THERMOREGULATION, SIDS AND THE UPPER AIRWAY

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Background - Thermal stress is a risk factor for the Sudden Infant Death Syndrome (SIDS). Apnea may precipitate the final sequence of events that leads to SIDS, and the laryngeal chemoreflex (LCR) is a common cause of apnea in infants. Hyperthermia prolongs the LCR in decerebrate neonatal piglets and anesthetized neonatal rats. This thermal response originates from heating in the region of the nucleus of the solitary tract (NTS), and the reflex mechanisms responsible for prolonging the LCR depend on release of gamma-aminobutyric acid (GABA). Activation of presynaptic adenosine A$_{2A}$ (Ad-A$_{2A}$) receptors tends to enhance GABAergic activity. Moreover, adenosine antagonists shorten and Ad-A$_{2A}$ agonists prolong the LCR under normothermic conditions. Therefore, we tested the hypotheses that 1) enhanced GABAergic activity in the NTS would prolong the LCR even under normothermic conditions; 2) an Ad-A$_{2A}$ receptor antagonist would prevent thermal prolongation of the LCR when injected unilaterally within the nucleus of the solitary tract (NTS); and 3) an Ad-A$_{2A}$ agonist, working through GABAergic mechanisms, would prolong the LCR under normothermic conditions.

Procedure - We studied decerebrate piglets aged 4-13 days. We elicited the LCR by injecting 0.1 ml of water into the larynx and recorded integrated phrenic nerve activity. Thermal prolongation of the LCR was elicited by warming the entire animal by ~ 2ºC, and drugs (a GABA reuptake inhibitor - nipecotic acid, an Ad-A$_{2A}$ antagonist - SCH-58261 or an Ad-A$_{2A}$ agonist – CGS-21680) were injected into the region of the NTS.

Results - The LCR was prolonged when the body temperature of each piglet was raised ~ 2ºC, and the Ad-A$_{2A}$ antagonist reversed the thermal prolongation of the LCR when injected into the NTS. Enhanced activity of GABA resulting from focal injection of nipecotic acid in the NTS prolonged the LCR. Focal injection of an Ad-A$_{2A}$ agonist into the NTS prolonged the LCR as well. Injections of vehicle alone into the NTS did not alter the duration of the LCR.

Conclusions - Hyperthermic activates GABAergic mechanisms in the region of the NTS that prolong the LCR. Adenosinergic processes, working through Ad-A$_{2A}$ receptors, modulate this GABAergic process and may amplify or attenuate the thermal prolongation of the LCR. Modulation of adenosinergic processes may provide an attractive pharmacological mechanism of reducing the risk of neonatal apnea and possibly of SIDS. Supported by NICHD grants 36379 and 42707.