent hypoxia

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Body: Objective: Obstructive sleep apnea (OSA) is highly prevalent and is associated with increased risk of cardiovascular disease. OSA is characterized by episodic cycles of hypoxia and normoxia during sleep. While OSA is considered as a proinflammatory condition, there is little data on cellular inflammation in OSA. The aim of this study was to examine the expression of lung tissue TLR4 mRNA and protein in mice under intermittent hypoxia condition. Methods: Eight-week old male C57BL/6J mice were exposed to intermittent hypoxia (30 s exposure to 5 % oxygen, followed by 30 s exposure to 21% oxygen) for 8 h/day during daytime or maintained under normoxic conditions for 2, 3, or 4 weeks. The mRNA expression levels of anti-TLR4, anti-nuclear factor-kappa B (NF- κ B), anti-inhibitory I kappa B protein (I- κ B), anti-transforming growth factor (TGF- β) and anti- β -actin antibody in lung tissue were measured by real time reverse-transcription PCR, and protein levels were assayed by Western blot. Results: Under intermittent hypoxia, the mRNA expression of TLR4 was increased more than that of the control group. There was a positive correlation between the mRNA and protein level of TLR4 in a time-dependent manner, although it was not statistically significant. The expressions of I- κ B and TGF- β were increased with the period of intermittent hypoxia. Conclusions: These results show that TLR4 expression is increased in lung tissue under intermittent hypoxia condition. These data suggest that intermittent hypoxia in OSA can influence TLR4 expression and TLR4-associated pathway may be related with systemic inflammatory response in OSA.