Force pathway to synaptic clustering at the neuro-muscular junctions of embryonic flies

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Abstract (Arial 10)

Memory and learning in animals are mediated by neurotransmitters that are released from vesicles clustered at the synapse. Vesicle clustering has been believed to result primarily from biochemical signaling processes that require the connectivity of the presynaptic terminal with the cell body, the central nervous system, and the postsynaptic cell. We show, using embryonic *Drosophila* motor neurons, that vesicle clustering at the neuromuscular presynaptic terminal depends on mechanical tension within the axons [1]. Neurons generate this tension within the first two hours of synaptogenesis, and actively maintain the tension of about 1 nN by employing acto-myosin machinery. If the rest tension is perturbed mechanically, axons restore the rest tension either by relaxing or by contracting over a period of about 15 min. Vesicle clustering vanishes upon severing the axon from the cell body, but is restored when mechanical tension is applied to the severed end of the axon. Clustering increases when intact axons are stretched mechanically. We finally reveal the underlying mechanism by which tension and vesicle clustering are linked [2]. The role of mechanical force in vesicle clustering is a new paradigm in the understanding of synaptic functions. This force paradigm may lead to new treatments for neurological diseases.

References

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[2] Fan A, Tofangchi A, De Venecia M, Saif MT. A simple microfluidic platform for partial treatment of insuspendable tissue samples with orientation control. *Lab Chip*, 2018, 18 (5), 735-742.

Figures

Figure 1. Nervous system of an embryonic Drosophila (left). The axons of motor neurons emanate from the Central Nervous System (CNS) to form Neuro Muscular Junction (NMJ) with muscle. One of the axons is resected by a laser beam. The neurotransmitter vesicles de-cluster after resection. But if the cut end is pulled by a pipette, vesicle clustering is restored.