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Tolperisone potently inhibits ouabaine-induced increase of cortical excitability in mouse brain slices

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Tolperisone is a centrally acting muscle relaxant drug, which has long been used for the treatment of muscle spasticity and pain associated with rheumatic diseases. It is thought to act via inhibition of sodium and calcium channels. Cortical spreading depression (CSD) is a pathological phenomenon characterized by abnormally increased neuronal activity and excitability. It is implicated in the pathomechanism of some central nervous system diseases such as migraine or ischemic brain damage due to injury or stroke. In a mouse brain slice model, we investigated the effect of tolperisone on the threshold concentration of ouabain to induce CSD. Tissue DC potential changes associated with CSD were recorded with glass electrodes. Slices were perfused with artificial cerebrospinal fluid. Thirty min later perfusion was switched to a solution containing ouabain so that the concentration of the excitatory substance in the slice chamber was elevated continuously in a nearly linear manner. When ouabain exceeded a threshold concentration a CSD was elicited. In control solution the latency of CSD initiation was 12.3±0.2 min, which corresponded to a ouabain concentration of about 100 μM. In the presence of tolperisone (12.5-200 μM) the latency increased dose-dependently, with a minimum effective concentration of 12.5 μM, where the latency increased to 14.5±0.4. Our model seems to be suitable for testing drug effect on cortical excitability in vitro.