Matching between adult neurons: feel abandoned? Just call on me

Plasticity in the central nervous system allows the adaptation of neural circuits to new circumstances, such as the recovery after brain injury. The mechanisms of neural plasticity include, among others, the formation of new synapses. An example of these plastic processes is reactive synaptogenesis: synapses formation after partial deafferentation of a given population of neurons. Usually, neurons receive inputs from different sources. If one of these inputs is depleted, the remaining afferents sprout their axon terminals, establishing new synapses with the target cell that, in turn, fill the vacant spaces left by the lost input.

The process of reactive synaptogenesis may lead to the reinforcement of the spared input. Depending on the nature of both groups of afferents, this may have two opposed consequences: first, if both afferents carry different signals, the strengthening of one of them with detriment of the other could alter the firing pattern of the postsynaptic neuron; second, if both inputs have related signals, then the original firing pattern may be finally restored.

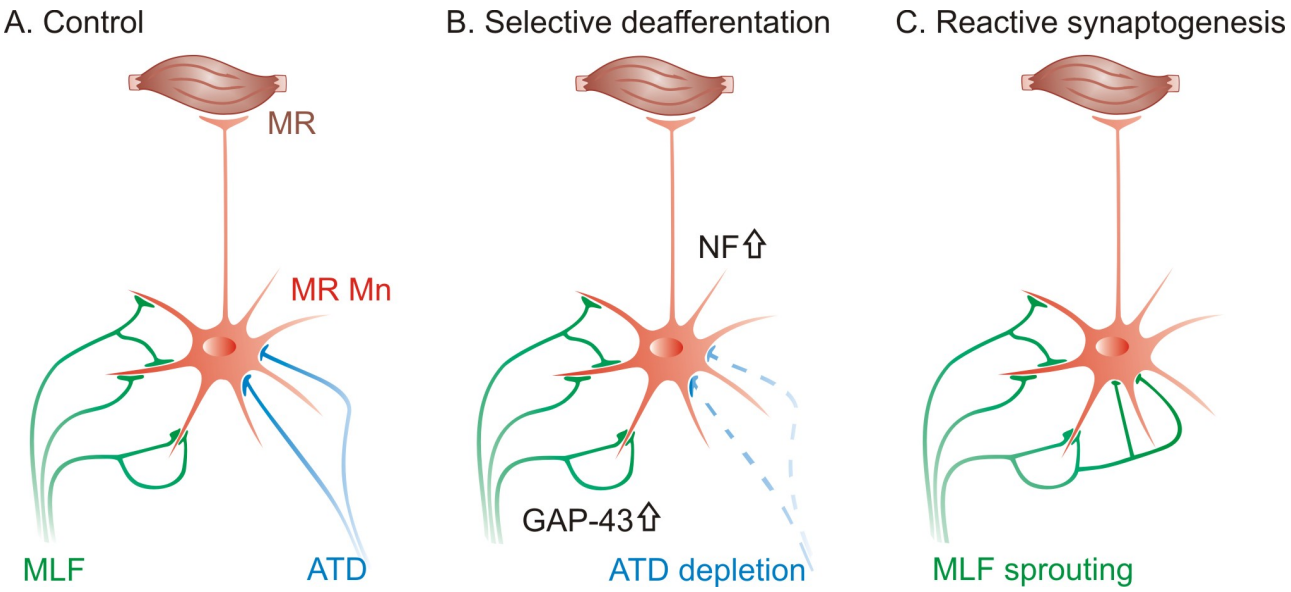

Fig. 1. **A.** Medial rectus motoneurons (MR Mn) receive afferents from the medial longitudinal fascicle (MLF) and the ascending tract of Deiters (ATD). **B**. After ATD depletion, the content of neurotrophic factors (NF) in medial rectus motoneurons is increased, as well as the amount of GAP-43 in the neuropil. **C**. 96 hours after lesion, the process of reactive synaptogenesis had started and an increase in afferent terminals was observed.

This seems to be the case for a population of midbrain motoneurons that innervate the extraocular

medial rectus muscle. These motoneurons receive two main inputs: second order vestibular neurons located at the ipsilateral lateral vestibular nucleus reach them through the ascending tract of Deiters (ATD), and pontine abducens internuclear neurons innervate them contralaterally through the medial longitudinal fascicle (MLF). Both afferents carry signals related to the position of the gaze and the velocity of eye movements in response to head movements. Previous studies of our laboratory demonstrated that the section of the ATD produced a reactive sprouting from abducens internuclear neuron axons that restored the normal firing pattern of medial rectus motoneurons. Besides, early after lesion, it was observed an increase in neurotrophin proteins. On the contrary, the transection of the MLF did not produce a strong enough reactive synaptogenesis in vestibular neurons. This different reaction to each selective deafferentation was explained in terms of quantity of axons, because the abducens projection is much more robust than the vestibular one.

The neurotrophin family of neuronal growth factors, composed mainly by nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) are implicated in the expression of growth-associated proteins such as GAP-43, but their actual role in reactive synaptogenesis is not fully understood. We evaluated the short-term events that occur after the transection of either the MLF or the ATD. By means of confocal microscopy, immunocytochemistry and retrograde labeling, a reduction in the synaptic coverage was described 24 hours and was more pronounced 48 hours after ATD lesion. Strikingly, 96 hours after lesion the number of synaptic terminals had increased. However, synaptic stripping after MLF transection was slower but irreversible.

Irrespective on the type of lesion or the time course of synaptic recovery, an increase in neurotrophin content was observed in partially deafferented motoneurons from the second day after lesion, before synaptic reinnervation. We argue that neurotrophins could have been released from motoneurons at synapses, captured by the axonal terminals of abducens internuclear neurons, and retrogradely transported to the soma, inducing an increase in the expression of axon growing molecules, that would lead to the process of reactive synaptogenesis.

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