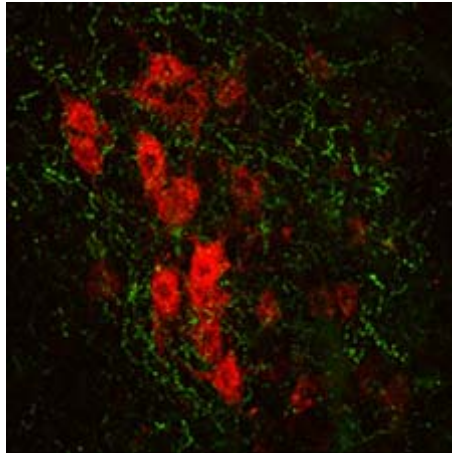


The Role of Age and Gender in Sleep-Related Breathing Disorders



Photomicrograph of serotonin containing axons (green) in close proximity to hypoglossal nerve cells (red).

My research involves how aging effects the neural control of breathing. Very little is known about the effects of age on regions of the brain and spinal cord that are involved in the control of respiration. We believe that aging results in structural and functional changes in these respiratory control areas that may predispose people to breathing disorders. Moreover, we hypothesize that age-associated changes in respiratory areas of the brain and spinal cord are quite different in men and women.

I am particularly interested in the role of the neurotransmitter serotonin in the control of breathing. We have found that in male rats with increasing age, serotonin levels decrease in areas of the brain that help to keep the upper airway functioning normally. In contrast, these changes are not seen in aging female rats. In other studies on rats, we have recorded an age-associated decline in the normal response to episodes of hypoxia in male rats. Once again, similar changes were not seen in female rats. These data led us to conclude that aging has a gender-specific effect on how serotonin can modulate the respiratory control system. For over a century it has been known that fluctuations in female hormone levels associated with the estrus cycle and with pregnancy have profound effects on breathing, and recent evidence supports a role for the female gonadal hormones, estrogen and progesterone in the neural control of breathing. The male gonadal hormone testosterone may also be involved in the control of breathing, as it can be converted to estrogen in the brain. Gonadal hormone levels decline with age. We believe that there is a link between increasing age, levels of gonadal hormones,

serotonin, and the neural control of breathing. Recent results from our laboratory show that levels of serotonin in brain regions involved in the control of breathing fluctuate during the rat estrus cycle, and decrease following gonadectomy. The responses of the respiratory system to episodes of hypoxia also change with hormone levels in both male and female rats. Taken together, our data support the hypothesis that gonadal hormones play a critical role in the maintenance of respiratory function with increasing age through their action on the serotonergic system in the brain. Furthermore, preliminary studies suggest that manipulations of gonadal hormone levels can reverse or delay the age-associated changes in the neural control of breathing. These ongoing studies will provide a better understanding of the age and gender-related contributions of the serotonergic system to sleep-associated breathing disorders such as obstructive sleep apnea (OSA). OSA is an age-associated disease that is far more prevalent in men than women, and also more prevalent in women after menopause who are not taking hormone replacement therapy.

Publications Relative to This Topic:

Behan, M. and M. S. Brownfield. 1999 Age-related changes in serotonin in the hypoglossal nucleus of rat: Implications for sleep-disordered breathing. *Neurosci. Lett.* 267:133-136. [\[Abstract\]](#)

Fuller, D.D., Baker, T.L., Behan, M. and G.S. Mitchell, 2001. Expression of hypoglossal long term facilitation differs between sub-strains of Sprague-Dawley rat. *Physiol. Genomics* 4;175-181 [\[Full text\]](#)

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Behan, M., and C.F. Thomas. 2005. Sex hormone receptors are expressed in identified respiratory motoneurons in male and female rats. *Neuroscience* 130:725-734. [\[Abstract\]](#)

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