The impact of Anxiety Sensitivity in asthma patients with panic disorder on respiratory response to a standard panic (CO₂) challenge

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Links between Anxiety and Asthma

- Link between anxiety and impaired airway function in asthma patients.
  - Increased dyspnea and bronchoconstriction

- Anxiety sensitivity (AS) is a trait associated with excessive fear of anxiety-related sensations based on beliefs about their harmful consequences.
  - AS is high in patients with Panic disorder

- Panic disorder (PD)
  - Sudden, recurrent panic attacks, episodes of intense fear or discomfort associated with cognitive and physiological symptoms
  - Common among asthmatics
  - Associated with worse asthma outcomes, possibly due to panic-induced respiratory changes.
CO$_2$ inhalation as a panic challenge

- CO$_2$ inhalation is also a well known panic challenge in PD patients

- Inhaling concentrations of CO$_2$ (e.g., continuous 7% or one vital-capacity inhalation of 35%) induces more anxiety and panic symptoms in PD patients

- Role of Anxiety Sensitivity in PD patients, who are undergoing a panic challenge is unclear
Aims

• To evaluate the impact of AS on respiratory measures in asthmatics with PD during a panic challenge.
  ▫ CO$_2$ production [VCO$_2$; ml/kg/min],
  ▫ O$_2$ production [VO$_2$; ml/kg/min],
  ▫ Ventilation rate [VE; L/min]
  ▫ Tidal volume [TV; L]
Methods

- 17 patients with physician-diagnosed asthma and PD

- Inclusion criteria: a primary diagnosis of asthma (chart evidence of previous positive methacholine test and/or bronchodilator reversibility); be non-smoking; aged 18-70 years.
  - Bronchodilators withheld for at least 8 hours prior to testing.

- Exclusion criteria: Chart evidence of a medical condition that was more severe than asthma (such as cancer, COPD); cognitive or language deficit that would have impaired providing informed consent
Panic Disorder and Anxiety Sensitivity

• Panic Disorder confirmed by meeting DSM-IV criteria for a primary diagnosis of PD.
  ▫ ADIS-IV; semi-structured interview, good to excellent inter-rater reliability (e.g., PD, $\kappa = 0.72$)

• Anxiety sensitivity index (ASI)
  ▫ 16-item questionnaire
    • measures the extent to which individuals are fearful of anxiety-related symptoms (trait anxiety sensitivity).
  ▫ High internal consistency ($\alpha = 0.83$) and test-retest reliability
Measures

• CO₂ Panic Challenge
  ▫ Completely exhale, then One vital capacity of 35% CO₂, then told to breath normally

• Breath by breath Respiratory Measures
  ▫ Jaeger Oxycon Pro

• Statistical Analyses:
  ▫ Mixed models assessed the impact of AS and time (pre and post 35% CO₂ inhalation) on respiratory measures.
Study design

PD and AS Assessment

Baseline (20 minutes)
• Continuous breath by breath recording

Recovery (20 minutes)
• Continuous breath by breath recording

35% CO₂ Inhalation
• Complete exhalation, then take one vital capacity inhalation of the gas, hold it for 4 seconds, and then breathe normally
## Results

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD) or % (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.5 (14.5)</td>
</tr>
<tr>
<td>Sex (% Women)</td>
<td>82.4 (14)</td>
</tr>
<tr>
<td>ASI Total Score</td>
<td>20.0 (9.9)</td>
</tr>
<tr>
<td>ACQ Mean Score</td>
<td>1.20 (1.12)</td>
</tr>
<tr>
<td>PC20 response to Metacholine challenge</td>
<td>0.71 (2.53)</td>
</tr>
<tr>
<td>Morisky Total Score</td>
<td>3.65 (2.1)</td>
</tr>
<tr>
<td>Resting VCO(_2) (ml/kg/min)</td>
<td>172.8 (75.5)</td>
</tr>
<tr>
<td>Resting VO(_2) (ml/kg/min)</td>
<td>174.4 (80.7)</td>
</tr>
<tr>
<td>Resting Ventilation Rate (L/min)</td>
<td>8.23 (3.3)</td>
</tr>
<tr>
<td>Resting Tidal volume (L)</td>
<td>0.70 (0.3)</td>
</tr>
</tbody>
</table>
Exhaled CO2

<table>
<thead>
<tr>
<th></th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASI</td>
<td>2.5</td>
<td>0.11</td>
</tr>
<tr>
<td>Time</td>
<td>0.58</td>
<td>0.44</td>
</tr>
<tr>
<td>ASI X Time Interaction</td>
<td>4.0</td>
<td>0.046</td>
</tr>
</tbody>
</table>

- No main effect of time
- No main effect of ASI
- Interaction effect for ASI by time
Exhaled CO₂ changes over time

- β (VCO₂ (ml/kg/min))
- Time (minutes)

High ASI
Low ASI
Exhaled $O_2$

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>ASI</td>
<td>1.24</td>
<td>0.27</td>
</tr>
<tr>
<td>Time</td>
<td>3.40</td>
<td>0.07</td>
</tr>
<tr>
<td>ASI X Time</td>
<td>2.45</td>
<td>0.12</td>
</tr>
</tbody>
</table>

- No main effect of time
- No main effect of ASI
- No interaction effect for ASI by time
Ventilation Rate

<table>
<thead>
<tr>
<th></th>
<th>F</th>
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</tr>
</thead>
<tbody>
<tr>
<td>ASI</td>
<td>6.85</td>
<td>0.008</td>
</tr>
<tr>
<td>Time</td>
<td>0.14</td>
<td>0.71</td>
</tr>
<tr>
<td>ASI X Time Interaction</td>
<td>1.91</td>
<td>0.17</td>
</tr>
</tbody>
</table>

- Main effect of time: Higher Ventilation Rate in high ASI
- No main effect of ASI
- No interaction effect for ASI by time
Tidal Volume

<table>
<thead>
<tr>
<th></th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASI</td>
<td>1.06</td>
<td>0.30</td>
</tr>
<tr>
<td>Time</td>
<td>0.09</td>
<td>0.77</td>
</tr>
<tr>
<td>ASI X Time Interaction</td>
<td>27.48</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

- No main effect of time
- No main effect of ASI
- Interaction effect for ASI by time
Tidal Volume changes over time

![Graph showing Tidal Volume changes over time with two lines representing High ASI and Low ASI. The x-axis represents time in minutes, ranging from -5 to 5, and the y-axis represents β (Tidal Volume (L)). The graph indicates a peak at time 0 for both lines, with the Low ASI line peaking slightly higher.](image)
Conclusion

- Asthma patients with PD and higher AS had increased and more prolonged \( VCO_2 \) and TV responses to the panic challenge than patients with PD and lower AS.

- This could indicate that in addition to PD, AS contributes above diagnoses of PD to respiratory responses to a panic-inducing challenge.

- As well as the presence of PD in asthma patients, AS seems to be critical in determining the respiratory response to a panic inducing challenge.
Acknowledgements

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- Emilie Dolan MSc (c)
- Members of MBMC
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Screened for eligibility 228

Excluded 106 (46%)
- Comorbid disease, severe psychopathology, substance abuse, or didn’t meet criteria for PD = 46
- Diagnosed with severe asthma = 46
- Smoking = 12
- Age criteria = 2

Eligible 122 (54%)

Refused to participate 56

Consenting participants 67 (55%)

Excluded from analyses due to an incomplete MCT 28
- Withdrawal = 12
- Baseline FEV\textsubscript{1} < 70% of predicted values = 10
- PC\textsubscript{20} $\geq$ 16mg/ml = 6

Final sample 39