

# Transcriptomic analysis identifies a unique, intermittent hypoxia mediated inflammatory profile: evidence from a cross-over randomised CPAP withdrawal trial with and without supplemental oxygen in OSA

## *Introduction*

OSA is associated with cardiovascular (CV) disease. It is not known to what extent inflammatory or other changes, mediated by intermittent hypoxia contribute to the development of CV disease in OSA.

## *Methods*

Patients received two-weeks of either supplemental oxygen (O<sub>2</sub>) – with partial attenuation of intermittent hypoxia – or air, instead of their usual CPAP, crossing over after two-weeks back on CPAP. At baseline and following two weeks of O<sub>2</sub> or air, peripheral blood leucocytes were collected. Messenger ribonucleic acid (mRNA) was extracted and RNA sequencing was performed. Differential expression and gene expression signatures were determined through standard bioinformatics analyses.

## *Results*

After adjustments for multiple comparisons, the expression of 25 genes were significantly altered (p.adj <0.05) following CPAP withdrawal onto air, but no genes were significantly altered with CPAP withdrawal onto O<sub>2</sub>. Gene set Enrichment analysis (GSEA) demonstrated a number of pathways upregulated by CPAP withdrawal onto both air and O<sub>2</sub>, such as upregulation of “Oxidative Phosphorylation” and “Reactive Oxygen Species” pathways (both p<0.001). However, the upregulation of the “Inflammatory Response”, “IL6-JAK-STAT3 signalling”, “TNFα signalling” and “IFN-alpha response” pathways (all p<0.001), seen with CPAP withdrawal onto air, were all attenuated by O<sub>2</sub>.

## *Conclusions*

Inflammatory pathways were upregulated following CPAP withdrawal and were attenuated by O<sub>2</sub>. This suggests that intermittent hypoxia in OSA causes inflammatory changes which may contribute to the development of CV disease.