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**Title** Neuroprotectant minocycline depresses glutamatergic neurotransmission and Ca<sup>2+</sup> signalling in hippocampal neurons.

**Text** The mechanism of the neuroprotecting action of the tetracycline antibiotic minocycline against various neuron insults is controversial. In an attempt to clarify such mechanism, we have studied here its effects on various electrophysiological parameters, Ca<sup>2+</sup> signalling, and glutamate release, in primary cultures of rat hippocampal neurons, and in synaptosomes. Spontaneous excitatory postsynaptic currents and action potential firing were drastically decreased by minocycline at concentrations known to afford neuroprotection. The drug also blocked whole-cell inward Na<sup>+</sup> currents (I<sub>Na</sub>) by 20%, and the whole-cell Ca<sup>2+</sup> current (I<sub>Ca</sub>) by about 30%. Minocycline inhibited glutamate-evoked elevation of the cytosolic Ca<sup>2+</sup> concentration ([Ca<sup>2+</sup>]<sub>c</sub>) by near 40%, and K<sup>+</sup>-evoked glutamate release from synaptosomes by 63%. Minocycline also depressed the frequency and amplitude of spontaneous excitatory postsynaptic currents (sEPSCs), but did not affect the whole-cell inward current elicited by GABA or glutamate. This pharmacological profile suggests that the neuroprotective effects of minocycline might be associated to the mitigation of neuronal excitability, glutamate release, and Ca<sup>2+</sup> overloading.

**Theme** C - Disorders of the nervous system  
Neurotoxicity, inflammation, and neuroprotection - Neuroprotective mechanisms