Nifedipine enhances neurotransmitter release in a mouse model of Spinal Muscular Atrophy

P06-06

A.M. López[I], R. Tejero[II], L. Tabares[II]

[I]Departamento de Fisiología Médica y Biofísica, Facultad de Medicina. Universidad de Sevilla., Sevilla, Spain, [II] Departamento de Fisiología Médica y Biofísica, Facultad de Medicina. Universidad de Sevilla., Seville, Spain

Spinal muscular atrophy (SMA), an autosomal recessive neurodegenerative disease, is caused by mutations in or loss of the Survival of Motor Neuron (*SMN1*) gene that reduces the level of the Survival of Motor Neuron protein. It is characterized by degeneration of spinal cord α-motoneurons, resulting in weakness and muscle atrophy. Furthermore, the quantal content at the neuromuscular junction (NMJ) is reduced about 50% in the SMA (SMNΔ7) mouse model.

We investigated the ability to modulate synaptic release in SMA motor nerve terminals by nifedipine (50 μM), a L-type voltage-dependent calcium channels antagonist that enhances neurotransmission in central synapses, as well as NMJ. Likewise, we studied its effect on the parameters that determine the quantum content: the probability of release(p_r) and the number of release sites(n). To this end, we performed electrophysiological intracellular recordings in the *Transversus abdominis* muscle in control and SMNΔ7 mice.

We found that nifedipine significantly increased the amplitude of the evoked end-plate potentials at low-frequency of stimulation (0.5 Hz) in both genotypes. In contrast, the amplitude of the spontaneous release was not affected although its frequency was increased. Quantal content was significantly increased after the application of the drug. Additionally, p_r significantly increased in the control terminals (≈170%), and n in the mutants (≈300%). At high-frequency of stimulation (20 Hz), nifedipine produced a great facilitation during the first phase of the train and a significant increase in the total number of released quanta in controls. However, the effect was much lower in mutants. We are now studying the mechanism by which nifedipine enhances neurotransmission.

Thus, we propose that neurotransmitter release in SMA terminals can be positively modulated through an increase in the number of active release sites after application of nifedipine.

Financial support BFU2013-43763-P, BFU2016-78934-P, BES2011-048901