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Commentary

Early signs of neurobehavioral improvement after short-term continuous positive airway pressure in obstructive sleep apnea

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Obstructive sleep apnea (OSA) is the most common respiratory sleep disorder with recent estimates reporting a significant rise in OSA prevalence to over 20% of the middle-aged population (Heinzer et al., 2015; Adams et al., 2012). OSA has been linked with excessive day time sleepiness and neurobehavioral abnormalities including attention/vigilance dysfunction and memory impairments. These abnormalities potentially contribute to elevated risk of road/work accidents and earlier onset of neurological disorders (Beebe et al., 2003; Tregear et al., 2009; Rosenzweig et al., 2015). Numerous studies report impairments in brain oxygenation and morphology in OSA patients, which may underpin the neurobehavioral impairments often observed in these patients (Torelli et al., 2011).

Despite the considerable neurobehavioral sequel associated with OSA, there is growing recognition that only a sub-set of at risk patients are negatively affected. There is significant disease heterogeneity in daytime function between individual patients which also varies across cognitive domains. For example, clinically, some patients may report significant daytime sleepiness and display clear vigilance/memory impairments, while others do not show obvious daytime neurobehavioral abnormalities. Similarly, response to treatment with continuous positive airway pressure (CPAP), considered the 'gold-standard' in treating OSA, is also highly variable, often with only partial effectiveness in reversing neurobehavioral abnormalities, even in compliant patients (Kushida et al., 2012; Antic et al., 2011). Thus, the relationship between OSA, the brain and neurobehavioral function is complex and not well understood highlighting the daily clinical challenge of identifying at risk OSA patients, and knowing who, how, when and for how long one should be treated to achieve effective therapy.

In this issue of *EBioMedicine*, Ivana Rosenzweig and colleagues (Rosenzweig et al., 2016) have partly addressed this challenge and provide new clinically useful information on the time course of improvements in cognitive/memory function and brain morphological changes in OSA patients treated with CPAP. The study examined the impact of CPAP on cognitive/memory function and brain morphology in a relatively large group of 55 patients using a randomized parallel group design. The novel aspect of the study was examining the impact of 1 month of CPAP therapy which is shorter term compared with existing literature where 3 or more months of CPAP have been previously used. Neurocognitive function focusing on memory and brain imaging was assessed at baseline in all OSA patients and compared to 35 age and education matched controls, which is a strength of the study. OSA patients were then randomized into two groups: 1) best supportive care (BSC) group, which comprised education on sleep, naps caffeine and sleep hygiene, or 2) BSC + CPAP group. All were re-assessed at 1 month follow-up.

The main finding of the study was that CPAP therapy for one month led to significant improvements in brain morphology, daytime sleepiness and verbal episodic memory function in the BSC + CPAP group compared with the BSC only group. These early hypertrophic morphological changes appeared to be specific to the right thalamus and linked regions. Furthermore, interesting relationships were observed between the morphological changes in the brainstem and improvements in daytime sleepiness in the BSC + CPAP group.

These findings are important and suggest that brain plasticity is initiated relatively early during CPAP therapy with rapid morphological changes in at least some brain regions. These neuroplastic changes may underlie improvements in at least some daytime abnormalities such as daytime sleepiness. Although the sample was relatively large in this study, the between subject design may have reduced the power to detect differences between the interventions and explore relationships between brain morphology and function. OSA is a complex disorder with significant heterogeneity in brain morphology, daytime functional outcomes as well as cardio-metabolic outcomes. Greater recognition of the complexity in sleep medicine and other medical fields is driving the move towards more personalized diagnosis and treatment approaches. Towards this more research is needed, adopting within-group repeated measures and randomized controlled cross-over designs to allow

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phenotyping and assessment of clinically useful neural markers that underpin functional daytime impairments in OSA. This would allow for early identification of patient most at risk of functional neurobehavioral and memory impairments and those who respond favorably/rapidly to therapy.

Disclosure

The authors declared no conflicts of interest.

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