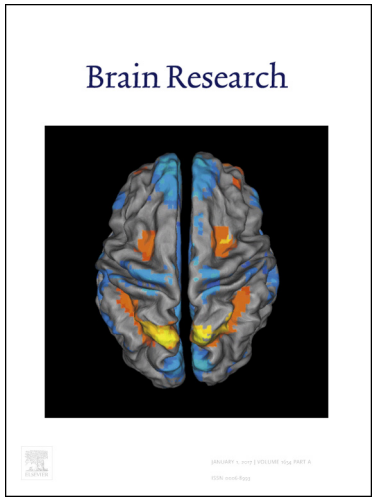

Research report

Melatonin decreases neuronal excitability in a sub-population of dorsal root ganglion neurons

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Melatonin decreases neuronal excitability in a sub-population of dorsal root ganglion neurons

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Abstract: Melatonin, a powerful antioxidant, participates in the regulation of important physiological and pathological processes. We investigated the actions of melatonin on neuronal excitability of intact dorsal root ganglions (DRG) from rats using intracellular recording techniques in current clamps. Melatonin blocked the generation of action potentials in a concentration-dependent manner. Bath applied melatonin (1.0-1000.0 nM) hyperpolarized the resting membrane potential, and increased the input resistance and rheobase. Melatonin also altered the active electrophysiological properties amplitude and maximum descendant inclination in a statistically significant way. In order to provide evidence on the mechanism of action of melatonin in the DRG, quantitative PCR (qPCR) was performed. Analyses were performed for melatonin membrane receptors, MT_1 and MT_2, and it was observed that the DRG expresses MT_1 receptors. In addition, we noted that the melatonin-induced effects were blocked in the presence of luzindole, a melatonin receptor antagonist. The minimal effective concentrations of melatonin (10.0 nM) and the blockade of effects caused by luzindole suggest that the effects of melatonin are hormonal, and are induced when it binds to MT_1 receptors.

Keywords: melatonin; DRG; dorsal root ganglion; excitability; MT_1; action potential.

1. Introduction

Melatonin (N-acetyl-5-methoxytryptamine) is a neurohormone produced and secreted at night by the pineal gland in all vertebrates following a circadian pattern. It is secreted with a daily rhythm and reaches its peak near the middle of the night (McIntyre et al., 1989). In humans and other mammals, detection of light drives activity in retinal ganglion cells that project to the suprachiasmatic nucleus (SCN) in the hypothalamus, causing the release of inhibitory gamma-amino butyric acid (GABA) that inhibits the circuit controlling melatonin synthesis and release. In darkness, the SCN synaptically evokes noradrenaline release from the superior cervical ganglion (SCG). Noradrenaline, consecutively, acts on β-adrenergic receptors in the pineal gland to provoke melatonin synthesis and secretion (Bedrosian et al., 2013; Ganguly et al., 2002; Moore et al., 1995).[1]

Melatonin is involved in circadian timing, but several other functions, in a variety of tissues, have been attributed to it. Melatonin regulates sleep (Brzezinski et al., 2005), promotes neuroprotection (Naseem and Parvez, 2014; Song et al., 2015), scavenges free radical molecules, has antioxidant and anti-inflammatory activities (Hardeland, 2005; Reiter et al., 2007), and is involved in pain modulation (Aviram et al., 2014; Lopez-Canul et al., 2015).

The molecular mechanisms of action of melatonin are either non-receptor-mediated, including inhibition of Ca^{2+}/calmodulin-dependent kinase II (Benítez-King et al., 1996) and direct scavenging of reactive oxygen species (Tan et al., 2002), or receptor mediated, such as circadian modulation and sleep promotion [see review (Reiter et al., 2014)]. Melatonin membrane receptors are G protein-coupled receptors. They are classified based on their kinetic properties and pharmacological profiles into MT_1 (Mel 1a) and MT_2 (Mel 1b) (Dubocovich and Markowska, 2005) and are high affinity binding receptors.

[1] Abbreviations: DRG: Dorsal Root Ganglia; AP: Action potential; MT_1: melatonin membrane receptor type 1; MT_2: melatonin membrane receptor type 2