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Intracerebroventricular administration of galanin decreases free water intake and operant water reinforcer efficacy in water-restricted rats ☆

Ariel Brewer [a,*], Ülo Langel [b], John K. Robinson [a]

[a] Department of Psychology, Biopsychology Program, Stony Brook University, Stony Brook, NY 11794-2500, USA
[b] Department of Neurochemistry and Neurotoxicology, Stockholm University, Stockholm, Sweden

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Abstract

The 29/30 amino acid neuropeptide galanin coexists with vasopressin in the hypothalamus and has been shown to inhibit the actions of vasopressin and aldosterone, suggesting an inhibitory role for galanin in physiological water retention mechanisms and water seeking and water consumption behavior. Little work, however, has examined a role for galanin in water intake regulation. Furthermore, many experiments that have reported galanin-induced impairments in the performance of tasks thought to measure learning and memory have used water restriction routines and water reinforcers to maintain responding. Therefore, the present study examined the effects of intracerebroventricularly administered galanin (5.0–20.0 μg/5 μl) on free water consumption during a 10 min test session and a follow up open field exploration, an operant progressive ratio (PR) schedule, a test used to assess reinforcer strength, and an operant fixed time schedule (FT 20) in 23.5 h water restricted rats. Finally, in an additional experiment that was designed to simulate the effects of a galanin-induced decrease in water reinforcer efficacy, the rats were allowed access to water prior to testing in an operant delayed non-matching to position (DNMTP) task. A galanin-induced decrease in water consumption was observed in both the free access test and the FT 20 at the 20 μg dose, but no significant galanin-induced alterations in open field behavior. A decrease in responses emitted and rewards received was observed on the PR schedule at the 5, 10, and 20 μg doses. Pre-session access to water significantly reduced the number of trials per session in the DNMTP but did not reduce accuracy. This study is the first to observe a galanin-induced reduction in water intake and reinforced operant behavior, and suggests that galanin may play a role in regulating water intake and reinforcement. However, the present data also suggest that DNMTP choice accuracy deficits observed previously cannot be attributed to a galanin-induced change in reinforcer efficacy.

Keywords: Galanin; Reward; Thirst; Vasopressin; Water intake

1. Introduction

Many years of research have supported a role for galanin in a variety of sensory, limbic, and cognitive processes (Bartfai et al., 1993; Bartfai, 1995). In particular, galanin reliably stimulates food intake when administered intracerebroventricularly (i.c.v.) or intrahypothalamically of the rat (Tempel et al., 1998; Kyrkouli et al., 1986; Crawley, 1999). Galanin receptors are present in high concentrations throughout the hypothalamus, including preoptic, supraoptic (SON) and paraventricular (PVN) nuclei (Skofitsch and Jacobowitz, 1985, 1986; Skofitsch et al., 1986; O'Donnell et al., 1999).

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* Corresponding author. Tel.: +1 631 632 7864; fax: +1 631 632 7876.
E-mail address: arbrewer@ic.sunysb.edu (A. Brewer).

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In contrast to the demonstrated effects on feeding, reports of galanin effects on drinking have been limited. For example, one study (Kyrkouli et al., 1990) showed no change in the proportion of time spent drinking compared to other activities in a one-hour test session following hypothalamic galanin infusion (0.32 μg). However, this study did not measure water consumption per se, and the amount of time the rat spent drinking was a very small proportion of the total and was at the measurement floor.

There is mounting evidence pointing to a role for galanin in regulating physiological water balance via the renin–angiotensin system and the resulting changes in both vasopressin and aldosterone (e.g., Skotfitsch and Jacobowitz, 1989; Kondo et al., 1991; Landry et al., 1995; Balment and al Barazanji, 1992; Ciosek and Cisowska, 2003). It has been well established that galanin is co-expressed in vasopressin producing cell bodies in the magnocellular hypothalamic neurons (Melander et al., 1986; Rökaeus et al., 1988; Skofitsch et al., 1989). Landry et al. (1995) reported a significant increase in vasopressin mRNA in dehydrated rats compared to controls. Galanin (0.32 μg i.c.v.) administered to the water-restricted rats decreased vasopressin mRNA content in the PVN and SON to the level of non-restricted controls. Furthermore, administration of the galanin antagonist M15 significantly increased vasopressin mRNA levels to that of the dehydrated rats, thus suggesting an inhibitory role of endogenous galanin on vasopressin expression in magnocellular hypothalamic neurons. Balment and al Barazanji (1992) reported a significant decrease in plasma aldosterone levels following galanin administration (infused for 40 min at 32 ng/min i.c.v.) in anesthetized rats receiving continuous i.c.v. hypotonic saline infusion when compared to saline only controls. Galanin infusion also produced an increase in urine flow, characteristic of reduced fluid retention, and an associated decrease in urine osmolarity, characteristic of reduced sodium balance. Following hypertonic saline treatment, a dose-dependent (12.5–100 pmol) decrease in plasma vasopressin levels were found when galanin was administered i.c.v., with maximum suppression at 10 min post injection (Kondo et al., 1991).

The question of galanin and water consumption is not only important at a basic level, but also has implications for behavioral studies involving galanin in tests of learning and memory that use water reinforcers. Many experiments that have reported galanin-induced impairments in the performance of tasks thought to measure learning and memory have used water-restriction routines and water reinforcers to maintain responding (e.g., Givens et al., 1992). For example, galanin produced non-specific delay-independent accuracy deficits and reduced the number of trials completed per session in the operant delayed non-matching to position (DNMTP) task when administered i.c.v. and intrahippocampally (Robinson and Crawley, 1993a,b, 1994; McDonald and Crawley, 1996). This galanin-induced decrease in the number of trials completed per session may reflect a change in the efficacy of the water reward, either through a direct effect on thirst, or an indirect effect on reward systems.

Neuroanatomical evidence provides support for the involvement of galanin in brain dopamine systems. Galanin containing fibers have been located in brain areas containing dopaminergic cell bodies and associated pathways (Skofitsch and Jacobowitz, 1985; Melander et al., 1986; Kordower et al., 1992; Perez et al., 2001). Galanin binding sites (Skofitsch et al., 1986; Melander et al., 1988; Kohler et al., 1989) and receptor mRNAs (Sullivan et al., 1997; Kolakowski et al., 1998; O'Donnell et al., 1999) have also been located in dopamine associated regions such as the ventral tegmental area, substantia nigra, and the nucleus accumbens. Functional evidence also points to a role for galanin in dopamine mediated pathways. For example, galanin was found to have an inhibitory effect on dopaminergic neurons in the rat median eminence (Nördstrom et al., 1987), and a dose-related decrease in tyrosine hydroxylase immunoreactivity was found in midbrain dopaminergic neurons following galanin treatment (Counts et al., 2002). Furthermore, galanin's ability to modulate reward and motor systems has been indicated by studies which measured DA synthesis and content in areas generally thought to play a role in reward systems. An in vivo microdialysis study revealed that microinjection of galanin into the lateral ventricles or PVN (1.6–16.0 μg/side) produced an increase in dopamine release in the nucleus accumbens (Rada et al., 1998). Additionally, a dose-dependent increase in DOPA accumulation was found in the nucleus accumbens and neostriatum following i.c.v. galanin administration (Ericson and Ahlenius, 1999). When galanin was infused into the ventral tegmental area, a significant increase in DOPA accumulation was only produced in the nucleus accumbens. The increases in DOPA accumulation were interpreted by the authors as a galanin-induced down regulation of dopamine synthesis.

Because of this evidence suggesting an involvement of galanin in water intake and dopamine-mediated reward systems, the present study examined the effects of i.c.v. galanin on several tests designed to assess the effects of galanin on free water access consumption and water reinforcer strength. First, free water consumption was assessed during a 10 min test session in 23.5 h water-restricted rats. Possible motor or other behavioral confounds that could account for observed changes in water intake were assessed in an immediate follow-up test in an open field. Second, patterns of responding were examined following galanin administration in an operant progressive ratio (PR) schedule, a test commonly