Correspondence

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Sildenafil Does Not Influence Autonomic Neurocardiac Control Assessed by Standard Measurements of Heart Rate Variability

To the Editor:

Recently, an excellent study by Phillips and colleagues¹ showed a significant increase in muscle sympathetic nerve activity (MSNA) in healthy young men after a single 100-mg dose of sildenafil. The MSNA increase did not, however, result in an increase in heart rate, from which the authors concluded that the sympathetic activation they observed was selective for the vascular sympathetic drive only. Given the highly differentiated nature of autonomic efferent activity, the measurement of MSNA as a pure index of peripheral sympathetic outflow might allow no definitive conclusions to be made about the autonomic control of the sinoatrial node.

A noninvasive method for evaluating autonomic neurocardiac control involves standardized investigations of heart rate variability (HRV). We recently investigated the 5-minute resting HRV. Measurements were obtained according to previously published protocols²−³ before and 90 minutes after a test dose of sildenafil (25 to 50 mg) in 21 men with an average age of 53.7±11.5 years (M.W. Agelink, MD, et al, manuscript in preparation, 2000). Sildenafil exerted no notable influence on the spectral low frequency (0.04 to 0.15Hz) and high frequency (0.15 to 0.4Hz) components assessed in absolute and normalized units; the sympathovagal balance expressed as the low/high frequency ratio was not displaced by sildenafil (4.3±2.9 before versus 4.7±3.3 after sildenafil; *P*=0.7). If one accepts the normalized low frequency power and the low/high frequency ratio as reasonable reflections of central nervous sympathetic outflow to the sinoatrial node, our results indicate that sildenafil does not influence the cardiac sympathetic resting tone or the sympathovagal balance. There was, however, a mean 8.9% reduction of systolic blood pressure combined with a mean 5.8% increase in heart rate 90 minutes after dosing with sildenafil, which suggests that the blood pressure decrease under sildenafil in older patients is more marked than in younger patients. Thus, an increased vascular sympathetic drive after application of sildenafil (expressed in the study of Phillips et al¹ as a sildenafil-induced increase in MNSA burst frequency) may be important in opposing the systemic vasodilator effects of sildenafil and maintaining blood pressure levels.

Ben-David and Zipes⁴ emphasized that autonomic nervous system occurs in a number of situations, not necessarily provide accurate insights into the autonomic control of the sinoatrial node. Differential activation of the autonomic nervous system occurs in a number of situations, including REM sleep² and the diving reflex.³ Even in healthy normal humans studied during resting conditions, there is considerable complexity in the interaction between sympathetic traffic and heart rate and their relative influences on blood pressure levels.⁴

The interesting data described by Agelink and colleagues do indeed suggest the possibility of an age-dependent potentiation in the hemodynamic effects of sildenafil. The relatively modest increase in heart rate in the setting of a presumed 10 to 15 mm Hg reduction in blood pressure is also quite intriguing. We thank these investigators for sharing their data with us.

Bradley G. Phillips, Pharm D
Masahiko Kato, MD, PhD
Catherine Pesek, DO
University of Iowa
Iowa City, Iowa

Krzysztof Narkiewicz, MD, PhD
Medical University of Gdansk
Gdansk, Poland

Mikołaj Winnicki, MD, PhD
Diane Davison, RN, MS
Virend Somers, MD, PhD
Mayo Clinic
Rochester, Minnesota

Marcus W. Agelink, MD
Heiko Ullrich, MD
Department of Neurocardiology
Institute of Biological Psychiatry & Neuroscience
Evangelische Kliniken Gelsenkirchen
Gelsenkirchen, Germany

Norbert H. Brockmeyer, MD
Department of Dermatology and Andrology
St. Josef Hospital
Ruhr-University of Bochum
Germany

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Marcus W. Agelink, Heiko Ullrich and Norbert H. Brockmeyer

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