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Pathophysiology of Obstructive Sleep Apnea & Its Role in Excessive Daytime Sleepiness

Announcer: Welcome to ReachMD.

This medical industry feature, titled “Pathophysiology of Obstructive Sleep Apnea & Its Role in Excessive Daytime Sleepiness” is provided in partnership with Jazz Pharmaceuticals, Inc. This program is intended for physicians.

Here’s Dr. Richard Bogan, Associate Clinical Professor at the University of South Carolina School of Medicine and Chairman and Chief Medical Officer at SleepMed, Incorporated.

Dr. Bogan is a paid consultant for Jazz Pharmaceuticals, Inc.

Dr. Bogan: Researchers continue to learn more about excessive sleepiness in obstructive sleep apnea or OSA.

Many factors, such as insufficient sleep, medication, or comorbid sleep disorders, can cause your patients with OSA to feel sleepy.

Recent studies have identified new findings about the potential consequences of OSA, including physiologic changes to the brain occurring as a result of chronic sleep disruption and chronic intermittent hypoxia.

Clinical and animal studies have suggested that sleep fragmentation and chronic intermittent hypoxia are associated with injury to wake-promoting neurons in the brain.

In one study involving a mouse model of chronic sleep fragmentation, data show that neuronal injury can occur when sleep is disrupted. Specifically, this research looked at the effect of chronic sleep disruption on wake neuron survival in 8-week-old male mice.

The data revealed that 14 weeks of chronic sleep fragmentation caused an approximate 50% reduction in the total number of noradrenergic neurons in the locus coeruleus and reduced dendrite projections in these wake-promoting neurons.

These effects were observed even after 4 weeks of normal sleep/wake conditions in mice.

In a different study of chronic intermittent hypoxia, the long-term intermittent hypoxia protocol was used in adult mice to model sleep apnea oxygenation patterns observed in patients with severe OSA. As compared with sham controls, 6-month exposure to hypoxia and subsequent reoxygenation resulted in a 40% loss of wake-active dopaminergic and noradrenergic neurons in the ventrolateral periaqueductal gray and locus coeruleus regions.

However, other wake-active neural groups, such as monoaminergic, cholinergic, and orexinergic neurons, were spared from injury.

The animal data tell us that OSA-associated chronic sleep fragmentation and intermittent hypoxia can result in injury to wake-promoting neurons, potentially resulting in excessive sleepiness.

Imaging studies in humans have also shown changes to brain physiology including white matter *and* gray matter.

In individuals with untreated OSA, changes in brain anatomy include a reduction in gray matter concentration in certain regions of the brain. Affected areas include the thalamus, anterior cingulate cortex, and frontal cortex.

These areas are involved in wakefulness and neurocognitive performance, such as those that mediate attention and higher-order cognitive processes—for example, executive functions.

White matter, which refers to myelinated neuronal pathways, also can be affected by OSA. Consider another recent study.

Diffusion tensor imaging was used to evaluate white matter neuronal tracts in patients who were adherent to CPAP for 6 or more hours per night for 30 days. One group had ongoing sleepiness while the other group did not.

The data indicate that whole brain mean diffusivity was significantly higher in the sleepy group compared with the nonsleepy group—a factor that indicates widespread changes in white matter.

Results do suggest that patients with OSA and sleepiness have altered white matter density compared with nonsleepy patients with OSA.

What we can conclude from the research is that excessive sleepiness is associated with structural changes to brain white matter.

This indicates that neuronal connectivity in patients with OSA who experience excessive sleepiness, may be compromised.

We continue to learn more about the pathophysiology and challenges of excessive sleepiness in OSA.

Announcer: This program was brought to you by Jazz Pharmaceuticals, Incorporated.

To find out more about the pathophysiology behind excessive daytime sleepiness in obstructive sleep apnea please visit EDAandOSA.com . That's E-D-A A-N-D O-S-A.com.

If you missed any part of this discussion or to find others in this series, visit ReachMD.com/SleepScience. This is ReachMD. Be part of the knowledge.

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