
Media Contact: Mindy Baxter

214-648-3404

melinda.baxter@email.swmed.edu

STRESS DOES NOT CAUSE PYRIDOSTIGMINE TO ENTER THE BRAIN

DALLAS – May 18, 2000 – Stress does not cause Pyridostigmine Bromide (PB) to enter the brain and therefore did not contribute to the Gulf War syndrome through this mechanism, according to UT Southwestern Medical Center at Dallas researchers.

In the “Highlight” section of the May issue of *Toxicology and Applied Pharmacology*, Dr. Christopher Sinton and colleagues report that, when administered to rats PB enters the brain in only small amounts but, when the rats are exposed to severe stress, the amount of PB entering the brain decreases. This finding is important because it contradicts an earlier study from Hebrew University in Jerusalem, Israel, suggesting that stress dramatically increased the entry of PB into the brain of experimental animals and thus might explain the symptoms of Gulf War veterans.

The UT Southwestern study is the fourth study published in peer-reviewed scientific journals to contradict the original Israeli finding. Also in the May issue of this journal researchers from the Israel Institute for Biological Research, unrelated to the original Israeli researchers, published similar findings failing to replicate the original Israeli study in mice. The same results were published by researchers from Brookhaven National Laboratory, New York, in 1999 and by French Army researchers in 1998.

The UT Southwestern study also demonstrates that regardless of whether animals are stressed, PB enters the brain in small amounts in proportion to the dose administered. This explains how PB might have contributed to any brain damage underlying Gulf War veterans’ symptoms even though stress did not augment its effect.

“This is the fourth of four published studies to show that stress does not cause PB to flood into the brain and cause brain damage,” said Dr. Sinton. “Contrary to popular medical assumptions, however, PB does get into the brain in small amounts normally and could have contributed to brain damage. It is just that stress is not a factor in this process.”

Of the 700,000 U.S. troops deployed to the Gulf War, an estimated 500,000 received PB tablets to protect from nerve gas exposure. Soon after the war the high rate of illness in Gulf War veterans without objective signs of disease was assumed to be a

psychological reaction to stress. The original Israeli study suggesting that stress increased penetration of PB into the brain gave strong backing to the role of stress.

Subsequently, however, UT researcher Dr. Robert Haley, a co-author of the new UT Southwestern study, demonstrated that the psychological studies leading to the stress theory were flawed and had failed to implicate stress in causing the veterans' illnesses.

“Our new findings, along with those from the three other negative studies, appear to have removed the last remaining scientific support for stress as a cause of the symptoms,” Haley concluded.

In the UT Southwestern study the researchers administered PB to two strains of rats with and without three types of stress-producing conditions. These included forced swimming, heat stress and restraint stress. All three types of stress were shown to increase the production of stress hormones in the rats, confirming that they were severely stressed. But each of the three stressful conditions, as well as the combination of forced swimming and restraint stress, caused the entry of PB into the brain to decrease, not increase.

References

Sinton CM, Fitch TE, Petty F, Haley RW. Stressful manipulations that elevate corticosterone reduce blood-barrier permeability to pyridostigmine in the rat. *Toxicology and Applied Pharmacology* 2000;165:88-105.

Grauer E, Alkalai D, Kapon J, et al. Stress does not enable pyridostigmine to inhibit brain cholinesterase after parenteral administration. *Toxicology and Applied Pharmacology* 2000;164:301-304.

Lallement G, Foquin A, Baubichon D, et al. Heat stress, even extreme, does not induce penetration of pyridostigmine into the brain of guinea-pigs. *Neurotoxicology* 1998; 19:759-766.

Telang FW, Ding YS, Volkow ND, et al. Letter to the editor. *Nuclear Medicine and Biology* 1999; 26:249-250.