Abstract View

NEUROPEPTIDE Y AND ITS RECEPTOR ANALOGS MODULATE ISCHEMIA-INDUCED NITRIC OXIDE PRODUCTION.

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We previously showed that intracerebroventricular (ICV) injection of neuropeptide Y (NPY) or Y1 agonist increased the infarct volume whereas administration of BIBP3226, a NPY Y1 antagonist, reduced the infarct volume. Nitric oxide (NO) is a mediator of ischemic damage. In this study, we examined the effects of NPY and its receptor analogs on NO production during middle cerebral artery occlusion. Male Sprague-Dawley rats were anesthetized with sodium pentobarbital. NPY (10 mcg/kg), [Leu31, Pro34]-NPY (30 mcg/kg), BIBP3226 (15 mcg/kg), NPY3-36 (15 mcg/kg) or vehicle was administered via a slow ICV injection at 2 minutes after onset of ischemia. NO measurement was made in the brain slices between Bregma levels +2 and -4 mm. NO trapping reagents, diethyldithiocarbamate and iron citrate, were administered via intraperitoneal and subcutaneous injection, respectively, at 15 minutes prior to ischemia. Tissue NO concentration was measured using electron paramagnetic resonance spectroscopy. Results from the ischemic side were expressed as a percentage of the non-ischemic side and compared among groups using two-tailed Student's t test. After 15 minutes of focal cerebral ischemia, the relative NO concentration increased to 131.9±8.0% (mean±SEM; n=8). NPY treatment further increased the NO signal (250.9±50.5%; n=8, $P<0.05$), whereas BIBP3226 reduced the NO signal (69.6±8.8%; n=8, $P<0.05$). Treatment with [Leu31, Pro34]-NPY and NPY3-36 did not affect the ischemia-induced NO signal (133.4±13.3%, n=8; 129.2±21.8%, n=8). Thus, exogenous NPY and its receptor analogs may affect the infarct volume via their effects on ischemic-induced NO generation.