TLR2 is involved in the acute reaction to intermittent hypoxia

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Introduction: Obstructive sleep apnea (OSA) is a prevalent chronic multisystem disease characterized by brief periods of repetitive upper airway occlusion, hypoxia, hypo/hypercarbia and sleep fragmentation. OSA has recently been linked to early cognitive decline and the Alzheimer's disease (AD), and even though the pathogenic mechanism behind this association is not clear, neuroinflammatory process has been suggested to play the role.[1] Neuroinflammation is increasingly recognized as one of the important possible precipitants of neurodegeneration, such as occurs in the AD. In AD microglia are able to bind to soluble amyloid beta via cell surface receptors, including Toll like receptors (TLR), and this process is thought to be part of the inflammatory reaction in AD. In this study we set to investigate the presence of neuroinflammation in the animal model of OSA using in vivo imaging of the TLR2 signal.

Methods: A customized set-up for exposing mice to intermittent hypoxia was designed. Transgenic TLR2-luc mice underwent 8 h daily of 90s periods of 5, 7% of oxygen and room air during 3 weeks, while the controls were kept near the setup to account for the stress of handling. All mice were regularly imaged after exposure throughout the period using a prolonged imaging protocol of 45 minutes for more precise signal acquisition.

Results: The mice that underwent chronic intermittent hypoxia showed a significant upregulation of TLR2 signal following the first day of exposure, after which the signal returned to baseline values. The signal had the highest intensity in the frontal region of the brain.

Conclusion: Our results suggest that TLR2 might play an acute role in mediating the neuroinflammatory response to intermittent hypoxia.

1. Rosenzweig I, Glasser M, Polsek D, Leschziner GD, Williams SC, Morrell MJ. Sleep apnoea and the brain: a complex relationship. *The Lancet Respiratory medicine* 2015.