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CONSTITUTIVE NITRIC OXIDE SYNTHASE (cNOS): A POSSIBLE KEY POINT IN PATHOGENESIS OF SECONDARY LESION AFTER SPINAL CORD INJURY

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Secondary lesion (LS) which follows a spinal cord injury is an early phenomenon, independent from inflammatory cells invasion of damaged tissue (1). Nitric Oxide (NO) has been indicated as having a role in its pathogenesis (2). There are two constitutive isoforms of NOS, endothelial (eNOS) and neuronal (eNOS), constantly active, and an inducible isoform (iNOS), synthesised only during inflammatory response and able to produce big amount of NO. High concentration of NO could be toxic, because of its conversion in peroxynitrates, highly reactive metabolites destroying biological structures of cells (3). For this reason, NO concentration is strictly and finely regulated in cells. We suppose that major inhibitory effect on the induction of iNOS expression is represented by the "physiological" concentration of NO synthesised by the cNOS, which would inhibite NF-kB activation (4). Aim of this study is to asses the role of the two cNOS in pathogenesis of secondary lesion after spinal cord injury in rat.
A compression of dorsal spinal cord injury has been performed on rats by a vascular clip (50 gr/mm2 for 15"). 15 and 60 minutes after trauma, the enzymatic activity of nNOS and eNOS (n=6 per group) and the activation of nuclear factors NF-kB and STAT 1 (n=3 per group), have been measured in the cervical, dorsal and lumbar segments of injured spinal cord. Other untreated rats served as control groups. Moreover in injured rats, 2 hours, 6 hours and 24 hours after injury, the expression of m-RNA for iNOS is under investigation by Northern Blotting.
In control rats, specific activity of nNOS is : 161±14 in cervical segment, 163±10,9 in the dorsal segment and 211±21,4 in the lumbar segment. In injured rats, 15 minutes after injury specific activity of nNOS is 187±18 in cervical segment, 150±11,6 in dorsal segment and 231±12 in lumbar segment, and 60 minutes after injury it is 165±14 in cervical segment, 87±10,9 in the dorsal segment and 51±21,4 in the lumbar segment. eNOS activity is subjected to an high variability itself. Dorsal spinal cord injury reduces after 60 minutes the activity of nNOS in dorsal and lumbar segment.
NF-kB shows a basal level in all uninjured spinal cord but it is strongly activated 1 hour after injury only in dorsal segment. STAT 1 is not present in uninjured spinal cord and it is activated just 15 minutes after injury only in dorsal spinal cord.
These results seem to confirm our hypothesis about the fine regulation of NO concentration following the cell damage occurring in spinal cord injury. A new therapeutic strategy for prevention of secondary lesion after a spinal cord injury, based on modulation of constitutive NOS in resident spinal cord cells, could be evaluated.

References

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