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Special Issue on Galanin

Electrophysiological studies on galanin effects in brain – progress during the last six years

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Abstract

The effects of galanin and galanin fragments have been studied on neurons in various brain regions of rodents using electrophysiological techniques. Here, we mainly review reports published during the last six years, that is after the second galanin symposium in 1998. These papers deal with locus coeruleus (LC), the hippocampal formation (HF), hypothalamus, the nucleus of the diagonal band of Broca (DBB) and the dorsal vagal complex (DVC). In most cases galanin has an inhibitory effect by increasing a potassium conductance or reducing a calcium conductance. In LC, beside a direct inhibitory effect, galanin exerts an indirect effect enhancing the noradrenaline-induced hyperpolarization. In the HF, galanin (1–15), but not galanin (1–29), induces hyperpolarization in CA3 pyramidal neurons. Inhibitory effects of galanin on several forms of synaptic plasticity including long-term potentiation, frequency facilitation and paired-pulse facilitation have also been demonstrated in normal and transgenic animals. In the hypothalamic arcuate nucleus galanin has a presynaptic action inhibiting glutamate release, as well as a postsynaptic effect via the galanin R1 receptor. In the DVC, galanin inhibits dorsal vagal motor neurons projecting to the stomach by activation of a postsynaptic galanin receptor. However, excitatory effects of galanin have also been reported in several regions, such as the DBB nucleus, where galanin increases excitability by decreasing a K^+ conductance. Taken together, electrophysiological studies have further supported the role of galanin as a neurotransmitter/neuromodulator in the brain.

Keywords: Galanin antagonists; GALR1,-R2,-R3 receptors; Hippocampal formation; Hyperpolarization; Hypothalamus; Locus coeruleus; Synaptic plasticity

1. Introduction

Galanin, a 29 amino acid neuropeptide (30 in humans) (Tatemoto et al., 1983), is widely distributed in the central nervous system (CNS) and, in many cases, coexists with classic transmitters (Melander et al., 1986b, 1988). Galanin has been suggested to be involved in numerous neuronal functions including learning and memory, pain and feeding behaviors (see book from the second Galanin Symposium edited by Hökfelt et al., 1998) and to exert trophic effects (see Wynick and Bacon, 2002). So far, cDNAs for three distinct galanin receptors, galanin receptor R1 (GALR1), -R2 (GALR2) and -R3 (GALR3), have been identified in rat, mouse and man (see Branchek et al., 2000). They belong to the superfamily of G-protein-coupled receptors (GPCRs). Activation of galanin receptors results in, for example, opening of K^+ channels and inhibition of cAMP synthesis (GALR1 and GALR3), as well as activation of phospholipase C and mobilization of intracellular Ca^{2+} (GALR2) (see Branchek et al., 2000).

Earlier electrophysiological studies revealed that in the CNS galanin produces predominantly inhibitory effects and were summarized by Pieribone et al. (1998) at the second galanin symposium. At the Third Galanin

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Symposium in 2004 in San Diego no electrophysiological studies were presented, with one exception. We therefore decided to compile a small review, mainly including papers published after the 1998 meeting, focusing on electrophysiologic effects of galanin application on to CNS neurons in rodents.

2. Locus coeruleus

The noradrenergic locus coeruleus (LC) cell group has a robust expression of galanin even under normal circumstances, and at least 80% of the noradrenergic LC neurons produce galanin (Melander et al., 1986b; Holets et al., 1988; Xu et al., 1998a). Also in the human brain galanin is expressed in the LC (Chan-Palay et al., 1990; Miller et al., 1999). ^{125}I-galanin binding sites are present over the LC region (Pieribone et al., 1995) and both GALR1 and GALR2 mRNA are expressed in LC neurons (Parker et al., 1995; O'Donnell et al., 1999). Earlier electrophysiological studies have shown that galanin reduces firing rate and induces hyperpolarization/outward current, which persists under conditions in which synaptic input is blocked (tetrodotoxin, TTX, plus low $Ca2^{+}$ medium), presumably via an increase in K^{+} conductance (Seutin et al., 1989; Sevcik et al., 1993; Pieribone et al., 1995). This effect is attenuated by the non-selective galanin receptor antagonist M15, but neither by M35 nor M40 (Xu et al., 1998b). These compounds are chimeric peptides developed by Bartfai et al. (1992). Beside this direct effect, an indirect, modulating action of galanin on LC neurons has been demon-

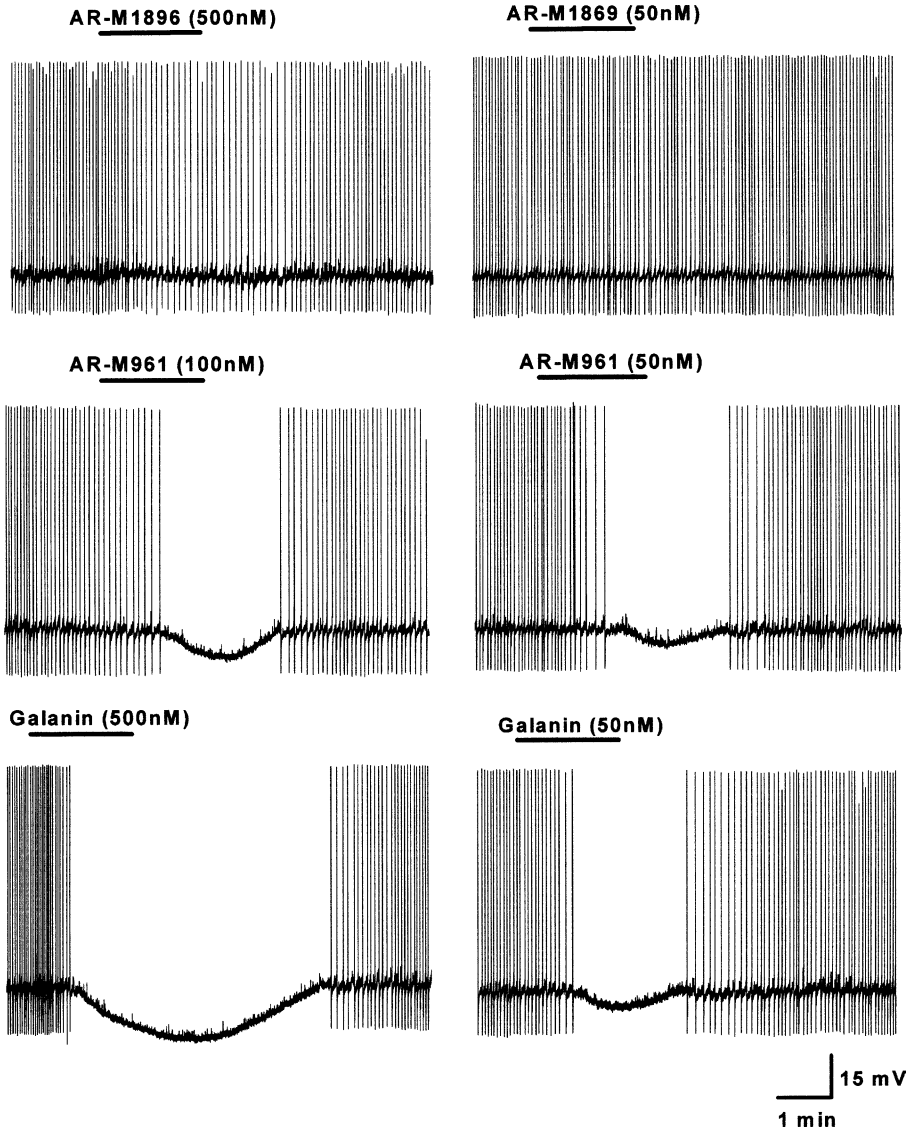

Fig. 1. Dose–response effect of AR-M1896, AR-M961 and galanin on the same LC neurons. Note that AR-M1896 has a distinctly weaker effect than AR-M961 (middle trace) and galanin (lower trace), causing hardly any hyperpolarization. The resting potential was –62 mV throughout the experiment. From Ma et al. (2001), with permission.