Short communication

Effects of lidocaine injections into the lateral parabrachial nucleus on dipsogenic and pressor responses to central angiotensin II in rats

Jose Vanderlei Menani a,b, Terry G. Beltz a, Alan Kim Johnson a,*

a Departments of Psychology and Pharmacology and The Cardiovascular Center, University of Iowa, Iowa City, IA 52242-1407, USA
b Department of Physiology, School of Dentistry, Paulista State University, Araraquara, SP 14801-903, Brazil
GUIDELINES FOR THE SUBMISSION OF MANUSCRIPTS

These can be found in the "front matter" of every last issue of each volume of Brain Research.

The preferred medium of submission is on disk with accompanying manuscript (see "Electronic manuscripts").
Short communication

Effects of lidocaine injections into the lateral parabrachial nucleus on dipsogenic and pressor responses to central angiotensin II in rats

Jose Vanderlei Menani a,b, Terry G. Beltz a, Alan Kim Johnson a,*

Departments of Psychology and Pharmacology and The Cardiovascular Center, University of Iowa, Iowa City, IA 52242-1407, USA
b Department of Physiology, School of Dentistry, Paulista State University, Araraquara, SP 14801-903, Brazil

Accepted 28 June 1995

Abstract

This study investigated the effects of bilateral injections of the local anesthetic, lidocaine, into the lateral parabrachial nucleus (LPBN) on the dipsogenic and pressor responses induced by intracerebroventricular (i.c.v.) injection of angiotensin II (ANG II). Centrally injected ANG II (50 ng/\mu l) induced water intake (1.2 ± 0.8 ml/h) and pressor responses (22 ± 1 mmHg). Prior bilateral injection of 10% lidocaine (200 nl) into the LPBN increased the water intake (14.2 ± 1.4 ml/h), but did not change the pressor response (17 ± 1 mmHg) to i.c.v. ANG II. Lidocaine alone injected into the LPBN also induced a pressor response (23 ± 3 mmHg). These results showing that bilateral LPBN injection of lidocaine increase water intake induced by i.c.v. ANG II are consistent with electrolytic and neurotoxic lesion studies and suggest that the LPBN is associated with inhibitory mechanisms controlling water intake induced by ANG II. These results also provide evidence that it is feasible to reversibly anesthetize this brain area to facilitate fluid-related ingestive behavior.

Keywords: Lateral parabrachial nucleus; Angiotensin II; Water intake; Arterial pressure; Thirst; Local anesthetic

The lateral parabrachial nucleus (LPBN) is a pontine structure that lies dorsal to the superior cerebellar peduncle. Recent studies from our laboratory have shown that the LPBN is an important hindbrain structure that is involved in the control of water intake [3,7,10-12]. Rats with electrolytic or neurotoxic (ibotenic acid) lesions of the LPBN show an increase in drinking to central or peripheral angiotensin II (ANG II) and to peripheral isoproterenol [3,10]. Since the water intake induced by central carbachol or subcutaneous hypertonic saline is not changed by LPBN lesions, a LPBN-associated mechanism has been proposed to be involved in the control of extracellular fluid depletion-induced thirst [11]. Similar increases in water intake have also been reported after lesions of the area postrema and adjacent medial nucleus of the solitary tract (AP/mNTS) [11]. The LPBN receives afferent projections from the AP/mNTS and sends efferent projections to areas of the forebrain involved in fluid and electrolyte balance such as the median preoptic nucleus and the central nucleus of the amygdala [2,6,9,15]. In this study, we investigated the effects of temporary, reversible lesions of the LPBN produced by bilateral injections of the local anesthetic, lidocaine, on the dipsogenic and pressor responses induced by intracerebroventricular (i.c.v.) ANG II.

Male Sprague-Dawley rats weighing 300-400 g were used. Rats were anesthetized with Equithesin (3.3 ml/kg b.w.) and placed in a Kopf stereotaxic instrument. The skull was leveled between lambda and bregma. Stainless steel 23 gauge cannulas (12 mm long) were bilaterally implanted into the LPBN using stereotaxic coordinates of 9.4 mm caudal to bregma, 1.9 mm lateral and 4.1 mm below the dura. The tips of the cannulas were positioned in the brain at points 2 mm above the LPBN. A third cannula (23 gauge × 12 mm long) was implanted in the left lateral ventricle (LV) at coordinates of 1.2 mm caudal to bregma, 1.5 mm lateral and 4.0 mm below the dura. The cannulas were fixed in the cranium using dental acrylic resin and small screws, and metal tubing (30 gauge) was used as an obturator to keep the cannulas patent.

Angiotensin II (50 ng/\mu l) and 10% lidocaine hydrochloride (Sigma, St. Louis, MO) were dissolved in 0.15 M NaCl (vehicle). Hamilton syringes (10 \mu l) were connected by PE-10 polyethylene tubing to needles (30 gauge) which...
were introduced into the brain through the previously affixed guide cannulas. The needles for injection into the LPBN and LV were 2 mm longer than the guide cannulas. Injection volumes into the LPBN were 200 nl and into the LV 1 µl. Vehicle or 10% lidocaine was injected into the LPBN immediately before i.c.v. ANG II was injected into the LV. The volume of water consumed over a period of 1 h after i.c.v. injection of ANG II was measured at 15 min intervals using burettes graduated with 0.1 ml divisions and fitted with metal spouts. Direct mean arterial pressure (MAP) was recorded in unanesthetized, unrestrained rats. On the day before the experiment, the rats were anesthetized with Equithesin (3.3 ml/kg b.wt.) and a PE-10 polyethylene tube connected to PE-50 was inserted into the abdominal aorta through the femoral artery. The cannula was tunneled subcutaneously to the back of the rat and was connected to a pressure transducer coupled to a multichannel recorder (Dynograph Recorder R611, Sensor Medics).

At the end of the experiments, the animals received bilateral injections of a dye (200 nl of methylene blue solution) into the LPBN. They were then deeply anesthetized with sodium pentobarbital (80 mg/kg) and perfused with saline followed by 10% formalin through the heart. The brains were removed, fixed in 10% formalin, frozen, cut in 50 µm sections, stained with Cresyl violet and analyzed by light microscopy with the aid of the brain atlas of Paxinos and Watson [13] to confirm the position of the injections into LV and LPBN.

Histological material was examined without knowledge of the results of the functional tests (i.e. 'blind'). Only animals that met the criteria of (1) ventricular cannulas with access to the LV, (2) caudal injection sites terminating bilaterally in the LPBN, and (3) each of the 200 nl Methylene blue injections confined to the LPBN were considered successful preparations. Functional data from only successful preparations were used for analysis. Experimental results are reported as means ± S.E.M. Analysis of variance and Student t-test were used for comparisons. Differences were considered significant at P < 0.05.

The bilateral injection of lidocaine (200 nl) into the LPBN significantly increased the water intake induced by i.c.v. ANG II (50 ng/1 µl; Fig. 1). Lidocaine alone injected into the LPBN induced no water intake in satiated rats. Bilateral injections of 10% lidocaine (200 nl) alone into the LPBN increased MAP (Fig. 2). The pressor response to lidocaine occurred immediately after the injections into the LPBN (peak response in 3 min). No change in the pressor response to i.c.v. ANG II (injected 5 min after lidocaine) was observed after the injection of 10% lidocaine into the LPBN (Fig. 2). The resting baseline MAP prior to lidocaine injection was 117 ± 3 mmHg, and the baseline MAP prior to ANG II after the treatment with lidocaine was 128 ± 3 mmHg.

The present results show that bilateral injections of lidocaine into the LPBN increase the water intake induced by i.c.v. ANG II. These results together with previous studies showing similar increases in water intake to ANG II-related stimuli after electrolytic or neurotoxic lesions of the LPBN [3,10–12] provide evidence of an inhibitory pathway associated with the LPBN that is important for the control of ANG II-induced water intake.

Studies have shown that the increase in blood pressure induced by ANG II impairs its dipsogenic effect [5,14,16]. Since prior injection of lidocaine into the LPBN produced no significant change in the pressor response to i.c.v. ANG II, the increased water intake is unlikely to be due to an impairment of the pressor effect of the peptide.

Lidocaine injected bilaterally alone into the LPBN increased MAP. This observation suggests that cells within or fibers passing through the LPBN may tonically inhibit
increases in arterial pressure. There may be a role for the LPBN in processing blood pressure and/or volume-related information that affects the control of drinking. Central representation of information derived from systemic receptors and afferent pressure/volume pathways may play an inhibitory role in the control of ANG II-induced water intake. Blocking this information by injection of lidocaine into the LPBN may be responsible for facilitating the dipsogenic action of central ANG II. However, it should not be concluded that there are no LPBN-associated excitatory mechanisms. Injection of glutamate into the LPBN increases arterial pressure [17]. The ultimate effects of electrolytic, neurochemical and anesthetic (lidocaine) lesions of the LPBN on functional responses in all likelihood reflect the net result of removing a combination of both excitatory and inhibitory influences.

An increase in water intake to i.c.v. ANG II similar to that produced by bilateral LPBN injections of lidocaine has also been observed [4,11] after AP/mNTS lesions. Ohman and Johnson [11] have suggested that AP/mNTS and LPBN may be linked in a common drinking-related inhibitory pathway. A recent study from our laboratory [12] showed that electrolytic LPBN lesions abolished the inhibition of water intake observed during the inflation of a right atrial balloon. The antipsogogenic effect of atrial stretch may be due to the activation of neural and/or humoral mechanisms. Neural input activated by changes in blood volume reaches the parabrachial nucleus [18]. However, an alternative or parallel (redundant) inhibitory mechanism might be a humoral mechanism that involves circulating atrial natriuretic peptide (ANP). It has been shown that central or peripheral administration of ANP reduces dipsogenic responses [1,8]. The AP is rich in ANP receptors. Since the AP lacks a blood–brain barrier, plasma ANP may activate receptive cells within the AP and this information is, in turn, carried via an ascending projection to the LPBN where it acts to inhibit drinking.

In summary, results showing that inactivation of a cerebral area (bilateral LPBN in this case) increases water intake to i.c.v. ANG II suggest that injection of a local anesthetic into specific areas of the brain can be used to study experimentally-induced dipsogenic responses.

Acknowledgements

This research was supported by National Heart, Lung, and Blood Institute Grants HL-14338 and HL-44546 and Fundacao de Amparo a Pesquisa do Estado de Sao Paulo Proc. 93/0167-7.

References

NEW AND FORTHCOMING TITLES IN ELSEVIER'S NEUROSCIENCE PROGRAMME

Progress in Brain Research Series

Neuroscience: From the Molecular to the Cognitive — Vol. 100, edited by F. Bloom

Biological Function of Gangliosides — Vol. 101, edited by L. Svennerholm

The Self-Organizing Brain — Vol. 102, edited by M.A. Corner and J. van Pelt

Neural Regeneration — Vol. 103, edited by F.J. Seil

******

Neuroscience Protocols — Module 3, edited by F. Wouterlood
Neuroscience Protocols — Module 4, edited by F. Wouterlood

OPAL Module 3: Immune Cells, by H.-P. Hartung and X. Zhang

OPAL Module 4: Endocrine Cells, by B. Cooke

For more information or a free OPAL Preview Disk, please contact Joyce Hobbelink, Elsevier Science, PO Box 1527, 1000 BM Amsterdam, The Netherlands, Fax: (31) (20) 485 3342, e-mail: j.hobbelink@elsevier.nl

SUBSCRIPTION AND PUBLICATION DATA 1995

Brain Research (including Molecular Brain Research, Developmental Brain Research, Cognitive Brain Research and Brain Research Reviews) will appear weekly and be contained in 53 volumes (108 issues): Brain Research, Volumes 669–705 (37 volumes in 74 issues), Molecular Brain Research, Volumes 26–32 (7 volumes in 14 issues), Developmental Brain Research, Volumes 84–90 (7 volumes in 14 issues), Cognitive Brain Research, Volume 3 (1 volume in 4 issues) and Brain Research Reviews, Volumes 20–21 (2 volumes in 6 issues). Please note that Volumes 26 and 27 of Molecular Brain Research were published ahead of schedule in 1994, in order to reduce publication time. The volume remains part of the 1995 subscription year. Discussions in Neuroscience, Volume 11 (1 volume in 4 issues) will be mailed as an integral part to all full-set subscribers to Brain Research in 1995. Separate subscriptions: Molecular Brain Research, Vols. 26–32, Developmental Brain Research, Vols. 84–90, Cognitive Brain Research, Vol. 3, and Brain Research Reviews, Vols. 20 and 21, may also be ordered separately. Prices are available from the Publisher upon request. Subscriptions are accepted on a prepaid basis only, unless different terms have been previously agreed upon.

Subscription orders can be entered only by calendar year (Jan.–Dec.) and should be sent to Elsevier Science B.V., Journal Department, P.O. Box 211, 1000 AE Amsterdam, The Netherlands, Tel.: (31) (20) 485 3642, Fax: (31) (20) 485 3598, or to your usual subscription agent.

Postage and handling charges include surface delivery except to the following countries where air delivery via SAL (Surface Air Lift) mail is ensured: Argentina, Australia, Brazil, Canada, Hong Kong, India, Israel, Japan, Malaysia, Mexico, New Zealand, Pakistan, P.R. China, Singapore, South Africa, South Korea, Taiwan, Thailand and USA. For all other countries air mail rates are available upon request.

Claims for missing issues must be made within six months of our publication (mailing) date, otherwise such claims cannot be honoured free of charge. In the United States and Canada: for further information concerning this or any other Elsevier Science journal, contact Elsevier Science Inc. Attn: Journal Information Center, 655 Avenue of the Americas, New York, NY 10010, U.S.A. Tel.: (1) (212) 633-3750; Telefax: (1) (212) 633-3990; Telex: 420-643 AEP UI.

Information for Advertisers. Advertising orders and enquiries can be sent to Elsevier Science B.V., Advertising Department, P.O. Box 211, 1000 AE Amsterdam, The Netherlands, Tel.: (31) (20) 485 3796; Fax: (31) (20) 485 3810. Office address for courier services: Molenwerf 1, 1014 AG Amsterdam, The Netherlands. For the U.K.: T.G. Scott and Son Ltd., Vanessa Bird, Portland House, 21 Narborough Road, Cosby, Leicestershire LE9 5TA, U.K., Tel.: (44) (116) 2750 520/2753 333; Fax: (44) (116) 2750 522. For the U.S.A. and Canada: Weston Media Associates, Daniel Lipner, P.O. Box 1110, Greens Farms, CT 06436-1110, U.S.A., Tel.: (1) (203) 261-2500, Fax: (1) (203) 261-0101.

ADONIS Identifier. This Journal is in the ADONIS Service, whereby copies of individual articles can be printed out from CD-ROM on request. An explanatory leaflet can be obtained by writing to ADONIS B.V., P.O. Box 839, 1000 AV Amsterdam, The Netherlands.

© The paper used in this publication meets the requirements of ANSI/NISO 239.48-1992 (Permanence of Paper).