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Overexpression of Glur2 and NR1 glutamate receptors in lizard spinal motoneurons following caudotomy and caudal regeneration

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The lizard regenerating tail has been used as a model to study the molecules involved in neuronal plasticity. The regrowing tail is innervated by the spinal motoneuron axons of the three spinal segments rostral to the amputation. During regeneration, these motoneurons display hypertrophy and nNOS, Bcl-2 and GAP-43 induction (Cristino et al., Neuroscience 101(451-458); 2000). It is known that, in mammals, axotomy induces intracellular Ca+2 increase which might cause neuronal death, and the glutamate receptors are involved in Ca+2 modulation. These receptors are of two types: AMPA and NMDA receptors. AMPA glutamate receptors include two subgroups based on Ca+2 permeability. The subgroup containing the GluR2 subtype reduces Ca+2 permeability, whereas the NR1 subtype of the NMDA group increases it.The above subtypes were immunodetected in the motoneurons of spinal cord sections of Gekko gecko with intact tails, by using anti human policlonal and monoclonal antibodies, at day 15 and 30 after caudotomy and with completely regenerated tails (240 days). nNOS immunofluorescence was performed on consecutive sections to correlate it with GluR2 and NR1 expression, nNOS activity being Ca+2-dependent On the treated sections was performed densitometric analysis.The results were the following:
GluR2 and NR1 increased at day 15 (OD 52.3 ± 0.8 and 34.32 ± 0.7, respectively; mean OD ± SEM) with respect to control animals (15.3 ± 0.6 and 16.3 ± 0.5), GluR2 expression dysplayed a peak and NR1 decreased at day 30 (56,7 ± 0.6 and 21.7 ± 0.4) and the expession of both subtypes decreased in regenerated tails (20.8 ± 0.3 and 43,7 ± 0.5). GluR2/NR1 double immunofluorescence showed no colocalization, while nNOS/GluR2 double immunofluorescence revealed colocalization in spinal motoneurons.
These data suggest a functional relationship of the neuroprotective type between the increase in GluR2, NR1 and the nNOS expression in axotomized motoneurons. This relationship would cause a block of the excitotoxic effects of Ca increase.