Erectile dysfunction related to sleep apnea may persist, but is treatable

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For sufferers of sleep apnea, erectile dysfunction (ED) is often part of the package. New research indicates that ED in cases of obstructive sleep apnea syndrome (OSAS) may be linked to the chronic intermittent hypoxia—oxygen deprivation— (CIH) that patients with OSAS experience during episodes of obstructed breathing.

In the first model to address this possibility experimentally, researchers from the University of Louisville found that after one week of being exposed to CIH similar to that which a human with PSAS would experience, mice showed a 55 percent decline in their daily spontaneous erections. After five weeks of CIFH exposure, the "latency to mount" period— the average interval between mounting a mate— increased 60-fold.

"Even relatively short periods of CIH...are associated with significant effects on sexual activity and erectile function," wrote David Gozal, M.D., professor of pediatrics at the University of Louisville.

The results appeared in the second issue for September of the *American Journal of Respiratory and Critical Care Medicine*, a publication of the American Thoracic Society.

The study examined the behavioral and physiological effects in mice exposed to CIH for anywhere from five to 24 weeks. Control mice were kept under identical conditions, but were not subjected to nocturnal CIH. The mice were evaluated on a series of complex sexual behaviors,

including erection frequency and mating behavior and measured associated biomarkers of sexual function that may be affected by CIH, such as testosterone and estradiol levels, and also the expression of endothelial and neuronal nitric oxide synthase (eNOS and nNOS respectively). eNOS, which is increased by drugs such as sildenafil (Viagra), plays a major role in male sexual drive and activity.

After just five weeks exposure to CIH, not only did latency-to-mount time increase by 60-fold, latency to intromission increased by 40-fold. Latency to ejaculation was also severely affected. In five out of seven mice tested, ejaculation did not occur at all, but in one mouse, latency to ejaculation was 660 minutes—eleven hours—whereas in control mice the median time to ejaculation was "only a few minutes, said Dr. Gozal. Interestingly, one mouse appeared to be unaffected in this respect.

"The disparity in responses among mice is very similar to the heterogeneity of the magnitude of end-organ morbidity in sleep apnea among patients, and shows that not everyone will be affected to the same extent," said Dr. Gozal.

While there were no differences in testosterone and estradiol levels, there was also a significant reduction in eNOS expression with mice exposed to CIH for eight weeks.

Even after six weeks' recovery time with standard oxygen levels, mice exposed to CIH for as little as one week only recovered 74 percent of their original erectile function. "[T]his could suggest either chronic residual deficits after CIH or that full recovery would require longer periods," wrote Dr. Gozal.

Despite the lingering negative effects of CIH on sexual behavior in mice, the researchers did find that it was largely reversible. In the second phase of the experiment, Dr. Gozal administered tadalafil, which increases the

availability of nitric oxide through PDE5. Treatment with tadalafil improved erectile and sexual functioning in CIH-exposed mice to near-normal levels in almost all cases.

"In the present study, tadalafil restored CIH-induced impairments of latencies to mounts, intromissions and ejaculations, significantly improving performance during spontaneous erections and during mating and noncontact activity," wrote Dr. Gozal. "The effects of tadalafil were not limited to the erectile tissue but extended to behavioral components, suggesting a possible role for PDE5 in central nervous system mechanisms that control sexual behavior."

"Further studies are needed to explore the effects of sleep disruption and episodic hypoxia during sleep on the central nervous system that mediates sexual drive," said Dr. Gozal. "Exploration of alternative interventions aiming at preventing and treating this infrequently spoken of, yet extremely frequent complication of OSA, will certainly require improved understanding of the complex mechanisms affecting sexual activity and how it is affected by diseases such as sleep apnea."

"These findings add sexual dysfunction to a long list of disorders associated with – and probably caused by – OSA," stated John Heffner, past president of the ATS. "Although this study was performed in research animals, chronic intermittent hypoxia has profound effects on multiple organ systems and a strong biologic plausibility exists that similar findings will be observed in humans. Early identification and effective therapy of OSA is critically important especially considering the high prevalence of this disorder."

Source: American Thoracic Society