

Hypoventilation at Peak Exercise in People with Congenital Central Hypoventilation Syndrome

Syndrome: Potential Role of *PHOX2B* Gene Variant

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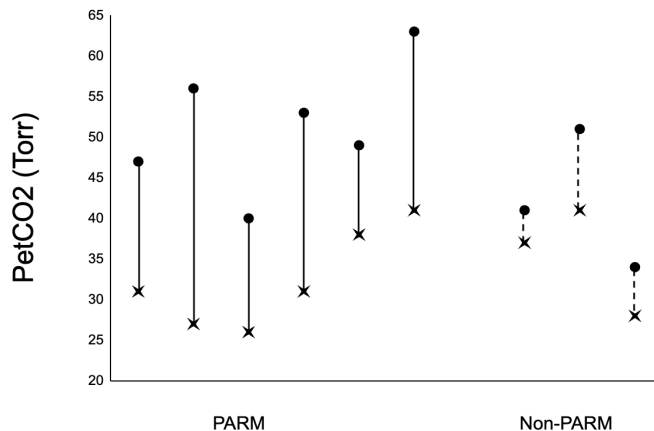
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Background: There is a paucity of data on exercise in individuals with genetically confirmed congenital central hypoventilation syndrome (CCHS). We hypothesize that 1) these individuals hypoventilate at peak exercise and 2) *PHOX2B* gene variant and/or BMI affect hypoventilation during exercise.

Methods: We performed a retrospective study of nine individuals with genetically confirmed CCHS, seen at Children's Hospital Los Angeles, who performed cardiopulmonary exercise stress testing (CPET). Demographics, BMI, *PHOX2B* gene variant, ventilatory support, medical history, polysomnography, and CPET results were collected.

Results: Nine people with CCHS aged 8-22 years were included; six with a *PHOX2B* polyalanine repeat mutation (PARM), three with a non-PARM. Three subjects were obese and one was overweight. Average end tidal P_{CO_2} ($P_{ET}CO_2$) during sleep was 30 ± 10 torr. $P_{ET}CO_2$ increased from rest (33 ± 6 torr) to maximal exercise (48 ± 9 torr; $p < 0.0006$). The difference in mean $P_{ET}CO_2$ at peak exercise minus at rest was greater for PARM (19 ± 6 torr) than for NPARM (7 ± 3 torr; $p = 0.019$). There was no difference in mean $P_{ET}CO_2$ at maximal exercise in the patients who were overweight/obese compared to those with healthy weight ($p = 0.44$).

Conclusion: Individuals with *PHOX2B* PARMs had worse hypoventilation during peak exercise than those with NPARMs. Hypoventilation was not affected by BMI.



X = $P_{ET}CO_2$ at rest. ● = $P_{ET}CO_2$ at peak exercise

Figure 1: Change in $P_{ET}CO_2$ from rest to peak exercise for each subject carrying PARM versus non-PARM variant.



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