Paroxysmal coughing: *in vivo* investigations and model simulations

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Paroxysmal coughing occurs in patients with chronic obstructive pulmonary disease and is responsible for significant morbidity. Anesthetized cats produces bouts of coughing that are similar to paroxysmal coughing. However, the spatiotemporal features of repetitive coughing are unknown. We speculated motor drive during successive coughs within a repetitive bout would be dynamic. Further, we hypothesized successive coughs could be modeled by manipulation of second order interneuronal elements in a model of the unified cough/breathing network. *In vivo*, cough esophageal pressures (Pes) and expiratory muscle electromyogram (EMG) magnitudes increased during successive coughs to peak and declined thereafter. First cough had the lowest magnitude (Pes=25.06 $\pm$ 3.9 cmH_20) and increased with successive coughs until reaching maximum at the 8^{th} cough (Pes=51 $\pm$ 5.6 cmH_20). A model of the brainstem cough/respiratory network previously incorporated a single population of second order cough interneurons to transmit airway sensory information to the rest of the network. A second cough interneuron population was added which interacted with the original group through inhibition at stimulus onset. Simulations of this modified model produced abdominal motor drive during repetitive coughing that mimicked patterns observed *in vivo*. We conclude that significant dynamic features of *in vivo* repetitive coughing can be modeled by incorporating a feed-forward inhibitory system into the extant model of the cough/respiratory network. These data suggest more than a simple "relay" of cough related afferent information to the CNS and support a model with cascading interactions that sequentially promote and limit reflex effects. Support: NIH HL 89104; HL 103415.