Title: PTSD-Induced Alterations of Cardiac Homeostasis

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Introduction: Cardiovascular disease (CVD) is the leading cause of death in the United States. Multiple studies indicate that Post-Traumatic Stress Disorder (PTSD) is a risk factor for CVD. Accordingly, we hypothesize that PTSD-induced chronic inflammation increases macrophage numbers in the heart, leading to increased cardiac fibrosis and the resetting of cardiac homeostasis.

Methods: To induce experimental PTSD, C57BL/6 male mice (8 months old) were given an intermittent foot-shock (IFS; 1.0 mA, 1 sec duration) 5 times within a 6 minute span. Before each shock, a tone was played to act as the PTSD-associated trigger. Control animals were identical to experimental animals but did not receive the foot shock. At 13-weeks post-IFS, mice underwent open field and fear conditioning chamber behavioral assessments to measure PTSD symptomology. Plasma was collected to determine circulating cardiac troponin I (cTnI) levels. Based on cTnI, mice were separated into 3 groups: no IFS (controls), IFS mice with a slight increase in circulating cTnI (non-responders), and IFS mice that had significantly elevated cTnI (PTSD-like) compared to controls. At tissue sacrifice (13-weeks after IFS), the left ventricle (LV) was collected and perfused with cardioplegic to arrest it in diastole. The LV was fixed in paraformaldehyde and paraffin embedded for picrosirius red (PSR) staining and macrophage immunohistochemistry.

Results: Thirteen weeks after IFS, mice that displayed an elevation in circulating cTnI also demonstrated symptoms of intrusion ($p=0.03$) and alterations in arousal ($p=0.01$) in response to the PTSD trigger, mimicking clinical symptoms of PTSD. Mice that had a more subtle elevation in cTnI did not show significant alterations in behavior, classifying them as non-responders ($p=0.31$). PTSD-like mice had increased collagen ($p=0.03$) and macrophages ($p=0.02$) in the LV compared to controls and non-responders. Non-responders had elevated collagen ($p=0.02$), but not macrophage numbers ($p=0.19$) when compared to controls.

Conclusions: In conclusion, our data suggests that 13 weeks post-IFS, mice that illustrate PTSD-like symptomology have increased macrophages and deposition of cardiac fibrosis indicating increased cardiac remodeling compared to controls and non-responders.

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