BRAIN STRUCTURAL CHANGES UNDERLYING COGNITIVE DISABILITIES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS): A VBM STUDY

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INTRODUCTION
Previous MRI studies have reported inconsistent findings on the association between the presence and severity of obstructive sleep apnea syndrome (OSAS) and brain tissue abnormalities [1]. So far, it still remains a matter of debate whether patients with OSAS present with an increased risk for developing a neurological impairment. The principal aim of this study was to assess, using voxel based morphometry (VBM) [2], the presence and extension of both gray (GM) and white matter (WM) changes in patients with OSAS at different clinical stages. The secondary aim was to ascertain the relationship between these changes and specific cognitive profiles.

METHODS
We recruited 16 patients (F/M=3/13; mean [SD] age=55.8 [6.7] years) suffering from OSAS as assessed by their Apnea/Hypopnea Index (AHI) (mean [SD] AHI=53 [26] h⁻¹). Twelve of them were characterized by a severe form of OSAS (AHI>30 h⁻¹), while the remaining 4 were at a moderate clinical stage (15≤AHI≤30 h⁻¹) [3].

RESULTS
Neuropsychological data analysis revealed that patients with OSAS had significantly lower scores than healthy controls on Rey’s 15 word list test (immediate recall) [6] which explores verbal memory. Patients with OSAS at a moderate stage did not reveal any significant difference in GM or WM volumes when compared either with healthy controls or patients with OSAS at a severe stage. Conversely, patients with OSAS at a severe stage compared to healthy controls showed a region of decreased GM volume in the right hippocampus (P_FWE cluster level corr. <0.05; MN Coordinates [x,y,z] = 30; -5; -48). The same contrast revealed also a symmetric region of GM loss in the left hippocampus, together with additional localisations within more lateral temporal areas, although none of these results survived after FWE correction (p uncorr.<0.001). Moreover, patients with severe OSAS compared to healthy controls showed two regions of reduced WM volume within the right temporal lobe (p uncorr.<0.001). Interestingly, one of them was localized nearby the hippocampal region also showing GM atrophy. Multiple regression analysis revealed a direct association between scores obtained on Rey’s 15 word list and GM volume in the left orbitofrontal cortex (OFC) (MNI Coordinates [x,y,z] = -6; 41; -24; p uncorr.<0.001).

DISCUSSION
The results of this study indicate that the brain tissue of patients with OSAS is vulnerable to recurrent episodes of apnea, with detectable abnormalities in the hippocampal regions of patients with a severe clinical form (AHI>30 h⁻¹). This finding is consistent with previous reports indicating the hippocampus as a brain structure particularly sensitive to hypoxia [10-12]. Additionally, the hippocampus is directly implicated in memory functions, which was found to be impaired in our cohort of patients.

WM atrophy was also present in a region nearby the right hippocampus of patients with severe OSAS. This suggests that not only regional GM atrophy, but also brain disconnection may contribute to cognitive deficits in patients with OSAS. Finally, a direct association was found between scores obtained on Rey’s 15 word list test and GM volumes in the OFC, a region known to take part in memory processing [13, 14]. Thus, it seems plausible that, in addition to the hippocampal involvement, the memory deficits observed in our patients might be linked also to changes in other regions.

References