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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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 spinous 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 amplitudes of first surface positive and first surface negative waves were measured. Both rCBF and EPs were determined repeatedly under resting conditions and at various 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®). Finally, MABP was reduced to 30 mmHg by fractional withdrawal of 10 ml of blood into a heparinized syringe. MABP was gradually increased to starting levels by re-infusion of blood and injections of noradrenaline. During experiments PaO2 was kept above 95 mmHg, PaCO2 was maintained within the normal range (27–33 mmHg), and arterial pH varied from 7.23 to 7.52.

**Results**

As reported elsewhere under standard conditions, i.e. during normocapnia and normotension, resting rCBF was significantly lower (Wilcoxon test: P < 0.005) in the dorsal horn of the lumbar spinal cord (40 ± 29.2 ml/100 g/min) than in somatosensory cortex (79 ± 38.6 ml/100 g/min). Below the limits of autoregulation (at approx. 80% of control MABP) blood flow in the cerebral cortex and in the spinal cord passively followed changes in MABP in a linear manner. 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 (P+) followed by a surface negative wave (N−) (fig. 2). In principle P+ may be considered as the presynaptic component representing conduction in afferent fibers, while N− primarily reflects the excitation of postsynaptic nerve cells. During normocapnia and normotension, P+ and N− 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, P+ ranging between 235 and 1817 μV and N− between 136 and 766 μV in the spinal cord, and P+ between 21 and 209 μV and N− 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 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...
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.

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.

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, neurophysiological 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
Symon et al. 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.

**FIGURE 4.** 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 post-synaptic 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.
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**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\(^6,7,14-17\) and may sustain severe decreases of blood pressure\(^6\) and/or complete ischemia for up to 15 min\(^18\) with little alteration. The cerebral cortex on the other hand is much more prone to a breakdown of synaptic transmission during ischemia.\(^19\) The postsynaptic components of cortical EPs disappear at flow values of 15–18 ml/100 g/min,\(^1\) while the presynaptic component may be preserved down to a residual flow of 12 ml/100 g/min,\(^4\) 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 excitatory process. Therefore, the failure to detect a significant linear regression on the cortical P\(_a\) 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-terposed 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**


FIGURE 5 Regression lines, and respective 95 percent confidence limits, of pre- and postsynaptic amplitudes of the spinal and cortical evoked potential (EP) on regional blood flow (rCBF), each given as a percentage of control.
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