Age associated iron deposition in basal ganglia increases with physical fitness

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Target Audience

Clinicians and scientists studying brain structure and aging.

Purpose

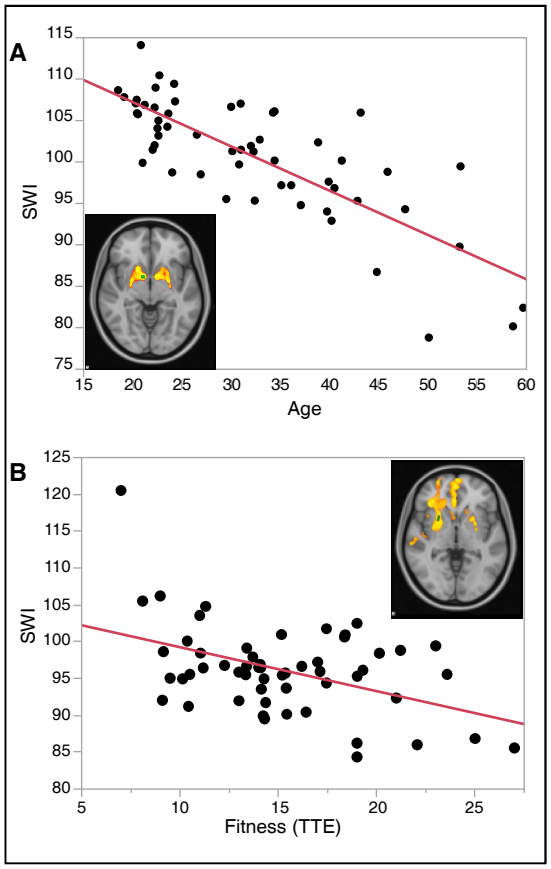
It has been well established that the amount of iron in several basal ganglia structures increases asymptotically with age and is a feature of neurodegenerative disease.[1,2] The significance of this iron accumulation is not well understood. The purpose of this study was to understand the relationship between age, fitness, cognition and iron deposition in the brain.

Methods

Using susceptibility weighted MRI scans, we estimated brain iron content on 56 participants between the ages of 18 and 59 (33 women, mean age 32.1, S.D. 10.8). Cerebral blood volume (CBV) was also measured using a contrast agent injection.[3] A battery of cognitive tests was administered to each participant including forward and backward digit span, the Rey-Osterrieth Complex Figure Drawing task (ROCF) task, semantic and verbal fluency, Rey Verbal Learning Test (RVLT), and the CES depression index. Physiological tests included a standard VO_2 max test administered on a stationary exercise bike. Ventilatory oxygen consumption was measured as well as Total Time to Exhaustion (TTE).

Results

As has been previously reported,[4] we found a linear increase in magnetic susceptibility with increasing age in the basal ganglia, with the strongest correlation in the putamen (TFCE corrected, $P<0.05$, Figure 1A). We also found regions in the putamen and medial frontal cortex in which susceptibility is positively correlated with fitness level (Figure 1B). This correlation is not explained by age, sex, or differences in vasculature as measured by cerebral blood volume (CBV). Additionally, we found a robust regional sex difference in estimates of iron content. Males showed higher iron estimates in superior cortical grey and white matter while females showed higher iron in cerebellum and subcortical structures including hippocampus (TFCE corrected, $P<0.05$). Unlike reported associations in older adults,[1,2] no correlations were found between iron estimates and several measures of cognitive function in our sample.



Discussion

Many existing studies of iron and susceptibility in the brain have focused on older participants and/or the potential role of iron accumulation in cognitive decline.[5-7] The current study is unique in that it focuses on a younger age group at a point when the slope of change in iron content, as measured in postmortem tissue, is significantly higher.[8] Our findings do not suggest any cognitive impact of the age-related accumulation of iron in the basal ganglia during young to middle adulthood. We also show that susceptibility correlates with fitness, suggesting iron deposition may be a by-product of cardiovascular activity. Finally, our results may help resolve some disagreement in the literature regarding sex difference in iron content.[1,9]

Conclusion

Although the cause and function of iron deposition in the basal ganglia remain unknown, our results suggests it does not have a negative affect on cognition in young to middle aged healthy adults and may be related to fitness and/or activity levels.

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