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# EXPERIMENTAL MODELS OF CEREBRAL ISCHEMIA: ROLE OF eNOS

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Stroke remains one of the major causes of death and disability throughout the world. The development of experimental models of cerebral ischemia has allowed for a better knowledge of its pathophysiology and for testing therapeutic strategies. The only models of spontaneous stroke are provided by the spontaneously hypertensive stroke-prone rats (SHRSP). In this animal model, spontaneous brain ischemia occurs as a consequence systemic and brain inflammation. The permanent and/or transient mechanical occlusion of middle cerebral artery (MCAO) is routinely used to test drugs aimed at reducing the extent of cellular damage in the acute phase of stroke, with various mechanisms. By the use of MRI techniques ($T_2$W and DWI) it is possible to identify in the same animal the early onset of brain lesion as well as to follow it. In this experimental model both nNOS and eNOS play a role in the development of brain lesions. In particular in nNOS knockout mice develop smaller cerebral infarctions than do wild type animals, suggesting that nNOS is involved in tissue damage. On the contrary eNOS knock out mice develop larger strokes after MCAO, probably because eNOS plays a role in maintaining cerebral blood flow. Indeed, recent data indicate that statins, which are capable to increase eNOS activity, exert protective effects on the development of cerebral focal ischemia in mice. Data obtained in rats, treated with lipophilic statins, indicate that these drugs increase eNOS expression in brain vessels, resulting in reduction of brain infarct size, as detected by MRI. Moreover, the protective effect of these drugs is observed not only when they are administered before but also after the ischemic insult. Overall these data suggest that the increases in eNOS activity or nitric oxide availability at vascular level represent a potential therapeutic approach in the prevention and treatment of brain ischemia.