Comparative Studies of Regional CNS Blood Flow and Evoked Potentials in the Cat

Effects of Hypotensive Ischemia on Somatosensory Evoked Potentials in Cerebral Cortex and Spinal Cord

M. Sato, M.D.,* G. Pawlik, M.D., C. Umbach, M.D., and W. -D. Heiss, M.D.

SUMMARY Functional resistance to graded hypotensive ischemia of various segments of the somatosensory pathway was determined in anesthetized cats by repeated concurrent recordings of regional blood flow measured by hydrogen clearance, and evoked potentials (EPs), of dorsal horn of lumbar spinal cord and cerebral cortex. During normal resting CNS blood flow (CBF), there were significant successive reductions of EP amplitudes, recorded from presynaptic spinal components (634, 424-949 μV; re-linearized mean and 95% confidence limits of log-transformed data) compared to postsynaptic spinal (359, 247-522 μV) and presynaptic cortical (50, 32-79 μV) and to postsynaptic cortical components (33, 22-50 μV). During ischemia amplitudes of EPs in spinal cord and cerebral cortex showed significantly different behaviors. The presynaptic spinal component was virtually independent of regional blood flow down to 12 percent of resting values, the postsynaptic cortical component exhibited strongest positive correlations (r = 0.45) with flow. In both regions postsynaptic amplitude was more sensitive to flow changes than respective presynaptic amplitudes. Despite similar regression coefficients for intermediate segments of somatosensory pathway, only postsynaptic spinal components were significantly correlated (r = 0.40) with regional flow. Presynaptic cortical amplitudes were variable and no significant flow dependence was demonstrated. Results suggested that in comparable degrees of regional ischemia of CNS functional integrity is determined by numbers of synaptic transmissions involved locally. Comparatively simple structures, e.g. the spinal cord, are less susceptible to ischemia and complex neuronal networks, e.g. the cerebral cortex, are more susceptible.

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IN ANOTHER SERIES OF EXPERIMENTS1 data indicated striking similarities between cerebral cortex and lumbar spinal cord of the cat as to their autoregulatory flow responses to manipulations of blood pressure. This observation might appear to contradict clinical evidence of lower incidences of symptomatic spinal cord ischemia compared to cerebral ischemic events during hypotension unless there are different susceptibilities to ischemic damage. Numerous studies have been reported using somatosensory evoked potentials (EPs) as indicators of CNS function, e.g. in ischemia or traumatic injury of the brain3-6 or spinal cord,7-8 but concurrent measurements of regional blood flow and EPs in both areas were not carried out. The present study was designed to provide comparative intra-individual measurements defining relationships of nervous function documented by evoked potentials with CBF measured by hydrogen clearance concurrently in the dosal horn of the lumbar spinal cord and contralateral somatosensory cortex during sciatic nerve stimulation.

Methods

Eleven cats of either sex weighing 1.5 to 2.8 kg were anesthetized by intraperitoneal injections of ketamine hydrochloride (25 mg/kg body weight) and by nitrous oxide. Anesthesia was maintained at all times according to recommendations of the American Heart Association and American Physiological Society. Catheters were inserted into the femoral vein for drug administration and blood withdrawal, and into the descending aorta via the femoral artery for continuous blood pressure monitoring and blood gas determinations. Following tracheostomy the animals were para-
lyzed with repeated doses of pancuronium bromide (0.24 mg/kg body weight every 2 hours) and artificially ventilated with a Starling breathing pump. Anesthesia was maintained with a 3 to 1 mixture of nitrous oxide and oxygen. Rectal temperature was kept at 37–39°C by means of a heating lamp.

The animal's head was fixed in a head holder, and a burr hole, 3–4 mm in diameter, was made in the frontal bone over the somatosensory cortex, 2 mm laterally from the sagittal and 4 mm anteriorly from the coronal suture. A spinal process was fixed in a special holder, and a small laminectomy was performed at L3. After incising the dura glass insulated platinum electrodes (10–20 μm in diameter with 1 mm bared) were inserted 2 mm deep into the somatosensory cortex and into the contralateral dorsal horn of the spinal cord at L3 (2 mm laterally from the midline), respectively. Blood flow was measured simultaneously in these two areas by recording the regional hydrogen clearance following inhalation of a gas mixture containing 5–12% H2. Flow values were calculated from H2-clearance curves starting 40 sec after terminating hydrogen inhalation by means of the equation: blood flow (in ml/100 g/min) = 69.3/T1/2. Steel needles were placed in the neck muscles and in the paravertebral muscles, to serve as indifferent electrodes for the EP recordings. During CBF measurements the sciatic nerve could be stimulated (5V, 0.3 msec, 2–3 Hz). Signals from cortical and spinal microelectrodes were passed through various filters (1-100 Hz band width), so that EPs could be isolated, amplified and stored in the memory of a DEC/MINC computer. The averages of 100 single evoked responses from the dorsal horn and the somatosensory cortex, respectively, were plotted and ampli-
tudes of first surface positive and first surface negative waves were measured. Both rCBF and EPs were deter-
mined repeatedly under resting conditions and at var-
ious levels of mean arterial blood pressure (MABP) after maintaining 10 min stabilization period. MABP was decreased from initial values (150 ± 29.9 mmHg, mean ± standard deviation) to 45 mmHg by repeated injections of trimethaphan camsylate (Arfonad®). Fi-

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Regression lines calculated from 34 measurements each (fig. 1) demonstrate similar relationships between MABP in the hypotensive range and rCBF in both regions.

Under resting conditions as well as within the range of hypotension studied, the somatosensory EPs in the cortex and in the dorsal horn of the spinal cord consisted of a well-defined first surface positive wave (P1) followed by a surface negative wave (N1) (fig. 2). In principle P1 may be considered as the presynaptic component representing conduction in afferent fibers, while N1 primarily reflects the excitation of postsynaptic nerve cells. During normocapnia and normotension P1 and N1 of each animal remained rather constant with an average coefficient of variation of 10% over long intervals of time. However, there was considerable interindividual variation, P1 ranging between 235 and 1817 μV and N1 between 136 and 766 μV in the spinal cord, and P2 between 21 and 209 μV and N2 between 14 and 110 μV in cerebral cortex. Significant (PAGE L-test: P < 0.01) and successive reductions of average EP amplitudes, from the presynaptic spinal to the postsynaptic cortical component, were observed (fig. 3).

Comparison of the EP-CBF relationships among 39 recordings was achieved concurrently in spinal cord and in cortex at various degrees of hypotensive ischemia. Because of substantial differences among animals, CBF and EP data were expressed as percentages of their respective values under control conditions. This transformation seemed appropriate in view of the significant positive correlations between cerebral and spinal cord CBF (r = 0.45, P < 0.005) as well as
SPINAL CORD VS CEREBRAL CORTEX RESISTANCE TO ISCHEMIA

FIGURE 2. Typical tracings of evoked potentials (averages of 100 single responses each, identical amplification) obtained by microelectrodes in the dorsal horn of the lumbar spinal cord and in the somatosensory cortex during sciatic nerve stimulation, permitting distinctions between the $P_1$ and $N_1$ amplitudes.

between logarithms of spinal and cortical peak-to-peak EP amplitudes ($r = 0.53, P < 0.005$). Figures 4 and 5 show individual EP data in relation to regional CBF with corresponding regression lines and respective degrees of confidence. Since no significant differences were found between EPs obtained either during the hypotensive interval or during subsequent pressure rise, all data were pooled. Both in the spinal cord and in the cerebral cortex the $N_1$ amplitudes were more susceptible to ischemia than presynaptic components. Within the domain of experimental ischemia $P_1$ was virtually independent of flow in spinal cord, and in cortex $P_1$ data were too scattered to yield significant regressions. Differences in flow-dependence between the presynaptic amplitude of spinal EPs and the postsynaptic amplitude of cortical EPs were highly significant (ANCOVA: $P << 0.001$). Cortical $N_1$ amplitudes were most sensitive to changes in rCBF.

Discussion

Rationale and Methodological Considerations

Simultaneous recordings of rCBF in various parts of the CNS were used to establish specific capacities of flow regulation. While limits of autoregulation are similar in spinal cord and in cerebral cortex, it is well known that the susceptibility to ischemic damage differs considerably among these parts of the CNS, suggesting differences in functional and metabolic activities which may be difficult to detect in diachronous experiments. When platinum microelectrodes are utilized for measuring H$_2$ concentration in tissues, and rCBF is estimated from clearance curves, neuro-physiological information can be obtained with the same electrodes at the same time by appropriate filtering and amplification of recorded evoked potentials. This concurrent recording technique yields rCBF and EP data from the same site, and relationships between parameters can easily be analyzed without experimental bias.

It is well established that various waves of the somatosensory potentials reflect propagation of stimulus dependent excitation at various stages of afferent pathways. The first surface positive deflection ($P_1$) of the EP in the dorsal horn of the spinal cord reflects the arrival of the impulse volley in the afferent fibers of the spinal root, the surface negative wave ($N_1$) the activation of the second afferent neurons and of the intermediate nerve cells. The first surface positive wave ($P_1$) of the EP in the somatosensory cortex is due to the arrival of impulses in the afferent fibers of the thalamocortical tract, the negative wave ($N_1$) indicating the activation of postsynaptic nerve cells in the somatosensory cortex. Evoked responses, therefore, provide some information on neuronal function of the entire somatosensory pathway from the bipolar spinal ganglion cell to the thalamus and farther up to secondary cortical cells.

EPs were used extensively for testing the function of the CNS under various pathological conditions. Changes in slope and amplitude as well as the disappearance of EPs may be related to the severity of tissue damage following experimental ischemia or trauma. Encouraged by results from animal experiments.

FIGURE 3. Pre- and postsynaptic amplitudes of the average somatosensory evoked potential (EP) in dorsal horn of the lumbar spinal cord and in contralateral cerebral cortex in 11 cats, showing successive decreases from spinal cord to cortex. Columns represent re-linearized means of log-transformed data, 95 per cent confidence intervals are indicated by vertical bars.
Symon et al\textsuperscript{13} used somatosensory evoked responses as an indicator of the severity of brain dysfunction in patients suffering from subarachnoid hemorrhage. A systematic comparative study of the ischemic vulnerability of EPs in the spinal cord and in the cortex has not been reported to date. In order to investigate regional resistances to ischemia in two CNS regions that are anatomically far apart systemic hypotension was induced in cats by drugs and, to produce low flow values, even by hypovolemia in addition. Although it is not known whether these procedures themselves may significantly alter evoked response, there was no evidence for a differential effect on EPs of either lowering or increasing blood pressure.

![Graphs showing the effect of regional spinal cord blood flow (rSCBF; a and b) and regional cortical blood flow (rCBF; c and d) on pre- (a and c) and postsynaptic amplitude (b and d) of spinal cord (SCEP) and cortical (CEP) somatosensory evoked potentials. Both EP amplitudes and flow are expressed as percentages of their respective resting values at the beginning of each experiment. In addition to individual data respective regression lines and equations are shown.](http://stroke.ahajournals.org/)
explained by a variable number of thalamic relays in the amplitude-flow relationships for postsynaptic spinal rCBF in spite of similar regression coefficients of final EPs and presynaptic cortical components may be citatory process. Therefore, the failure to detect a significant dependence of pre- and postsynaptic amplitudes of the spinal and cortical evoked potential (EP) on regional blood flow (rBF), each given as a percentage of control.

**EP-rCBF Relationships**

Some structures in the spinal cord, particularly the spinal roots and the white matter tracts, are known to be resistant to traumatic and ischemic injury and may sustain severe decreases of blood pressure and/or complete ischemia for up to 15 min with little alteration. The cerebral cortex on the other hand is much more prone to a breakdown of synaptic transmission during ischemia. The postsynaptic components of cortical EPs disappear at flow values of 15-18 ml/100 g/min, while the presynaptic component may be preserved down to a residual flow of 12 ml/100 g/min, probably demonstrating higher resistance to ischemia of white matter.

In line with these qualitative observations the present data indicate that the sensitivity to ischemia increases from lower to higher stages in the afferent somatosensory pathway. This flow dependence apparently corresponds not only with the absolute level of regional perfusion under standard conditions, but also with the complexity of the neuronal network and the number of synaptic transmissions involved in the excitative process. Therefore, the failure to detect a significant linear regression on the cortical P, amplitudes on rCBF in spite of similar regression coefficients of the amplitude-flow relationships for postsynaptic spinal EPs and presynaptic cortical components may be explained by a variable number of thalamic relays in the path of somatosensory impulses from spinal cord to cerebral cortex.

**Conclusions**

Experimental results clearly demonstrate that irrespective of a similar autoregulatory capacity, probably because of simpler neuronal networks the spinal cord has a greater resistance than cerebral cortex to ischemia of comparable degrees. This finding provides a neuro-physiological basis for the high frequency of cortical ischemic events compared to spinal cord in clinical practice.

**References**

Comparative studies of regional CNS blood flow and evoked potentials in the cat. Effects of hypotensive ischemia on somatosensory evoked potentials in cerebral cortex and spinal cord.
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