Respiratory Neural Drive in Down Syndrome

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Background

- Pulmonary complications are a leading cause of medical emergencies and mortality in Down syndrome (DS)[1].
- While research emphasis in DS is primarily on structural abnormalities of airways, respiratory muscles, and immune compromise, the role of a respiratory neural drive remains unexplored.
- Studies in DS animal models demonstrate the presence of respiratory neural drive deficit, however, no studies have been conducted in humans.

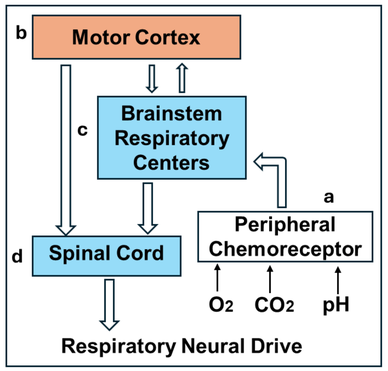
Hypothesis

Our central hypothesis is undiagnosed neural drive deficits impairs volitional and automatic respiratory effort in children with DS.

Objective

Determine whether respiratory central neural drive is reduced in DS due to:

a. Changes in Chemosensitivity that detect the level of O2 and CO2 in the blood.
b. Reduced Volitional Drive from Motor Cortex
c. Reduced Automatic Drive from Brainstem
d. Changes in spinal cord circuitry hat controls the respiratory muscles.



Schematic Diagram of Control Of Breathing

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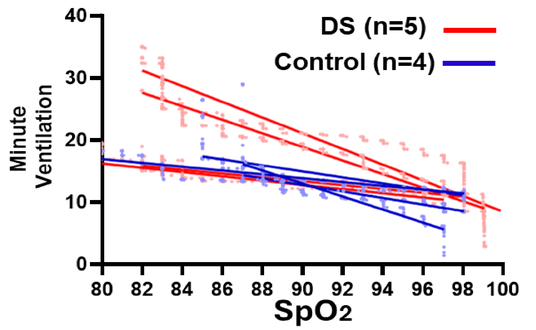
Preliminary Results

Assessment of Brainstem Neural Drive (Automatic Breathing)

Chemosensitivity

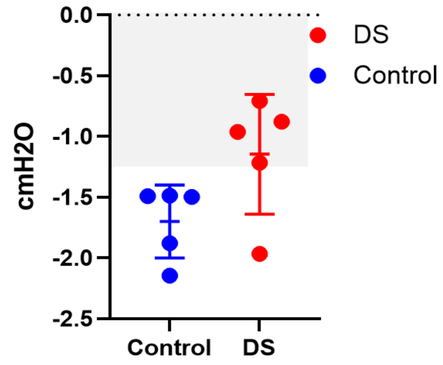
Two participants with DS had increased chemosensitivity



Minute Ventilation= Tidal volume x Breathing Frequency

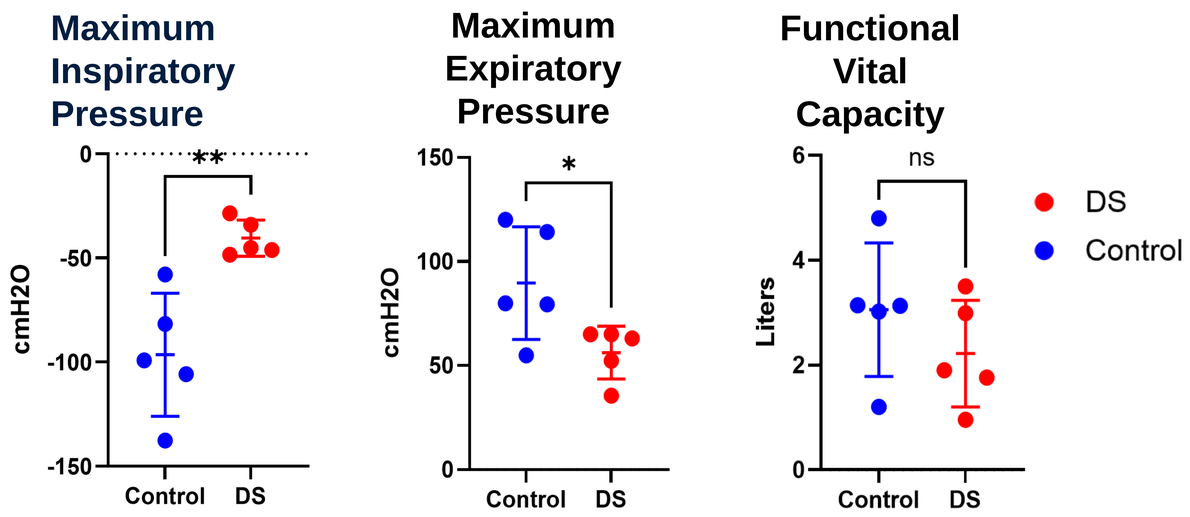
Mouth Occlusion Pressure at 0.1 sec (P0.1)

All participants with DS (except 1) had lower P0.1 values suggesting a reduced brainstem respiratory drive in DS



Clinical Pulmonary Function Test (Volitional Breathing)

All participants with DS had significantly reduced ability to generate volitional maximum inspiratory and expiratory pressure. However, these volitional tests were challenging to conduct due to increased cognitive load, poor mouth seal causing air leaks, and inconsistent motivation or effort



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Methods

Design: Cross Sectional Study

Demographics

Control	DS
11 (M)	13 (M)
12 (M)	13 (F)
15 (M)	22 (F)
17 (F)	29 (F)
22 (M)	29 (F)

Respiratory Testing

Volitional Pulmonary Function Test

The volitional tests included:

1. **Maximum Inspiratory Pressure**
2. **Maximum Expiratory Pressure**
3. **Functional Vital Capacity**

Automatic Breathing Tests

A non-rebreathable mask system was used to assess automatic brainstem drive to breathe via two tests:

1. **Chemosensitivity**—changes in ventilation and oxygen saturation after 1.5 minutes of breathing 9% O_2, 4% CO_2 (balance N_2);
2. **P0.1**—mouth pressure 0.1 seconds after unexpected airway occlusion.

Conclusion

Preliminary findings suggest a neurophysiological basis for respiratory vulnerability in children with DS, particularly reduced automatic brainstem drive, which are not assessed routinely in the clinic.

Future Directions

- We are currently analyzing transcranial (TMS) and cervical (CMS) magnetic stimulation evoked diaphragm responses to determine conduction delays and changes in neural excitability in DS.
- We are also planning to conduct an MRI diffusion tensor imaging of the brainstem and spinal cord circuitry to assess early correlates and biomarkers of respiratory impairments in DS.
- Once we establish the presence and cause of reduced respiratory neural drive in DS we will begin to explore targeted use of noninvasive and medical management strategies aimed at improving central respiratory drive in this group.

References:

Acknowledgement:

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