SMN PROTEIN EXPRESSION IN AXOTOMIZED FACIAL MOTOR NEURONS IN THE RAT: A DEGENERATION PARADIGM

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Spinal muscular atrophy (SMA) is a common autosomal recessive disease of childhood. It is characterized by progressive degeneration of motor neurons and amyotrophic muscle weakness leading to respiratory failure. The Survival Motor Neuron (SMN) gene is the SMA-determining gene. The SMN protein has several proposed housekeeping cellular roles in pre-mRNAs maturation and splicing and in regulating transcription. However, the pathogenic mechanisms linking the loss of the SMN protein to the selective motor neuron death of SMA is still unclear. We have previously demonstrated that the SMN protein is markedly expressed by developing and mature spinal cord motor neurons, and that it is present in the axonal compartment of motor neurons during the pre-natal and the early post-natal development. In the present study, we investigated the plasticity of SMN expression in rat facial motor neurons after peripheral axotomy. Confocal double and triple immunofluorescence labeling experiments were carried out with specific anti-SMN antibodies and different neuronal and glial markers after facial axotomy at post-natal day 7 and different survival times (1 to 7 days). After axotomy, an increasing number of degenerating motor neurons were present in the ipsilateral facial nucleus at progressively longer survival times. Positive neuronal nitric oxide synthase (nNOS) staining was evident in the most lateral part of the axotomized facial nucleus. In the same location within nucleus, we observed quite a number of motor neurons with a clear shift of the SMN expression from the cytoplasm to the nucleus. These motor neurons were specifically surrounded by microglial cells and characterized by loss of axo-somatic synaptic contacts. These data clearly demonstrate that the SMN expression in motor neurons may be induced or modified by external noxious stimuli. Experiments are now in progress to verify whether the different SMN sub-cellular distribution reported here is a marker for surviving neurons in regeneration or neurons already committed to degeneration.