A PERIPHERAL AND CENTRAL CHOLINERGIC PATHWAY MODULATES STRESS-INDUCED HYPERTHERMIA IN THE RAT EXPOSED TO AN OPEN FIELD

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Exposure to an open-field is psychologically stressful and leads to an elevation in core temperature (T_c). We suspect that peripheral and central cholinergic pathways modulate T_c during open field exposure and other types of stress. We recently found that methyl scopolamine (MS), a peripheral muscarinic antagonist, had an antipyretic effect on stress-induced elevations in T_c caused by handling and cage-switch stress. Pyridostigmine (PYR), an inhibitor of acetylcholinesterase activity (AChE) that leads to cholinergic stimulation in peripheral tissues, should reverse the effects of MS on T_c during open field stress. Two experiments were performed to assess the role of peripheral and central cholinergic receptors in the control of open field hyperthermia. In the first experiment, we assessed the effects of MS and PYR on open field hyperthermia**.** Male, Sprague Dawley rats at 90 days of age were housed individually at an ambient temperature (T_a) of 22°C. T_c and motor activity (MA) were monitored with radiotelemetry units implanted under Nembutal anesthesia (50 mg/kg; IP) at least 10 days prior to testing. The open field chamber consisted of an illuminated Plexiglass box (61 $\times$ 61 $\times$ 61 cm) maintained at a T_a of 22°C. Rats were dosed IP at 1200 hr with saline, 1.0 mg/kg MS, 0.1 mg/kg PYR, or a combination of MS and PYR and placed immediately inside the open field chamber for 60 min. T_c of rats injected with saline increased by 0.7°C during open field exposure. The hyperthermic response to open field exposure was suppressed immediately by MS and enhanced by PYR. T_c increased by 0.3°C in the MS-treated animals. The hyperthermic response in the PYR group was nearly 0.6°C above that of rats dosed with saline. In addition, co-administration of PYR and MS led to a T_c response identical to that of rats injected with saline. In the second experiment, we assessed if a low dose of the organophosphate pesticide chlorpyrifos (CHP) would alter open field hyperthermia with and without administration of MS. CHP irreversibly inhibits AChE and leads to cholinergic stimulation in the CNS and peripheral tissues. At 900 hr the rats were gavaged with corn oil or 10 mg/kg CHP. This CHP treatment had no effect on resting T_c or MA. The rats were then dosed IP with saline or 1.0 mg/kg MS at 1200 hr and subjected to open field stress for 1 hr. T_c of the corn oil/saline group underwent a 1.2°C increase during open field exposure, whereas T_c of the CHP/saline group was significantly attenuated. Administration of MS attenuated the open field hyperthermia of rats treated with corn oil and CHP. We expected that a low dose of CHP would have a similar effect on open field hyperthermia as did PYR. However, CHP attenuated the hyperthermic response. Overall, activation of peripheral muscarinic receptors modulates the magnitude of hyperthermia during open field exposure. CHP leads to peripheral and central cholinergic stimulation. Since CHP attenuated open field hyperthermia, it appears that central cholinergic suppresses the hyperthermic response to open field exposure.

This abstract does not necessarily reflect EPA policy.

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