BMJ Helping doctors make better decisions

NEWS

Stress may disturb the blood-brain barrier

BMJ 1996; 313 doi: 10.1136/bmj.313.7071.1505a (Published 14 December 1996)
Cite this as: BMJ 1996;313:1505.2

Severe stress can disturb the blood-brain barrier that protects the brain from drugs and other chemicals that enter the circulatory system, say Israeli researchers. Their discovery may help to explain why soldiers given the drug pyridostigmine to protect against nerve gas poisoning during the Gulf war reacted differently from soldiers given the drug in peace time.

Professor Hermona Soreq, a neurobiologist at Jerusalem's Hebrew University, and Dr Alon Friedman, a neurosurgeon at Beersheba's Soroka Hospital who was a doctor in Israel's defence forces during the Gulf war, reported their research in Nature Medicine (1996:2:1382-5). They caused severe stress in a group of mice by forcing them to swim for eight minutes and then injected them with pyridostigmine. The drug was found in the brain cells in the mice in the experimental group but not in those in a comparable control group. After this surprising finding, the researchers tested other substances, including dyes, and these too entered the brain in stressed animals.

The brain is unique among organs in that, due to an elaborate membrane structure, few chemicals have been known to pass into it from the blood. Pyridostigmine, an inhibitor of the neurotransmitter carbamate acetylcholinesterase, has been regarded as the most effective drug for protecting people exposed to nerve gas and was believed not to cause central nervous system symptoms because it “did not permeate” the blood-brain barrier.

However earlier research had shown that Israeli soldiers given pyridostigmine during the Gulf war showed a greater than threefold increase in the frequency of reported central nervous system symptoms than soldiers given the same regimen during clinical trials. This increase was not due to enhanced absorption or decreased elimination of the drug.

This latest research in mice supports the theory that the stress situation associated with war induces disruption in the blood brain barrier and allows pyridostigmine to penetrate the brain. “These findings suggest that peripherally acting drugs administered under stress may reach the brain and affect centrally controlled functions,” the authors say.

The authors also postulate that changes to the blood-brain barrier may explain the vulnerability of stressed animals to viral infections of the central nervous system. And further understanding of the mechanisms underlying these alterations in the permeability of the blood-brain barrier may have far reaching clinical implications with regard to the delivery of drugs or gene therapy agents to the brain.—JUDY SIEGEL-ITZKOVICH, medical correspondent, Jerusalem Post