Homeostatic effects of the neuropeptide Galanin on neuronal cortical excitability

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The neuropeptide Galanin has pleiotropic functions ranging from influencing the release of hormones and in hypothalamus, control of the release of neurotransmitters in hippocampus, control of food intake, of sleep and of stress resilience. Here, we investigated its effects on cortical spreading depolarization (CSD) and neuronal excitability represented in parameters of the electroencephalographic activity. In spontaneously breathing anesthetized adult rats (sodium thiopentone, 100 mg/kg, i.p.) we recorded the electrocorticogram with arrays of glass microelectrodes in two areas (treated and untreated) at cortical depths of 400 and 1200 µm that were separated by a wall made from dental acrylic. CSD was induced by KCl microinjection. CSD-related direct current (DC) potential shifts, changes in extracellular potassium concentration and in regional cerebral blood flow were continuously monitored. We applied either Galanin at doses of 1 µM to 0.1 nM, or the Galanin receptor 2 (GalR2) antagonist M871 at a concentration of 3 nM for 2 h as pretreatment, followed by 2 h application of Galanin at 0.1 µM. This antagonist was also tested in co-application with Galanin at same doses for 4h. Untreated control brain slices were stained for GalR1/2 localization.

After topical application of Galanin on cortex we found a decrease of brain excitability (decrease of CSD amplitudes and propagation velocity), the reduction of propagating CSD and the increase of the application time of KCl to ignite a CSD. M871 prevented Galanin effects on CSD, but induced the development of ictal activity patterns in some animals. The GalR1 and GalR2 were stained in cortical neurons with different pattern (GalR2 in all; GalR1 in 50% neurons of layer IV/V), being GalR2 more relevant for Galanin actions in cortex.

We conclude that Galanin controls cortical neuronal activity, with the maintenance of excitability via the GalR2, since its blockade prevented all effects on CSD.