Changes in the Somatosensory Cortical Evoked Potential Produced by Hypovolemic Shock[1] (35428)

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The central nervous system (CNS) is acutely sensitive to the effects of circulatory insufficiency. Complete interruption of cerebral circulation is followed within seconds by loss of consciousness—within minutes by irreversible pathological changes (1). The importance of the integrity of the CNS to cardiovascular function is emphasized by the experiments of Sagawa (2) who found that systemic arterial pressure regulation was unstable and developed oscillations at cerebral perfusion pressure levels below 30 mm Hg. That specific areas of the brain are involved in the coordination of cardiovascular responses can be demonstrated by experiments such as those of Forsyth (3), who showed that electrical stimulation of the hypothalamus produced profound changes in blood flow distribution. Such findings indicate the potential value of critical analysis of the interaction between neural and cardiovascular effects associated with changes produced by stress.

Recently, Meldrum and Brierly (4) and Brierly *et al.* (5) described the pathological changes in the brain of the rhesus monkey following relatively brief periods of very profound arterial hypotension (pressure levels below 25 mm Hg). They concluded that the EEG was of little predictive value but changes in the somatosensory cortical evoked potential correlated closely with the severity of brain damage. The purposes of the present study were first, to determine whether or not the evoked potential would be altered when systemic arterial pressure was maintained for prolonged periods at levels between 35–45 mm Hg, and second, to evaluate the relationships between changes in the somatosensory evoked potential and the progression of hemorrhagic shock, especially the development of irreversibility.

Methods. The principles of laboratory care established by the National Society for Medical Research were followed carefully. The experimental model was the classical reservoir system for producing a controlled low blood pressure level. Studies were done in 10 cats and 8 dogs anesthetized with pentobarbital (30 mg/kg). The animals were placed in the supine position and a femoral vein was cannulated for the addition of supplemental anesthesia. Animals were maintained as lightly anesthetized as possible and no supplemental doses were given during the recording phase of the experiment. A large cannula was placed in one femoral artery, connected to the reservoir, and kept closed with a clamp until completion of the other preparations. The other femoral artery was cannulated for measurement of arterial pressure using a Microdot MS-5 transducer. The pressure reference point was the midthoracic line. The neurophysiological manipulations required slight elevation of the head, but this never exceeded the height of the pressure gauge by more than 10 cm.

After placement of the cannulas the animal was turned over and the forelimb superficial radial nerve was isolated and connected to a Grass S-4 stimulator. A midline contralateral craniotomy exposed the pericruciate sulcus of the cortex and the somatosensory evoked potential was recorded from a spring-mounted monopolar electrode in contact with the brain surface. This electrode also served as a recording electrode for the EEG. The reference electrode was placed on the skull. A tungsten microelectrode was used for recording from the cuneate nucleus.

The animals were ventilated with room air

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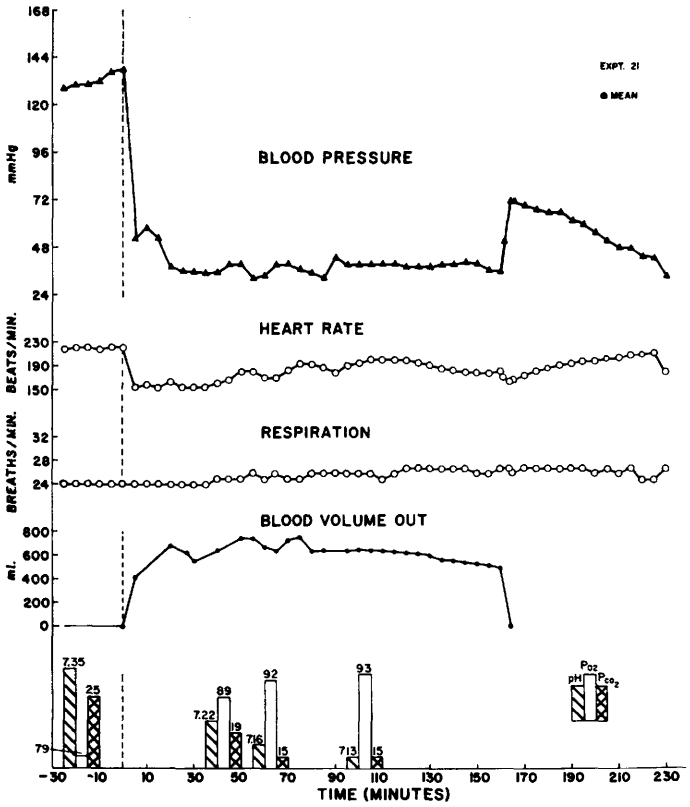

FIG. 1. Data from one experiment illustrating typical changes produced by reservoir model of hemorrhagic shock.

using a Harvard positive-pressure respirator to avoid the occasional premature termination of the experiment by abrupt respiratory failure. The respirator was adjusted to just suppress spontaneous respiration. Body temperature was measured with a Yellow Springs telethermometer and a rectal probe and maintained in the range of 36 to 37° by a Gorman-Rupp circulating water system. Periodic arterial blood samples were obtained through the pressure-measuring catheter for pH, pO_2, pCO_2, and hematocrit measurements using Radiometer equipment and an Adams microhematocrit centrifuge. After completion of all preparations, the animal was heparinized, control records were made, the line to the arterial reservoir was opened, and the reservoir height was adjusted to maintain arterial pressure at 35 to 45 mm Hg.

All parameters with the exception of the evoked potentials were monitored continuously on an 8-channel Grass recorder and simultaneously stored on magnetic tape. The evoked potentials were elicited by supramaximal stimuli to the superficial radial nerve delivered at a rate of 0.1/sec. During control periods, the evoked potential was very reproducible and could be maintained for hours.

Results. The changes in measured parameters were typical of those previously noted to occur with this preparation (Fig. 1) (6). The initial volume increment produced a rapid fall in pressure to 40 mm Hg. Maintenance of this pressure was associated with gradual transfer of additional blood into the reservoir. After a variable period of time, the reservoir volume decreased as blood returned to the animal. In the example illustrated (Fig. 1), the animal began to take up blood spontaneously from the reservoir after 110 min of maintaining a mean systemic pressure between 40–45 mm Hg. The arterial pressure

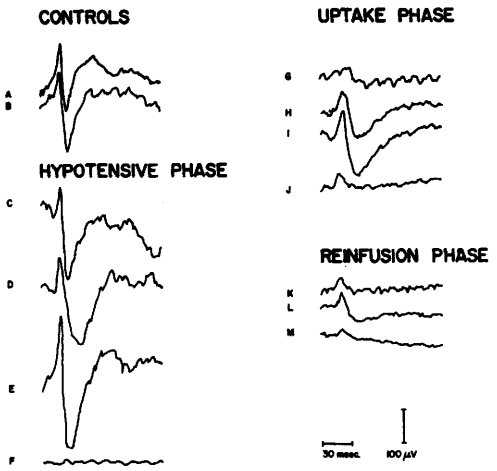

FIG. 2. Changes in somatosensory cortical evoked potential produced by hypovolemic shock: (A,B) control records; (C–E) progressive enhancement of potential with hypotension; (F) abrupt disappearance of potential as uptake phase began; (G–J) potentials during uptake phase (note transient recovery); (K–M) potentials following return of all remaining shed blood (again transient recovery).

was maintained at the constant low levels until 30% of the maximum reservoir volume was taken up; at that point, all remaining shed blood was infused. There was some recovery noted in the mean pressure with infusion. No animal, however, was able to sustain its pressure for any length of time following infusion. The progressive postinfusion fall in pressure marked irreversibility. The initial heart rate response was a bradycardia which gradually developed into a tachycardia. The terminal phase of the experiment was marked by a second bradycardia. The changes in pH, pO_2, and pCO_2 were typical of the classic observations of a progressive metabolic acidosis with attempted respiratory compensation.

Changes in the cortical evoked potential associated with the progression of shock in one animal are shown in Fig. 2. During the control period the evoked responses were quite reproducible as illustrated in the first two wave forms in Fig. 2. Subsequently, there were progressive changes in the appearance of the waveform as the duration of shock progressed, although the arterial mean pressure stayed relatively constant. An increase in peak-to-peak amplitude of the cortical potential frequently occurred as the period of shock progressed (Fig. 2, C–E). The onset of uptake was marked by a dramatic decrease in amplitude of the cortical evoked potential which rapidly fell to zero. In other animals, the change was not always so abrupt but showed a steady decrease in amplitude with the maintained low pressure until the potential disappeared.

Changes in the evoked potential generally followed the same course during the uptake and postinfusion phases (Fig. 2). There was frequently some recovery of the cortical evoked potential amplitude following return of the shed blood, but this was transient and progressively fell in the postinfusion phase. In 6 out of 8 dogs, and 6 out of 10 cats, the evoked potential was abolished prior to or coincident with the onset of the spontaneous uptake period. In the other 4 cats, the potential decreased in amplitude prior to uptake but did not disappear. Only 2 dogs failed to show a change in the evoked potential before the postinfusion period. No difference was observed between changes in amplitude of the negative and positive components of the cortical potential associated with the progression of shock (Fig. 3).

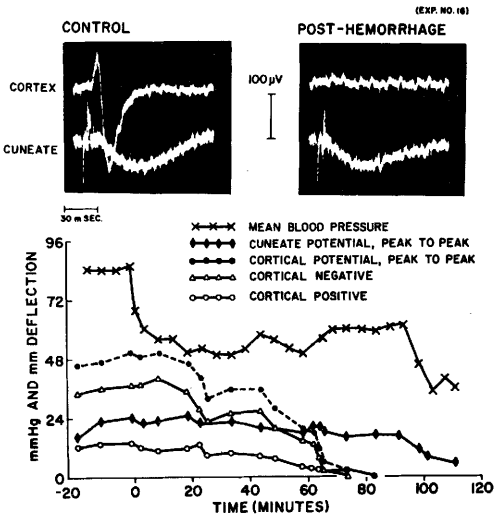

FIG. 3. Changes in cortical and cuneate evoked potential with the progression of shock inserts at top: photographs of the potentials before and after hemorrhage. Spontaneous uptake of blood from the reservoir began after 50 min of hypotension.

Cortical and cuneate evoked potentials were recorded in two of the experiments with cats (Fig. 3). The evoked potential persisted at the cuneate level even though the cortical potential had disappeared. Figure 3 depicts graphically the association of changes in both cortical and cuneate potentials with the progression of shock. Note that in the postinfusion period the cuneate evoked potential amplitude decreased.

The EEG was monitored from the same areas as the evoked potential. In almost every case, the evoked potential persisted after the EEG activity disappeared. Changes in the EEG record as shock progressed were variable and difficult to quantify or correlate with mean pressure changes. The changes in evoked potential were much easier to follow.

Discussion. Our study has shown that characteristic changes in the somatosensory cortical evoked potential occur as shock progresses. Changes in this potential predicted failure of the circulation to maintain systemic arterial pressure with the available intravascular blood volume. In the majority of cases, a decrease in amplitude of the cortical potential preceded the fall in mean pressure which occurred when reservoir outflow fell behind the intravascular blood volume requirements. Meldrum and Brierly (4) and Brierly *et al.* (5) indicated that in order to abolish the evoked potential they had to drop the blood pressure rapidly below 25 mm Hg. However, we have shown that the same result occurs if a higher level of blood pressure is maintained for a prolonged period of time. The frequent return of the evoked response after infusion would suggest that in these animals the functional impairment is reversible. Meldrum and Brierly found a close correlation between disappearance of the cortical evoked potential and the development of permanent damage. In their study, moreover, not all animals taken to the same low pressure developed irreversible changes, and those animals without permanent damage maintained the evoked response. The EEG changes were an unsatisfactory index of the ischemic stress as judged by the ultimate pathology. Meldrum and Brierly concluded that the changes in amplitude with time of the sensory evoked response permitted differentiation of the extent of irreversible brain damage in monkeys and that perfusion pressure and EEG alterations did not. Ochs (7) also found that direct cortical responses were sensitive to the arterial pressure level.

Our results indicate that in the majority of cases, irreversible hypovolemic shock produces characteristic changes in the somatosensory cortical evoked potential suggesting profound and variable damage of the central nervous system. There was no correlation between changes in systemic blood gas levels or pH and the disappearance of the electrical potentials. Some of the variability in our results could be related to the depth of anesthesia since pentobarbital decreases cerebral metabolism and a decreased metabolic rate could reduce or delay ischemic effects (4). It is possible that withdrawal of a quantity of blood enhanced anesthetic action, which resulted in the depression of the cortical potential. However, in our experiments the evoked potential was maintained for 30 to 120 min following the withdrawal of blood. If the sensitivity of the cortical potential to the anesthetic increased with hypovolemia, a more immediate effect would have been expected.

A basic cause of the neural alterations with shock undoubtedly lies in the failure of adequate perfusion of the central nervous system. A low perfusion pressure has been found to result in maximal vasodilation of central vessels so that pressure becomes the major determinant of cerebral blood flow. Harper and Glass (8), in the dog, found that, at a mean arterial pressure of 50 mm Hg, cortical blood flow was not influenced by changes in arterial pCO_2, presumably because of maximal dilatation of cerebral vessels. It is thus likely that at the pressure levels used in the present study, cerebral perfusion was greatly reduced. There is also evidence that uneven distribution of cerebral flow occurs with low perfusion pressures. In the postrecovery pathological studies of Meldrum and Brierly (4) damage was particularly likely to occur at arterial boundary zones. These boundary zones are at the junctions between the anterior, middle, and posterior cerebral arteries. Hypotension caused characteristic boundary zone lesions in parieto-occipital sulci and other areas of the neocortex, but damage was

frequently scattered through the cortex, thalamus, and the cerebellum. It is thus apparent that severe and variable damage can occur throughout the brain. This could account for our findings that the cortical evoked potential was more sensitive to hypovolemia than were the cuneate responses.

Summary. Cortical and cuneate evoked responses and the EEG were studied during the various stages of hypovolemic shock. In 16 out of 18 animals, a decrease in amplitude of the cortical evoked response preceded or was concomitant with the period of spontaneous uptake of blood. Changes in amplitude and frequency of the EEG paralleled the changes noted in the cortical response but were much more variable. There was no correlation between changes in systemic blood gas levels or pH and the disappearance of the electrical responses. The fall in evoked cortical potential appears to provide a good indication of impending failure to maintain systemic arterial pressure.

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