Anesthesiology
73:485–490, 1990

The Effects of Intravenous Succinylcholine on Cerebral Function and Muscle Afferent Activity Following Complete Ischemia in Halothane-anesthetized Dogs

William L. Lanier, M.D., Paul A. Iaizzo, Ph.D.,† James H. Milde‡*

The effects of iv succinylcholine (SCh) on cerebral blood flow (CBF), the electroencephalogram (EEG), muscle afferent activity (MAA), electromyographic activity (EMG), and Pa_{CO_2} were tested in six halothane-anesthetized dogs (1.0 MAC) more than 1 h after a 10-min period of complete cerebral ischemia. All dogs received treatments of both iv SCh (1.0 $mg \cdot kg^{-1}$) and saline placebo in a random sequence. Fasciculations and substantial increases in EMG activity were observed in all dogs following SCh administration. At the onset of fasciculations, there was an increase in MAA to a peak value of 353 ± 74% of control (mean ± SE; n = 5 for MAA; n = 6 for all other variables) at the 1-min measurement point. Thereafter, MAA gradually declined toward control values. There were delayed increases in Pa_{CO_2} throughout the 45-min study period, achieving values of 106 ± 1% to 118 ± 4% of control (an increase in Pa_{CO_2} of 2–7 mmHg). Despite the increases in MAA and Pa_{CO_2}, there were no significant increases in CBF during the study. The control EEG 1-h after complete cerebral ischemia, but immediately before administering the drug treatments, consisted predominantly of a delta rhythm, denoting cerebral dysfunction. In one dog, SCh administration produced transient attenuation of the delta rhythm, a change consistent with cerebral stimulation. In the remaining five dogs, SCh had no effect on the EEG. Treatment with saline placebo did not affect any variable measured. The authors conclude that, in the electrically dysfunctioning brain (*e.g.*, as occurs following resuscitation from complete cerebral ischemia), the cerebral (*i.e.*, CBF and EEG) response to iv SCh is attenuated when compared to the previously reported response in normal brain. (Key words: Anesthetics, volatile: halothane. Brain: blood flow; electroencephalogram; intracranial pressure; ischemia; metabolism; oxygen consumption. Muscle, skeletal: afferent activity; electromyograms. Neuromuscular relaxants: succinylcholine.)

INTRAVENOUS ADMINISTRATION of the depolarizing neuromuscular relaxant succinylcholine (SCh) is reported to produce activation of the electroencephalogram (EEG) and increases in cerebral blood flow (CBF) and intracranial pressure (ICP) in lightly anesthetized dogs with normal brains.[1,2] These cerebral effects have been attributed primarily to SCh-induced increases in muscle afferent activity (MAA) producing cerebral stimulation and secondarily to SCh-induced increases in Pa_{CO_2}.[1,2] In lightly anesthetized humans having normally functioning brains, SCh also is reported to produce EEG activation[3,4] and, in patients having intracranial mass lesions, increases in ICP.[5,6] As in dogs, these effects are assumed to be related primarily to SCh-induced increases in MAA.[3–6]

In the single published report in which the cerebral effects of SCh were evaluated in subjects having preexisting global cerebral dysfunction (*i.e.*, coma), SCh did not produce an increase in ICP.[7] There are several possible explanations for this finding; the most likely is that the electrically dysfunctioning brain is unable to process MAA input and respond with the arousal response observed in normal brain. To test this hypothesis, we simultaneously examined the effects of SCh on cerebral function and muscle afferent activity following complete ischemia in lightly anesthetized dogs.

Methods

The study protocol was approved by the Institutional Animal Care and Use Committee. The studies were performed immediately after studies in normal, anesthetized dogs (as described in a recent publication from our laboratory[2]) so that comparisons could be made between the two groups of studies.

Six mongrel dogs weighing 13.3 ± 1.3 kg (mean ± SE) were studied. Dogs were anesthetized while in a Plexiglass induction box using halothane in O_2. The trachea was intubated without the use of neuromuscular relaxants, and ventilation was controlled. During the preparatory period, anesthesia was maintained with 1.0–2.5% halothane inspired in N_2 and O_2. Ventilation and FI_{O_2} were adjusted to maintain Pa_{O_2} near 150 mmHg and Pa_{CO_2} near 40 mmHg (Instrumentation Laboratory; electrodes at 37° C). Inspired and end-expired concentrations of O_2, CO_2, and halothane were measured using a mass spectrometer (Perkin-Elmer Model 1100). Cannulae were inserted into a femoral artery for blood sampling and pressure measurements and into femoral and forelimb veins for fluid and drug administration. For mean central venous pressure (CVP) measurement, a PE90 catheter (Becton Dickinson Co.) was inserted *via* the right jugular vein to the level of the junction of the superior vena cava

* Associate Professor of Anesthesiology.
† Assistant Professor of Anesthesiology.
‡ Instructor in Anesthesiology.

Received from the Anesthesia Research Laboratories, Department of Anesthesiology, Mayo Clinic and Mayo Medical School, Rochester, Minnesota. Accepted for publication April 10, 1990. Supported in part by a "Starter Grant" from the American Society of Anesthesiologists, and Research Grants NS-07507 and HL-07111 from the National Institutes of Health, Public Health Service.

Address reprint requests to Dr. Lanier: Department of Anesthesiology, Mayo Clinic, Rochester, MN 55905.

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/73/3/485/637048/0000542-199009000-00019.pdf by guest on 04 April 2024

and right atrium. Heart rate (HR) was determined from a lead II electrocardiogram. The EEG was recorded from a three-lead bipolar system (bifrontal, biparietal, and bioccipital) using electrodes glued to the exposed calvarium. During the preparatory period, dogs were given 0.9% saline solution in 10 ml · kg^{-1} increments as needed to maintain mean arterial blood pressure (MAP) > 60 mmHg. Bicarbonate was given as needed to maintain a buffer base near 40 mEq · l^{-1}. The ears of all dogs were plugged with cotton, and the eyes were taped shut.

Following preparations for physiological monitoring, dogs were prepared for the production of complete cerebral ischemia using an aortic cross-clamp model described previously.[8–10] Briefly, through a right-sided thoracotomy, umbilical tapes were placed around the ascending aorta and venae cavae. After reducing halothane concentrations to 0.87% end-expired for 20 min, complete cerebral ischemia for 10-min duration was produced by simultaneously occluding the aorta and venae cavae. This technique confined the cardiac output to the coronary and pulmonary circulation. Occlusion was verified by a femoral MAP of zero and rapid onset of an isoelectric EEG. Coincident with the EEG becoming isoelectric, halothane was discontinued, and the dogs' lungs were ventilated with O_2 and N_2. At the end of the 10-min period, the tape around the aorta was released, with the tapes around the venae cavae having been released 15–20 s earlier.

Immediate postischemic treatment consisted of sodium bicarbonate (20 mEq), 0.9% saline solution (100–300 ml iv), and transient hyperventilation. Using this methodology, all dogs had an MAP > 60 mmHg within 90 s after ischemia (mean time, 39 ± 10 s). Halothane 0.87% end-expired was reinstituted within 10 min after restoration of cerebral blood flow (*i.e.*, after the MAP had exceeded 60 mmHg but before there was return of any EEG activity).

When complete cerebral ischemia is produced in the above manner, it results in an initial period of cerebral hyperemia lasting less than 1 h followed by a prolonged period of diminished CBF.[9,10] The period of diminished CBF, termed the "delayed postischemic hypoperfusion state," lasts for 6 h or more following the restoration of normal cerebral perfusion pressure.[10] Following production of cerebral ischemia in the current study, and while awaiting the establishment of the delayed hypoperfusion state, dogs were prepared for the additional measurements of CBF, cerebral metabolic rate for oxygen consumption ($CMRO_2$), ICP, MAA, and electromyographic activity (EMG).

Muscle afferent activity from the right hindlimb gastrocnemius muscle was measured using techniques described previously.[2] Briefly, a branch of the tibial nerve passing to the gastrocnemius muscle was severed near its proximal origin, and electrical activity from the distal nerve branch was detected using a shielded, bipolar, platinum electrode. The EMG from the same gastrocnemius muscle was measured using fine nichrome wire electrodes placed within the muscle near the motor point. Both MAA and the EMG were amplified using DC amplifiers, visually displayed on a storage oscilloscope, and recorded using an FM tape recorder for later analysis. Thereafter, MAA was quantified using a saturating diode-integrating circuit. The biphasic MAA signal was bisected so that only positive deflections above background noise were directed to the integrating circuit. The MAA recordings from this study were analyzed concurrently with recordings from a previous study.[2] The same techniques and circuit settings to eliminate background noise were used to allow direct comparisons between studies.[2]

Cerebral blood flow was measured using an established venous outflow technique. After administration of heparin (300–400 units · kg^{-1} iv), the sagittal sinus was exposed, isolated, and cannulated as described previously.[11] This procedure allowed blood sampling and provided for the direct measurement of CBF from the anterior, superior, and lateral portions of both cerebral hemispheres representing approximately 54% of the total brain weight.[12] Blood flow was continuously recorded using a square-wave electromagnetic flow meter (ET 300 API, Carolina Medical Electronics).[13] Blood oxygen contents were calculated from measurements of oxyhemoglobin concentrations (CO-oximeter, Instrumentation Laboratories, electrodes).[14] The $CMRO_2$ was calculated as the product of CBF and the arterial to sagittal sinus blood O_2 content difference. The ICP was monitored using a parietal, epidural, fiberoptic device (LADD Research Industries). Brain temperature was monitored by a parietal, epidural thermistor and maintained at 37° C using heat lamps.

The study period did not begin for a minimum of 60 min after resuscitation from ischemia (range, 60–129 min) and a minimum of 15 min after return of the continuous EEG. Once these criteria had been satisfied, ventilation and FI_{O_2} were again adjusted to produce arterial blood gases within protocol limits. Throughout the postischemic period, a cerebral perfusion pressure (CPP) of >50 mmHg was maintained (using continuous low-dose infusions of phenylephrine [40 $\mu g \cdot ml^{-1}$], if needed).

For a minimum of 15 min before control measurements and throughout the study period, no further adjustments were made in ventilation, anesthetic concentration, or phenylephrine infusion rate, nor were additional iv fluids given. After control measurements were obtained, three dogs were given SCh at concentrations of 1.0 mg · kg^{-1}, and physiologic, cerebral, and muscle variables were measured for 45 min. After a 30–45 min pause at which time cerebral and muscle variables had stabilized at pre-SCh control values, a second control period was obtained,

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/73/3/485/637048/0000542-199009000-00019.pdf by guest on 04 April 2024

and the above sequence was repeated using saline placebo at a volume of 0.05 ml · kg^{-1}. In the remaining three dogs, SCh and saline placebo treatments were given as above, except their sequence was reversed. At the completion of the studies, all dogs were killed with iv KCl during anesthesia. The brains were removed and weighed so that CBF and $CMRO_2$ could be expressed as a function of brain weight.

Following the administration of each drug, the average cerebral and systemic responses were calculated for each dog for the time periods 0–15, 15–30, and (when applicable) 30–45 min. Data following treatments with SCh from these time periods were compared to data following placebo treatments using paired *t* tests. In addition, data from the individual data points (*e.g.*, the 1-min, 2-min, or 3-min data points) following SCh *versus* placebo treatments were compared using analysis of variance (ANOVA) and a one-factor, completely randomized design. The Spearman rank correlation coefficient (rs) was used to assess the correlation between CBF and ICP changes. Fisher's exact test was used to compare the incidence of fasciculations in SCh- *versus* placebo-treated dogs. All statistical comparisons were made on raw data, and $P < 0.05$ was considered significant. All data are expressed as mean ± SE.

In addition to the statistical analysis comparing raw data, data from each dog were expressed as a percent of the dog's control values. This provided for easier recognition of the temporal relationship between cerebral and systemic changes, as displayed in the accompanying figures. However, statistical analyses were not performed on percent of control data.

Results

Control systemic and cerebral variables measured before the administration of either SCh or placebo treatments are listed in table 1. The groups were well-matched for both cerebral and systemic data.

TABLE 1. Control Variables Before Succinylcholine (SCh) or Placebo Treatments in Six Dogs

	Treatments	
	SCh 1 mg · kg^{-1} iv	Placebo iv
Pa_{O_2} (mmHg)	151 ± 8	153 ± 3
Pa_{CO_2} (mmHg)	40 ± 1	41 ± 1
*p*H	7.33 ± 0.02	7.33 ± 0.01
BB+ (mEq · l^{-1})	42 ± 1	42 ± 1
CVP (mmHg)	6 ± 1	5 ± 1
Brain temperature (° C)	36.9 ± 0.1	37.1 ± 0.01
MAP (mmHg)	75 ± 3	80 ± 5
Heart rate (beats · min^{-1})	133 ± 7	130 ± 9
Measured halothane (% expired)	0.87 ± 0.00	0.87 ± 0.00

There were no significant differences between treatments.
Data are presented as means ± SE (n = 6).

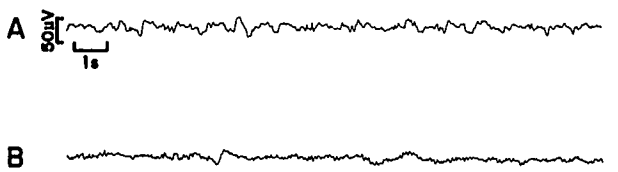

FIG. 1. Electroencephalographic activity following complete cerebral ischemia. The typical EEG pattern consisted of a mixture of 4–7 Hz theta activity superimposed upon a background of 1–2 Hz delta activity (*A*). SCh had no effect on this pattern in five dogs. In the remaining dog, SCh produced a transient attenuation of the delta activity, and the attenuation was most prominent in the frontal and parietal EEG leads (*B*). (In these examples, EEG data are recorded from the bifrontal EEG.)

Following SCh treatment, fasciculations were observed visually and recorded by the EMG in all six dogs ($P < 0.05$ *versus* placebo). Electromyographic evidence of fasciculations began at 22 ± 3 s following SCh and persisted for 30 ± 5 s (range, 21–55 s). During violent fasciculations in one dog, the onset of bleeding around the MAA recording electrode precluded the measurement of MAA data from that dog. In the remaining five dogs, a small increase in MAA began shortly before the onset of visible fasciculations. With the onset of fasciculations, there was a dramatic increase in MAA in five of five dogs and a small, numerical increase in CBF in five of six dogs (range, 110–130% of control at the 1-min measurement point). The CBF changes, however, did not achieve statistical significance. The postischemic control EEG pattern consisted of a mixture of two electrical patterns: one in the delta frequency range and one in the theta range. The delta pattern consisted of predominantly 1–2 Hz, 20–180 μV activity. In the occipital EEG, the delta activity tended to have a higher amplitude and was more rhythmic than in the parietal or frontal EEG. The theta pattern was more prominent in the anterior leads and consisted of 4–7 Hz, 10–30 μV activity. A representative sample of the control EEG is presented in figure 1A. The administration of iv SCh had no effect on the postischemic control EEG in five of six dogs. In the remaining dog, SCh produced an attenuation of the delta activity in the frontal and parietal leads (fig. 1B). The delta activity attenuation began with the completion of fasciculations and persisted for less than 2 min. Thereafter, the EEG returned to the control pattern.

Following placebo treatment, no fasciculations were observed, MAA and CBF remained stable, and the EEG remained in the postischemic control pattern throughout the study.

When comparing 15-min measurement periods (table 2), SCh produced significant changes in MAA and Pa_{CO_2}, and the values following SCh were significantly greater than those following placebo at both the 0–15 and 15–30 min measurement periods. In contrast, SCh

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/73/3/485/637048/0000542-199009000-00019.pdf by guest on 04 April 2024

TABLE 2. Cerebral Blood Flow (CBF), Muscle Afferent Activity (MAA), Pa_{CO_2}, Intracranial Pressure (ICP), and Cerebral Metabolic Rate (CMR_{O_2}) Responses to iv Succinylcholine (SCh) and Placebo in Dogs After Complete Ischemia

Variable Measured	Time (min)	SCh 1.0 mg·kg iv	Placebo iv
CBF (ml·100 g^{-1}·min^{-1})	Control	25 ± 3	25 ± 3
	0–15	27 ± 4	25 ± 3
	15–30	27 ± 4	26 ± 3
	30–45	28 ± 4	—
MAA (% control)	Control	100 ± 0	100 ± 0
	0–15	238 ± 38†	102 ± 3
	15–30	173 ± 22*	99 ± 8
	30–45	142 ± 12	—
Pa_{CO_2} (mmHg)	Control	40 ± 1	40 ± 1
	0–15	46 ± 1†	41 ± 1
	15–30	44 ± 0*	41 ± 1
	30–45	43 ± 1	—
ICP (mmHg)	Control	8 ± 2	8 ± 3
	0–15	10 ± 3	8 ± 2
	15–30	8 ± 2	8 ± 3
	30–45	4 ± 1	—
CMR_{O_2} (ml·100 g^{-1}·min^{-1})	Control	3.12 ± 0.16	3.20 ± 0.17
	0–15	3.20 ± 0.13	3.15 ± 0.16
	15–30	3.17 ± 0.16	3.16 ± 0.14
	30–45	3.23 ± 0.19	—

All data are presented as mean ± SE (n = 5 for MAA; n = 6 for all other variables).

* $P < 0.02$ between SCh and placebo treatments.

† $P < 0.01$ between SCh and placebo treatments.

produced no significant changes in CBF, $CMRO_2$, ICP, CVP, MAP, or heart rate.

The temporal relationship between CBF, MAA, and Pa_{CO_2} following SCh is presented in figure 2. After the injection of SCh, no noticeable changes occurred until the onset of MAA increases, fasciculations, and EMG activation. With the onset of these changes in muscle activity, the subtle frontal EEG changes noted above occurred in one dog. There was also a numerical increase in CBF in five of six dogs; however, the CBF alteration was not statistically significant. The largest increase in MAA (353 ± 74% of control) occurred at the 1-min measurement point and was followed by a progressive decrease with time. Cerebral blood flow at the period of greatest MAA (*i.e.*, the 1-min measurement point) was 115 ± 5% of control (not significantly different from placebo values). Pa_{CO_2} increased after iv SCh, achieving values of 106–118% of control (a 2–7 mmHg increase) throughout the 45-min study period.

Using comparisons between individual data points (ANOVA), CBF and ICP never differed significantly between SCh and placebo treatments. There also was no correlation between CBF and ICP following either the SCh or placebo treatments.

Discussion

In lightly anesthetized subjects having normal cerebral electrical activity, intravenous SCh has been reported to produce EEG activation[1–4,15] and increases in CBF[1,2] and ICP.[1,2,5,6] These cerebral effects have been attributed primarily to the influence of SCh-induced MAA increases on the cerebral state of arousal[1–6,15] and secondarily to SCh-induced increases in Pa_{CO_2}.[1,2]

The proposed mechanism by which SCh affects cerebral function by an MAA-mediated mechanism is as follows: SCh is a potent agonist for increasing afferent activity generated from muscle spindles, presumably because the drug interacts with gamma efferent receptors on the spindles.[2,16,17] Activation of the intrafusal fibers of the muscle spindles will subsequently result in an increase in MAA (*i.e.*, by altering the gain of the receptor). The action potentials generated by the spindles are transmitted by peripheral nerves to the dorsal spinal cord. This MAA information is then directed to higher central nervous system centers *via* several different neuronal pathways,[18,19] and these pathways converge on both the motor cortex (area 4) and the somatosensory cortex (area 3a).[18–20] Thus, increases in MAA have the potential to influence the functional activity within large areas of brain. In accordance with afferentation theory, increases in MAA in lightly anesthetized subjects can produce a generalized

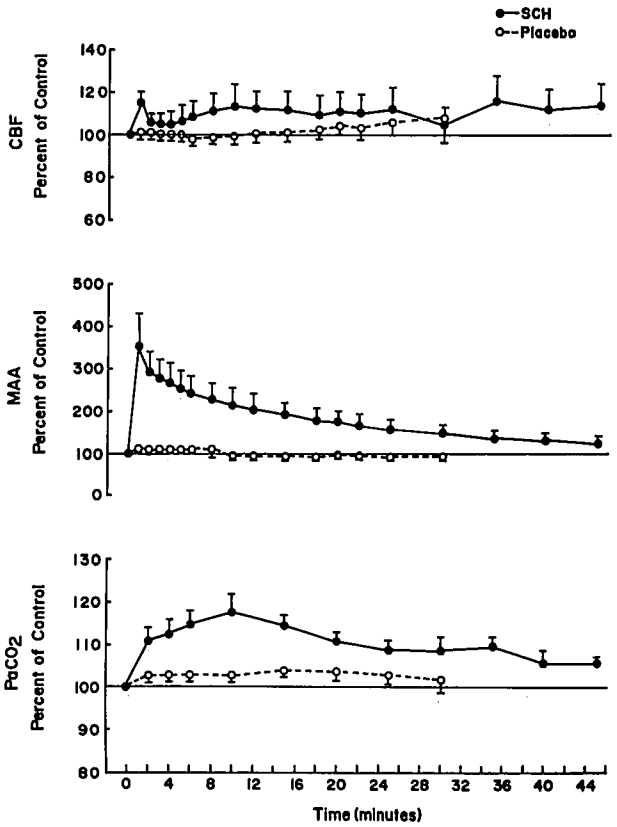

FIG. 2. The temporal relationship of changes in CBF, MAA, and Pa_{CO_2} after iv administration of SCh 1.0 mg·kg^{-1} or placebo in dogs anesthetized with 1.0 MAC halothane following a period of complete ischemia. All values are expressed as mean % of control ± SE (n = 5 for MAA; n = 6 for CBF and Pa_{CO_2}).

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/73/3/485/637048/0000542-199009000-00019.pdf by guest on 04 April 2024

cerebral arousal. The manifestation of this arousal response as EEG activation and CBF increases without $CMRO_2$ increases[1,2] is similar to the cerebral response elicited in lightly anesthetized dogs following afferent input into the brain induced by electrical stimulation of the sciatic nerves.[21]

The cerebral response to iv SCh can be attenuated or abolished by a variety of factors (*e.g.*, pretreatment with nondepolarizing relaxants or increase of anesthetic depth), and these factors appear to fall into one of two categories: 1) they either prevent a muscle response following SCh (*i.e.*, they prevent increases in MAA or increases in CO_2 production) or 2) they interfere with the brain's ability to respond to increased MAA induced by iv SCh. Lanier *et al.* demonstrated that when dogs were pretreated with paralyzing doses of pancuronium (0.2 $mg \cdot kg^{-1}$ iv), the cerebral response to SCh was abolished.[1] Similarly, Minton *et al.* reported that pretreatment with paralyzing doses of vecuronium (0.14 $mg \cdot kg^{-1}$ iv) prevented the cerebral response to SCh in humans.[5] Subsequent studies in dogs demonstrated that these large doses of pancuronium and vecuronium also prevented an EMG and MAA response following SCh[2]§ Thus, the pretreatment that abolished the muscle response also abolished the cerebral response. Lanier *et al.* also demonstrated that increasing anesthetic depth would abolish the cerebral response to SCh, presumably because the brain was unable to respond to SCh-induced increases in MAA.[1]

In 1982, White *et al.* evaluated the effect of SCh on the ICP response to tracheal suctioning in patients whose lungs were mechanically ventilated.[7] Their subjects were 15 intensive care unit patients, all of whom had "diffuse brain injuries" and were comatose. The baseline ICP was 16 ± 2 mmHg. After measurement of the baseline ICP, patients were treated with 1.0 $mg \cdot kg^{-1}$ iv SCh, followed 1–2 min later by suctioning of the endotracheal tube. Intravenous SCh did not increase intracranial pressure in these patients; quite the contrary, SCh administration resulted in an ICP response to tracheal suctioning that was significantly less than the response following saline placebo. This occurred presumably because SCh prevented the increases in ICP during coughing that have been attributed previously to increases in venous pressure.[7] Based on the data of White *et al.*, we hypothesized that the lack of an ICP increase following SCh was related to their selection of comatose patients[1]: in the series of patients they studied, the brain would have been unable to respond in a normal fashion to the MAA increases following SCh.

In our study, which also evaluated subjects having baseline alterations in cerebral electrical (*i.e.*, EEG) activity, only one of six dogs had EEG evidence of cerebral arousal following iv SCh. Furthermore, there were no significant increases in CBF or ICP, as we observed previously following SCh in normal dogs using this model.[1,2] The minimal cerebral response to SCh occurred even though there was a large increase in MAA. We interpret these data and the data of White *et al.*[7] as demonstrating that during periods of altered cerebral electrical activity, whether that altered activity is produced by ischemia or deep anesthesia,[1] the brain is unable to mount a response to SCh-induced MAA increases.

In the current study, cerebral dysfunction was induced by exposing the dogs' brains to a global ischemic insult. The duration of ischemia was chosen because, using this model, 10 min of complete ischemia typically will result in a dog that survives the insult but sustains moderate to severe neurologic functional injury.[22] Our studies identified that there was a lack of a cerebral response to SCh in the diffusely dysfunctional, postischemic brain, a finding that may have clinical relevance in certain types of patients. One of the limitations of our study, however, was that it did not allow us to identify the specific location of brain or spinal cord responsible for the lack of cerebral response to SCh. Thus, it is not clear whether the lack of response was due to dysfunction in a single area or multiple areas of the central nervous system. Furthermore, it is not clear whether the lack of a CBF response was due to an alteration in the vasculature or a neuronal injury that, in turn, was responsible for modulating vascular function. Further studies will be needed to resolve these issues.

Our previous work supports the hypothesis that the cerebral response to SCh in normal brain is secondarily influenced by SCh-induced increases in Pa_{CO_2}.[1,2] These Pa_{CO_2} increases are presumably due to SCh-induced increases in muscle O_2 consumption and, thus, CO_2 production.[23] In previous reports, we established that in normal dogs anesthetized with 1.0 MAC halothane, CBF increases approximately 4% for each mmHg increase in Pa_{CO_2}.[1,2] This value is consistent with the experience of other laboratories in which studies were conducted in subjects having normal brain.[24] In contrast, when the effects of Pa_{CO_2} alterations on CBF have been studied in subjects shortly after a period of global cerebral ischemia, the CBF response has been reported to be either attenuated or absent, depending on whether the cerebral ischemia was modest or severe, respectively.[25,26] The current study supports the assumption that the post-ischemic brain has a diminished CBF response to Pa_{CO_2} alterations. When we calculated the line of best fit between the observed increases in CBF and the measured increases in Pa_{CO_2}, our data suggest that in the model used in the current study, CBF increased only 2% for each 1 mmHg increase in Pa_{CO_2} (fig. 3). (These calculations assume that MAA does not influence the CBF response in dogs to 1.0 $mg \cdot kg^{-1}$ of SCh after the 15-min measurement point. This assumption is consistent with previous observations

§ Unpublished data, Lanier WL.

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/73/3/485/637048/0000542-199009000-00019.pdf by guest on 04 April 2024

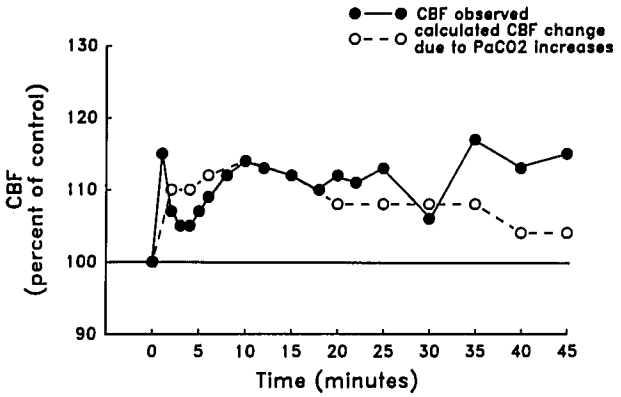

FIG. 3. The observed CBF and the calculated contributions of Pa_{CO_2} to the CBF response after SCh 1.0 mg · kg^{-1} in postischemic dogs anesthetized with 1.0 MAC halothane. Each point represents the mean response for six dogs. A 2% increase in CBF per mmHg increase in Pa_{CO_2} was used to generate the calculated CBF curve (see text for discussion).

in normocapnic dogs anesthetized with 1.0 MAC halothane.[1,2])

In summary, results from the current study demonstrate that in dogs having cerebral dysfunction produced by an earlier period of complete ischemia, the cerebral response to SCh is less than has been reported previously in dogs having normal cerebral function.[1,2] This attenuated response occurred in the presence of a normal MAA response to SCh.[2] We interpret these findings as proof that when the brain has global cerebral electrical dysfunction, its ability to mount an arousal response to MAA increases is attenuated.

The authors wish to thank Frank W. Sharbrough, M.D., for confirming the interpretation of electroencephalographic data; John D. Michenfelder, M.D., for his expert advice throughout this project; and William Gallagher, Richard Koenig, and Rebecca Wilson for their technical assistance.

References

1. Lanier WL, Milde JH, Michenfelder JD: Cerebral stimulation following succinylcholine in dogs. ANESTHESIOLOGY 64:551–559, 1986
2. Lanier WL, Iaizzo PA, Milde JH: Cerebral function and muscle afferent activity following i.v. succinylcholine in dogs anesthetized with halothane: The effects of pretreatment with defasciculating doses of pancuronium. ANESTHESIOLOGY 71:87–95, 1989
3. Mori K, Iwabuchi K, Fujita M: The effects of depolarizing muscle relaxants on the electroencephalogram and the circulation during halothane anesthesia in man. Br J Anaesth 45:604–610, 1973
4. Oshima E, Shingu K, Mori K: EEG activity during halothane anesthesia in man. Br J Anaesth 53:65–72, 1981
5. Minton MD, Grosslight K, Stirt JA, Bedford RF: Increases in intracranial pressure from succinylcholine: Prevention by prior non-depolarizing blockade. ANESTHESIOLOGY 65:165–169, 1986
6. Stirt JA, Grosslight KR, Bedford RF, Vollmer D: "Defasciculation" with metocurine prevents succinylcholine-induced increases in intracranial pressure. ANESTHESIOLOGY 67:50–53, 1987
7. White PF, Schlobohm RM, Pitts LH, Lindauer JM: A randomized study of drugs for preventing increases in intracranial pressure during endotracheal suctioning. ANESTHESIOLOGY 57:242–244, 1982
8. Goldstein A Jr, Wells BA, Keats AS: Increased tolerance to cerebral anoxia by pentobarbital. Arch Int Pharmacodyn Ther 161:138–143, 1966
9. Fleischer JE, Lanier WL, Milde JH, Michenfelder JD: Effect of lidoflazine on cerebral blood flow and neurologic outcome when administered after complete cerebral ischemia in dogs. ANESTHESIOLOGY 66:304–311, 1987
10. Steen PA, Milde JH, Michenfelder JD: Cerebral metabolic and vascular effects of barbiturate therapy following complete global ischemia. J Neurochem 31:1317–1324, 1978
11. Michenfelder JD, Messick JM Jr, Theye RA: Simultaneous cerebral blood flow measured by direct and indirect methods. J Surg Res 8:475–481, 1968
12. Takeshita H, Michenfelder JD, Theye RA: The effects of morphine and N-allylnormorphine on canine cerebral metabolism and circulation. ANESTHESIOLOGY 37:605–612, 1972
13. Artru AA, Michenfelder JD: Canine cerebral metabolism and blood flow during hypoxemia and normoxic recovery from hypoxemia. J Cereb Blood Flow Metab 1:277–283, 1981
14. Theye RA: Calculation of blood O_2 content from optically determined Hb and HbO_2. ANESTHESIOLOGY 33:653–657, 1970
15. Motokisawa F, Fujimori B: Arousal effect of afferent discharges from muscle spindles upon electroencephalograms in cats. Jpn J Physiol 14:344–353, 1964
16. Brinling JC, Smith CM: A characterization of the stimulation of mammalian muscle spindles by succinylcholine. J Pharmacol Exp Ther 129:56–60, 1960
17. Guyton AC: Textbook of Medical Physiology, seventh edition. Philadelphia, W. B. Saunders, 1986, pp 607–612
18. Weisendanger M, Miles TS: Ascending pathway of low-threshold muscle afferents to the cerebral cortex and its possible role in motor control. Physiol Rev 62:1234–1270, 1982
19. Ghosh S, Brinkman C, Porter R: A quantitative study of the distribution of neurons projecting to the precentral motor cortex in the monkey (M. fascicularis). J Comp Neurol 259:424–444, 1987
20. Lucier GE, Ruegg DG, Wiesendanger M: Responses of neurones in motor cortex in area 3a to controlled stretches of forelimb muscles in cebus monkeys. J Physiol (Lond) 251:833–853, 1975
21. Kuramoto T, Oshita S, Takeshita H, Ishikawa T: Modification of the relationship between cerebral metabolism, blood flow, and electroencephalogram by stimulation during anesthesia in the dog. ANESTHESIOLOGY 51:211–217, 1979
22. Steen PA, Newberg LA, Milde JH, Michenfelder JD: Nimodipine improves cerebral blood flow and neurologic recovery after complete global ischemia in the dog. J Cereb Blood Flow Metab 3:38–43, 1983
23. Muldoon SM, Theye RA: The effects of succinylcholine and d-tubocurarine on oxygen consumption. ANESTHESIOLOGY 31: 437–442, 1969
24. Lassen NA: Cerebral and spinal cord blood flow, Anesthesia and Neurosurgery, second edition. Edited by Cottrell JE, Turndorf H. St. Louis, C. V. Mosby Co., 1986, pp 1–21
25. Miller CL, Alexander K, Lampard DG, Brown WA, Griffiths R: Local cerebral blood flow following transient cerebral ischemia. II. Effect of arterial p_{CO_2} on reperfusion following global ischemia. Stroke 11:542–548, 1980
26. Schmidt-Kastner R, Hossmann K-A, Grosse Ophoff B: Pial artery pressure after one hour of global ischemia. J Cereb Blood Flow Metab 7:109–117, 1987

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/73/3/485/637048/0000542-199009000-00019.pdf by guest on 04 April 2024