Brain imaging studies indicate that people with obstructive sleep apnea (OSA) have structural changes in the brain, such as decreased gray matter volume in areas of the brain that are involved in memory, attention, planning, organizing, and strategizing.

These changes may explain reduced concentration, reduced attention level and impaired memory noted in people with OSA. Some research indicates that continuous positive airway pressure (CPAP) treatment can reverse the damage to these brain tissues in people with OSA.

In OSA, a person stops breathing (i.e., has apnea) intermittently during sleep. The cessation in breathing occurs because upper airway muscles relax excessively during sleep, which allows the upper airway tissues such as the tonsils and adenoids to collapse into the airway and obstruct airflow. The blood oxygen level consequently decreases. When it falls to a certain level, the brain triggers an arousal which restores upper airway muscle tone, opens the airway, and thereby restores airflow. Once a person resumes sleep, the process can recur. A person diagnosed with OSA has five or more OSA episodes for each hour of sleep during a sleep period.

Animal studies indicate that the hippocampus, a small structure at the base of the brain that is involved in memory, is especially sensitive to and damaged by hypoxia (low oxygen level). In humans, structural changes have been noted in the hippocampus and in the white matter and gray matter of the brains of people with OSA. These brain alterations may be associated with the intermittent episodes of oxygen desaturations that occur during apnea episodes.

People with OSA often have problems with concentration and other aspects of cognition; however, after successful OSA treatment (the most common is CPAP treatment in which pressurized air is blown through the nose or nose and mouth to prevent upper airway collapse), concentration and cognition improves. Therefore, researchers Vincenza Castronovo and colleagues hypothesized that patients with severe OSA would have altered white matter integrity in the brain (and subsequently altered cognition) and that OSA treatment would improve the structural damage and cognitive impairment. Using diffusion tensor imaging to measure white matter integrity in the brain and various neuropsychological tests to measure cognitive performance, the researchers assessed 17 untreated patients with OSA before treatment and at three months and 12 months after treatment.

Diffusion tensor imaging is a form of magnetic resonance imaging (MRI) that detects how molecules such as water flows (i.e., diffuses) through a tissue. In fibrous tissues (e.g., nerve or muscle tissue), water diffuses more quickly along the axis of the fibers. This factor is used to detect if a tissue is intact.

The diffusion tensor images of the OSA patients were compared to those of 15 matched healthy individuals without OSA (who were only measured once at baseline). Castronovo found that before treatment OSA patients had impaired cognitive functions, impaired mood and sleepiness. Statistical analyses showed that these factors were associated with diffuse areas of reduced white matter fiber integrity. After three months of CPAP, some abnormalities in the white matter had decreased; after 12 months of CPAP treatment, the white matter abnormalities were nearly reversed in all affected regions in treatment-compliant patients. There were also significant improvements in memory, attention and executive-functioning (i.e., the ability to connect past experience with present action to perform actions such as planning, organizing, strategizing and remembering details) that paralleled the improvement in white matter integrity.

Other researchers have similarly noted reduced white matter volume in the brains of people with OSA. For example, Hsiu-Ling Chen and colleagues used diffusion tensor imaging to assess white matter integrity in people with severe OSA (> 30 respiratory events per hour of sleep). They found white matter damage in certain regions in the brain and that the degree of this alteration was associated with the degree of disease severity. Hyun Kim and colleagues polysomnographically assessed 503 study participants (age, 59 ± 7.8 years) for OSA; they were subsequently classified as having no OSA, mild OSA (5–15 events per hour), or severe OSA. The participants then underwent brain magnetic resonance imaging (MRI), which detected alterations in white matter in 39.6 percent of the participants with moderate or severe OSA.

Other researchers have noted reductions in gray matter volume in the brains of people with OSA. For example, Nicola Canessa and colleagues and colleagues used voxel-based morphometry (VBM) to map brain regions in people with and without OSA. Voxel-based morphometry uses a unit, called a voxel (often depicted as a cube), to analyze the length, width, mass, area and other features of a structure. By using voxels, scientists can determine whether a structure is larger or smaller than normal. Before treatment, Canessa noted reduced gray matter volume in the left parahippocampal gyrus (also called the entorhinal cortex), left posterior parietal cortex, and right superior frontal gyrus in people with severe OSA. After three months of CPAP therapy, the gray matter volume increased in certain hippocampal regions (e.g., left subiculum and bilateral entorhinal cortex) and in frontal regions. The overall gray matter volume increased after three months of CPAP treatment. Canessa furthermore noted that OSA severity was positively correlated with the degree of post-treatment hippocampal gray matter volume increase in areas within or near the hippocampus (e.g., right entorhinal cortex and...
in the left subiculum). Improvement in memory, attention, and executive functioning paralleled gray matter volume increases in hippocampal and frontal structures.

Macey and colleagues noted diminished regional and unilateral gray matter loss in multiple brain sites (e.g., the frontal and parietal cortex, temporal lobe, anterior cingulate, hippocampus, and cerebellum) in patients with OSA. Many of these areas are involved in the motor regulation of the upper airway (which may contribute to upper airway collapse) and in areas involved in cognitive function.

However, some researchers have not found that gray matter volume increases after CPAP treatment or that white matter or gray matter is significantly reduced in people with OSA. For example, Fergal O’Donoghue and colleagues noted diminished regional and unilateral hippocampal and frontal structures. However, others have noted scattered areas of gray matter loss in the temporal lobe and hippocampus in untreated people with OSA. All patients underwent a MRI study before initiating CPAP treatment and then underwent another MRI study six months after initiating CPAP treatment. However, the MRI scans at six months showed no significant change in the gray matter volume in the treated patients. From this finding, O’Donoghue concluded that CPAP treatment has no effect on gray matter volume. O’Donoghue cautions that this finding does not indicate that no neural changes occur in people with OSA. It may be that their criteria for including patients in their study may have excluded patients who may have had changes in these brain structures (i.e., the patients in their study may have been more resistant to the neurologic and cardiovascular complications of OSA) or it may be that the adverse effects of OSA on cerebral structure may only occur after decades of untreated disease (the patients in O’Donoghue’s study were on average 49 years old).

Mary Morrell and colleagues noted reduced gray matter volume in the left hippocampus of male patients with OSA who had an apnea-hypopnea index of 25–40 respiratory events per hour. However, they found no changes in the gray matter volume in the right hippocampus or other brain regions.

Because of reductions in gray and white matter volume in people with OSA, some scientists speculate that OSA may be a risk factor for the early development of dementia or mild cognitive impairment in older people. Early treatment for OSA may help decrease this risk. This has yet to be assessed.

The finding of reduced gray and white matter volume in people with OSA raises new questions about OSA. For example, could it be that this alteration is actually a causative factor of OSA rather than a consequence of OSA? Could reduced gray matter volumes in areas involved in the motor aspects of respiration play a role in upper airway collapse? To what extent can the recovery of white matter and gray matter volume be improved by CPAP or other apnea treatments?

A better understanding of brain structures involved in the pathogenesis of OSA or impacted by OSA could improve treatment for this disorder. For now, scientists continue to focus on determining exactly how structural changes in the brain and OSA are related. Future neuroimaging studies may help to identify patients who are at the greatest risk of a poor treatment outcome.

This information could be used to customize OSA treatment for patients and improve treatment compliance and treatment outcomes.

References