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Behavioral Stress Results in Reversible Myocardial Dysfunction in a Rodent Model

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Clinical reports suggest that emotional stress alone is sufficient to cause reversible myocardial dysfunction in patients. We report that a combination of prenatal stress followed by restraint stress (PS + R) results in echocardiographic evidence of myocardial dysfunction compared with control rats subjected to the same restraint stress (control + R) (45.8 ± 3.9 vs 61.9 ± 2.4%; $P < .01$). Catheter-based hemodynamic studies in freely ambulatory awake rats revealed both systolic (+dp/dt; 10,438 ± 741 vs 12,111 ± 652) and diastolic (−dp/dt; −8,287 ± 444 vs 10,440 ± 364) dysfunction in PS + R vs control + R ($P < .05$, for both). PS + R also demonstrated a significantly attenuated ($P < .05$) hemodynamic response to increasing doses of the beta-adrenergic agonist, isoproterenol. Pretreatment with the p38 MAP kinase inhibitor, SB203580, prevented the baseline reduction in +dp/dt and −dp/dt as well as the blunted isoproterenol response in vivo. Cardiac myocytes from PS + R also revealed diminished fractional shortening (6.7 ± 0.8 vs 12.7 ± 1.1%, $P < .01$) and blunted inotropic responses to isoproterenol ($P < .01$). In vitro treatment with SB-203580 blocked p38 MAP kinase phosphorylation, reversed the depression in fractional shortening, and partially ameliorated the blunted adrenergic signaling seen in adult rat ventricular myocytes from PS + R. We conclude that p38 MAP kinase activation in cardiac myocytes by behavioral stress may lead to reversible myocardial dysfunction in this animal model of human disease.