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## Abstract 20

### 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) ( $45.8 \pm 3.9$  vs  $61.9 \pm 2.4\%$ ;  $P < .01$ ). Catheter-based hemodynamic studies in freely ambulatory awake rats revealed both systolic (+dp/dt;  $10,438 \pm 741$  vs  $12,111 \pm 652$ )

and diastolic ( $-dp/dt$ ;  $-8,287 \pm 444$  vs  $10,440 \pm 364$ ) 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 ( $6.7 \pm 0.8$  vs  $12.7 \pm 1.1\%$ ,  $P < .01$ ) 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.