Longitudinal Dopamine D2 Receptor Changes and Cerebrovascular Health in Aging

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Study Question
What is the magnitude of longitudinal dopamine D2 receptor (DRD2) losses in aging, and what are the determinants of individual differences in DRD2 change?

What Is Known and What This Paper Adds
Numerous cross-sectional human in vivo studies demonstrate DRD2 reductions with aging. A major shortcoming of many of these studies is their cross-sectional design, and the few longitudinal DRD2 studies have short follow-up intervals. This study’s results show longitudinal DRD2 decline in select brain regions over 5 years of aging, and that cerebrovascular health contributes to individual differences in DRD2 decline rates.

Methods
This study analyzed data from healthy older adults randomly selected from the population and enrolled in the longitudinal Cognition, Brain and Aging study (baseline: n = 181, ages: 64–68 years, 100 men and 81 women; 5-year follow-up: n = 129, 69 men and 60 women). Eligible participants were free from disorders that can alter brain and cognitive functioning. Participants had undergone 11C-raclopride/PET, MRI, cognitive testing, blood sampling, and collection of demographics, health, and lifestyle data. The primary outcome was 5-year change in DRD2 availability (binding potential), which was estimated within MRI-defined brain regions through t tests and univariate difference score models. Second, changes in cerebrovascular health, estimated through white matter lesion volumes and cerebral blood flow after MRI, were assessed in relation to DRD2 change through multivariate regression models. Lead-lag and change-change associations were assessed through bivariate difference score models.

Results and Study Limitations
DRD2 availability declined over 5 years within the striatum (approx. −2 to −5%, p < 0.05). This decline was, however, lower than cross-sectional estimates (approx. −8% per decade). DRD2 decline was also observed in select extrastriatal regions (approx. −6 to −8% for the orbitofrontal cortex, hippocampus, and anterior cingulate cortex, p < 0.05). DRD2 changes correlated across the dorsal striatum and anterior cingulate cortex (r’s = 0.37 to 0.57) and were associated with increments in white matter lesion volumes (r = −0.22). Similarly, DRD2 changes correlated between the nucleus accumbens and orbitofrontal cortex (r = 0.57) and were associated with cortical perfusion changes (r = 0.27). Limitations of this study include the narrow age range of this sample that may limit generalizability of the findings, and the dropout rate may have led to selection bias.

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