Effects of Hemorrhagic Hypotension on the Cerebral Circulation

II. Electro cortical Function

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SUMMARY The effects of graded hemorrhagic hypotension on electrocortical function was investigated in 12 cats anesthetized with α-chloralose. Cerebral function was assessed both in terms of spontaneous activity (EEG) and the somatosensory evoked response. No significant changes in the EEG trace or in the amplitude of the positive/negative waves of the primary evoked response were observed at mean arterial pressures of between 120 mm Hg and 40 mm Hg. At levels of systemic arterial pressure of less than 40 mm Hg cortical rhythms became slower as pressure was decreased and an isoelectric EEG was recorded in the pressure range 10–30 mm Hg. The earliest sign of any change in the amplitude of the primary evoked response was observed at arterial pressures of approximately 35–40 mm Hg. Below this value the amplitude decreased with decreasing systemic pressure and became zero in the pressure range 15–25 mm Hg.

SEVERE HYPOTENSION produces a loss of cerebral function, the extent and reversibility of which depends on the degree and duration of the period of hypotension. Recent studies have described the changes in cerebral function over periods of sustained hypotension.1–4

The present study forms part of a systemic investigation which attempts to correlate the changes in cerebral blood flow during graded hemorrhagic hypotension with the subsequent alteration in cerebral functional activity and the development of hypoxic brain damage.

This communication reports the changes observed in cerebral functional activity during hypotension and relates these changes to the arterial pressure and to the corresponding alterations in the cerebral circulation. The detailed accounts of the impairment of the cerebral circulation and development of brain damage due to hypotension are given in the accompanying papers.5,6

It has been suggested7 that the somatosensory evoked response is a more accurate guide than the EEG to brain damage during hypotension. Therefore, both these parameters were measured in this study.

Methods

General Description

The effect of graded hemorrhagic hypotension on electrocortical activity was determined in 2 parallel studies in a total of 12 cats, of either sex, weighing between 1.6 and 4.8 kg. Anesthesia and general preparation of the animals were identical to those described previously.5

Measurement of Somatosensory Evoked Response

Six cats were used to study the effects of hypotension on the somatosensory evoked response. The cats were placed in a head-holder and the scalp was incised along the midline and reflected. A small craniotomy (approximately 1.5 × 1.0 cm) was made over the sensory cortex, using a saline-cooled dental drill, and a reference silver-electrode was implanted in the neck muscle. A supramaximal stimulus (0.5–2V, 0.2 msec, 1 Hz) was applied via a DISA type 14 E12 time base unit to the contralateral superficial radial nerve. Bipolar silver ball-tipped recording electrodes were then positioned (1 cm apart) on the surface of the dura to obtain maximal potential. Signals from the recording electrodes were amplified with a band width of 2–500 Hz and the average of 16 evoked potentials recorded with a DISA type 14 G01 digital averager from which the measurements were taken and of which a photographic record was kept.

The somatosensory evoked response was recorded for a control period of 30 min and then the animal was subjected to stepwise hypotension induced by controlled hemorrhage.5 Mean arterial pressure was decreased by approximately 10 mm Hg at each step and allowed to stabilize for approximately 10 min at each new level before the potentials were recorded. The effect of this hypotension on the evoked response was assessed in terms of the average peak-to-peak amplitude of the positive/negative sequence of the primary evoked response8 and the amplitude expressed as a percentage of the control amplitude (i.e. that recorded at normotension).

Electroencephalographic Recording

The 6 cats used in the EEG study were initially prepared as described previously. Following exposure
of the skull, small burr holes were made at 7 stereotactically determined sites (1 cm apart) over each hemisphere. The holes were threaded, and nylon screws carrying silver/silver-chlorided ball electrodes inserted to allow epidural recording. The wires from these electrodes were soldered to the terminals of a Cannan 15-way connector and this was fixed securely in place with dental acrylic.

A period of approximately one hour was allowed for stabilization of the animal before 8-channel, bipolar EEG recordings were commenced and continued throughout the experiment. A global stage analysis of electrocortical activity (Prior et al, *) was made at every level of mean arterial pressure: these stages range from 1 (continuous activity) to 6 (isoelectric). Intermediary stages were classified according to the duration of suppression of activity and the amplitude of bursts of cerebral activity appearing in the tracing.

**Results**

**Somatosensory Evoked Response**

The primary evoked response comprised an initial surface-positive potential, with peak latency of 10–14 msec, followed by a surface-negative wave with peak latency of 14–22 msec. The positive and negative waves showed similar changes with hypotension. Therefore, the amplitude of the primary response was measured as the peak-to-peak amplitude of the positive-negative sequence.

The amplitude of the primary response remained essentially unchanged over the arterial pressure range 120 mm Hg to 40 mm Hg. The earliest change in amplitude was observed at arterial pressures of 35–40 mm Hg.

One example of the change in the evoked response during hypotension is illustrated in figure 1. This demonstrates that not only does the amplitude of the evoked response decrease at arterial pressures below 40 mm Hg, but that, in addition, the peak latency of the positive and negative potentials increases. Generally, the surface-positive wave showed slightly less change in peak latency and amplitude than the surface-negative wave at each level of arterial pressure. In figure 2 the individual observations are combined in 5 mm Hg arterial pressure bins (e.g. 30–34, 35–39 mm Hg).

At arterial pressures below the threshold level (35–40 mm Hg) the amplitude of the evoked response decreased with decreases in arterial pressure and reached zero at 16–26 mm Hg. At pressures just below the threshold level, the amplitude of the evoked response diminished rapidly at each new level of arterial pressure and reached a stable value within 2–3 min. Recording for a further 15 min, at a steady arterial pressure, brought no further change in the size of the potential.

No measurement of blood flow was performed in those animals subjected to electrocortical analysis. However, by interpolation from the previous study, it could be shown that the amplitude of the evoked response...
response remained unchanged until cerebral blood flow had been decreased to approximately 50% of baseline values (i.e. 28 ml/100g min) although at this value zero flow was observed in certain electrodes. Below this level, the evoked response decreased progressively with decreases in blood flow and by extrapolation it would be expected that complete loss of the evoked response would occur at about 15–20% of baseline blood flow, i.e. at 8–11 ml/100g min.

Electroencephalogram

The base line tracings could be classified generally as Stage 2 or 3 (fig. 3) according to the global stage analysis chart of Prior, et al. and they remained constant over an arterial pressure range of 120–40 mm Hg. The scatter of the individual recordings is shown in figure 4.

At arterial pressures below 40 mm Hg, the cortical rhythms became slower with decreasing arterial pressure. A critical level of 30–35 mm Hg was observed, at which point a marked slowing of the EEG was apparent in most animals.

At arterial pressures below 25 mm Hg, electrocortical activity decreased in amplitude and abundance until an isoelectric tracing (Stage 6) was obtained. This isoelectric stage was observed over the pressure range 15–30 mm Hg.

By interpolation from the accompanying study of cerebral circulation during hypotension, it is evident that there was no change in EEG staging until cerebral blood flow was reduced to about 30% of control which represents a flow of about 17 ml/100g min.

Discussion

Previous studies on the spontaneous electrocortical activity during systemic hypotension have yielded very varied results, due primarily to the differing methods and rate of induction of hypotension. Differences in the anesthetic and animals may increase also the variation in these findings (see Kovach and Sandor). However, some comparisons can be made.

Electroencephalogram

The results in the current study showed that when systemic hypotension was induced slowly, the EEG activity was unchanged until the arterial pressure had decreased below 40 mm Hg. This suggests that the
EEG is more susceptible to impairment in the unanesthetized, than the anesthetized animal, perhaps due to the decrease in cerebral metabolic requirements in the latter case. Evidence for this is that the EEG is impaired at arterial pressures of 50-60 mm Hg, and an isoelectric EEG develops after 20-30 min at 30-40 mm Hg in unanesthetized dogs and cats. Further, the degree of EEG impairment seems also to depend on the rate of hemorrhage. Marked loss of EEG activity is seen in anesthetized cats at arterial pressures below 60 mm Hg if blood withdrawal is very rapid, although Yashon et al. report no loss of EEG activity in dogs subjected to rapid hemorrhage from 120-30 mm Hg and maintained for up to 2 h. This might have been due to protection of the brain by the barbiturate anesthesia which is known to reduce cerebral metabolic demand.

In the present experiment the changes in the evoked cortical response paralleled those observed in spontaneous activity. There are few reports comparing these parameters during hypotension, but Meldrum and Brierley and Brierley et al. found that the EEG was more sensitive than the somatosensory evoked response to lowered arterial pressure, but they claimed that the latter was of greater value than the EEG in predicting brain damage during profound hypotension. However, the induction of hypotension was very rapid in their study, which may have impaired selectively the EEG, for in a graded, slowly induced hypotension we found no difference between the levels of arterial pressure at which the initial alterations in EEG and evoked activity occurred. One further contrast between the 2 studies is that Brierley and colleagues induced hypotension by a combination of ganglion-blocker, withdrawal of blood and head-up tilt, rather than by hemorrhage alone as in our study. Other reports suggest that the EEG is a good guide to estimating the severity of brain damage in hemorrhagic shock in unanesthetized sheep and traumatic shock in patients, and Kovach found good correlation between irreversible brain damage and EEG changes in hemorrhagic shock in anesthetized baboons. Our results agree with these authors and, as reported in the accompanying communication, we found cell damage only at levels of hypotension at which marked loss of electrocortical function (both the EEG and the evoked response) was apparent.

In this study, the earliest detectable changes in the EEG occurred only at values of cerebral blood flow of less than 50% of baseline, the point at which Williams observed first signs of cerebral malfunction in patients. Below this threshold value of blood flow, further decreases in flow produced progressive loss of spontaneous activity.

Somatosensory Evoked Response

The primary evoked response is dependent on the functional state of the specific afferent pathway and involves 3 sites (dorsal column nuclei, ventrobasal nucleus of thalamus and the somatosensory cortex). Of these, the cortical component is probably the most sensitive to decreases in energy supply. This latter point may explain partly the minor differences between the present results and those of Branston et al. who observed no decreases in the amplitude of the evoked response until a cerebral blood flow of 16 ml/100g/min had been reached. Following occlusion of the middle cerebral artery in baboons these workers noted complete loss of the evoked response at a cerebral blood flow of 12 ml/100g/min. In the present experiments, complete loss of the evoked response was calculated to occur at 8-11 ml/100g/min, a value in agreement with those quoted above from Branston and colleagues, although it must be noted that the earliest evidence of a change in amplitude was observed at a higher value (approx. 30 ml/100g/min) in the present study. It is possible that the difference in the animal species used by the 2 groups of workers could explain such a discrepancy, but it would seem more likely that the difference is a function of the 2 different models of brain hypoxia used. In the study by Branston et al. hypoxia was produced acutely and was regional in distribution, whereas in the present investigation hypoxia was produced gradually over 2 to 3 hours and was global in distribution. Furthermore, in Branston's study ischemia was induced initially and then hypotension was superimposed.

In the present study, the decrease in the evoked response could have resulted also from failure of neuronal and synaptic transmission at other sites such as the thalamocortical projection, since blood flow will be decreased also in the thalamus during systemic hypotension.

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References

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