Stress related neural activity: potential mechanism contributing to benefit of physical activity on heart failure incidence

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Background: We previously observed that: 1) physical activity (PA) decreases stress-related neural activity (SNA) in a dose-dependent manner and 2) resting SNA predicts incident heart failure (HF). Thus, we hypothesize that PA may decrease the risk of incident HF in part through its beneficial effect on SNA.

Methods: Self-reported PA data were acquired from Partners Biobank participants. Metabolic equivalent of task-minutes per week (MET*minutes/week) were calculated and participants were categorized according to their adherence to current PA recommendations (<500 and ≥500 MET-min/wk). In a subset with clinically indicated 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET) imaging (n=744), SNA was measured as a ratio of amygdalar to ventromedial prefrontal cortical activity. Subsequent HF and baseline CVD risk factor data were obtained using International Classification of Diseases Codes. Kaplan-Meier and Cox regression analyses were used to evaluate the relationship between PA vs HF risk. Mediation analysis was used to test whether PA’s impact on SNA significantly mediated the association between PA and HF.

Results: Among 50,363 participants (median age 59 years [IQR 42, 70], 40% male), 13,850 (11.6%) were diagnosed with HF over a median period of 3.1 years. PA within recommendations was associated with lower risk of subsequent HF (hazard ratio (HR) [95% confidence interval (CI)]: 0.849 [0.760, 0.948], p=0.004, Figure 1) in a model adjusted for CVD risk factors and history of myocardial infarction. As noted previously, higher SNA associated with higher risk of subsequent HF (HR [95% CI]: 1.34 [1.08, 1.66], p=0.007); and PA within guideline recommendations (vs.below) associated with lower SNA (Zscore ± SD: −0.14±0.92 vs 0.02±1, p=0.037). Moreover, mediation analysis shows that exercise reduces HF risk in part via reductions in SNA, accounting for 9% of the total relationship between exercise and HF risk (p<0.05, Figure 2).

Conclusion: PA associates with reductions in: A) stress-associated neural activity and B) subsequent HF risk. Moreover, the mechanism by which PA reduces HF risk may involve salutary effects on stress-related neural pathways.