Sleep Apnea and Function of the Upper Airway

- Describe the anatomic regions of the upper airway and sort structure and function into active and passive components
- List the features of the respiratory control system relevant to apnea
- Define treatment modalities for obstructive sleep apnea in physiological terms
Part I

Describe the anatomic regions of the upper airway and sort structure and function into active and passive components
The Upper Airway is a Multipurpose Passage

• Transmits air (per nose and mouth) and liquids and solids (per mouth).
• Acts as a heat exchanger.
• Highly adapted for vocalization in humans.
  – As a result it is semi-rigid and therefore prone to collapse.
Regions of the Upper Airway
• Nose
• Nasopharynx
• Oropharynx
• Laryngopharynx
• Larynx
Regions of the Upper Airway
• Nose
• Nasopharynx
• Oropharynx
• Laryngopharynx
• Larynx

Maxilla

Mandible

Hyoid
Mechanical Features of Upper Airway Structures

• Slowly Varying Properties
  – Craniofacial form (base of the skull and mandible)
  – Tissue Mass and Orientation (including gravitational effects and mucosal thickness)

• Rapidly Varying Properties
  – Linkage between Lung and Pharyngeal volume
  – Blood volume and airway lining fluids
  – Neural Control of muscles at valves and for airway functions
Muscles of the Upper Airway

- Alae nasi (widens nares)
- Levator palatini (elevates palate)
- Tensor palatini (stiffens palate)
Muscles of the Upper Airway

- Genioglossus  
  (protrudes tongue)

- Geniohyoid  
  (displaces hyoid arch anterior)

- Sternohyoid  
  (displaces hyoid arch anterior)

- Pharyngeal constrictors  
  (form lateral pharyngeal walls)
MRI of the Upper Airway

Thickening of Lateral Pharyngeal Walls in Patient with Sleep Apnea

Normal MRI

Patient MRI (reduced lateral dimensions)

Promoting Airway Collapse

- Lower Nasal Pressure
- Extra luminal Pressure (Positive)
  - Fat
  - Mandibular size/position

Promoting Airway Patency

- Pharyngeal Dilator contraction
- Lung Volume by traction
The Starling Resistor

Concepts for Upper Airway Collapsibility (Pcrit)

\[ V_{\text{max}} = \frac{\left( P_{\text{US}} - P_{\text{crit}} \right)}{R_{\text{US}}} \]

Inspiratory Airflow Limitation

Increasing Downstream Pressure does not help.

Adapted from Gold AR & Schwartz AR, Chest. 1996; 110(4):1077-1088
Pressure-Flow Curves

Pcrit for an OSA patient

Summary Graph

Data

Mechanical States for a Startling Resistor

\[ V_{\text{max}} = \frac{(P_{\text{US}} - P_{\text{crit}})}{R_{\text{US}}} \]
Review:
Critical Closing Pressure ($P_{CRIT}$)

Comparison of Pcrit among Clinical Groups

NREM Sleep

<table>
<thead>
<tr>
<th>Pcrit (cm H₂O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Snorer</td>
</tr>
<tr>
<td>UARS</td>
</tr>
<tr>
<td>Obstructive Hypopnea</td>
</tr>
<tr>
<td>Obstructive Apnea</td>
</tr>
</tbody>
</table>

Neuromuscular Blockade

<table>
<thead>
<tr>
<th>Pcrit (cm H₂O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Mild Obstructive Apnea</td>
</tr>
<tr>
<td>Mod Obstructive Apnea</td>
</tr>
</tbody>
</table>

Adapted from:
Gleadhill, et al. ARRD 1991;143:1300
Isono et al. J Appl. Physiol. 1997;82:1319
Pcrit Determination for Active and Passive Properties of the Upper Airway

Advanced Learning slide
An Analytical Approach to Distinguish Active and Passive Features

$V_{1max}$ (ml/s)

$P_{crit}$

$V_{max}$ (ml/s)

$\Delta P_{crit_{A-P}}$

$P_N$ (cm H$_2$O)

Part II

List the features of the respiratory control system relevant to apnea
Feedback Control of Breathing

Controller

Sensors
- Carotid body
- Brainstem

Pressure Receptors

Controlled System

Nerves and muscles

afferents

circulation
Neuromuscular Activity and Upper Airway Obstruction

Remmers, 1978
Neural Control and State Changes
Upper Airway Reflexes are Blunted during Sleep

Wheatley et al, 1993
Upper Airway Mechanical Loads and Neural Responses

- Apnea
- Hypopnea
- Snoring
- Normal

$P_{\text{Crit}}$ (cmH$_2$O)

Compensatory Neuromuscular Responses

Mechanical Loads

Patil SP et al., J Appl Physiol. 2007; 102(2):547-56
Patterns of Sleep Apnea
Ventilatory Drive in obstructive and central apneas.

UA = DIA

UA > DIA

Cherniack, 1979
Recurrent Apneas are Ventilatory Arrhythmia.

From Lynn, 1998
Recording of an Obstructive Apnea during Sleep

Principles and Practices of Sleep Medicine 2nd Ed.
Obstructive Sleep Apnea is a Neuromechanically Unstable Upper Airway

Strohl and Redline, 1986
Ventilatory Instability and Upper Airway Obstruction

Summary Idea:
Loop Gain and $P_{crit}$

A. Wellman 2008 by permission

Size Compliance

From Lynn, 1998
Risk Factors in the History

- Obesity (7-8 fold risk)
- Gender (M : F :: 3-4 : 2)
- Family History
- Sleepiness itself
- Cardiovascular Disease itself

Possibility of Finding Another Family Member with Sleep Apnea

Number of Family Members with Known OSAHS

Redline and Tishler, 2000
Recurrent Sleep Apnea is a **biologically Complex Trait.**
A Whole-Genome Scan for 24-Hour Respiration Rate: A Major Locus at 10q26 Influences Respiration During Sleep

E. J. C. de Geus,1,* D. Posthuma,1,* N. Kupper,1 M. van den Berg,1 G. Willemsen,1 A. L. Beem,1 P. E. Slagboom,2 and D. I. Boomsma1

1Department of Biological Psychology, Vrije Universiteit, Amsterdam; and 2Department of Molecular Epidemiology, Leiden University Medical Center, Leiden, The Netherlands

Identification of genes causing variation in daytime and nighttime respiration rates could advance our understanding of the basic molecular processes of human respiratory rhythmogenesis. This could also serve an important clinical purpose, because dysfunction of such processes has been identified as critically important in sleep disorders. We performed a sib-pair–based linkage analysis on ambulatory respiration rate, using the data from 270 sibling pairs who were genotyped at 374 markers on the autosomes, with an average distance of 9.65 cM. Uni- and multivariate variance-components–based multipoint linkage analyses were performed for respiration rate during three daytime periods (morning, afternoon, and evening) and during nighttime sleep. Evidence of linkage was found at chromosomal locations 3q27, 7p22, 10q26, and 22q12. The strongest evidence of linkage was found for respiration rate during sleep, with LOD scores of 2.36 at 3q27, 3.86 at 10q26, and 1.59 at 22q12. In a simultaneous analysis of these three loci, >50% of the variance in sleep respiration rate could be attributed to a quantitative-trait loci near marker D10S1248 at 10q. Genes in this area (GFRA1, ADORA2L, FGR2, EMX2, and HMX2) can be considered promising positional candidates for genetic association studies of respiratory control during sleep.

Introduction

Billions of mammals, including humans, depend on rhythmic breathing to regulate one of the foremost aspects of homeostasis: the appropriate exchange of oxygen and carbon dioxide. Although a number of theoretical models...
On Physical Examination
(often normal)

- Obesity (BMI > 30 kg/m²)
  - Neck circumference*
- Mallampati score *
- Craniofacial
  - Soft tissues in nose and pharynx
  - Head Form

*M Accepted pre-test factor
Craniofacial Findings I

Tonsil Grade
Craniofacial Findings II

Nasion → Retrognathia

Gnathion →
Part III

Define treatments for obstructive sleep apnea in physiological terms
Optimal OSA Treatment Would Restore:

• Upper Airway Patency during Sleep
• Sleep Continuity
• Adequate Gas Exchange
• Quality of Life
  – Sleepiness
  – Neurocognitive Function
• A lower diurnal blood pressure
• A decrease in Mortality
Treatment Targets

Mechanical Loads
- Size and anatomy
- Collapsibility

Neural Drive
"Conservative” Therapy

- Treat hypothyroidism or acromegaly (if present)
- Weight loss
  - Case series*
- Fitness
  - Case series
- Nasal Splinting
  - Case series with mixed success
- Positional Therapy (Sleep on side, pillows)
  - Case series
- Sprays
  - No data
- Spousal Advice
  - Ear plugs

* Bariatric Surgery for BMI >35-40: ~85% effective
OSAHS Rx. CLASSES

Introduction

Therapy Directed at the Upper Airway

– By-pass upper airway: tracheostomy
– Continuous positive pressure therapy (CPAP)
– Surgery (UPPP, mandibular advancement)

– Oral Appliances
– Experimental
  • Electrical stimulation of nerves
  • Drug therapy
CPAP Effects

Patient Awake

Schwab et al, 1995

Patient Asleep

Strohl and Redline, 1983
CPAP increases Upstream Pressure

\[ \text{P}_{\text{N}} = 0 \]
\[ \text{P}_{\text{N}} < \text{P}_{\text{crit}} \]
\[ \text{P}_{\text{N}} > \text{P}_{\text{crit}} \]
\[ \text{P}_{\text{crit}} = +1 \]
\[ \text{P}_{\text{crit}} > \text{P}_{\text{ph}} \]

Apnea

Flow-Limitation

\[ \text{R}_{\text{us}} \]
\[ \text{P}_{\text{N}} = +5 \]
\[ \text{P}_{\text{N}} > \text{P}_{\text{crit}} \]
\[ \text{P}_{\text{ph}} = +5 \]
\[ \text{P}_{\text{crit}} = +1 \]
\[ \text{P}_{\text{crit}} > \text{P}_{\text{ph}} \]

Normal Breathing with CPAP

\[ \text{P}_{\text{us}} = +15 \]
\[ \text{P}_{\text{N}} > \text{P}_{\text{crit}} \]
\[ \text{P}_{\text{crit}} = +1 \]
\[ \text{P}_{\text{ph}} = +5 \]
\[ \text{V}_{\text{max}} = (\text{P}_{\text{N}} - \text{P}_{\text{crit}})/\text{R}_{\text{N}} \]

\[ V = (\text{P}_{\text{N}} - \text{P}_{\text{ph}})/\text{R} \]

Adapted from Gold et al. Chest 1996;10:1077-1088
EFFECTS OF 12 cmH2O

Sullivan et al, 1981
Various Approaches

- Uvulopalatopharyngoplasty (UPPP)
- Hyoid suspension
- Nasal septal surgery
- Tongue reduction
- Mandibulomaxillary Advancement
UPPP (Fujita, 1981)

Most common procedure

- Treatment for Retropalatalal Collapse
- No randomized controlled trials
- 20-70% success at 2 years
  - Patient selection
  - AHI fall <50% or to
UPPP effects

Oral Appliances* will:

- Be as effective as CPAP in mild to moderate OSA
  - Better success: Lower BMI, positional apnea, and ability to protrude tongue
- Help patients utilize CPAP in those intolerant of high pressures

* Randomized Controlled Trials
Selective Stimulation of the Hypoglossal Nerve

Summary Idea: Loop Gain and P_{crit}

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Size Compliance
**Drug Therapy**

Drugs that selectively affect loop gain.
- Respiratory stimulants
- But no consistent effects across medications

Drugs that alter mechanical loads.
- Weight loss (no studies on OSA effects)

Drugs to reduce sleepiness
Structure and Function of the Upper Airway

Implications for Sleep Apnea: Review of Objectives

• Describe the anatomic regions of the upper airway and sort structure and function into active and passive components
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