P-28

MILD HEAT EXPOSURE STIMULATES PROLIFERATION OF NEURONAL STEM CELLS *IN VITRO*

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During exercise, the body core temperature increases by a few degrees. Our group has reported that constant exposure to moderate heat facilitates neuronal progenitor cell proliferation in the hypothalamus. Voluntary exercise also promotes the proliferation of neuronal progenitor cells in the hypothalamus and hippocampus.

In this study, we investigated whether temperature has any direct effects on proliferation of neuronal stem cells (NSCs). To evaluate the effects of mild heat exposure on proliferation of NSCs *in vitro*, NSCs obtained from 14.5-day-old rat embryos were propagated as neurospheres at two different temperature conditions: 37°C and 38.5°C. Cell viability was measured, the diameter of neurospheres was analyzed and the number of cells from dissociated neurospheres were counted.

Mild heat exposure increased cell viability, cell count and the diameter of neurospheres. Moreover, the phosphorylation of CREB (cAMP response element-binding protein) and mRNA levels of brain-derived neurotrophic factor (BDNF) were higher in cells cultured at 38.5°C than those cells cultured at 37°C. Furthermore, the mRNA levels of heat shock protein 27 (HSP27) and 70 (HSP70) were increased after mild heat exposure while the mRNA level of HSP90 remained unchanged.

These data suggest that treatment with mild heat stimulates the proliferation of NSCs *in vitro* possibly by activating CREB, inducing BDNF and heat shock protein mRNAs. The direct effects of temperature on NSCs might be one of the mechanisms involved in heat-induced and exercise-induced neurogenesis.

Keywords: Heat acclimation, Neurogenesis, Heat shock proteins, CREB, BDNF

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