Reconstruction of synaptic inputs to pre-Bötzinger complex neurons in situ

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The pre-Bötzinger complex (pre-BötC) is an essential component of the brainstem respiratory rhythm-generating circuitry and receives convergent synaptic inputs from numerous neuron populations. Phasic excitatory and inhibitory synaptic inputs during the respiratory cycle are thought to dynamically shape membrane potential trajectories and spiking patterns of pre-BötC neurons, but the temporal fluctuations of synaptic conductances have not been well characterized. We applied sharp microelectrode intracellular recording techniques to characterize spiking patterns, membrane potential trajectories, and synaptic conductances of pre-BötC respiratory neurons within in situ perfused brainstem-spinal cord preparations of mature rats, which provide favorable conditions for intracellular recording analysis of synaptic mechanisms during inspiratory (I) and expiratory (E) phases in a functionally intact brainstem. We distinguished different types of I and E pre-BötC neurons and analyzed changes of excitatory (Ge) and inhibitory (Gi) conductances throughout the respiratory cycle from current- and voltage-clamp recordings. The different types of neurons showed characteristic patterns of Ge/Gi fluctuations. Pre-I and ramp-I neurons exhibited strong excitatory inputs with maximal Ge of up to 80% and 60% of neuronal leak conductance, respectively. In pre-I neurons Ge increased in mid-E, was maximum during the I phase (defined by phrenic nerve activity) with peak Ge at the end of I. Gi was maximal at the IE transition and decreased through the first half of E (i.e. during the post-I period). In contrast, ramp-I neurons exhibited a rapid increase of Ge at I onset with maximal values at the end of I. Gi rapidly increased at the I-E transition and remained high throughout E. In pre-BötC E neurons (post-I and augmenting-E) the dominant synaptic inputs were inhibitory. Gi in post-I cells increased in mid-E, reached maximum values during I and then rapidly declined at I termination. Ge occurred primarily during the post-I period and was nearly an order of magnitude lower. Gi in aug-E neurons was maximum during I with lower, gradually declining values during the first half of E. The reconstructed patterns of Ge and Gi allow us to define and classify the types of respiratory neural populations involved in the respiratory rhythm generation and establish their interactions. The resultant network architecture was generally consistent with circuit architectures proposed in our previous models to account for a 3-phase rhythmic respiratory pattern.

Supported by: NIH R01 NS057815, R01 NS069220, Intramural NINDS/NIH.