

TITLE: ELECTRICAL CORRELATES OF BRAIN INJURY RESULTING FROM SEVERE HYPOTENSION AND HEMODILUTION

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INTRODUCTION: Both controlled hypotension (HT) and hemodilution combined with hypotension (HD/HT) have been used to reduce surgical blood loss and transfusion requirements. These techniques can put the brain at risk by decreasing oxygen delivery. We sought to define the threshold and electrical correlates of brain injury induced by HT, HD and HD/HT in a non-human primate model. The electroencephalogram (EEG) and somatosensory (SEP) and auditory (AEP) evoked potentials were compared to the degree of stress imposed and eventual neuropathologic outcome.

METHODS: Forty-one male monkeys (*M. fascicularis*, mean body wt 3.9 kg) were anesthetized with halothane in O₂, paralyzed, intubated, and ventilated mechanically to achieve a PetCO₂ of 35 mm Hg. Anesthesia was maintained with 0.8% halothane in 50% O₂-50% N₂. Arterial blood gases and hematocrit (hct) were measured every 10 min during the three experimental periods: control, stress and recovery. Acid-base status was maintained normal by adjusting minute ventilation and giving NaHCO₃ solution. Temperature was controlled at 37.4 ± 0.7 (SD) °C. Six EEG leads were implanted in the skull in a bilateral parasagittal array. Power spectral analysis of the EEG was performed on-line and recorded as a time-compressed array. SEPs were elicited by percutaneous electrical stimulation of the left superficial radial nerve, recorded from the right parietal electrode referred to an electrode at the nose, and averaged by computer. AEPs were elicited by binaural clicks and recorded from a vertex electrode referenced to an electrode at the mastoid process. After control recordings, hypotension was induced in the HT group (n = 10) using trimethaphan (1.2-10 mg/kg IV bolus). After the 30-min hypotensive period, blood pressure was restored by infusion of lactated Ringer's solution and 0.01% phenylephrine when necessary. The HD group (n = 4) was hemodiluted by withdrawing a predetermined blood volume and replacing 3:1 with lactated Ringer's solution. In the HD/HT group (n = 23), the added stress of hypotension was induced with trimethaphan. HD and HD/HT animals were resuscitated following the 30-min stress period by

reinfusion of blood and pressor support when necessary. Four animals which served as controls were not given trimethaphan or hemodiluted. Three days after the experimental period electrical recordings were repeated under the same anesthetic conditions and then the brain was perfusion fixed for histopathologic examination.

RESULTS: One control, 3 HT and 7 HD/HT animals died prior to the 3 day post-stress recording period. Diffuse edema and cerebellar tonsillar herniation were found in these animals. Of the 3-day survivors, none of the control HD or HT animals had evident brain cell injury despite hct's in the HD group ranging from 11 to 15% and mean arterial blood pressures (MABP) in the HT group ranging from 17 to 36 mm Hg. Of the animals surviving HD/HT (ranges: MABP 19-37 mm Hg, hct 12-20%), 44% showed multifocal ischemic changes in cerebrum, cerebellum and basal ganglia. High frequency EEG activity was decreased in intensity during hypotension to similar degrees in the HD and HD/HT groups. Neurologic outcome, therefore, could not be predicted on the basis of EEG changes alone. Comparison of evoked potential amplitudes showed that the depression of SEP wave P₂ (latency 12 ms) correlated best with the degree of hypoxic insult to the brain. The mean P₂ amplitude was depressed more during the stress period in surviving animals with subsequent brain injury (60 ± 21% [SD]) than in non-injured animals (22 ± 15%). No surviving animal maintaining a P₂ amplitude greater than 53% of control incurred brain damage; half of the survivors whose P₂ amplitude did decrease below this level did sustain brain injury. In all groups P₂ amplitude returned to control by 3 days post-stress, showing no correlation with the existing cellular injury at that time.

CONCLUSIONS: There appears to be a threshold for hypoxic brain injury which can be approximated for combinations of hypotension and hemodilution. The SEP can indicate the degree of hypoxic stress imposed and may indicate when a subject is at substantial risk of brain injury.

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