NEUROSCIENCE

Roles of glutamate and GABA of the Kölliker-Fuse nucleus in generating the cardiovascular chemoreflex

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Abstract

The Kölliker-Fuse (KF) nucleus is a part of the parabrachial complex, located in the dorsolateral pons. It is involved in the chemoreflex-evoked cardiovascular and respiratory changes, but the role of GABA and glutamate in cardiovascular chemoreflex has not been shown yet. This study was performed to determine the role of GABA, glutamate, and their interaction in the KF, in cardiovascular chemoreflex in anesthetized rat. The antagonists were microinjected into the KF, and arterial pressure, heart rate, and single-unit responses were recorded simultaneously. The chemoreflex was evoked by i.v. injection of KCN, consisted of a short pressor followed by long bradycardia responses. Both responses were significantly attenuated by injection of a synaptic blocker ($CoCl_2$) into the KF, confirming involvement of the KF in generating the reflex. Microinjection of AP5, an NMDA receptor antagonist, into the KF significantly attenuated the pressor and bradycardia responses, while blocking the AMPA receptors by CNQX had no significant effect. Blockade of $GABA_A$ receptors by bicuculline methiodide (BMI) potentiated both responses. Co-injection of BMI and CNQX potentiated the responses too. Co-injection of BMI and AP5 had no significant effect on the pressor response but significantly attenuated the bradycardia response. In conclusion, the KF plays a role in generating cardiovascular chemoreflex via its glutamate NMDA but not AMPA receptors. GABA inhibits both components of this reflex through $GABA_A$ receptors. There is an interaction between $GABA_A$ and NMDA receptors in regulating the bradycardia response of the reflex. Single-unit results were also presented which were correlated with and supported the homodynamic findings.

Keywords Cardiovascular chemoreflex · Kölliker-Fuse · Single-unit · Glutamate · GABA

Introduction

The parabrachial complex is located in the dorsolateral pons. It can be divided into several distinct subnuclei, including the parabrachial nuclei and the Kölliker-Fuse (KF) region [2]. Reciprocal tract tracing studies have demonstrated that nuclei of the KF area are major ascending targets for the nucleus tractus solitarius (NTS), which receives inputs from various visceral sensory afferents via the vagal and glossopharyngeal nerves [19, 25, 31]. The KF nucleus send dense descending projections to A5 area, the entire lateral respiratory column in the medulla oblongata, the NTS, the nucleus ambiguus [10,

13, 19], the spinal cervical phrenic motoneurons [14, 32], and the spinal motoneurons that supply the intercostal and abdominal respiratory muscles [11, 33].

The KF has widespread interconnections with brain areas involved in cardiovascular, respiratory, and pain regulation [8, 22, 34]. Previous studies have reported a role of KF in chemoreflex-evoked cardiovascular and respiratory changes [7, 9, 22, 24, 37]. Furthermore, large numbers of neurons in the KF are activated following stimulation of cardiac sympathetic afferents [15, 21].

Studies using c-Fos-immunoreactive expression as a marker of neuronal activity showed intense activation of the KF region after hypoxia, hypercapnia, or stimulation of the carotid sinus nerve [3, 4, 6, 20, 39]. Lesion of the dorsolateral pons, including KF, decelerated the respiratory responses to hypoxia [36] or hypercapnia [27, 35] and augmented the carotid sympathetic chemoreflex response [23, 35].

The KF region contributes to central and peripheral cardiorespiratory responses to chemoreflex activation by hypercapnia or systemic administration of potassium cyanide (KCN),

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