SUMMARY  Brain retraction and induced hypotension are surgical adjuncts capable of compromising cerebral blood flow. To evaluate their effects upon brain function, cortical evoked potentials, neurological status and cortical histological changes were determined as a function of graded levels of brain retractor and systemic perfusion pressure in the dog.

Somatosensory evoked potentials recorded from the site of application of brain retraction showed a decrement as a function of both the amount of retraction pressure and the systemic perfusion pressure. An electrode distant from the retractor site showed similar, though reduced and more variable changes in amplitude. For higher levels of brain retractor pressure, induced hypotension to 50 mm Hg systemic perfusion pressure produced greater reductions in evoked potentials than in normotensive subjects. It was demonstrated that a reduction of 50% of the evoked potential amplitude after sixty minutes brain retraction signaled, with high probability, the occurrence of postoperative sensory and/or motor deficits and cortical histopathology. It was concluded that cortical evoked potentials represent a reliable indicator of the functional effects produced by applied cortical retraction pressure at several levels of systemic perfusion pressure. It was suggested that the recording of evoked potentials would prove most useful during neurosurgical procedures employing induced hypotension and brain retraction.

GIVEN THE LIMITS of the autoregulatory capacity of the brain, surgical adjuncts which can compromise cerebral blood flow may be critically important considerations, especially in patients with suspected or demonstrated brain pathology. Two such procedures are brain retraction and induced hypotension. Both are factors affecting cerebral vascular transmural pressure;1 the first a force directed from the outside and the latter a reduction in the force directed from the inside of the vessel. The potential deleterious effects of combining the two procedures are widely recognized. However, no investigation of their combined effects upon brain function has been reported. The present study attempts to provide data on changes in three measures of brain function following experimental induction of hypotension and brain retraction. These data may be especially relevant to the surgical treatment of cerebral vascular tumors and anomalies wherein both induced hypotension and brain retraction are employed in combination.

To evaluate the effects of these two factors acutely we have chosen to monitor brain function with measurement of somatosensory evoked potentials (SEP) during the application of various levels of brain retraction (P) and systemic perfusion pressure (SPP) in the dog. To test for the subsequent effects of these procedures and to assess the significance of acutely observed SEP changes, postoperative neurological status and brain histologic changes were evaluated.

Evoked potentials were selected as the monitor of the effects of brain retraction since they have been shown to be sensitive indicators of cerebral blood flow (CBF) and to correlate well with those factors affecting CBF. Secondly, the early component of the evoked potential is topographically specific so that the site of retractor application and the cortical response area can be the same. Since we have found the techniques of evoked potential recording easily implemented in the surgical setting, we sought experimental data and experience that might prove helpful in application of the monitoring techniques to neurosurgical procedures.

Methods

Fifty-four mongrel dogs weighing 15-20 kg were arbitrarily partitioned into normotensive and induced hypotension groups. Anesthesia was induced with sodium pentobarbital (Nembutal) 25 mg/kg i.v. The animals were intubated and ventilated with a respirator. The respiratory parameters were adjusted for stable pH, Pco₂ and Po₂ and checked by discontinuous blood gas measurement. Arterial and central venous pressures were monitored with femoral artery and vein catheters attached to standard monitoring equipment. Lead 2 of the ECG was also monitored continuously.

Under sterile conditions, craniotomy was performed over the right temporo-parietal area. The dura was incised and reflected. Stainless steel recording electrodes were placed on the pial surface at the level of the somatosensory cortex. One was placed laterally under the retractor and one was placed medially under bone. Reference and ground electrodes were placed subcutaneously anteriorly and posteriorly to the cranial defect. A specially modified DeMartel type brain retractor with microcircuit strain gauge pressure monitoring unit was fixed into a micro-manipulator and calibrated. The retractor was gently placed over the lateral electrode site (0 mm Hg retractor pressure) and an initial somatosensory evoked potential (SEP) in response to median nerve stimulation was taken. Animals were randomly assigned to groups in accordance with applied retractor pressure. In the normotensive group, retractor pressure was then adjusted to either 0, 10, 20, 30, 40, or 50 mm Hg and SEP's recorded every 15 minutes for the one hour retraction and the half hour recovery period. Retractor pressure was monitored continuously and adjusted when necessary to maintain a constant value. The dural defect was then repaired and the wound closed. Neurological status was assessed for three days using Tarlov's rating system for sensory and motor
function. The animal was then sacrificed and the brain removed and placed in formalin for histological study. The same procedures were followed in the hypotensive group except that sodium nitroprusside was administered by intravenous drip to lower the femoral arterial-venous pressure difference (SPP) to 50 mm Hg after which a retractor pressure of 0, 10, 20, or 30 mm Hg was applied.

Cortical responses were amplified with a band pass of 3 to 3KHz and led to a Nicolet Model 1072 Signal Averager with a low pass filter time constant of 4 msec. One hundred twenty-eight sweeps of 100 msec duration were averaged. Responses were printed on an X-Y recorder for further analysis. Median nerve stimuli consisted of capacitively coupled 1 msec constant current square wave pulses delivered at a rate of 3/sec. Stimulus amplitude was uniformly adjusted to twice the current necessary to elicit a motor response.

Results

Normotensive Animals

The systemic perfusion pressure (SPP) encountered in these animals ranged from 67 to 220 mm Hg (μ ± S.D. = 119 ± 27.4 mm Hg). As expected, SPP was a significant determinant of SEP amplitude during retraction. Early in the study it was observed that animals with high arterial pressure were less affected by identical levels of brain retraction than those with low arterial pressure. Combining all animals into one group (i.e. ignoring retraction pressure differences) a Spearman Rank Correlation Test indicated a high correlation between SPP and the reduction of SEP's seen following a one hour application of 0 to 50 mm Hg brain retraction (r = .037, n = 28, p < 0.05). One might speculate that a chance assignment of hypotensive animals to the high retraction pressure groups produced the above correlation. In argument against this and indicating a random distribution of blood pressures, an analysis of variance showed no significant difference in the perfusion pressures among the six retraction pressure groups (F6, 22 = 0.43, p > 0.75). Therefore, on the average, for a given level of retraction pressure (Pr), the animals with lower perfusion pressures demonstrated greater reductions in SEPs.

The most consistent and profound reductions in SEP amplitudes were seen in the higher retraction pressure group (Pr = 30 to 50 mm Hg). Although there was a trend for the evoked potentials to decrease with maintained retraction, most of the SEP decrement was seen by 15 minutes of retraction (see figs. 1, 2 and 3). A most dramatic example of the reduction of SEPs with retraction is illustrated in figure 1 in recordings taken from a normotensive group animal (SPP = 98 mm Hg) subjected to 50 mm Hg retractor pressure. The significance of the decrements in SEP amplitudes for the various levels of retractor pressure was assessed with an analysis of variance. An arc sine transformation of the data represented as percentage of control amplitude means and the standard errors for the 0 to 30 mm Hg and 40 to 50 mm Hg retraction pressure groups is shown in figure 2A. There it can be seen that although some recovery is evident for the 40 and 50 mm Hg animals, the evoked potentials remain severely depressed (58% pre-retraction values) for at least 30 minutes after the retractor was removed. In addition to the high magnitude of SEP change in the Pr = 40 and 50 mm Hg groups, a Spearman Rank Correlation Test on the data from all groups showed a high degree of correlation between the 60 minute SEP amplitude and applied retraction pressure (r = 58, n = 28, p < .005). From these findings one can conclude that the
FIGURE 2. SEP changes with retraction. A. Changes in time of median nerve evoked cortical potentials with application of retractor pressure in normotensive animals. Upper trace, average of groups showing no significant difference in amplitudes of SEPs compared to controls, $P_r = 0$ to $30$ mm Hg. Lower trace, average of groups with SEPs significantly reduced as compared to controls, $P_r = 40$ and $50$ mm Hg. B. As above, for induced hypotension animals. Upper trace, $P_r = 0$ and $10$ mm Hg. Lower trace, $P_r = 20$ and $30$ mm Hg.

degree of reduction of the SEP is a function (at least in part) of applied brain retraction pressure.

The electrode distant to the site of retractor pressure application showed similar reductions in SEP amplitudes. However, the variations in amplitude were not always consistent. A Spearman Rank Correlation Test indicated no significant correlation between the SEP's of the two electrode sites for the $P_r = 40$ and $50$ mm Hg groups ($r_s = .05$).

Since the observed reductions in SEPs seems to be both a function of systemic perfusion pressure and applied retraction pressure, in a given case, measurement of one alone might not serve as a predictor of significant changes in SEP amplitudes. SEP amplitude decrements with increased retractor pressure ($P_r$) and/or decreased systemic perfusion pressure (SPP). Combining these two terms by subtraction ($SPP - P_r$) yields a single term descriptive of their relationship to evoked potential amplitude and postoperative neurological status and histopathology. As expected, the term $SPP - P_r$ is highly correlated with SEP amplitude ($r_s = .53$, $n = 28$, $p < .005$).

Hypotensive Group

With the induction of systemic hypotension by intravenous infusion of sodium nitroprusside the effects of graded brain retraction pressure were more pronounced. With the induced nominal systemic perfusion pressure of $50$ mm Hg a significant difference among retractor pressure groups was seen at the $p < .01$ level ($F_{8,16} = 5.78$). Compared to the hypotensive control group ($P_r = 0$ mm Hg), both the $20$ and $30$ mm Hg groups had their $60$ minute evoked potentials significantly reduced ($p < .05$ and $p < .005$ respectively) whereas the $10$ mm Hg group showed no significant difference ($p > .5$). Figure 2B illustrates the changes in time of the evoked potentials in the hypotensive animals. By comparison with figure 2A it can be seen that for the higher retractor pressure groups, the evoked potentials for the hypotensive animals are more severely depressed than the equivalent normotensive group. The data presented above is only from animals surviving for three days postoperatively.

FIGURE 3. SEP changes in normotensive dogs. Three point moving average of SEP amplitude as a function of the difference between systemic perfusion pressure and brain retraction pressure ($SPP - P_r$). Normotensive animals. Vertical Scale; SEP amplitude after $60$' brain retraction as a percentage of no-retraction SEP amplitude.
Whereas all normotensive animals survived these procedures, for hypotensive subjects, two out of seven animals subjected to 20 mm Hg retraction pressure and four out of nine from the 30 mm Hg group died within 48 hours of operation.

Finally, it appears that induced hypotension with sodium nitroprusside slightly depresses the evoked potential in time. However, a one-tailed Mann-Whitney comparison of the 60 minute evoked potential amplitudes of the normo- and hypotensive control groups (P_t = 0 mm Hg) showed no significant difference (p = .143).

**Histopathology and Neurological Status**

With only two exceptions, all 16 animals exhibiting a three day postoperative neurological deficit also showed greater than 50% reduction in their 60 minute SEPs. On the other hand only two of the remaining animals without three day postoperative neurological deficit showed a greater than 50% reduction in SEPs. However, these last two animals did have large deep cortical lesions (> 0.3 cm³). Similarly, with one exception, only animals exhibiting large deep cortical lesions (> 0.3 cm³) showed a greater than 50% reduction in the 60 minute SEP recordings.

In general, the greater the retraction pressure the greater the neurological deficit and the larger the lesion produced. In most cases, exceptions to these findings could be rationalized by considering the SPP – Pr term. For example, one animal with a mean arterial pressure of 220 mm Hg and subjected to 50 mm Hg retraction pressure (SPP – Pr = 170 mm Hg) showed no SEP change, no neurological deficit and a lesion of only 0.13 cm³. Another animal subjected to 30 mm Hg retraction pressure showed severe sensory and motor loss with a SPP – Pr of 69 mm Hg.

**Discussion**

The findings presented above indicate that somatosensory evoked potentials represent a meaningful measure in monitoring the effects of brain retraction. Additionally, for this experimental model, the findings also provide maximum allowable retraction pressures for a 60 minute application to avoid pathological consequences. For normotensive animals the maximum is between 30 and 40 mm Hg and with induced hypotension of P_m = 50 mm Hg it is between 10 and 20 mm Hg. On the average, a reduction of the SEP to 50% of control values is consistent with the local PO₂ and evoked potential recordings of Branston et al. The failure of evoked potential recovery was associated with greater depths of ischemia and tissue hypoxia and the oxygen tension data suggested that some regional non-perfusion was established.

Similarly the finding of correlation between reduction of evoked potentials with applied retractor pressure is, in general, in agreement with most reports in which evoked potentials were monitored during maneuvers which severely restrict cerebral blood flow (CBF), produced by increased intracranial pressure, was sufficient to abolish the direct cortical response to electrical stimulation. With a lesser reduction in CBF a significant correlation between changes in cortical perfusion pressure and changes in the amplitude of the direct cortical response was demonstrated. From figure 3 it can be seen that a definite threshold effect occurs in that the SEP is unaffected until the SPP – Pr value is reduced to approximately 90 to 100 mm Hg. Thereafter the SEP diminishes somewhat linearly with reducing SPP – Pr values. The term SPP – Pr, is related to, but not identical to cerebral perfusion pressure. With craniotomy, retraction pressure is analogous locally to intracranial pressure in the usual sense. Therefore, the transmural pressure of the vessel under the retractor would be proportional to the difference between blood vessel intraluminal pressure and the transmitted retractor pressure. Branston et al. showed that following middle cerebral artery occlusion in the baboon, areas in which a steady blood flow of 16 ml/100 g/min was maintained, the evoked potential was not affected. Below 12 ml/100 g/min the evoked potentials were abolished and in between these values the amplitude of the evoked potential was critically dependent on flow. With high retraction pressures we visualize a central area under the retractor in which flow has been critically reduced (with SEP loss), a marginal zone wherein the SEP is reduced and beyond that an area in which the neurons are unaffected. Since the SEP is generated over a large area one can assume that increasing retraction pressure would compromise the blood supply to an increasing number of neurons. Thus, once the SPP – Pr values reach a critical value, a somewhat linear decrease in SEP amplitude might be expected. This interpretation is further supported by the observations that for animals surviving high retraction pressures the SEP was never abolished and necrotic lesions were seen.

The above findings only apply to the animals surviving the procedure. Six hypotensive animals subjected to 20 and 30 mm Hg retraction pressure died as a result of these procedures. In every case their SEPs were profoundly depressed to less than 20% of control values by the time retraction was removed. Subsequently SEP loss either preceded or was coincident with deteriorating bodily functions and eventual death. Although the imposed reduction in cerebral blood flow was the causative agent, a number of precipitating events were observed. These included continued depression of blood pressure, loss of spontaneous respiration and profound brain edema. In another report the duration of absence of the evoked potential and EEG (of less than 5 minutes) determined animal survival. In the present report, no animal that had a complete SEP loss survived. This would tend to support Yashon et al. who concluded that in dogs, the electrocortical recovery patterns are reliable indicators for determining the prognosis following cerebral circulatory deprivation. It is clear that in all cases presented, relief of retraction is indicated whenever the SEP is depressed by at least 50%.

The hypotensive control group data indicates that neither the toxic effect of nitroprusside nor maintenance of SPP = 50 mm Hg for 60 minutes were, by themselves, deleterious. Under these conditions neither neurologic nor histological pathology were evident and no significant changes in SEPs occurred. At this level of drug induced...
hypotension autoregulation of CBF can be presumed and this conclusion is augmented by the reported correlation between CBF and evoked potentials as well as the reported absence of brain lesions in monkeys subjected to a greater degree of systemic hypotension.

Simple mechanical transmission of pressure can account for the reduction of SEPs seen at an electrode site distant to the point of application of retraction. As in this study, the selection of type and location of peripheral stimulation will probably be determined primarily by the selection of the area of applied retraction. However, one example where pathology must be considered is where evidence exists of compromise of blood flow in the middle cerebral artery. Symon et al. reported that following unilateral middle cerebral artery occlusion the median nerve evoked potential was not affected whereas profound reductions in the trigeminal nerve cortical evoked responses were seen. This difference corresponded to the measured changes in regional blood flow at the two recording sites. Similarly the presence of vascular anomalies or other pathology might produce more severe consequences at such areas even though the retractor was applied at a distant site. For the one situation presented here the greatest reduction in neuronal function was seen at the site of retractor application. For monitoring at other cortical sites one need only select the appropriate modality. Considering the distribution of cortical evoked potentials for visual, auditory and somatosensory stimulation much of the cortical surface is available for monitoring during retraction. Indeed, if the direction of retraction is directed toward the brainstem, recording of auditory “far-field” or brainstem potentials may be useful in monitoring conduction through this area.

Except for the reminder that gentle retraction be used, findings specific to brain retraction seldom appear in the literature. A marked exception is the report by Aserman in which several deaths are attributed to the effects of “retractor anemia.” The assumptions in that report are that the brain more readily transmits applied pressure with induced hypotension and that the findings of histopathology (only at points distant to the operative site) could not be attributed to the surgery per se. Our results do not support Aserman’s contention since, in the present study, lesions only appeared at the retraction site. However, evidence of transmission of pressure was seen in the reduction of the evoked potentials at a site distant to the point of retractor application. Also, it is reasonable to assume that the application of retraction directed toward so-called arterial border zones, especially in the presence of vascular anomalies or pathology, might produce ischemia at distant sites. However, with craniotomy, transmission of pressure is greatly reduced and most of the force is absorbed by compression of the brain at the site of retraction. While theoretically possible, Aserman’s argument is weakened by his report of a complete absence of pathology at the site of retractor application.

In earlier years, reports on the use of induced hypotension as a surgical adjunct included the conclusion that 60 mm Hg was the safe minimum in normotensive subjects, that a rate of reduction of mean arterial pressure of 10 mm Hg per minute was the safe maximum and numerous morbid consequences of its use were reported. Apparently, with use, different drugs, improved monitoring and application techniques such limits have not been well supported. Most recent reports, at least in the application of the technique to neurosurgery, have found it to be a safe adjunct with little morbidity attributable directly to the induced hypotension. For instance, in reviewing others and their own experience, Yashon et al. and Sellery et al. report good to excellent results in 143 of 163 grade 1 aneurysm surgery patients where 40 mm Hg was the target mean arterial pressure. No morbidity or mortality in these patients was attributable to the induced hypotension. Patient selection, as always, remains a factor especially in those conditions where vasodilatory action of the brain’s vasculature is compromised.

The degree and duration of hypotension pressures employed in this study fall within the ranges reported in the clinical literature. Although not directly comparable because of protocol differences, the 50 mm Hg SPP herein employed is also well above perfusion pressures in dog at which the EEG is abolished and just above the level at which cerebral autoregulation is lost for drug induced hypotension. Unfortunately the degree and duration of brain retraction pressure employed were not reported in the neurological literature surveyed. To determine the range of retraction pressures to be used in this study we relied on the report of Albin et al. There, during several neurological procedures, maintained retractor pressures of 25 mm Hg were encountered. Although qualified by species differences, the occurrence of such high levels of retraction if combined with moderate hypotension would be expected to produce cerebral damage. The lack of morbidity attributed to the use of hypotension in the cited clinical literature may mean that gentle retraction was indeed employed in those cases. On the other hand, morbidity was seen and, in some cases, was attributed to other causes including vasospasm. Without measures of brain function or retractor pressure measurement, one can only conjecture. One can avoid the occurrence of excessive brain retraction by employing the technique of retraction pressure monitoring of Albin et al. The presumed ischemia produced by combining the two techniques has been documented to occur at higher levels of retraction and moderately deep hypotension in the dog. Somatosensory evoked potentials reliably signaled the occurrence of the combinations of these limiting pressure values and may prove to be a valuable monitoring technique in a number of neurosurgical procedures.

Acknowledgment

The authors wish to acknowledge the fine technical assistance of Marion Lebanik, B.S.

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Stroke. 1977;8:487-492
doi: 10.1161/01.STR.8.4.487

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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