

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

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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 sub-type; 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, motoneuron, autophagy