Dysfunctional breathing and the upper airway: Those scary things that go bump in your throat!

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Learning Objectives:
◇ To add light to a dark and murky literature, by discussing the role of the upper airway in:
   ◇ normal respiration,
   ◇ and dysfunctional breathing.
◇ To explore how processes linking the CNS, ANS, and the upper airway may play a role in dysfunctional breathing.
◇ I have no conflicts to disclose.

A Literature of Goofy Words
- Munchausen’s stridor
- Psychosomatic wheezing
- Fictitious asthma
- Hysteric croup
- Psychogenic stridor
- Pseudoasthma
- Laryngoneurosis
- Functional laryngeal stridor

Do upper airway problems have 1st psych causes?
A Literature of Goofier Logic

These problems are called “Functional”
Which really means they are “Dysfunctional”
– But, if Dysfunctional = Not Functional
– Then Functional = Not Functional!!!!!

Do upper airway problems have physiological basis?

Mini-Med School
- - The Upper Airway - -

- Conduit that extends to larynx/vocal cords
- Conditions and filters incoming air
- Monitors & modulates respiratory airflow
- Defends the airway
- Smell & speech

Can exceed ability to condition/filter air
- - The case of Olympic athletes - -

- Nordic Combined & XC Skiers
  – Ventilation to 200 l/min of cold, dry air
  – Chronic cough=86%; AHR/asthma=15%
- Alpine and Ski-Jumpers
  – Chronic cough <30%; AHR/asthma <4%
- Figure/Speed Skaters, Hockey Players
  – Poor air quality in indoor rinks
  – AHR/asthma = 12%

Can exceed ability to condition/filter air  
- - World Trade Center Disaster - -

WTC residents and responders have shown high rates of cough, rhinosinusitis, GERD, VCD, and AHR.

Dose-effect link; in part 2° to inhalation of caustic dust


Mini-Med School  
- - The Upper Airway - -

- Monitors & modulates respiratory airflow
- Upper airway dilates with I, contracts with E
- Effects important in:
  - Sleep, dilation inhibited
  - Exercise, mixed effects
  - Disease, “auto-PEEP” in asthma & COPD

Repetitive collapse and reopening of upper airway induces inflammation

- A rat model of sleep apnea inducing inflammation
- S-D Rats were subjected to 5 hours of periodic, recurrent mechanical modulation of upper airway pressure to induce mild collapse and reopening.
- 10-40 fold increase in gene expression of pro-inflammatory biomarkers in soft-palate and larynx.
- No evidence of histopathological or Pcrit changes.
- May contribute to vicious cycle of progressive OSA.

Allergy and irritants are linked; and the “One Airway” hypothesis

- Allergy and irritation are distinct but interact
  - Exposure to inhaled irritants (e.g., diesel or SHS) can lead to increased allergic sensitization
  - Airway allergies can intensify responses to irritants
- Upper airway inflammation affects the lower airway, and vice versa.


Mini-Med School - - The Upper Airway - -

- Protective reflexes and defense of the airway
  - Reflexes to prevent inhalation of foreign material into lungs
    - Nose/nasopharynx – olfactory & trigeminal (CN I & V)
    - Pharynx - glossopharyngeal & vagus (CNs IX & X)
    - Larynx – vagus (CN X)
- Mechanical, thermal and chemical/irritant sensors

Neuromodulation and Central Sensitization

- Allergic and inflammatory mediators can increase nerve excitability, not just acutely, but over the long-term!

Animal Models of Central Sensitization

Lung irritant exposure causes “central sensitization” of vagal reflexes
- Exposure to certain lung allergens and irritants
  - Capsaicin, ETS, isocyanates, URI viruses
- Activates C-fibers to nucleus tractus solitarius
- Causing increased & persistent NTS excitability
- Via tachykinin release (subst. P, neurokinin-A)
- Leading to persistent hyperactive CNS reflexes
  - Altered respiration (rapid, shallow breathing)
  - Increased (i.e., lowered threshold) cough reflex
  - Increased mucus production
  - Bronchoconstriction
  - Increased bronchial hyperresponsiveness


Certain dysfunctional breathing syndromes may arise from hyperactive CNS protective reflexes

Hypothesis: A family of dysfunctional breathing syndromes may arise due to induced “central sensitization” of key CNS areas that keep short-term protective reflexes “stuck on.”
- Reflexes such as panic anxiety, cough, fast and shallow breathing, glottic closure, rhinorrhea, GER, light unstable sleep.
- Possible role in fibromyalgia, IBS, MCS, sleep apnea/hypopnea???

The Irritable Larynx Syndrome

Central sensitization as response to repetitive nocistimulation
- Inflammation→altered autonomic tone→hyperactive reflexes
- Larynx shifts into a “spasm-ready state” with clear triggers
- Symptoms = chronic dry cough, globus, dysphagia, VCD
- Similar to lowered pain thresholds in chronic pain
- Reflex hyperactivity likely to be caused and/or worsened by:
  - Airway insults, e.g., asthma, GERD, rhinosinusitis, URIs
  - Environmental factors, e.g., inhaled irritants, ETS, odors
  - Psychological factors, e.g., anxiety, trauma, ?CNS viruses?

Vocal Cord Dysfunction (VCD)

- Paradoxical inspiratory closure of vocal cords (folds) observed via laryngoscopy after symptom provocation
- Airflow obstruction occurs in upper airway
- Audible wheeze or stridor in upper airway
- Common asthma mimic (10-25%)
- Etiology unknown but stress &/or psychopathology emphasized
- Treatments mainly nonspecific but usually focus on breathing

Clinical & Psychosocial Factors in VCD

- Originally described in young, female, health care workers, with abuse history; called conversion disorder
- Now recognized in several, different groups:
  - Respiratory disease, allergy, irritant exposure, or post-URI
  - Athletic competition (including race horses); military service
  - After neck surgery, with use of vagal stimulators
- Overlap with chronic cough, hyperventilation, OSAHS
- No established relationship with psychological distress or psychiatric illness

Adolescents with Asthma and VCD

- Prospective data on 84 inpatients admitted for severe, intractable asthma
- Self, parent &/or teacher report psych/family measures
- Structured psychiatric interview and family observation
- Pulmonologist blind to psych data assessed VCD
- 12 patients with VCD matched to patients with asthma and no VCD by race, gender, daily prednisone dose

Psychological Assessments: Anxiety Prominent in VCD

<table>
<thead>
<tr>
<th></th>
<th>VCD Patients Mean (SD)</th>
<th>Asthma Only Mean (SD)</th>
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</thead>
<tbody>
<tr>
<td>Family Functioning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self report</td>
<td>2.13 (0.33)</td>
<td>1.97 (0.42)</td>
</tr>
<tr>
<td>Observed</td>
<td>4.26 (1.07)</td>
<td>4.26 (0.74)</td>
</tr>
<tr>
<td>Child Adjustment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety (p &lt; .01)</td>
<td>1.96 (3.80)</td>
<td>-1.61 (1.84)</td>
</tr>
<tr>
<td>Acting Out</td>
<td>0.79 (3.13)</td>
<td>-1.27 (2.07)</td>
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Psychiatric Diagnoses: Anxiety Prominent in VCD

<table>
<thead>
<tr>
<th>Lifetime Psychiatric Diagnoses</th>
<th>VCD Patients N</th>
<th>Asthma Only N</th>
</tr>
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<tbody>
<tr>
<td>Separation Anxiety and/or Overanxious Disorder</td>
<td>8/12 (67%)</td>
<td>2/12 (17%)</td>
</tr>
<tr>
<td>Anxiety Disorder before Asthma</td>
<td>5/8 (63%)</td>
<td>0/2 (0%)</td>
</tr>
<tr>
<td>Depression comorbid with Anxiety Disorder</td>
<td>5/5 (100%)</td>
<td>0/2 (0%)</td>
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Reigning Theories about Panic Anxiety

- Psychiatry = Amygdala as “Fear Center”
  - Panic = one type of Fear Response or Circuit
  - Possible role of Classical Conditioning?

- Psychology = “Upstream” Cortical Influences
  - “Anxiety Sensitivity”
  - Misinterpretation of Body Sensations
  - Propensity to Catastrophic Interpretations

- “Downstream” Brainstem Influences
  - Interoception via UA/Lung Sensors & Vagal Afferents
**PD as a Respiratory Control Disorder**

- Rates Panic Disorder ↑ in Respiratory Disorders & vice versa
- Respiratory Control Abnormalities (“Unsteadiness”)
  - ↑ Compensated hyperventilation (↑PaCO₂, ↓Bicarb, nl pH)
  - ↑ Variability in Vt & RR (↑Sighs, Yawns, Gasps, Coughs)
  - ↑ Hypercapnic Drive (ΔVₖ/ΔCO₂)
  - CO₂ Inhalation or lactate infusion => Panic Symptoms

**Respiratory Control Abnormalities Normalize with Treatment**


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**PD and Traumatic Suffocation (TS)**

- - An Initiating or Triggering Factor? - -

- Higher rates of TS in PD patients vs Other Psychiatric Dx
- Higher rates in those with mostly “respiratory PD” = 76.5% versus those with other subtypes: “CV” =14.7%, “GI” =0%
- Higher rates of PD if suffocation used during torture
- TS history associated with panic after inhaling 35% CO₂


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**Panic Disorder without Fear**

- “Somatically expressed PD,” “masked anxiety,” “alexithymic PD”
- Meet DSM criteria for PD except for subjective fear or anxiety
- Prevalence = 30 to 40% of PD in medical populations
  - These patients seek treatment outside of mental health world
  - Bulk of “non-clinical panickers” in epidemiologic studies
- Similar demographic, clinical, prognostic features with “true” PD
  - May have less agoraphobic avoidance; more stoic, religious
  - + lactate challenge and anti-panic medication response
- Treatment reduces somatization, health care utilization


Hyperventilation Syndrome (HVS)
- 50-60% overlap with Panic Disorder
- 60-70% overlap with Agoraphobia
- 29 patients referred for chronic HVS
- 21 confirmed as hypocapneic by ETCO$_2$ x 5 min
  - 3 had abnormal V-P scan
  - 10 had anxiety disorders (panic or phobias)
  - 6 were “normal” (panic disorder without fear?)
  - 2 had positive histamine challenge (asthma/VCD?)

Summary
- The upper airway is NOT a passive conduit, but rather is actively and dynamically involved in respiration in both normal and disease/dysfunctional states.
- The upper airway affects the lower airway, and vice versa.
- CNS reflexes and regulation of the upper airway are involved in both functional and dysfunctional processes.
- The role of psychological processes/disorders in the upper airway are overemphasized, but understudied.

Research Implications
- Do psychological processes such as Anxiety Sensitivity or Traumatic Stress initiate or predispose to upper airway dysfunction? If so, how and in what contexts?
- How do single versus repeated environmental insults lead to upper airway problems and problems (and what are the key characteristics of these insults)?
- Are there “initiating” factors and “perpetuating” factors?
- What actually changes in the brain and rest of the body during these reactive processes?
- How are the ANS/vagal tone/HPA axis involved?
- How can these be altered/changed/prevented?