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Presentation Abstract

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Title: Control of respiratory pattern by interacting pontine and pulmonary feedback loops

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Abstract: We developed a computational model of interactions between the pontine and pulmonary inputs in the control of the respiratory pattern. The underlying hypothesis was that the peripheral pulmonary feedback loop and pontine input control respiratory phase durations via the same key medullary neurons, responsible for the onset and offset of inspiration. In addition, pontine and pulmonary inputs control the gain of each other via interaction in nucleus tractus solitarius (NTS) and pons. In our model, the pontine neurons receive excitatory inputs from the medulla and provide excitation to the medullary neurons responsible for the onset and termination of inspiration. Similarly, vagal feedback provides excitation to the same medullary neurons via excitatory pump cells of the NTS. At the same time, NTS neurons project to the pons providing presynaptic inhibition of medullary inputs to pontine neurons (i.e., the vagal feedback loop suppresses the pontine-medullary loop). Using our model, we investigated the effects of (1) “vagotomy” (breaking the peripheral control loop), (2) suppressing medullary inputs to the pons reducing the effect of pontine-medullary loop on the respiratory pattern, and (3) both these perturbations on the durations of inspiration (TI) and expiration (TE). In our simulations, vagotomy produced increases in both TI and TE; suppression of pontine-medullary interactions with vagal feedback intact caused an increase in TI at relatively constant TE; both perturbations resulted in “apneusis”, characterized by significantly prolonged TI.

To test our modeling predictions, experiments were performed *in vivo* in anesthetized, artificially ventilated adult rats (n=12). The respiratory pattern (phrenic nerve activity) was recorded under control conditions and either after vagotomy, or after pontine suppression by MK801 or AP-5 with vagus intact, or after both perturbations. The results of these experiments confirmed that both the peripheral (pulmonary feedback) and the pontine-medullary loops contribute to control of the respiratory pattern (TI and TE durations) with vagal feedback suppressing pontine control of the respiratory pattern. We also found that removal of the vagal control loop reduces respiratory pattern variability whereas a suppression of pontine control loop increases this variability. We conclude that specific changes in the inspiratory and expiratory durations and their variability reflect changing the balance between pontine and vagal control mechanisms and may be specific for particular cardio-respiratory diseases.

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