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Research Report

Effect of tooth pulp and periaqueductal central gray stimulation on the expression of genes encoding the selected neuropeptides and opioid receptors in the mesencephalon, hypothalamus and thalamus in rats

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ABSTRACT

Nociceptive stimulation has been considered to affect the expression of genes encoding endogenous neuropeptides and their receptors. The effect of electric stimulation of the tooth pulp and/or periaqueductal gray (PAG) in rats on mRNA levels of the selected neuropeptides and opioid receptors (ORs) was investigated in comparison with control group, without stimulation. The levels of mRNA for the selected neuropeptides: galanin (GAL), vasopressin (AVP), oxytocin (OT), substance P (SP), somatostatin (SOM), vasoactive intestinal peptide (VIP), endomorphin-2 (EM-2), and opioid receptors: MOR, DOR and KOR in mesencephalic, hypothalamic and thalamic tissues were determined by real-time PCR. It was demonstrated that in the control group expression of the tested neuropeptides was at a very low level in the mesencephalon and thalamus, but at the higher level in the hypothalamus. The highest expression of ORs was observed in the mesencephalon. Nociceptive tooth pulp stimulation had the strongest effect in the hypothalamus, elevating mRNA levels of all tested neuropeptides except SOM. Electric stimulation of PAG either did not change or down-regulated mRNA levels of the neuropeptides in the cerebral structures. Simultaneous stimulation of PAG and tooth pulp either did not affect mRNA levels of the investigated neuropeptides or caused their slight decrease versus tooth pulp stimulation. The noxious stimulation of tooth pulp increased also the levels of OR mRNAs, while stimulation of PAG had the opposite effect. The above results demonstrated that tooth pulp stimulation significantly up-regulated the mRNA levels for a number of neuropeptides and all three types of ORs in the rat brain, which would result in more potent antinociception. In contrast, PAG stimulation down-regulated the mRNA levels of several neuropeptides and ORs in the cerebral tissues, which would cause decreased synthesis of ORs. The obtained results represent a new insight into the mechanism of orofacial pain.

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1. Introduction

The perception of pain is determined by activation of afferent nociceptive impulsation in combination with appropriate sensitivity of mesencephalic, hypothalamic and thalamic centers to such impulsation (Shiraishi et al., 1995; Tang et al., 2009). The sensitivity of neurons in these cerebral regions is affected by numerous neuromodulators – substances which enhance or reduce the excitability of neurons in response to nociceptive stimuli (Rang et al., 1991; Dray and Bevan, 1993).

Stimulation of afferent sensory fibers of the trigeminal nerve (n.V) and, in particular, their endings in the tooth pulp causes the release of neurohormones and neurotransmitters, produced in the brain tissue, to the cerebrospinal fluid (CSF). These substances can act competitively to modulate the function of nervous centers situated in the vicinity of the cerebral ventricles and the fundus of the fourth ventricle, where the sensory and motor centers of the trigemino–hypoglossal reflex are located (Zubrzycka and Janecka, 2002). The mesencephalic, hypothalamic and thalamic centers form, via afferent and efferent nervous fibers, mutual connections with periaqueductal central

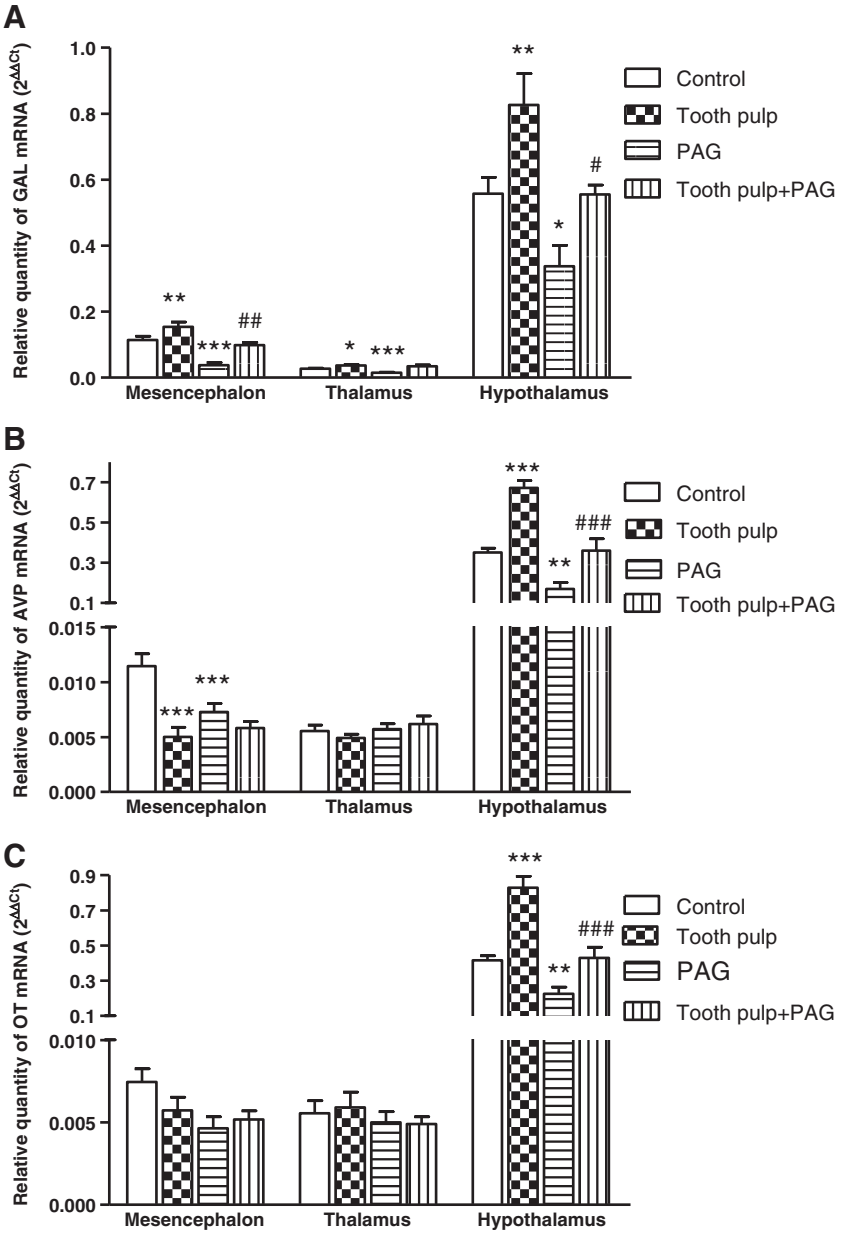

Fig. 1 – Quantitative RT-PCR analysis of: A) GAL, B) AVP, C) OT, D) SP, E) SOM, F) VIP, G) EM-2 mRNA expression in mesencephalon, thalamus and hypothalamus induced by tooth pulp, PAG, tooth pulp and PAG stimulation. The data represent mean ± SEM of 10 rats per group. Statistical significance was assessed using one-way ANOVA and a post-hoc multiple comparison Student–Newman–Keuls test. *; $p<0.001$; **; $p<0.01$; *, $p<0.05$ as compared to control. ###, $p<0.001$; ##; $p<0.01$; #, $p<0.05$ for tooth pulp + PAG stimulation vs. tooth pulp stimulation.**