Title : HETEROGENEOUS LOCAL BRAIN METABOLIC EVENTS DURING LIDOCAINE SEIZURES

Authors : M. Ingvar, M.K. and H.M. Shapiro, M.D.

Affiliation: Department of Anesthesia, Veterans Administration Hospital, San Diego, University of California, San Diego, La Jolla, California, 92093, University of Lund, Lund, Sweden

Introduction. Lidocaine in low doses has an anticonvulsant action and reduces cerebral metabolic rate (CMR); in higher doses it causes seizures and increases overall CMR by 12%. Electroneurophysiologic studies indicate that the lidocaine seizure focus is within the hippocampus. Such localized brain electrical activity could be expected to cause marked heterogeneity in brain metabolism which cannot be tested in studies of overall CMR (above). Utilizing a quantitative autoradiographic technique for determining the metabolic rate for glucose (1-CMRg), we report localized areas of CMR reduction and increase during lidocaine seizures.

Methods. Following surgical preparation with halothane anesthesia and local lidocaine infiltration, halothane was withdrawn and two groups of rats (n=7) stabilized under 60% nitrous oxide, 40% oxygen anesthesia for 20 minutes prior to determination of 1-CMRg. Muscle relaxation was obtained with gallamine (6 mg q 20 min) and both groups of rats ventilated to obtain the following blood gas status: PaO_2=166 mmHg, $PaCO_2$=36.5 mmHg and pHa 7.43. During lidocaine infusion, the arterial pressure fell to 63±1mmHg while it was 142±8mmHg ($p<.01$) in the control group. The electroencephalogram (EEG) was monitored continuously with biparietal needle electrodes and the convulsive dose of lidocaine (20mg/kg) given intravenously to obtain a burst suppression pattern. Additional doses of lidocaine (4mg/kg) were given to maintain this pattern throughout the 30 min. period required for 1-CMRg determination. Seizures were established 3-5 min. prior to infusion of ^{14}C-2-deoxyglucose. Statistical significance is considered to be at $p<.01$ as determined with student's unpaired "t-test".

Results. 1-CMRg measured in 25 brain structures is summarized in Figure 1. In 15 areas 1-CMRg was significantly reduced by about 20% to 60%. These metabolic depressions occurred over large areas of the cerebral cortex and included many brain stem nuclei. Two structures, the hippocampus and the choroid plexus, significantly increased 1-CMRg by 23% and 65% respectively.

Discussion. Our major finding is that marked localized increases in brain metabolism can accompany lidocaine induced seizures. This demonstration may explain the very small increase in CMR previously reported in studies determining metabolic rate for the entire brain. The increase in hippocampal 1-CMRg of over 200% is compatible with that determined during generalized continuous seizure activity (200-300%). These results point out the requirement for localized brain metabolic measurements when evaluating the consequences of nongeneralized seizure activity. Since the hippocampus is recognized to be extremely vulnerable to hypoxia, therapy should be immediately directed to suppressing lidocaine induced hippocampal discharges which we have found to cause a marked metabolic demand upon that brain structure. The mechanism for increased choroid plexus metabolism is not known; however, we have previously reported enhanced metabolism in that structure during seizures caused by enflurane.

Figure 1. Local cerebral metabolic rate of glucose (1-CMRG) for 25 structures expressed as per cent change from awake values. NS=non-significant ($p > .01$). All other structures were significantly different ($p < .01$) from awake values.