

The detrimental effect of aging and ischemia on cerebrovascular reactivity, and potential benefits of nimodipine.

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Introduction: Under physiological conditions, CO₂ inhalation induces hypercapnic vasodilation. We set out to investigate the effect of both aging and ischemia on cerebrovascular reactivity. Since preserved cerebrovascular responses may offer therapeutic benefit, we evaluated the potential protective properties of nimodipine on the hyperemic response.

Methods: Young and old isoflurane anesthetized male Wistar rats were used (n=24). In an open cranial window, CBF was measured by laser Doppler flowmetry, the local field potential was recorded by a glass capillary microelectrode, and nimodipine was administered topically at a dose of 100 µM. Cerebral ischemia was induced by bilateral common carotid artery occlusion. CO₂ challenge (10% CO₂ inhalation for 20s) was performed repeatedly (5 times) at an interval of 3 min. Finally, transcardial perfusion with 4% paraformaldehyde was performed and brain slices were prepared for immunohistochemistry.

Results: The relative amplitude of the CBF response to the hypercapnic challenge decreased significantly in the old animals (14.3±4.4 vs. 32.6±2.9%, old vs. young), and under ischemia produced in young animals (4.7±6.4 vs. 32.6±2.9%, ischemia vs. control). Likewise, the area under the curve (AUC) decreased with age (289±88 vs. 785±40%×s, old vs. young) and ischemia (235±101 vs. 785±40%×s, ischemic vs. control). Nimodipine elevated the relative amplitude of the CBF response impaired by aging (20.8±2.8 vs. 14.3±4.4%, old nimo vs. vehicle), also reflected by the AUC (430±44 vs. 289±88%×s, old nimo vs. vehicle).

Conclusions: Cerebrovascular reactivity becomes impaired by under ischemia and as a result of aging. Nimodipine emerges as a promising drug candidate to rescue cerebrovascular responses in aging.

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