Exercise suppresses apoptosis by stimulating IGF1/Akt and AMPK/SIRT1 survival signaling in the hippocampus of induced aging rats

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Abstract

Background: Aging is a natural phenomenon, the accumulation of molecular and cellular damage throughout life leads to age-related pathological condition. Extensive damage in the brain can cause neuronal dysfunction and trigger apoptosis. Exercise is presumed to delay the aging process and promote healthy since it seems to improve the function of most of the mechanisms involved in aging. Our purpose of this study was to evaluate the effects of exercise training on brain apoptotic and survival pathways in D-galactose-induced aging SD rats.

Material and Methods: Rats were allocated to the following groups：(1)young control group (control, n=6)；(2)young rats with swimming exercise group (exercise, n=6)；(3)aging control group (induced-aging, n=6), aging rats were induced and injected by the intraperitoneal injection of D-galactose (150mg/kg of body weight) which was dissolved in distilled water. D-galactose was injected at 6.00 P.M. once daily for 8 weeks to induce aging. (4)aging rats with swimming exercise group (aging-exercise, n=6). The exercise and aging with exercise were made to perform swimming exercise for 5 days per week gradual increases from the first week of every 20 min to 60 min for 8 weeks. Finally, the H&E stain and Western blotting were performed.

Results: The Fas-dependent apoptotic and mitochrondrial dependent apoptotic pathway components, such as Fas ligand, Fas, caspase 8, Bad, cytochrome C, caspase 9 and caspase 3, were all significantly increased in the induced-aging group relative to the control group whereas they were decreased in the aging-exercise group. The inflammation pathway marker, TNFα, p-NFκB, iNOS and COX-2, were mass expression in D-galactose-induced aging brain, exercise significantly inhibited the inflammatory signaling activity. The components of brain survival pathway (insulin-like growth factor I (IGFI), IGFI-receptor (IGFIR), phosphatidylinositol 3’-kinase (PI3K) and protein kinase B (Akt)) and the pro-survival Bcl-2 family proteins (Bcl-2 and Bcl-xL) were all significantly decreased in the induced-aging group compared with the control group whereas they were increased in the aging-exercise group. Additionally, the anti-aging pathway marker, p-AMPKα and SIRT1, were significantly reduced in D-galactose-induced aging group compared to those in the control group and obviously increased after exercise training.

Conclusion: This study demonstrated that exercise training not only reduced aging-enhanced brain apoptosis and inflammatory signaling activity, but also enhanced the IGF-I/Akt and SIRT1 survival pathways in the hippocampus from aging-exercise rats, which provides one of the new beneficial effects for exercise training in aging brain.

Results

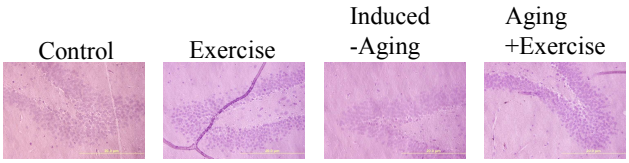

Figure 1. Representative results of hippocampus with HE staining.

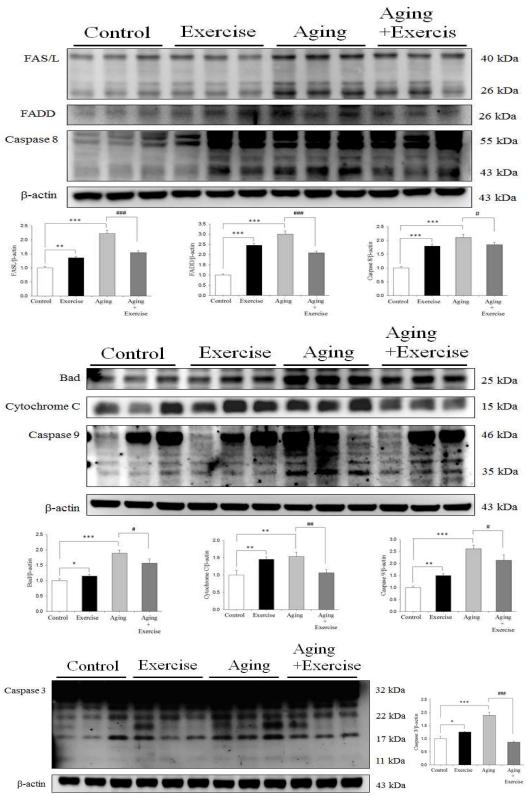

Figure 2. **Exercise training inhibited components of Fas-dependent and mitochondrial-dependent apoptotic pathways activation in hippocampus of D-galactose-induced aging rats.** The representative protein levels of Fas ligand, activated Fas receptor, FADD, activated Caspase 8, Bad, Cytochrome C, Caspase 9 and Caspase 3 prepared from hippocampal homogenates in the control, exercise, aging and aging+exercise rats were measured by Western blotting analysis.
*P＜0.05, **P＜0.01, ***P＜0.001 vs. Control ；#P＜0.05 , ##P＜0.01, ###P＜0.001 vs. Aging

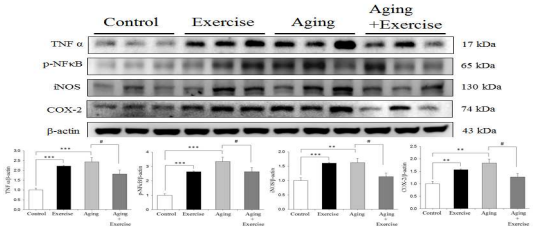

Figure 3. **Effect of exercise training on inflammatory proteins.** The representative protein levels of TNFα, p-NFκB, iNOS and COX2 prepared from hippocampi in the control, exercise, aging and aging+exercise rats were measured by Western blotting analysis.
*P＜0.05, **P＜0.01, ***P＜0.001 vs. Control； #P＜0.05, ##P＜0.01, ###P＜0.001 vs. Aging

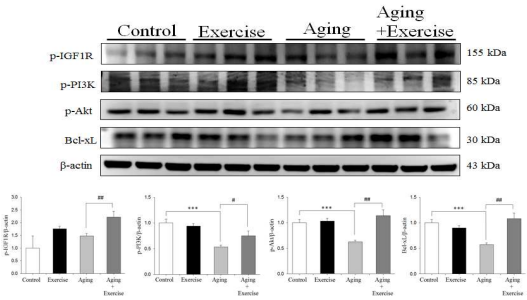

Figure 4. **Exercise training enhanced IGF1/Akt survival pathway in D-galactose-induced aging rat hippocampus.** The representative protein levels of survival proteins p-IGF1 receptor (p-IGF1R), p-PI3K, p-Akt and pro-survival Bcl family of Bcl-xL prepared from hippocampi in the control, exercise, aging and aging+exercise rats were measured by Western blotting analysis.
*P＜0.05, **P＜0.01, ***P＜0.001 vs. Control ；#P＜0.05 , ##P＜0.01, ###P＜0.001 vs. Aging

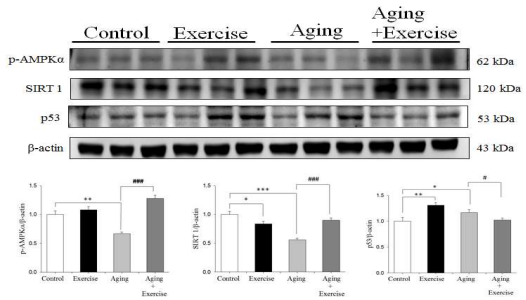

Figure 5. **Exercise training enhanced AMPK/SIRT1 anti-aging pathway in D-galactose-induced aging rat hippocampus.** The representative protein levels of p-AMPKα, SIRT1 and p53 prepared from hippocampi in the control, exercise, aging and aging+exercise rats were measured by Western blotting analysis.
*P＜0.05, **P＜0.01, ***P＜0.001 vs. Control ；#P＜0.05 , ##P＜0.01, ###P＜0.001 vs. Aging

Conclusion

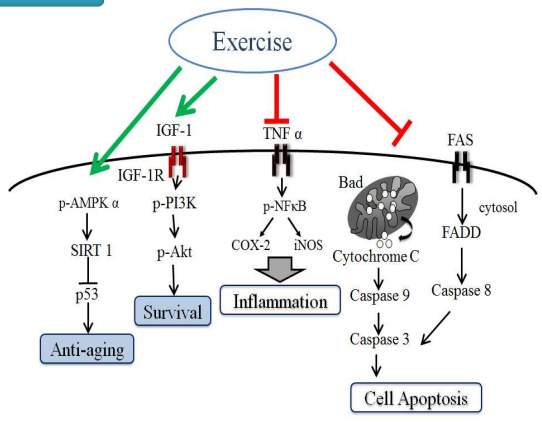

Figure 6. **The schematic representation exercise training not only ameliorates hippocampus apoptosis in D-galactose-induced aging rat by down-regulating the activities of Fas-dependent, mitochondrial-dependent apoptosis and inflammatory-related signaling pathways, but also enhanced the IGF/AKT and SIRT1 survival pathways.**