Title: CEREBRAL EFFECTS OF SUCCINYLCHOLINE IN DOGS HAVING DISRUPTED BLOOD-BRAIN BARRIER

Authors: W. L. Lanier, M.D. and J. H. Milde

Affiliation: Department of Anesthesiology, Mayo Clinic and Mayo Medical School, Rochester, MN 55905

Introduction. In lightly anesthetized subjects having normal brain and intact blood-brain barrier (BBB), i.v. succinylcholine (SCh) produces EEG activation and increases in cerebral blood flow (CBF).[1] These effects have been attributed to factors other than a direct stimulation of cerebral neurons, for SCh does not cross the BBB.[1] In contrast, when SCh is placed topically on the cerebral cortex, the drug produces seizures.[2] This suggests that i.v. SCh may produce intense cerebral stimulation or seizures if the drug is allowed to bypass the BBB and come into direct contact with neuronal elements. The present study tested that hypothesis by examining the cerebral effects of SCh versus placebo in dogs having osmotically disrupted BBB.

Methods. Twelve dogs weighing 10.7 + 0.5 kg (mean + SE) were anesthetized with 0.87% end-expired halothane (1.0 MAC), the trachea was intubated without the use of relaxants, and ventilation was controlled. Cannulae were inserted into a femoral artery for blood sampling and mean arterial pressure (MAP) measurements, and into femoral and peripheral veins for fluid and drug administration. PaO_2 was maintained near 150 mmHg, $PaCO_2$ near 40 mmHg, and esophageal temperature near 37°C. Sodium bicarbonate was given as needed to maintain buffer base near 40 $mEq \cdot l^{-1}$. Phenylephrine 40 $\mu g \cdot ml^{-1}$ in saline was given i.v. if needed to prevent the tendency to hypotension with the administration of mannitol and Evans blue dye. CBF was measured by direct cannulation of the sagittal sinus, and cerebral metabolic rate for O_2 consumption ($CMRO_2$) was calculated as the product of CBF and the arterial to sagittal sinus O_2 content difference.[1] The EEG was recorded from bifrontal, biparietal, and bioccipital electrodes. Following control measurements, each common carotid artery was injected with mannitol 25% 2.0 $ml \cdot kg^{-1}$ (1 dog per group) or 3.0 $ml \cdot kg^{-1}$ (5 dogs per group). Three minutes later, dogs received either SCh 1.0 $mg \cdot kg^{-1}$ i.v. (N=6) or saline placebo (N=6). Disruption of the BBB was confirmed by i.v. injection of Evans blue dye 3%, 4 $ml \cdot kg^{-1}$ at 15 min after SCh or placebo injection, and examination of the brains at the conclusion of the study. Unpaired t tests were used to compare data between groups, and $p < 0.05$ was considered significant.

Results. The SCh- and placebo-treated groups were well matched for control cerebral and physiologic variables. Control values in the placebo-treated group were MAP = 97 + 4 mmHg, CBF = 70.4 + 6.4 $ml \cdot 100g^{-1} \cdot min^{-1}$, and $CMRO_2$ = 3.88 + 0.17 $ml \cdot 100g^{-1} \cdot min^{-1}$. Control values in the SCh-treated group were MAP = 100 + 3 mmHg, CBF = 66.9 + 4.6 $ml \cdot 100g^{-1} \cdot min^{-1}$, and $CMRO_2$ = 3.64 + 12 $ml \cdot 100g^{-1} \cdot min^{-1}$. Intracarotid mannitol plus i.v. SCh produced a transient cerebral hyperemia to a peak CBF value of 116.6 + 8.5 $ml \cdot 100g^{-1} \cdot min^{-1}$ at 1 min after i.v. SCh. There were no $CMRO_2$ increases, prolonged EEG activation, or EEG spike and wave activity denoting intense cerebral stimulation or seizures. This effect was similar to the effect of intracarotid mannitol plus i.v. placebo (Fig). All 12 dogs had intraparenchymal Evans blue dye at autopsy, indicating BBB disruption.

Discussion. The cerebral effects of the relaxant d-tubocurarine and the antibiotic penicillin are both enhanced in the presence of BBB disruption, resulting in CBF increases and seizures, respectively.[3,4] In contrast, our study demonstrated no enhancement of the reported cerebral stimulating effects of SCh when given after BBB disruption. Specifically, i.v. SCh is not a convulsant when given in the presence of a normal brain having disrupted BBB.

References.

1. Lanier WL, Milde JH, Michenfelder JD: Cerebral stimulation following succinylcholine in dogs. Anesthesiology 64:551-559, 1986
2. Tan U: Electrocorticographic changes induced by topically applied succinylcholine and biperiden. Electroencephalogr Clin Neurophys (suppl) 42:252-258, 1977
3. Vesely R, Hoffman WE, Gil KSL: Cerebrovascular effects of curare and histamine in the rat. Anesthesiology 65:A336, 1986
4. Dobell ARC, Wyant JD, Seamans KB, Gloor P: Penicillin epilepsy: studies on blood-brain barrier during cardiopulmonary bypass. J Thorac Cardiovasc Surg 52:469-475, 1986

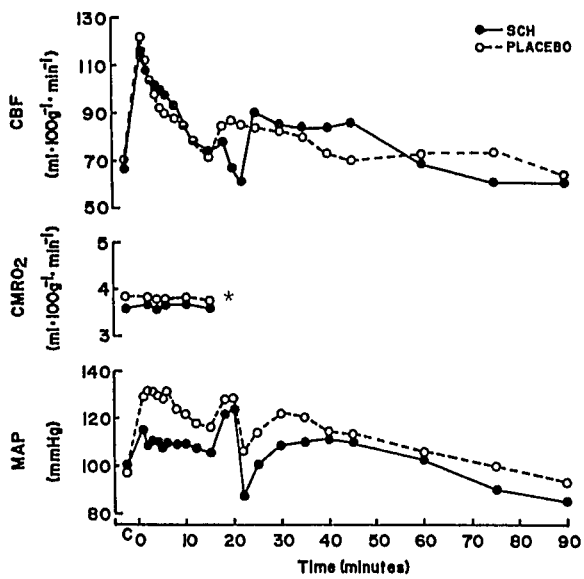

Figure: CBF, $CMRO_2$ and MAP data. Each point represents the mean response for 6 dogs. There were no significant differences between groups. (C = control). (* Blood O_2 content - and thus $CMRO_2$ - could not be measured spectrophotometrically after i.v. Evans blue dye.)