Title: POST ANESTHETIC SHIVERING IN PRIMATES: EFFECTS OF LOW BODY TEMPERATURE, SKIN WARMING AND NEUROTRANSMITTERS

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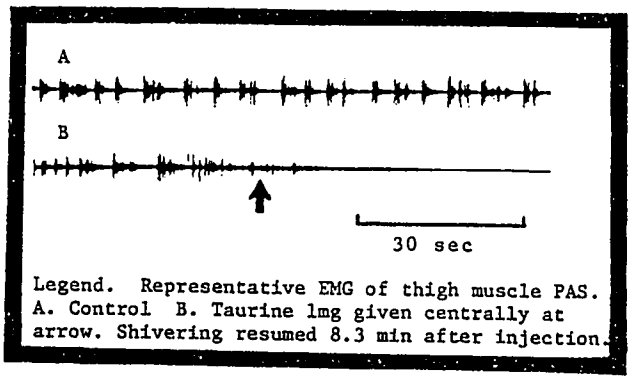
Introduction Post-anesthetic shivering (PAS) is a well-known clinical phenomenon. The many potential deleterious effects of PAS include hypoxia, which can be critical in patients with compromised cardiopulmonary systems, and damage to operative structures. A number of causative factors in PAS have been suggested, including: specific anesthetic agent(s), duration of anesthesia, type or site of surgical procedure, degree of fall in body temperature, alteration of central thermoregulatory set-point, and age, body weight and sex characteristics. However, basic research into determinants of PAS when uncomplicated by surgery and using specific physiological or pharmacological interventions has not been pursued. The experiments on a subhuman primate model described below were designed to determine: 1) if decreases in core temperature induced by halothane are associated with shivering, 2) if PAS has characteristics in common with cold-induced shivering seen in other situations, 3) if stimulation of peripheral warm receptors alone can inhibit PAS and 4) if administration of certain putative neurotransmitters known to alter thermoeffector activity can be used to control PAS.

Methods Nine squirrel monkeys (Saimiri sciureus) 7-14 yrs of age were tested in a thermoneutral environment (23°C). No preanesthetic agent was administered. Anesthesia was induced via face mask. The monkeys were then intubated (2.0 mm endotracheal tube) and maintained with 2-3% halothane and N_2O for 30 min. Electrical activity of thigh muscles was recorded using a dual EMG electrode assembly. Rectal and tail skin temperature were recorded continuously (YSI probes, #401 & 409). Heart rate was monitored via ECG electrodes. Physiological parameters were recorded using a Grass Instruments polygraph model 7 PCM12 equipped with an integration channel for EMG activity. Respirations were counted for 20 sec every 5 min throughout the procedure. A heat lamp and/or an electrical heating pad were used to maintain body temperature during anesthesia in certain experiments. Test substances were injected centrally via a chronic cannula (Kopf Instruments #201) implanted into a lateral cerebral ventricle, and were administered according to a random assignment of treatments.

Results/Discussion All animals in which body temperature was allowed to fall (avg. 2.5°C) during anesthesia developed significant shivering that was characteristic in gross electrographic appearance (magnitude and frequency) to cold-induced shivering.[1] Since no animal shivered when deep body temperature was maintained at pre-induction levels (38.5-39.5°C), PAS may have been driven primarily by low core temperature. Shivering ceased immediately after a heat lamp was directed upon the animals and resumed within 3 sec after the lamp was removed even though there was no change in the low core temperature (35.5 - 36.5°C). The powerful and immediate overriding effect of peripheral heat receptors on shivering is remarkable, and it suggests one practical method of PAS control. Central injection of α-MSH (100-300ug), an endogenous neuropeptide known to be antipyretic in low central and peripheral doses and to predominantly block heat conservation pathways when given in higher doses,[2] had no effect on shivering. This result suggests that pathophysiological events common to fever and/or tissue destruction are not responsible for shivering in these unoperated animals. On the other hand, central injection of the sulfonated inhibitory neurotransmitter taurine (1 mg), which affects both heat production and conservation,[3] delayed the onset of shivering in certain pretreatment experiments and abolished PAS within 30 sec in others.

Summary The results indicate that the effector mechanisms involved in PAS include central activation of heat production pathways, and that agents such as the amino acid taurine, which block heat production pathways, may be useful in controlling the shivering. We recognize that the results of these experiments may not apply to all instances of PAS. Surgery, additional medications and different anesthetics undoubtedly contribute to PAS and perhaps account for shivering in certain normothermic and hyperthermic patients. Conversely, such factors may also contribute to the lack of shivering seen in markedly hypothermic post-surgical patients. Identification of peripheral pathology and possible drug interactions responsible for shivering and/or its absense will require additional systematic basic research. (This work supported in part by NS 10046.)



Legend. Representative EMG of thigh muscle PAS. A. Control B. Taurine 1mg given centrally at arrow. Shivering resumed 8.3 min after injection.

References

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3. Clark SM, Lipton JM: Hypothermia produced in aged squirrel monkeys by central administration of taurine. Exp Aging Res 7:1, 17-24, 1981