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Intermittent Exercise Activates NRG1-SERCA2a Pathway to Improve Cardiac Function in Myocardial Infarction Rats

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Objective Intermittent exercise can improve cardiac function in rats with myocardial infarction. The Neuregulin-1(NRG1)/SERCA2a plays a critical role in maintain cardiac function. We want to investigate the effect of Neuregulin-1 (NRG1) on NRG1-SERCA2a signaling pathway activated by intermittent exercise and on improves cardiac function in rats with MI.

Methods 32 male sprague-dawley rats were randomly divided into four groups (n=8): Sham-operated group (S), sedentary MI group (MI), MI with interval training group (ME), ME with inhibitor AG1478 group (MA). ME and MA model after the MI model was established by ligation of the left anterior descending coronary artery, and began training 1 week after MI surgery. The S model only by threading without ligation. Rats in ME and MA model taken one week adaptive training, then began 8-week interval training. MA model were injected with inhibitor AG1478, once every two days. The 24h after training, rats were anesthetized, the LVSP, LVEDP, $\pm dp/dt$ max were tested by carotid artery intubation which in order to evaluate cardiac function. The protein expression of NRG1, PI3K, Akt, eNOS, PKG, PLN, SERCA2a in myocardium were measured by Westernblotting, themRNA expression of *serca2a* were tested by RT-qPCR.

Results Compared with S, the protein expression of NRG1, PKG, peNOS, pAkt, pPLN, pPI3K and SERCA2a decreased, *serca2a* mRNA expression decreased, LVSP and $\pm dp/dt$ max significantly decreased, LVEDP significantly increased; Compared with MI, the protein expression of NRG1, PKG, peNOS, pAkt, pPLN, pPI3K and SERCA2a increased, *serca2a* mRNA expression increased, LVSP and $\pm dp/dt$ max significantly increased, LVEDP decreased, and the effect of exercise were weakened by inhibitor AG1478. Correlation analysis showed that the myocardial pPLN and SERCA2a protein expression both were positively correlated with LVSP, $\pm dp/dt$ max, and negatively correlated with LVEDP.

Conclusions Intermittent exercise can increased myocardial NRG1 protein expression and activates NRG1-SERCA2a signaling pathway, improve myocardial infarction cardiac function.