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Optogenetics Active SNc DA Neurons Improve Locomotor Activity on Exercise-Induced fatigue Rats

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Objective After optogenetics activating SNc DANs, locomotor activity ability of exercise-induced fatigue rats were recorded to research the role of nigra-striatum DA system in central mechanism of motor control.

Methods Used male SD rats (220~240g), randomly divided into 6 groups: sham control group (SCG), optogenetics control group (OCG), fatigue group (FG), sham fatigue group (SFG) and optogenetics fatigue group (OFG). Virus were injected in the right SNc at coordinates (AP:-5.30 mm, R: 2.00 mm, H-8.00 mm). The SCG/SFG injected 1 μ l saline, OCG/OFG injected 1 μ l mixed virus(ChR2 with TH Cre,1:1), the fiber implantation site was deeper than the virus injection about 1 mm. Three weeks after surgery, rats attend 7D exhaustive treadmill exercise. After fatigue running, OCG/OFG/SCG/SFG were in the open field. We used two different light delivery schedules: 10 ms pulses at 20 Hz (10s) and 10 ms pulses at 3 Hz (10s). Sampling time were quiet state, 1D exhaustion, 7D exhaustion and recovery 24h. Animals were euthanized after completion of the behavioral tests. Brains were sectioned coronally in 50- μ m slices, images were taken using a fluorescence microscope and determined the anatomical location of the optical fiber.

Results (1) OCG/OFG obtain expression of ChR2 in DANs, this was not observed in SCG/SFG; Activation of OCG DANs with 20Hz increased the normalized mean global activity (laser on/laser off), and a significant increment in normalized mean global activity (laser on/laser off) when DANs were activated with 3Hz/20Hz in OFG ($p < 0.05$), showing successful transfection of OCG/OFG. (2) Stimulation at 20 Hz was sufficient to improve global activity, the effects of 3 Hz did not significant, showing 20Hz stimulation possibility be related to motor regulation. (3) The global activity and total distance of rats after 7D exhaustion were significantly lower than of quiet state ($p < 0.05$), the difference from the quiet state and after 24h recovery is not significant, indicating that the decline in locomotor ability caused by exercise induced-fatigue is reversible. (4) The 20 Hz stimulation significantly improved the global activity of 1D and 7D exhausted rats ($p < 0.05$), indicating that 20 Hz stimulation can effectively improve the rats locomotor activity with exercise-induced fatigue compared with 3 Hz stimulation.

Conclusions (1) ChR2 virus transfection can effectively active the nigra-striatum DA system, causing changes in motor performance and increasing the locomotor ability of rats; (2) The locomotor ability of rats with exercise-induced fatigue to decrease. The total distance and global activity decreased significantly with exercise-induced fatigue; (3) Photoactivation of SNc DANs can improve the locomotor activity of rats with exercise-induced fatigue. From the perspective of stimulating effect, 20Hz is the most obvious activation reference point (NSFC: 31401018, SKXJX: 2014014, Corresponding houlj@bnu.edu.cn).