

Obstructive sleep apnea linked to cancer growth in mice

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A new study links the intermittent interruption of breathing that occurs in patients with obstructive sleep apnea (OSA) to enhanced proliferation of melanoma cancer cells and increased tumor growth in mice, according to researchers in Spain. The study also found tumor cells of OSA mouse models tended to contain more dead cells, indicating a more aggressive type of cancer.

The results of the study will be presented at the ATS 2011 International Conference in Denver.

"To our knowledge, this study is the first one providing experimental evidence that a high-rate intermittent lack of oxygen, or hypoxia, mimicking the one experienced by OSA patients enhances tumor growth," said Ramon Farre, PhD, professor of physiology at the University of Barcelona School of Medicine Biophysics and Bioengineering Lab.

Recurrent hypoxia is one of the hallmarks of OSA, which may affect around 5 percent of Americans. OSA has been associated with an increased risk of cardiovascular disease, including [high blood pressure](#), as well as [daytime sleepiness](#) and a lower quality of life.

"Although earlier studies in animals have shown that [lack of oxygen](#), or hypoxia, plays an important role in regulating the various stages of [tumor formation](#) and progression, the results obtained from human studies including large groups of OSA patients are not easy to interpret because

there are other contributing conditions, most notably obesity," Dr. Farre added. "This well-controlled [mouse model](#) study allowed us to ensure that the only variable under study was [intermittent hypoxia](#)."

In this study, mice injected with melanoma [tumor cells](#) were divided among two groups. In the first group, mice were exposed to intermittent hypoxia, where oxygen was restricted for 20-second periods at a rate of 60 periods per hour for six hours per day, and normal [oxygen levels](#) for the remainder of the day. In the second group, mice received normal levels of oxygen (normoxia). Tumor volume was measured throughout the study and at the end of the study period. At the end of the 14-day study period, tumors from all mice were removed and weighed and tumor necrosis (indicated by the numbers of [dead cells](#) present) was measured to determine the aggressiveness of the tumors.

The authors found that while tumor volume progressively increased with time in both the intermittent hypoxia and control groups, the increase was higher in the mice subjected to intermittent hypoxia. Tumor weight and necrosis in the intermittent hypoxia group were almost two times that of the tumors in the control group.

"With the limitations of any animal model study, these results suggest that the intermittent hypoxia characterizing obstructive [sleep apnea](#) could enhance the growth of tumors," Dr. Farre said, adding that although the results were not entirely unexpected based on earlier studies connecting hypoxia with tumor growth, a link between breathing abnormalities specific to OSA and [tumor](#) progression had not previously been demonstrated.

"It was well known that continuous hypoxia promotes the growth of [cancer cells](#) and tumors," he said. "However, there were no data concerning the effects of the fast rate changes of oxygenation in sleep apnea on cancer."

Dr. Farre said the results of this study could have future clinical implications if the results are confirmed in large-scale human studies. "There are still several questions that need to be answered, both at the basic science and clinical levels," he said.

Future studies would need to evaluate whether intermittent hypoxia also triggers the initial formation of tumors and whether it promotes metastasis, or spread of tumors from one organ to another. Because this study focused on melanoma, Dr. Farre said additional studies should also explore whether intermittent hypoxia affects other types of cancer.

Extended population studies should also determine if there is a relationship between the incidence of cancer and the severity of OSA, as well as addressing the issue of obesity, which has been linked with OSA.

"Intermittent hypoxia is not the sole cancer-promoting challenge experienced by OSA patients," Dr. Farre said. "Obesity is also known to enhance cancer morbidity and mortality, and it is not clear to what extent intermittent hypoxia and obesity could interact to increase cancer growth in OSA patients.

Clarifying these questions certainly will require additional studies," he said. "If the current results in an animal model are confirmed by further clinical research, the public health impact of obstructive sleep apnea would be greater than currently known."

Provided by American Thoracic Society

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