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Research report

A5 region modulation of the cardiorespiratory responses evoked from parabrachial cell bodies in the anaesthetised rat

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Abstract

We have examined the importance of the A5 region modulating cardiorespiratory responses evoked from the parabrachial complex (PB) in spontaneously breathing rats. Cardiorespiratory changes were analyzed in response to electrical stimulation and glutamate microinjections into the PB (10–20 nl, 1–2 nmol) before and after ipsilateral microinjection of muscimol (50 nl, 0.25 nmol) or lidocaine (50 nl, 0.5 nmol) within the A5 region. Stimulation of medial parabrachial and Kölliker–Fuse nuclei (mPB-KF) evoked a decrease in respiratory rate ($P<0.001$) with a rise in blood pressure ($P<0.001$) and heart rate ($P<0.05$). After muscimol or lidocaine microinjections within the A5 region, the pressor and heart rate responses to mPB-KF stimulation were reduced ($P<0.05$, both cases). Muscimol within the A5 region altered the respiratory response to glutamate stimulation of mPB-KF, evoking an increase in respiratory rate ($P<0.05$). Lidocaine abolished the respiratory response to mPB-KF stimulation. Stimulation of the lateral parabrachial nuclei (lPB) caused an increase in respiratory rate ($P<0.001$) with a rise in blood pressure ($P<0.001$) and heart rate ($P<0.05$). Muscimol or lidocaine microinjections within A5 region decreased heart rate ($P<0.05$) and pressor responses ($P<0.05$) evoked from lPB. The increase of respiratory rate persisted unchanged. To confirm functional interactions between A5 and PB, extracellular recordings of putative A5 neurones were obtained during PB stimulation. Eighty-three A5 cells were recorded, 35 were activated from the mPB-KF (42%). The results indicate that neurones of the A5 region participate in the cardiorespiratory response evoked from the different regions of the PB complex. The possible mechanisms involved in these interactions are discussed.

Introduction

The respiratory rhythm is generated by the activity of neurones located within the medulla oblongata while pontine neurones are involved in the modulation of the pattern of respiration (for reviews see Refs. [17], [34], [41]). Lesions in specific pontine nuclei produce profound changes in respiration, which have led to the classical description of a 'pneumotaxic centre'. Previous studies have described that, in the rat, one of these pontine regions, the parabrachial complex, modulates respiration in two different ways. Neurones located in the medial region of the parabrachial complex and Kölliker Fuse nucleus are involved in the prolongation of expiration, while neurones located in the lateral parabrachial nucleus evoked a decrease in the duration of expiration together with a facilitation of inspiratory activity [4], [6], [28]. Parabrachial neurones are involved also in topographic organized control of bulbar laryngeal motoneurones [26]. In addition, activation of these 'respiratory' regions also evokes cardiovascular responses: this comprises an increase of blood pressure and heart rate [3], [28].

Whilst the parabrachial complex has the appropriate anatomical connections with the medulla to produce these cardiorespiratory changes [8], [25], [36], [38] little is known about the pontine pathways that are activated during specific stimulation of the cell bodies of the parabrachial complex. It is known that the parabrachial complex is connected with the A5 region [36]. We have previously described that, after electrical stimulation of the medial or lateral nuclei of the parabrachial complex an increase of c-Fos-like protein immunoreactivity in the A5 pontine catecholaminergic area is observed [9].

The A5 group of catecholamine-containing neurones is located in the ventrolateral pons, between the root of the facial nerve and the superior caudal olivary nucleus. When stimulated with glutamate it produces cardiorespiratory and laryngeal responses similar to those observed with medial parabrachial stimulation, that is an expiratory facilitatory response associated with an increase in blood pressure, heart rate [10] and subglottic pressure [26]. The A5 region provides a major component of the noradrenergic input to the sympathetic preganglionic neurones of the intermediolateral cell column of the spinal cord [1], [31], [40]. Also it has connections with the nucleus tractus solitarii in the medulla oblongata, the medial, Kölliker–Fuse and lateral parabrachial nuclei in the pons and with the perifornical area and the paraventricular region of the hypothalamus [2], [43]. These connections with regions of CNS involved in cardiorespiratory regulation are indicative for a role of the A5 region in the control of both the sympathetic activity and respiratory function [8], [37].

The similarity of the responses to stimulation of the medial parabrachial complex and the A5 region suggest a possible interaction between these two pontine regions. Accordingly in the present study muscimol and lidocaine microinjections have been delivered within the vicinity of the A5 neurones before, and after, chemical stimulation of the different regions of the parabrachial complex in order to characterize the possible role of the A5 region in mediating the cardiorespiratory responses to parabrachial activation. To further confirm the interactions between these regions extracellular recordings of putative A5 cells were made during parabrachial stimulation.

Section snippets

General procedures

Experiments were performed on 33 spontaneously breathing Sprague–Dawley rats (body weight 250–300 g), anesthetized with sodium pentobarbitone (60 mg/kg i.p., initial dose, supplemented with 2 mg/kg i.v., as necessary). The trachea was cannulated below the larynx to measure airflow through a Fleisch pneumotachograph. An air-filled catheter was introduced into the esophagus for the indirect measurement of pleural pressure. The femoral artery and vein were cannulated to measure arterial pressure…

Medial parabrachial and Kölliker–Fuse (mPB-KF) stimulations before and after A5 microinjections

mPB-KF stimulation (nine rats) produced a response characterized mainly by a decrease in both respiratory rate and peak phrenic activity lasting 5.36±1.3 s. The accompanying cardiovascular response at these locations involved an increase of blood pressure and heart rate. Saline injections were ineffective. The histologically verified electrode positions are shown in Fig. 1.

Both electrical and glutamate stimuli decreased respiratory rate (P<0.001 in both cases; see Table 1, Fig. 2, Fig. 3). The…

Discussion

The aim of this study has been to determine functional interactions between two important pontine areas involved in autonomic central regulation: the parabrachial complex and the A5 region. The primary observation of this paper is that the two patterns of cardiorespiratory response that can be elicited from parabrachial nuclei are modified by the microinjection of muscimol or lidocaine into the A5 region. The expiratory facilitation evoked from mPB-KF was changed to an inspiratory facilitatory…

Acknowledgements

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…Electrical stimulation allowed us to tightly regulate the onset and offset of HDA activation. We selected the most usual stimulation parameters used in previous studies (Dawid-Milner et al., 1995, 2001, 2003; Diaz-Casares et al., 2009; Lara et al., 1994, 2002; Silva-Carvalho et al., 1993). Blockade of glutamate receptors located in the PBc was performed by unilateral microinjections of kynurenic acid (glutamate receptor unspecific antagonist), MK-801 (subtype NMDA glutamate receptor specific antagonist), CNQX (subtype non-NMDA glutamate receptor specific antagonist) and MCPG

(antagonist of metabotropic glutamate receptors)....

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