2. SPECIFIC AIMS

Obstructive sleep apnea syndrome (OSAS) has been reported to occur in approximately 50% in morbidly obese children [1], compared to only ~2% in the general pediatric population [2]. This marked difference in prevalence rates becomes even larger if one were to include other forms of sleep-related breathing disorders (SRBD) such as hypoventilation and hypercapnia or hypoxemia without frank obstructions. Although 45% of obese children have adenotonsillar hypertrophy, adenotonsillectomy eliminates OSAS in less than half of the obese subjects who elect to undergo this form of treatment [3]. These data along with other recent findings suggest that, although upper airway anatomy is a key mediator in OSAS, other factors affect dynamic changes in upper airway patency, such as chemoreflex control and state dependence, play important roles [4]. Moreover, the pool of subjects with obesity-related SRBD display a large variation of polysomnographic and clinical characteristics [1,4]. These may be classified broadly into the following 4 phenotypic categories: (a) primary snorers with no abnormalities of gas exchange, respiratory pattern or sleep disruption; (b) obstructive hypoventilation with hypercapnia or hypoxemia with near-normal respiratory or sleep patterns; (c) high arousal frequency without prominent gas exchange abnormality, obstructive apneas or hypopneas (includes upper airway resistance syndrome); (d) traditional OSAS with recurrent episodes of obstructive hypopnea and apnea.

We hypothesize that this diversity in phenotypic behavior results from the existence of different underlying physiological mechanisms, and that a quantitative dynamic model, informed using a novel dynamic MRI study, would allow us to better delineate the mechanistic differences. To test this hypothesis, we propose the following specific aims:

Aim #1: To establish a database of information pertinent to upper airway and ventilatory control dynamics in overweight/obese pediatric subjects that fall into one of the aforementioned 4 phenotypic categories, derived from high temporal resolution dynamic magnetic resonance imaging (DMRI) and other noninvasive physiological measurements made during wakefulness and sleep.

Aim #2: To estimate the key parameters of a closed-loop minimal computational model of SRBD in individual subjects using measurements of respiratory effort, airflow and gas exchange obtained during wakefulness and sleep, and to determine how these parameters may differ across the 4 phenotypic categories.

Aim #3: To extend the existing computational model using the detailed information of upper airway dynamics derived from DMRI, and to use the extended computational model to predict the observed characteristics of SRBD (e.g. average apnea-hypopnea index, periodicity of ventilatory oscillations, duration of upper airway obstruction, central vs. obstructive apneas) in individual subjects across the 4 phenotypic categories.

High temporal resolution dynamic imaging of the upper airway constitutes a key component of this project. As such, improvements to the current MRI methodology will be pursued in parallel with the above scientific objectives as separate technological aims. Specifically, we will seek to: (A) improve patient comfort by minimizing acoustic noise, and (B) improve spatio-temporal resolution by incorporating the use of parallel imaging and compressed sensing. We hypothesize that acoustic noise can be reduced by at least 50%, and spatio-temporal resolution can be improved by a factor of 4 to 12.