Effect of Pyridoxamine Treatment on Arterial Stiffness and Cognitive Function in Old Mice

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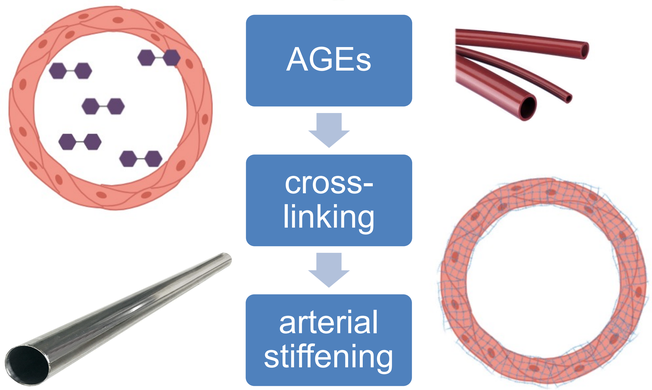
Abstract

With advancing age, large arteries experience increased stiffness in their walls, while small arteries maintain elasticity. Arterial stiffening can occur when advanced glycation end-products (AGEs) form, resulting in collagen in the extracellular matrix becoming cross-linked. Age-induced large artery stiffness is associated with cognitive impairment and heightened risk for developing neurodegenerative disease. The formation of AGEs and collagen cross-linking have been shown to be inhibited by pyridoxamine. It was hypothesized that pyridoxamine treatment would prevent age-related arterial stiffness and attenuate cognitive impairment. Pyridoxamine was administered via drinking water to old C57BL/6 mice for six months, with old and young control groups. Aortic stiffness was measured by pulse wave velocity (PWV), while carotid and middle cerebral artery stiffness were measured ex vivo. Nest building was performed to measure cognitive ability. Old pyridoxamine treated mice had lower aortic PWV and a trend for lower carotid stiffness compared with old control mice. There was no difference in cerebral artery stiffness across groups, indicating that pyridoxamine specifically targets age-related arterial stiffening. Nest building was impaired in old control mice compared with young, but old pyridoxamine treated mice were not different from either group. These results shed light onto potential pyridoxamine treatments for preventing large artery stiffness to preserve cognitive function.

Background



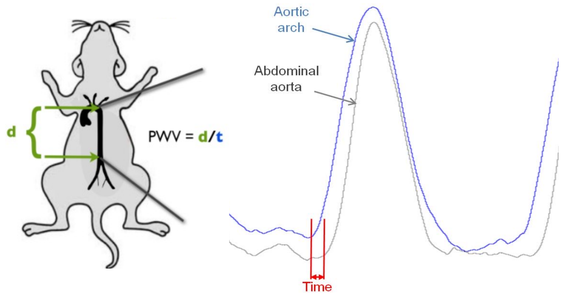
Hypotheses

- Pyridoxamine treated mice will have decreased pulse wave velocity
- Pyridoxamine treated mice will have higher nest building scores
- Pyridoxamine treated mice will have lowered beta stiffness parameters

Methods

Large Artery Stiffness Assessment

- Stiffness of the aorta was assessed by pulse wave velocity.
- Under isoflurane anesthesia, pulse waves were obtained via Doppler at the aortic arch and abdominal aorta.
- PWV analyzed in Doppler Signal Processing Workstation.



Cognitive Function Assessment

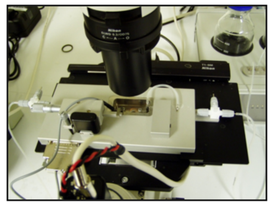
- Cognitive ability was assessed by nest building cognitive test.
- Using a five-point scoring scale, mice were assessed in their ability to build a nest overnight.
- Score of 0: Nestlet left untouched.
- Score of 5: Defined nest with high walls constructed in the corner of the cage.

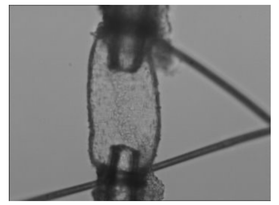
Score: 0

Score: 5

Ex-Vivo Passive Stiffness Test

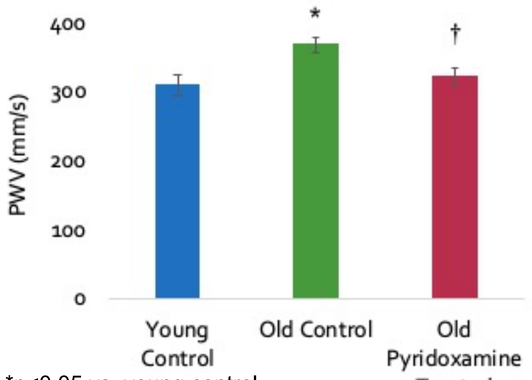
- Passive stiffness was evaluated ex-vivo via DMT pressure myograph.
- Carotid and middle cerebral arteries were exposed to increasing static pressures.
- Resistance to increasing pressure was assessed by measuring changes to lumen diameter.





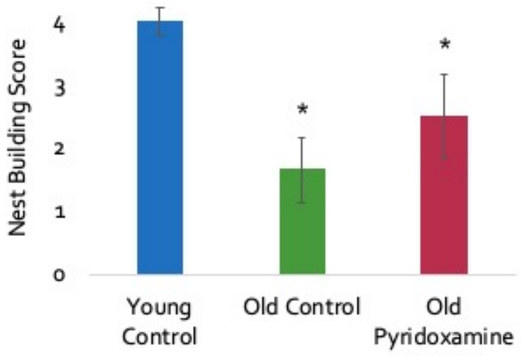
Results

Figure 1. Pyridoxamine treatment attenuated age-related large artery stiffness.



*p<0.05 vs. young control
†p<0.05 vs. old control

Figure 2. Pyridoxamine does not attenuate age-related cognitive impairment.



*p<0.05 vs. young control

Results continued

Figure 3. Pyridoxamine alleviated age-related large artery stiffness.

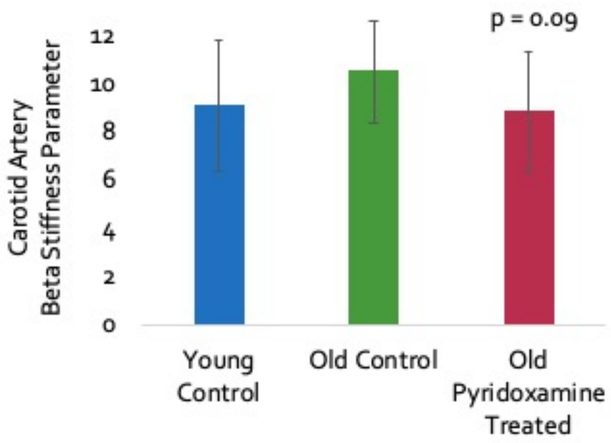
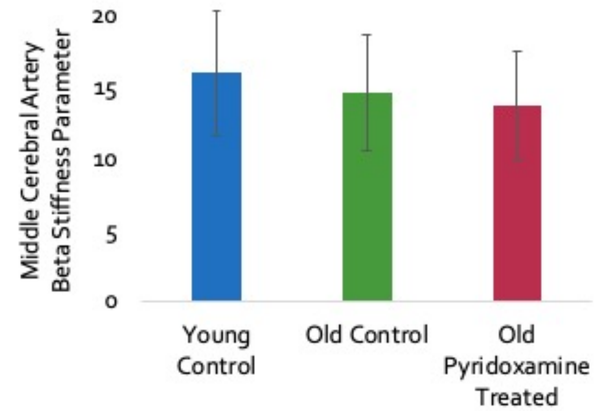


Figure 4. Pyridoxamine has no effect on stiffening of small arteries.



Conclusions

Pyridoxamine is a promising potential treatment for preventing the stiffening of large arteries and preserving vascular health to combat age-related health risks. Cognitive impairment was not significantly attenuated in pyridoxamine-treated mice, and future research must be conducted to assess contributing factors to this data, including potential sex differences, environmental factors, and insufficient sample size.

Acknowledgments

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