Glycerotoxin synchronises spontaneous quantal neurotransmitter release independently of action potentials

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Glycerotoxin (GLTx) is a novel neurotoxin recently purified from *Glycera convoluta* (Meunier *et al.*, 2002). GLTx produces an increase in neurotransmitter release at the neuromuscular junction (NMJ) by up-regulating N-type Ca^{2+} (Cav2.2) channels (Schenning *et al.*, 2006). GLTx enhances both spontaneous and evoked neurotransmitter release at the NMJ (Meunier *et al.*, 2002). The increase in miniature end-plate potentials (MEPPs) and miniature end-plate currents (MEPCs) occurs in a burstic manner. Interestingly, GLTx greatly increases the amplitude of some MEPPs. Analysis of interburstic events demonstrates that GLTx promotes a degree of quantal synchronisation even in the presence of tetrodotoxin (1mM). Two hypotheses have been tested: that GLTx induces a propagated release of intracellular calcium that triggers the synchronised spontaneous release; or that GLTx induces localised synchronisation of transmitter release from a few active zones along nerve terminal branches. Dual electrode recording techniques and nerve terminal visualisation suggests the latter hypothesis to be valid. Our results demonstrate that by interacting with Cav2.2 channels GLTx increases the synchronisation of spontaneous release, a process previously thought to solely rely on the presynaptic action potential mediated by Na^{+} channels. Our results suggest that Cav2.2 channels are directly participating in the molecular mechanism responsible for synchronising synaptic vesicle fusion events - a critical process that has received very little attention so far.

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