Hormone levels in women using contraception affect nerve activity involved in vessel constriction

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After menopause, women's levels of estrogen and progesterone fall. Their formerly lower risk for heart disease equals, even surpasses, men's risk. One possible contributing explanation for the change in risk is that sex hormones affect the sympathetic nervous system (SNS), which controls constriction of blood vessels and participates in the fight or flight response.

A new study by researchers at Western Ontario University is among the first to look at the hormone/SNS relationship in young women taking hormone contraceptives. It is the first to observe differences in the frequency of firings of the SNS neurons between high and low hormone phases of the menstrual cycle. It is also the first to examine how the SNS responds to chemoreflex stress (in this study, several moments of rebreathing oxygen-depleted air, then a breath held as long as possible). The study also examined the rarely studied strength of nerve firings, called burst amplitude. Using this unique approach, results that had been ambiguous or conflicting in other studies became clearer. The findings also provide new insight into mechanisms through which lower hormone levels may make the body more susceptible to damage caused by stress and the chronic elevation of the fight or flight response. A pattern consistent with these findings is observed in postmenopausal women.

The article is entitled "Hormone phase-dependency of neural responses to chemoreflex-drive sympatho-excitation in young women using

hormonal contraceptives." It appears in the online edition of the *Journal of Applied Physiology*, published by the American Physiological Society.

Methodology

Study participants were 10 women between the ages of 22 and 26 (average age 24). All were healthy nonsmokers of normal weight, who exercised regularly. All were taking some form of hormone contraception. The women were studied once during the first four days of menses (low hormone phase) and again between day 20-24 (high hormone phase). For these studies, each woman was connected to an instrument that measures the amount of oxygen in the lungs. Lying down, each breathed normally through a special mouthpiece. After five minutes, a valve on the mouthpiece changed room air to that in a bag with air earlier expired by the woman. Rebreathing used air resulted in lower oxygen and higher carbon dioxide levels in the blood. This chemoreflex stressor maximized response of the SNS. When oxygen levels fell to a specific point, the woman was asked to hold her breath as long as she could. Throughout the breathing sequence, investigators also monitored heart rate, blood pressure, and cardiac output. Tiny needles inserted into a nerve in the woman's leg measured frequency and "bursts" of SNS activity.

Results

Hormone contraception affected the regulation of muscle sympathetic nerve activity differently, depending on sex hormone levels and on the presence and severity of chemoreflex stress.

When the women were at rest, they experienced more frequent nerve firings during phases of their cycle when their hormone levels were highest. There was no difference in the amplitude (the scientific term for

magnitude or size) of neural bursts between high and low hormone phases. During episodes of stress, however, the women experienced greater increases in the number and amplitude of nerve bursts when their hormone levels were lowest. The more severe and long-lasting the stress was, the higher the amplitude was.

Importance of the Findings

The study findings show that the SNS uses different methods to control blood flow to the muscles. Depending on hormone levels and stress, the SNS alters the frequency and amplitude of nerve firings. The effect of these alterations helps explain how higher hormone levels in younger, premenopausal women protect against damage to the cardiovascular system through greater ability to control the SNS. The findings also suggest how stress can elevate the SNS in ways that, in the presence of lower hormones, may make the cardiovascular system more susceptible to the damage caused by chronic elevation of the fight or flight response. A pattern consistent with these findings is observed in postmenopausal women, where chronically low hormone levels are associated with increases in cardiovascular disease.

This more precise understanding about the relationship of hormones and the SNS also helps explain the mystery of why, as is known, males and females have different SNS responses while at rest and different responses to stress.

Study Team

First author is Charlotte W. Usselman, a doctoral student of Kevin Shoemaker, School of Kinesiology, and Department of Physiology and Pharmacology, Western University, London, Ontario. Dr. Shoemaker's Neurovascular Research Laboratory explores the pathways in the brain

associated with recruitment of sympathetic nerve activity and the physiological effects of these different pathways. The study team also includes Torri A. Luchyshyn and Chantelle A. Nielson, both master degree students; undergraduate Tamara I. Gimon; and endocrinologist Stan H M. Van Uum, Department of Medicine, Western University.

More information: The article is available online at jap.physiology.org/content/ear … 1.2013.full.pdf+html

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