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Exogenous VD3 alleviates chronic fatigue syndrome by activating MEKs/ERKs-SIRT1 signaling pathway in skeletal muscle

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Objective To investigate the effects of exogenous VD3 on exercise-induced chronic fatigue syndrome (CFS) and its mechanism.

Methods 80 male mice were randomly divided into 5 groups ($n=16$). One group was named as quiet control group (C) while the other four were used to build CFS model by forced swimming. Among the four groups, three were selected for feeding VD3 1 h before exercise (bVD), 15 min after starting exercise (mVD) and 1 h after exercise (aVD) respectively, and the group without VD3 feeding was CFS model group (CFS). The behavior and condition of mice was observed during the whole process. After the training was completed totally, the tail suspension test and the forced swimming test were implemented, and then the blood and quadriceps were dissected. Serum testosterone and corticosterone content, as well as the antioxidant system indexes in the quadriceps, including malondialdehyde (MDA), total antioxidant capacity (T-AOC), glutathione peroxidase (GSH-PX) and total superoxide dismutase (T-SOD), were measured. Routine western blotting experimentation was used to measure signal pathway indicators, containing SIRT1, SIRT3, ERK1/2, p-ERK1/2 and MEK1/2.

Results Compared with C group, CFS group appeared serious damage caused by fighting, and the concentration of serum testosterone decreased significantly ($p<0.01$ or $p<0.05$) while cortisol concentration increased significantly ($p<0.01$ or $p<0.05$). Regarding antioxidant stress system indexes, the expression of MDA, T-SOD and GSH-PX significantly increased ($p<0.05$). The concentration of MEK and SIRT3 decreased significantly ($p<0.01$ or $p<0.05$). Compared with CFS group, VD intervention group (bVD, mVD and aVD) showed less damage caused by fighting and significantly lighter body weight ($p<0.05$), and the concentration of serum testosterone increased significantly ($p<0.05$) while that of cortisol decreased significantly ($p<0.01$ or $p<0.05$). The expression of MDA decreased significantly ($p<0.05$), on the contrary, T-AOC, T-SOD and GSH-PX increased significantly ($p<0.05$). The expressions of MEK, p-ERK/ERK, SIRT1 and SIRT3 were significantly upregulated ($p<0.01$ or $p<0.05$).

Conclusions Exogenous VD3 could alleviate CFS, which probably related to activate the MEKs/ERKs-SIRT1 signal transduction axis and hence regulate the expression of SIRT3.