# TOPIRAMATE DOSE-DEPENDENTLY MODIFIES SLOW INHIBITORY POST SYNAPTIC POTENTIALS EVOKED IN RAT OLFACTORY CORTICAL NEURONES *IN VITRO*

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Topiramate (TPM) is a new generation antiepileptic drug, licensed for patients with partial and secondarily generalized seizures. Thus far, its cellular mechanisms include: blockade of voltage-activated $Na^+$ channels, modulation of HVA $Ca^{2+}$ channels, potentiation of $GABA_A$ currents inhibition of AMPA/KAI glutamate currents and a $K^+$-dependent hyperpolarization[1]. We tested TPM on transverse *in vitro* brain slices of olfactory cortex prepared from Wistar rats as previously reported[2]. This 'limbic' brain area is known to be important in the development and maintenance of experimental kindling and also has a potential role in the genesis and spread of certain forms of human epilepsy *e.g.* temporal lobe epilepsy with partial seizures. Stable intracellular recordings were made from neurones in the deep cell layer II-III using 4M K acetate-filled microelectrodes. Data are presented as mean ± S.E.M. As previously reported, in neurones maintained at –70 mV membrane potential by steady current injection, bath-application of TPM induced a slow membrane hyperpolarization, which was accompanied by a decrease in membrane input resistance[2]. Synaptic stimulation was delivered through a bipolar nichrome wire electrode (25μm diameter; 15μm inner core diameter) placed in cortical layer I, in order to activate afferent and association fibres projecting to layer II/III. Postsynaptic potentials (PSPs) were evoked in response to stimuli of increasing intensities (5–20 V, 0.2 ms) delivered by a Digitimer isolated DS2 stimulator. Stimulus strength was adjusted so that the synaptic response was just sub-threshold for evoking orthodromic action potentials. All measurements were performed before, during and after bath-application of TPM, so that each neurone served as its own control. Control PSPs recorded at -70mV were usually characterized by a fast excitatory component (fEPSPs) and a slow inhibitory component (sIPSPs). Control sIPSPs were characterized by a averaged peak amplitude of -6.47±0.73 mV with a averaged time to peak of 229.7±31 ms. TPM 10μM induced an increase in peak amplitude (+74,75%) and in the time to peak (+20.33%). Inversely, TPM 20 and 40μM induced a decrease of peak amplitude -46.58% and -61.73% for 20μM and 40μM, respectively. The latter dose reduced significantly also the time to peak of -28.38%. At the dose of 50μM, TPM induced a complete block of the sIPSPs these effects of TPM were usually fully reversed after a 30 min washout period. Such effects could contribute to the clinical antiepileptic efficacy of this drug.

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