THE BRAINSTEM, SIDS, AND THERMOREGULATION

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Background - Overheating and over bundling are important epidemiological risk factors for the Sudden Infant Death Syndrome (SIDS). Many SIDS Infants have decreased 5-HT1A receptor binding and increased numbers of serotonergic (5-HT) neurons in the medullary raphe and adjacent regions of the brainstem important for modulating many autonomic functions, including thermoregulation. The medullary raphe contains 5-HT neurons that project to the spinal cord; evidence suggests that they contribute to sympathetic outflow controlling brown adipose tissue (BAT) metabolism, peripheral vasoconstriction, and heart rate (HR). It is less clear whether raphe 5-HT neurons contribute to shivering, a major source of thermoregulatory heat production. We hypothesized that local activation of 5-HT1A receptors, presumably decreasing 5-HT neuronal activity, would decrease shivering, HR and vasoconstriction induced by cooling.

Procedure - We studied 6-15 day old piglets, chronically instrumented to measure EEG, EOG, nuchal EMG, ECG, surface and core temperatures. Neurochemicals were dialyzed directly either unilaterally into the more lateral paragigantocellularis lateralis (PGCL) or into the midline medullary raphe. Studies were performed in a temperature controlled whole body plethysmograph. Animals were cooled to approximately 5 °C below the lower threshold of their TNZ. After a control period of artificial CSF (aCSF) dialysis, either aCSF was continued or 8-OH-DPAT (DPAT), a selective 5-HT1A agonist, was dialyzed for 20 minutes, followed by a post control period of aCSF dialysis. Results - Dialysis of DPAT into either the raphe or adjacent PGCL abolished REM sleep and decreased shivering, HR, body temperature, and ear vasoconstriction. The effects of DPAT dialysis were abolished by prior local dialysis of WAY 100635, a selective 5-HT1A antagonist.

Conclusions - The results of these studies, and those of other investigators, support the hypothesis that 5-HT1A receptors located in the medullary raphe are important in the regulation of a number of thermoregulatory mechanisms, including BAT metabolism, vasoconstriction, and shivering. There is some evidence that 5-HT1A receptors provide an inhibitory feedback mechanism to prevent excessive 5-HT production. We speculate that decreased binding to these receptors in SIDS infants may allow excessive 5-HT activity when stressed leading to overheating. NIHCD 36379; First Candle SP30.