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# Rho-kinase Inhibition Improves Erectile Function in Aging Male Brown-Norway Rats

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Physiological aging is a significant risk factor in the on-set of male erectile dysfunction (ED) and an imbalance in factors that modulate cavernosal smooth-muscle tone may play a role in these altered penile hemodynamic mechanisms. To evaluate the association between aging and male erectile function, we monitored neurogenic erectile response and its correlation to systemic arterial pressure changes in old (21-23 months of age) vs young (6-9 months of age) Brown-Norway (BN) rats. We tested the hypothesis that age-associated ED is due to unregulated vasoconstrictive tone, contributed in part by an increased Rho-kinase activity, and that antagonism of Rho-kinase activity attenuates the age-related decline in male erectile function. We also examined the hypothesis that a combination of Rho-kinase antagonism and phosphodiesterase-5 (PDE-5) inhibition has a synergistic effect in improving the erectile response in these aging animals. Erectile function in old BN rats was evaluated before and after intracavernosal injection of a specific inhibitor of Rho-kinase (Y-27632) alone or in combination with zaprinast, a PDE-5 inhibitor. Erectile capabilities of the young and old BN rat groups were significantly different in corpus cavernosum pressure response after electrical-field stimulation of the major pelvic ganglion. Y-27632 administration attenuated the aging-related changes in male erectile function seen in BN rats. Rho-kinase antagonism and PDE-5 inhibition had a synergistic effect in improving erectile function in old rats. Our data indicate that aging leads to impairment in the neurogenic erectile response in BN rats involving a possible derangement in penile hemodynamic mechanisms of the erectile tissue. Rho-kinase inhibition may be of value in treating age-related ED.

**Key words:** Muscle, smooth, drug effects, penis physiology, biological aging, penile erection

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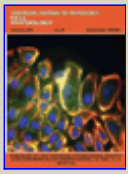
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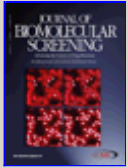
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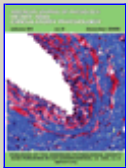
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