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Main Cavinton® metabolite cAVA increases neuronal excitability

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The sodium channel blocking activity of Cavinton (vinpocetine) is implicated in its anti-excitotoxic actions. Clinical- as well as animal experimental data indicate that vinpocetine has a memory enhancing effect. However, inhibition of sodium channels, which decreases excitability, is difficult to reconcile with a positive effect on memory. Vinpocetine is readily metabolised to cis-apovincaminic acid (cAVA) in rats. We investigated if cAVA could play a role in the memory enhancing effect of vinpocetine, by analysing the effects of cAVA on neuronal excitability in models of cortical spreading depression (CSD) and in spinal reflex experiments. In the rat hemisected spinal cord model, ventral root reflexes recorded from the L5 ventral root following the stimulation of the ipsilateral dorsal root, were dose-dependently enhanced by cAVA (25-400 μM). In brain slices, cAVA (100-200 μM) markedly increased the excitability of cortical tissue. CSDs could have been evoked more easily by application of high-potassium containing medium in the presence of cAVA. In vivo, when CSDs were recorded from the frontoparietal cortex, pre-treatment of rats with cAVA (20 mg/kg; i.v.) elevated the mean amplitude of DC potential shifts without altering the number of CSD events compared to vehicle control. Our findings indicate that cAVA, in contrast with vinpocetine, can directly enhance neuronal excitability. This suggests that the memory enhancing effect of vinpocetine may be due to its bioconversion to cAVA.