8) CINELLI, Elenia
2° anno Dottorato in Scienze Fisiologiche e Nutrizionali
Dip. Scienze Fisiologiche, Università di Firenze
elenia.cinelli@unifi.it

Respiratory role of GABA and glycine receptors within the bötzinger complex of the rabbit

Elenia Cinelli, Fulvia Bongianni, Donatella Mutolo, Tito Pantaleo
Dipartimento di Scienze Fisiologiche, Università degli Studi di Firenze, Viale G.B. Morgagni 63, I-50134 Firenze, Italy

The Bötzinger complex (BötC) is an important component of the respiratory network and one of the main source of inhibition for inspiratory activity. Synaptic inhibitory mechanisms mediated by GABA and glycine have been involved in the control of breathing, especially in adult mammals. However, the specific role of inhibitory mechanisms within the BötC remains to be investigated. To address this issue, experiments were carried out on α-chloralose-urethane anesthetized, vagotomized, paralysed and artificially ventilated rabbits. Respiratory output was monitored as phrenic nerve activity. Bilateral microinjections (30-50 nl) of GABA and glycine receptor agonists and antagonists were performed into the BötC. $GABA_A$ receptor blockade by bicuculline (5 mM) or gabazine (2 mM) induced strong depression of respiratory activity up to apnea. Glycine receptor blockade by strychnine (5 mM) induced mild decreases in both respiratory frequency and peak phrenic amplitude. Since strychnine at high concentration may also block $GABA_A$ receptors, the effects of the $GABA_A$ receptor agonist muscimol were studied both in control conditions and during glycine receptor blockade. Muscimol (0.3 mM) caused low-amplitude, high-frequency irregular oscillations superimposed on tonic phrenic activity and eventually the disappearance of respiratory rhythmicity in the presence of intense tonic inspiratory discharges. Muscimol-induced respiratory responses were not altered by prior microinjections of strychnine (5 mM) at the same site. $GABA_B$ receptor blockade by CGP-35348 (50 mM) did not affect respiratory activity. Microinjections of $GABA_B$ receptor agonist baclofen (1 mM) increased respiratory frequency, without appreciable changes in peak phrenic amplitude. The results demonstrate that GABA and glycine receptors are expressed within the BötC of the rabbit. The effects induced by bicuculline and strychnine appear to be related to disinhibition of BötC inhibitory neurons. Thus, $GABA_A$ and glycine receptors may have an intense modulatory role on inspiratory activity depending upon the inhibitory input they receive, with a major role played by $GABA_A$ receptors. The source of inhibitory inputs to the BötC remains to be investigated. $GABA_B$ receptors do not appear to be involved in the control of basal respiratory activity, although their activation may exert excitatory influences on respiration. Present findings also support the view that BötC neurons are important components of the neural mechanisms underlying the genesis of the normal pattern of breathing.