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CASTRATION CAN ACT VIA TESTOSTERONE DEPLETION TO PROTECT MICE FROM HEAT-INDUCED HYPOTHALAMIC APOPTOSIS AND DEGENERATION

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Background- Heatstroke is characterized by hyperpyrexia, multiple organ failure, and predominant central nervous system dysfunction. Many evidences showed that testosterone exhibits the negative effects on many disease models such as sepsis, shock and severe injury. However, it remains unknown on the heatstroke animal model. Here we demonstrated castration can protect mice from heat-induced hypothalamic neuronal damage and lethality. **Procedure** - ICR male mice (6- to 8-wk-old) were random divided into four groups. The first group of mice was exposed to room temperature and used as normothermic controls. Another three groups: sham-operated mice, castrated mice with vehicle treatment, and castrated mice with testosterone replacement, were all subjected to whole body hyperthermia (WBH) at 41.2°C for 1 hour and then allowed to recover at room temperature (25°C). Mice that survived on day 4 of heat treatment were considered survivors. Plasma concentration of testosterone was measured by enzyme immunoassay. For heat-induced apoptotic study, mice were sacrificed at 2.5 hours post-WBH to excise the organs for TUNEL assays or H-E staining. **Results** – The fraction survival and core temperature of sham-operated mice at + 4 h post-WBH were found to be 5/15 and 34.4°C±0.3°C, respectively. Castration decreased the plasma levels of testosterone almost to zero, protected the mice from heat-induced death (fraction survival, 13/15) and reduced the hypothermia (core temperature, 37.3°C). The beneficial effects of castration in lethality and hypothermia can be significantly reduced by testosterone replacement. Heat-induced apoptosis (indicated by TUNEL) and neuronal damage (indicated by cell shrinkage and pyknosis of nucleus) in the hypothalamus were significantly prevented by castration and also reversed it by testosterone supplement. **Conclusions** - Castration can act via testosterone depletion to protect mice from heatstroke-induced hypothalamic apoptosis, degeneration and lethality. (The experimental protocol has been approved by the Animal Ethic Committee of Chi Mei Medical Center under guidelines of NIH publication No.85-23, revised 1996).