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Relationship between Heat Failure Caused by Sympathetic Activation through Acquisition of Salt Sensitivity and Depression via Brain Sigma Receptors

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Summary

Depression often coexists with cardiovascular disease, such as hypertension and heart failure, in which sympathetic hyperactivation is critically involved. Reduction in the brain sigma-1 receptor (S1R) functions in depression pathogenesis via neuronal activity modulation. We hypothesized that reduced brain S1R exacerbates heart failure, especially with pressure overload via sympathetic hyperactivation and worsening depression. Male Institute of Cancer Research mice were treated with aortic banding and, 4 weeks thereafter, fed a high-salt diet for an additional 4 weeks to accelerate cardiac dysfunction (AB-H). Compared with sham-operated controls (Sham), AB-H showed augmented sympathetic activity, decreased % fractional shortening, increased left ventricular dimensions, and significantly lower brain S1R expression. Intracerebroventricular (ICV) infusion of S1R agonist PRE084 increased brain S1R expression, lowered sympathetic activity, and improved cardiac function in AH-H. ICV infusion of S1R antagonist BD1063 increased sympathetic activity and decreased cardiac function in Sham. Tail suspension test was used to evaluate the index of depression-like behavior, with immobility time and strain amplitude recorded as markers of struggle activity using a force transducer. Immobility time increased and strain amplitude decreased in AB-H compared with Sham, and these changes were attenuated by ICV infusion of PRE084. These results indicate that decreased brain S1R contribute the relationship between heart failure and depression in a mouse model of pressure overload.