Impaired cerebrovascular in obese children with obstructive sleep apnea compared to healthy controls

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Introduction: Obesity is a common cause of obstructive sleep apnea (OSA) in childhood (1) and obesity related OSA has a prevalence of 13-60%. With childhood obesity at epidemic levels, the incidence of OSA is rising (2). OSA is characterized by intermittent episodes of nocturnal hypoxia, hypercapnia and sleep disruption. Moreover, intermittent hypoxia leads to oxidative damage of the endothelial cells, resulting in endothelial dysfunction which compromises vasodilatory capacity and increases the risk of cerebrovascular damage (3). There is also impaired neurocognitive ability and poor school performance in the obese OSA population which is linked to cerebrovascular damage (4). Reduction in vasodilatory capacity can be quantified experimentally using MR based cerebrovascular reactivity (CVR) which is defined as the change in cerebral blood flow in response to a vasoreactive stimulus and reflects the vasodilatory capacity of the cerebral blood vessels (5). As such, MR based CVR measures can play an important role in understanding the mechanism of cerebrovascular injury in children with OSA and could serve as an early physiological imaging marker for cerebrovascular abnormalities associated with neurocognitive deficits. We hypothesize that obese children with OSA will have reduced CVR, both globally and regionally, compared to controls with no OSA.

Methods: 5 obese patients with OSA and 7 healthy controls were imaged on a 3T MRI scanner using a 32-channel head coil. CVR data were acquired using a blood-oxygen level dependent (BOLD) sequence during a computer-controlled administration of a vasoactive stimulus. The stimulus paradigm consisted of programmed cycles of normocapnia and hypercapnia levels of CO_2 through a rebreathing mask. The BOLD CVR images were acquired with TR/TE = 2000/40ms, FOV = 220mm, matrix size = 64×64, slices = 25, slice thickness = 4.5mm, volumes = 240, time = 8 min. High resolution CVR maps were computed using FSL v4.1 and then converted into surface maps through the Civet pipeline. Next, the surface maps were coregistered into the MNI pediatric MRI Atlas, which was segmented into the AAL regions (6). The MATLAB based program SurfStat was used to obtain global and regional CVR values and SPSS v22 was used to perform Student's t-tests on CVR between the groups.

Results: Global CVR levels in grey matter were significantly reduced in obese OSA patients compared to healthy controls. The regions of interest analysis revealed a number of AAL areas (inferior frontal, anterior cingulate, posterior cingulate, superior temporal gyrus) that showed significantly reduced CVR levels in the obese OSA group ($p < 0.01$) compared to healthy controls.

Discussion: In this study, we have demonstrated significantly reduced CVR in obese OSA patients compared to healthy controls. Reduced CVR may expose children who suffer from obesity related OSA to higher risk of cerebrovascular damage which could potentially manifest behaviourally as neurocognitive deficits and poor school performance in the obese OSA population. Future studies should assess regional CVR abnormalities in obese related OSA in combination with neurocognitive testing.

References: 1. Arens R, Muzumdar H: *J Appl Physiol* 2010; 108:436–44. 2. Speiser PW et al.: *J Clin Endocrinol Metab* 2005; 90:1871–87. 3. Cereda CW et al.: *Stroke* 2013; 44:1175–8. 4. Torelli F et al.: *Neuroimage* 2011; 54:787–93. 5. Yonas H, Pindzola RR: *Cerebrovasc Brain Metab Rev* 1994; 6:325–40. 6. Tzourio-Mazoyer N et al.: *Neuroimage* 2002; 15:273–89.

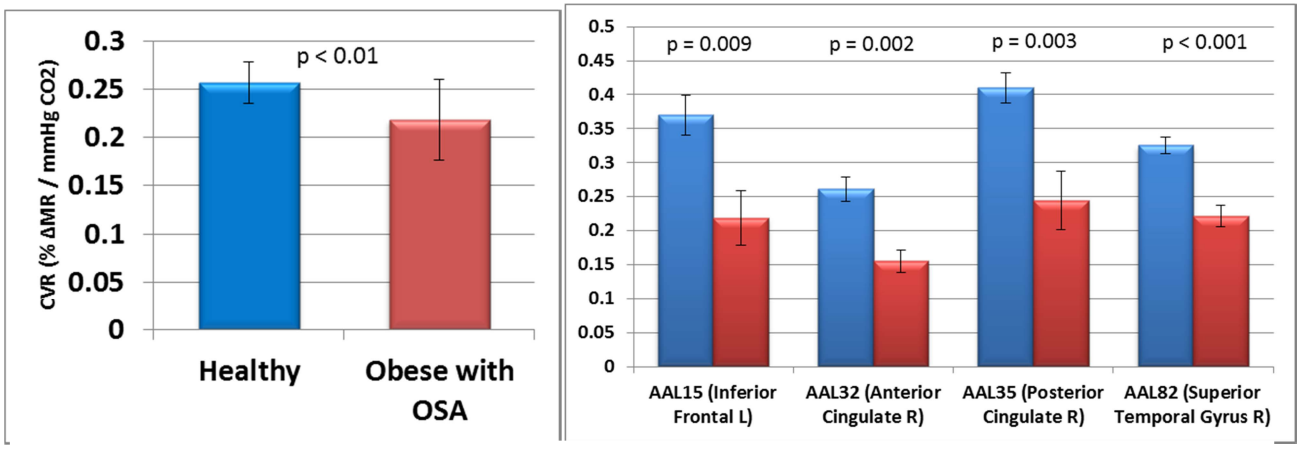

Fig. 1 Global and regional CVR Values between healthy (Blue) and Obese patients with OSA (Red)