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Letter to the Editor

Comment on "Neuronal nitric oxide synthase inhibition reduces brain damage by promoting collateral recruitment" in a cerebral hypoxia-ischemia mice model

Dear Editor,

A research paper by Zhang et al[1] was recently published in your journal reporting a role for neuronal nitric oxide synthase (nNOS) inhibition in the establishment of collateral recruitment in a cerebral hypoxic-ischemic mice model. This report has strongly challenged us at two levels as following:

1) The authors used adult mice, which underwent transient middle cerebral artery (MCA) occlusion by the insertion of a filament in the internal carotid artery (ICA) through the external carotid under isoflurane anesthesia in O_2. This model is a pure ischemia-reperfusion model, called intraluminal model[2], and not a model of hypoxia-ischemia produced by the ligation of an artery followed by a variable (according to the developmental stage) exposition to hypoxia (8% FiO_2)[3].
2) The authors used the 7-nitroindazole (7-NI at 25 mg/kg) as a competitive and selective nNOS inhibitor as we[4] and Pinard et al[5] previously used. Under basal conditions, a single dose of 7-NI significantly reduced mean blood-flow velocity (mBFV) in the ICAs, but not in the basilar trunk (BT) [Figure 1 in (4); Figure 2 in (1)]. However, in the text and Figure 3B Zhang et al[1] reported that 7-NI decreased mBFVs in the BT, although representative Doppler velocity waveforms showed an increase of the mBFV (blue line in Figure 3A – right).

An increase in blood flow (BF) in the BT during ischemia in the P7 rat was illustrative of the establishment of a collateral supply[6]. In adult rodents, the plasticity of collateral supply is less extended and less rapid to establish, and thus the modifications of BF in the ICA were more illustrative of the cortical collateral supply through the posterior or the anterior cerebral arteries when the MCA was occluded, and not the modifications in the BT.

Altogether, these thoughts impose to take the findings reported by Zhang et al[1] with caution.

Conflict of interest

The authors declare no conflicts of interest.

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