Dorsolateral Periaqueductal Grey Matter stimulation modifies laryngeal activity and subglottic pressure in spontaneously breathing anaesthetized rats

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Background

Abduction and adduction of the larynx allow changes in airflow necessary for the vibration of the vocal folds and emission of voice. It is known that stimulation of the Periaqueductal Gray matter (PAG) and nucleus retroambiguus (nRA) produces vocalization (Holstege et al., 1989) and lesions in PAG cause mutism in animals and humans (Esposito et al., 1999). The nRA is the perfect target to turn passive into active expiration modifying the activity of laryngeal motoneurons located in the nucleus ambiguus (Subramanian et al., 2009). We have shown that rostral and ventral pontine structures are involved in changes of laryngeal caliber (Lara et al., 2002). It has been also demonstrated a high expression of FOXP2 protein at mesencephalic and pontine regions (PAG, Parabrachial complex and A5 Region) involved in cardiorespiratory control. FOXP2 is a transcription factor required for brain and lung development and it is closely related to vocalization (Stanic et al., 2018).

Objectives

The aim of this study was to characterize the relations between mesencephalic regions (dlPAG) involved in cardiorespiratory control and their possible role in modulating laryngeal activity and their effects on vocalization.

Methods

Experimental studies were carried out with non-inbred male rats (n=14), SPF, Sprague-Dawley (250-300 g) housed under standard conditions. Animals were anesthetized with sodium pentobarbitone (60 mg/kg i.p., initial dose, supplemented 2 mg/ kg, i.v., as necessary). A double tracheal cannulation to develop the classical technique of the "isolated glottis in situ" and for the recording of respiratory airflow was carried out. Subglottic pressure was recorded with an aneroid transducer (Hugo Sachs Elektronik D-7801, ± 0,1 psi) by passing a stream of humidified warm medical air upwards through the larynx at a constant rate of 30-70 ml/min with a thermal mass digital air flow meter controller (Bronkhorst Hi-Tec F-201CV-AGD-22-V). Thus, at constant air flow, changes in pressure indicate changes in laryngeal resistance.

Bilateral parietostomy allowed access to dlPAG. Microinjections of PBS-Evans Blue (250 nl, pH 7.4 ± 0.1, 5-s duration) or glutamate (0,25M, 250 nl) were performed. Respiratory flow, pleural pressure, blood pressure, heart rate and ECG activity were also recorded.

Results

dlPAG PBS-Evans Blue microinjections did not produce any significant changes in any of the cardiorespiratory variables recorded. However, glutamate microinjections within the dlPAG evoked a decrease of laryngeal resistance (subglottal pressure) ($p<0,001$) accompanied with an inspiratory facilitatory response consisted of an increase in respiratory rate ($p<0,001$), together with a pressor ($p<0,05$) and tachycardic response ($p<0,001$).

Conclusions

The results of our study contribute with new data on the role of the mesencephalic neuronal circuits in the control mechanisms of subglottic pressure and laryngeal activity.

Keywords

Subglottic Pressure, Laryngeal Motoneurons, DMH-PeF, dlPAG, Nucleus Ambiguus