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Short communication

Role of lateral parabrachial nucleus in the inhibition of water intake produced by right atrial stretch

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Abstract

Rats with either bilateral electrolytic or sham lesions of the ventrolateral portion of the lateral parabrachial nucleus (VLLPBN) were implanted with latex balloons that lay at the right superior vena cava/atrial junction (RSVC/AJ). Water intake in response to isoproterenol was measured both with and without inflation of the balloon. Water intake of the sham-lesioned rats was significantly depressed by balloon inflation during the first hour of the experiment. In contrast, water intake in the VLLPBN-lesioned rats was unaffected by balloon inflation. These results suggest that the VLLPBN is involved in the processing of afferent input from stretch-activated RSVC/AJ receptors.

Keywords: Atrial volume receptor; Water intake; Lateral parabrachial nucleus; Isoproterenol; Rat

The role of vascular volume receptors located on the low pressure side of the systemic circulation (i.e., located in the atria and great veins; a.k.a. cardiopulmonary receptors) in the control of water intake is unclear. There is some evidence, albeit largely circumstantial, that input from these receptors may facilitate water intake in states of extracellular volume depletion [7,23]. In contrast, however, evidence suggesting that the volume receptors contribute to satiety (i.e., the termination of drinking) is more complete. Activation of mechanoreceptors in the rat by inflation of a small balloon in the right superior vena cava/atrial junction (RSVC/AJ) has been reported to attenuate spontaneous night-time water intake, as well as drinking in response to 24 h water deprivation, treatment with the hyperoncotic colloid polyethylene glycol and isoproterenol [10]. This manipulation had no effect on drinking induced by the infusion of hypertonic saline. Similar findings have been reported in the dog, with the exception that volume receptor activation in this species also attenuates water intake stimulated by cellular dehydration [19].

It is likely that volume information is integrated into the 'visceral' neural network that is involved in the control of drinking behavior. Anatomical evidence indicates that the lateral parabrachial nucleus (LPBN) is one site where peripherally derived inputs might converge. The LPBN, particularly the ventrolateral portion of the LPBN (VL-LPBN), receives the most prominent ascending projection of both the area postrema and nucleus of the solitary tract [16,17,26] and is involved through a rich communication network with hypothalamic nuclei known to be important in the maintenance of body fluid balance [6,17]. In addition, functional data exist linking the LPBN to the control of water intake [4,20,21].

The purpose of this experiment was to test the hypothesis that the VLLPBN mediates, at least in part, the reduction of water intake following activation of RSVC/AJ receptors. Isoproterenol, which to a degree mimics extracellular volume depletion (e.g., see Ref. [23] for review and references), was chosen as the experimental dipsogen.

This experiment was carried out on male Sprague–Dawley rats weighing between 300–420 g at the time of testing. The animals received either a bilateral electrolytic or sham lesion of the VLLPBN. Lesions were made by passing a 1.6 mA direct current through a stainless steel electrode for 4 s. Following a 2-week recovery period, atrial balloons were implanted in both groups of rats following the procedure described by Kaufman [10]. Briefly, the balloon was constructed of latex securely tied over the end of PE 50 tubing. The latex and PE tubing

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were covered with silastic tubing so that only the tip of the balloon was allowed to expand. The balloon was introduced through the right external jugular vein, and was advanced until the tip lay near the RSVC/AJ. The tubing was anchored to the right clavicle, as well as the muscle near the external jugular vein, and was subcutaneously tunneled to the nape of the neck and secured.

After a 1-week recovery period, drinking tests were begun. The atrial balloon was inflated in half of the rats in each group. This was accomplished by manual infusion of 0.05 ml water immediately prior to isoproterenol (30 μg/kg s.c.) administration. The balloons remained expanded throughout the 120-min test session. Rats in the balloon deflation condition simply received the injection of isoproterenol. Cumulative water intake was recorded at 15, 30, 60 and 120 min after dipsogen delivery. The balloons were deflated at the end of the test period. The conditions were reversed on a subsequent test day so that water intake in response to isoproterenol was measured in all rats under both balloon inflation and deflation conditions. Forty-eight hours intervened between consecutive tests.

Upon completion of testing, the lesioned and sham-lesioned animals were transcardially perfused with physiological saline followed by 10% buffered formalin. The brains were sectioned and stained with Cresyl violet in order to histologically verify the lesion placement. Histological criteria for a good lesion have been described previously [20]. The chest cavity of each animal was opened to reveal the right superior vena cava and atrium. The balloon was inflated and placement was visually verified. Rats that did not drink at least 1 ml during the balloon deflation condition were eliminated from the study. A repeated measure ANOVA was used to compare water intake during balloon inflation and deflation conditions for each group at each time point. Differences between group water intake were analyzed using one-way ANOVAs. Statistical significance was defined as $P < 0.05$. All values are reported as means ± S.E.M.

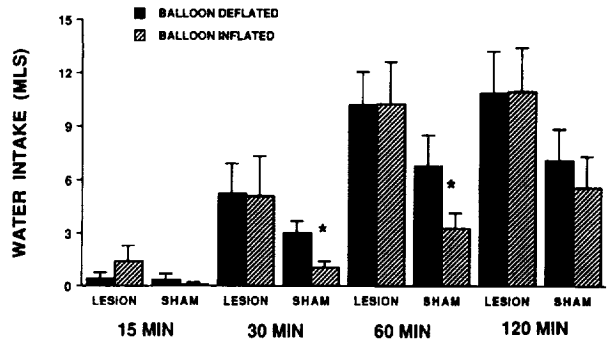

Fig. 2. Drinking in response to isoproterenol is shown for the VLLPBN (LESION) and sham (SHAM) lesioned rats at 15, 30, 60, and 120 min after dipsogen delivery. Water intake during the balloon inflation condition is depicted by hatched bars, solid bars represent water intake while the balloon was deflated. * Indicates a significant difference between inflation and deflation conditions. Significance is $P < 0.05$.

Six rats were determined to have both good VLLPBN lesions and accurate balloon placements. The lesions are comparable to those presented in previous publications [20,21] from our laboratory and a representive VLLPBN lesion from the present study is presented in Fig. 1. The brains of sham-lesioned animals were examined to ensure there was no damage to the VLLPBN, and balloon placement was also verified. Eleven rats met both criteria. Water intakes are presented in Fig. 2. Very little drinking occurred within the first 15 min following isoproterenol administration and balloon inflation did not significantly alter water intake in either the lesioned (inflation: 1.4 ± 0.9 ml; deflation: 0.4 ± 0.4 ml) or sham-lesioned (inflation: 0.1 ± 0.1 ml; deflation: 0.4 ± 0.3 ml) group. However, 30 min after drug administration, water intake was significantly decreased in sham-lesioned rats during balloon inflation (inflation: 1.1 ± 0.4 ml; deflation 3.0 ± 0.7 ml).

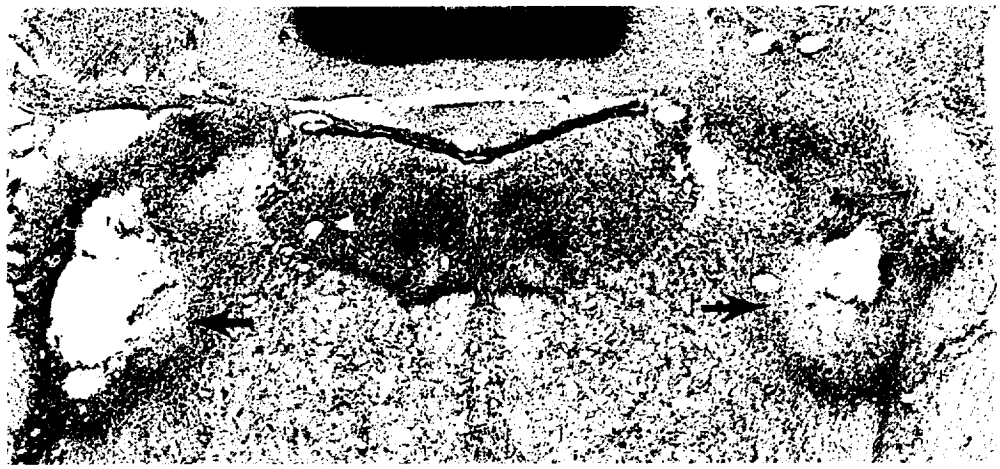

Fig. 1. Typical bilateral lesions (arrows) of the ventrolateral portion of the lateral parabrachial nuclei (VLLPBN).

Balloon expansion had no effect on drinking behavior of the VLLPBN-lesioned rats at this time point (inflation: 5.1 ± 2.2 ml; deflation: 5.3 ± 1.6 ml). A similar trend was seen at 60 min post-isoproterenol delivery. Drinking in the sham-lesioned rats was significantly suppressed by RSVC/AJ stimulation (3.3 ± 0.9 ml) as compared to the control condition (6.7 ± 1.8 ml), whereas water intake in the lesion group was unaltered by balloon expansion (inflation: 10.3 ± 2.3 ml; deflation: 10.2 ± 1.9 ml). By the end of the experiment, 2 h after isoproterenol administration, water intake was no longer significantly decreased by RSVC/AJ expansion in the sham-lesioned rats (inflation: 5.5 ± 1.8 ml; deflation: 7.2 ± 1.7 ml). Water intake in the VLLPBN-lesioned rats remained unaffected by this stimulus (inflation: 11.0 ± 2.5 ml; deflation: 10.8 ± 2.4 ml). Although there was a tendency for the VLLPBN-lesioned rats to drink more than the sham-lesioned animals, this trend did not reach statistical significance during the balloon deflation condition.

These results confirm previous work indicating that isoproterenol-induced water intake is attenuated by stretch of the RSVC/AJ [10,19] and suggests that the VLLPBN is critically involved in the mediation of the attenuation of drinking to this manipulation. It is unlikely that the reduced drinking exhibited by the sham-lesioned rats was the result of a debilitating effect of balloon expansion, as water intake was unaltered by this manipulation in the VLLPBN-lesioned rats. These data support the hypothesis that activation of cardiopulmonary volume receptors by stretch of the RSVC/AJ signals contribute to the termination of drinking, but it appears that this inhibitory signal adapts. That is, by the end of the experiment, the cumulative water intake of the sham-lesioned rats was not different between experiment conditions. Adaptation and resetting of vascular stretch receptors on both the high and low pressure sides of the circulation are well-described phenomena (see Refs. [2] and [27] for reviews).

It is reasonable to hypothesize that the VLLPBN is involved in volume receptor-induced inhibition of water intake. This region is heavily innervated by both the area postrema and nucleus of the solitary tract [16,26,28], nuclei known to receive input from cardiac and aortic arch baroreceptors via the vagus and glossopharyngeal nerves [3,9]. In addition, the lateral subdivisions of the parabrachial nucleus share reciprocal projections with the median preoptic nucleus, paraventricular nucleus, central nucleus of the amygdala, and other forebrain nuclei involved in the control of body fluid balance [6,17]. Therefore, the LPBN appears to be a component of a neural network capable of integrating information related to cardiovascular status and body fluid balance. Furthermore, the VLLPBN has been previously implicated in the attenuation of drinking. Bilateral electrolytic or chemical lesions of this nucleus augment drinking in response to centrally and peripherally administered dipsogens which simulate an extracellular fluid deficit [4,20,21]. It will be necessary to repeat the present balloon inflation studies in rats where chemical lesions (e.g., as in Ref. [4]) are used in order to discern whether the present effects are due to destruction of neurons with soma located in the LPBN or disruption of fibers of passage.

While the data presented here suggest that the VLLPBN plays a role in the volume receptor-induced attenuation of water intake in response to isoproterenol, it is not clear whether this is a neurally or humorally mediated event. There is evidence to suggest that the observed decrease in drinking is the result of direct neural stimulation of central nervous system (CNS) centers involved in drinking. Moore-Gillon and Fitzsimons [19] reported that inflation of a balloon implanted at the left pulmonary vein and atrial junction in the dog reduced water intake in response to isoproterenol and that blockade of the left vagus nerve prohibited this inhibitory action. Further, unilateral cervical vagotomy significantly increased water intake in the rat following the administration of isoproterenol [18]. Together these findings suggest that decreased drinking following volume receptor stimulation is the result of impulses traveling to the CNS via the vagus nerve.

Alternatively, it is possible that this information is relayed to the brain via a humoral rather than neural mechanism. Isoproterenol-induced water intake is believed to be largely mediated by the renin-angiotensin system [5,8,23]. Left atrial stretch has been demonstrated to inhibit renin release in the dog [15,25], suggesting that the observed attenuation of water intake might be due to reduced plasma renin levels. This is unlikely, however, since Kaufman found no significant change in plasma renin activity during right atrial expansion by balloon in the rat [11]. However, atrial natriuretic peptide (ANP) is also released by atrial distention, and may underlie this phenomenon [14]. Administration of ANP has been demonstrated to attenuate drinking in response to a number of dipsogenic challenges [1,12,13], and water intake itself has been reported to elevate circulating levels of the peptide [24]. A high density of ANP binding sites has been found in the area postrema, a circumventricular organ [22], and circulating ANP acting through this nucleus may activate CNS pathways involving the VLLPBN to inhibit drinking. It should be noted, however, that RSVC/AJ distention does not diminish water intake in response to all dipsogenic stimuli [10], which would be expected if ANP release via atrial stretch was solely responsible for the termination of drinking.

In summary, activation of RSVC/AJ receptors has been shown to attenuate isoproterenol-induced water intake in intact rats and this inhibition is abolished by ablation of the VLLPBN. These findings support the hypothesis that the VLLPBN is involved in the inhibition of drinking mediated by volume receptor stimulation. These results add to the growing body of evidence suggesting that the VLLPBN is involved in the termination of thirst stimulated by a variety of dipsogenic challenges.

Acknowledgements

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