Model-based quantification of loop gain using clinical polysomnography in patients with obstructive sleep apnea

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Abstract—Clinical physiologists have developed methods of estimating the stability of breathing (Loop Gain, LG), by deliberately perturbing the control system and observing the response. Such techniques have shown that elevated LG is an important physiological trait contributing to obstructive sleep apnea (OSA) which can be targeted with therapy. However, techniques to measure LG are currently interventional and laborious, which has hampered its use in the clinical environment. Here we propose and evaluate a novel method to estimate LG using the information available in a routine clinical polysomnogram.

I. INTRODUCTION

Airway obstruction (apnea/hypopnea) results in a LG-dependent build-up in chemical drive to breathe, which is observable when the airway re-opens. It is proposed that by fitting an appropriate ventilatory control model to these periods, it is possible to estimate LG.

II. METHODS

Observed ventilation is modeled as:

\[ v_e = v_{chem} + v_{around} \]  \hspace{1cm} (1)

where chemical drive \( v_{chem} \) is a function of time-delay (\( \delta \)), time-constant (\( \tau \)) and the steady state loop-gain (\( G \)):

\[ v_{chem} = \frac{G e^{-\delta / \tau}}{1 + s \tau} \]  \hspace{1cm} (2)

Two approaches for modeling the additional drive due to brief arousal from sleep \( v_{around} \) (ventilatory response to arousal, VRA) were tested: an additive factor \( v_{around} = \alpha \) or a multiplicative co-efficient of chemical drive \( v_{around} = \alpha \cdot v_{chem} \).

This methodology was evaluated in two stages: (1) The method was applied to overnight polysomnograms from 54 OSA patients to identify the best VRA model (based on minimum mean-square-error); and (2) the method was applied retrospectively to polysomnograms of 12 patients with OSA both at baseline and following oral acetazolamide (ACZ) treatment (500mg 2x daily for 1 week) [1]. On separate nights, LG was also measured using the CPAP drop method [2].

III. RESULTS AND DISCUSSION

VRA was best modeled as a multiplicative coefficient of chemical drive, with one coefficient applied to breaths during a scored arousal and a second applied to the breath following. Our method also detected a reduction in LG with ACZ treatment (0.52±0.14 vs. 0.40±0.16, \( p<0.05 \); quantified at 1 cycle/min) matching the reduction in LG measured using the gold-standard (0.60±0.1 vs. 0.36±0.1, \( p<0.05 \)). Reduced LG was also observed at frequencies of 2 cycles/min (LG2) and at the natural frequency (LGn; note LGn>1 defines instability; see Fig. 1).

![Figure 1. Detecting the acetazolamide-induced reduction in loop gain in OSA](image)

Our novel method allows LG and ventilatory drive to be measured in OSA patients using routine polysomnography alone. The method provides the major step necessary for quantifying the pathological traits causing OSA clinically and targeting these with appropriate therapy.

REFERENCES
