View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Firenze University Press: E-Journals

IJAE Vol. 115, n. 1/2 (Supplement), 2010

Validation of experimental models of spinal muscle atrophy (SMA): a neuroanatomical study

Federica Fulceri[1], Livia Pasquali[2], Leonardo Settimini[1], Feng Xia[1], Michela Ferrucci[1], Antonio Paparelli[1]

[1] Department of Human Morphology and Applied Biology, University of Pisa, Italy
[2] Clinical Neurology, Department of Neurosciences, University of Pisa, Italy

Spinal muscular atrophy (SMA) is an autosomal recessive disorder characterized by degeneration of spinal cord motoneurons and it is associated with muscle paralysis and atrophy. Based on symptom onset and disease severity, SMA is classified in three subtype; type I (severe), type II (intermediate) and type III (mild). All of these are due to loss or mutation of the telomeric survival of motor neurons gene (*SMN1*). *SMN1* is duplicated with a highly homologous copy called *SMN2* and both genes are transcribed. The pathophysiology of SMA remains unknown and no cure is available due to the paucity of reliable animal models. In this study we firstly characterized the anatomy and behaviour of a type III SMA mice. Our transgenic SMA model is characterized by the genotype Smn1 -/-, Smn2 +/+, Smn1A2G +/-. The motor test used are Rotarod test, the Paw Grip Endurance and the stride length test. All mice presented a progressive motor worsening evidenced by the rotarod test.

Analysis of the spinal cord of Smn1 -/-, Smn2 +/+ e Smn1A2G +/-, at lumbar level, shows severe cell death involving motor neurons within the lamina IX. The size of spared motor neurons is augmented in SMA mice.

We found that chronic autophagy stimulation delayed disease onset and progression.

Key words
Neurodegeneration, spinal cord, spinal muscle atrophy, motorneuron, autophagy