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Ascorbic Acid Infusion Improves Cerebrovascular Reactivity in Middle-Aged and Older Adults

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Aging is associated with reductions in cerebral blood flow and reduced cerebrovascular reactivity (CVR), both of which may contribute to the development of Alzheimer's Disease. In the peripheral vasculature, increased oxidative stress is associated with aging, and is linked to vascular dysfunction. Infusion of the antioxidant ascorbic acid (AA) has been shown to ameliorate peripheral vascular dysfunction in older adults; however, its effect on cerebrovascular function in humans is not entirely understood. **PURPOSE:** To determine whether oxidative stress reduces CVR in middle-aged and older adults (MA/O). We hypothesized that AA infusion would increase CVR in MA/O but not young adults (YA). **METHODS:** Young (18-29 years) and middle-aged and older (55-79 years) adults were recruited for two identical experimental visits. Each visit consisted of the same measures performed both before and after the infusion of either AA or a control solution (SAL). Infusions were administered in a random order and researchers were blinded to the treatment. CVR was defined as the change in mean middle cerebral artery blood flow velocity (MCAv) during hypercapnia, which was achieved using a computer-based gas blender that increased the subjects' end-tidal partial pressure of carbon dioxide (P_{ET}CO₂) 9 mmHg above baseline for a 3-minute period. MCAv was recorded using a transcranial Doppler ultrasound probe placed over the temporal window. Two-way ANOVAs were used to assess the effect of AA and SAL on CVR. Fisher's LSD tests were used to assess main effects when necessary. **RESULTS:** 8 YAs (25 ± 2 years) and 14 MA/Os (65 ± 6 years) completed the experimental visits. No main effect of either age or condition (pre/post) was observed in response to hypercapnia following either AA or SAL infusion. However, a significant age x condition interaction effect was observed for CVR (p = 0.016) following the infusion of AA, but not following infusion of SAL. Post hoc testing indicated that the difference in CVR was due to an increase in CVR the MA/Os (3.3 ± 1.7 %/mmHg pre vs. 4.1 ± 1.9 %/mmHg post, p = 0.006) following AA infusion. **CONCLUSION:** Our main finding is that AA infusion restores CVR in MA/Os, but not YAs. This suggests that age related increases in oxidative stress may impair cerebrovascular function and contribute to the development of cognitive impairment. **SIGNIFICANCE/NOVELTY:** These findings are significant as they indicate that oxidative stress may impair the functioning of cerebral blood vessels, providing a potential therapeutic mechanism for future interventions to delay or prevent the development of age-related cognitive impairment.

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