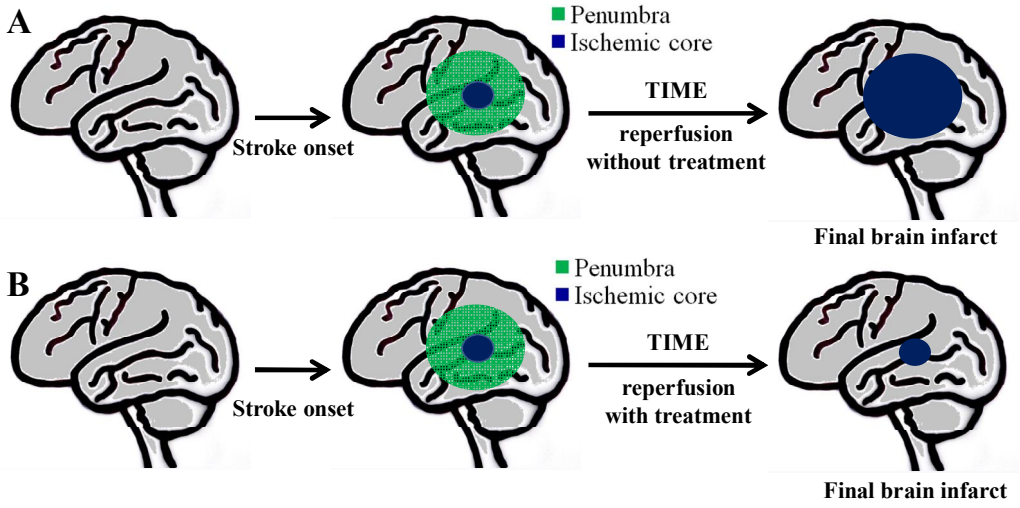
The purpose of the study is to elucidate the mechanisms underlying the neuroprotective action of a specific agonist of the Y2 receptors (Y2R) for the neuropeptide Y (NPY) in an experimental model of focal cerebral ischemia – middle cerebral artery occlusion with reperfusion (MCAO/R) in rats with essential hypertension (SHR). Previous studies conducted by our team in normotensive and SHR rats showed that the administration of NPY(13-36) 30 minutes after the onset of ischemia or 30 minutes after reperfusion, significantly reduced the volume of post-ischemic brain infarction and gait deficits. The background of this protective effect is unexplained.

During the first seconds or minutes of stroke, the ischemic area differentiates spatially into the necrotic ischemic core and the surrounding penumbra, where collateral circulation maintains blood flow at a level sufficient for cell survival for an extended period. In the course of an ischemic cascade, the penumbra is recruited into the ischemic core over time. Therefore, the goal of stroke therapy is to save the penumbra (picture 1). The mechanisms of ischemic stroke and damage of the penumbra are extremely complex, but several key processes can be indicated: overexcitation and transient, spontaneous activation of large number of neurons; loss of communication: neuron – astrocyte – blood vessel; dysfunction of cerebral microcirculation, apoptosis and inflammation. In addition, concomitant cardiovascular disease, such as arterial hypertension, worsen the course of stroke.

Our studies will determine the effect of NPY(13-36) on these ischemic cascade processes and further evaluate whether the test substance has a stimulatory potential of endogenous protective and repair processes: the recruitment of collateral circulation to the area of the penumbra and the formation of the new blood vessels (angiogenesis). The research will be carried out using electrophysiological methods, optical/laser measurements of cerebrocortical microflow changes and molecular biology methods.

Ischemic stroke is a serious disease that often results in death or significant and permanent disability of affected persons. Post-stroke disability impairs the functioning of the whole organism, exacerbates a patient's comfort and requires the involvement of financial resources and family care. The WHO epidemiological estimates show a high percent of cases of ischemic stroke with a tendency to increase. Despite intensive research and promising experimental results indicating the possibility of pharmacological protection of the brain against the effects of ischemia, no protective substance has been found to be effective in patients. This study provides hope for a more effective treatment of stroke in the future and to explore the possibilities of neuroprotective treatment in general.



Picture 1. The ischemic core and penumbra, theoretical basis of the neuroprotection therapy.
Panel A – stroke without treatment, panel B – neuroprotection therapy.