Differential regional decline in striatal and medial temporal dopamine receptor availability across adulthood

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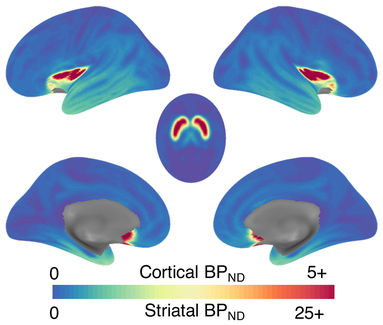
Introduction

The dopamine system has been implicated in episodic memory function, value-based decision making, and reward processing. In a recent study using a measure of percentage difference in D2R per decade, we reported evidence for regional variation in decline (right) such that subcortical and ventromedial cortical regions showed less decline than superior and lateral cortical regions. These initial analyses were conducted with atlas-based regions of interest that averaged across structures. **The present study used voxel-wise analyses to examine potential gradients of age-related decline within the striatum and medial temporal lobes.**

Region	% difference [95% CI]
Postcentral gyrus	−16.37 [−19.39, −11.95]
Middle frontal gyrus	−15.82 [−18.36, −12.62]
Precentral gyrus	−14.17 [−17.88, −8.48]
Inferior frontal gyrus	−13.28 [−16.11, −9.67]
Cingulate gyrus, posterior	−13.04 [−15.96, −9.11]
Superior parietal gyrus	−12.31 [−16.01, −6.53]
Superior frontal gyrus	−12.12 [−14.97, −7.58]
Pre-subgenual frontal cortex	−4.47 [−7.49, −0.85]
Fusiform gyrus	−4.31 [−6.05, −2.48]
Putamen	−3.62 [−4.76, −2.53]
Amygdala	−2.73 [−4.39, −0.91]
Thalamus	−2.70 [−3.98, −1.43]
Subcallosal area	−1.78 [−4.90, 2.40]
Ventral striatum	−1.43 [−3.38, 0.44]
Hippocampus	−0.83 [−3.47, 1.69]
Pallidum	−0.18 [−2.37, 2.05]

Methods

153 healthy adults between the ages of 20-83 completed a PET scan with [18F]fallypride during rest to measure D2R non-displaceable binding potential (BP_{ND}).



GE Discovery STE PET/CT

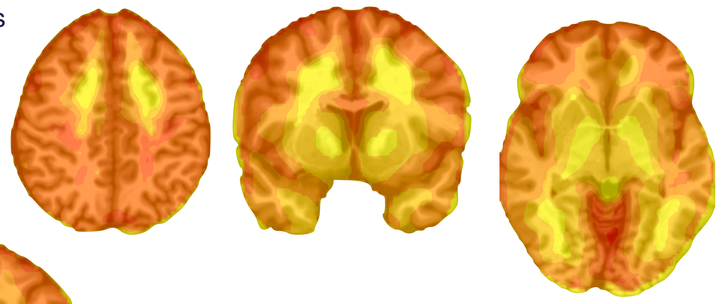
A voxelwise map of percentage difference per decade was calculated by:

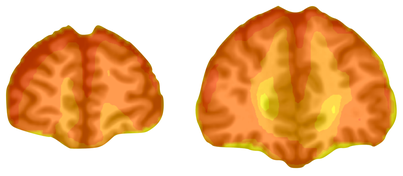
(1) fitting a linear model with a single predictor (age) to the voxelwise BP_{ND} data
(2) regression equation used to estimate BP_{ND} at age 20 and age 30
(3) percent difference per decade was calculated for each voxel using the formula:

$$\text{Percentage difference per decade} = \frac{(BP_{ND\_30} - BP_{ND\_20})}{BP_{ND\_20}}$$

Results

Expanded data set (n = 153) showed the same pattern as the published ROI-based analyses (n = 132). Regions of the striatum, medial temporal lobe (MTL), and other ventromedial cortical and subcortical regions showed relatively less age-related decline in D2R (yellow) compared to lateral and more superior cortical regions which showed the steepest declines (orange, red).



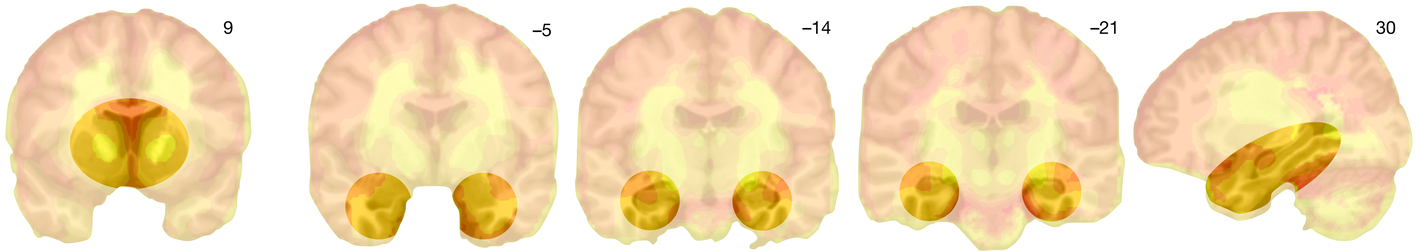


Percentage difference per decade

0-4%	5-8%	9-12%	13-17%	18-21%

We did not find evidence for gradients across the striatum beyond what was observed in the ROI analyses.

There was evidence for potential non-linear gradients across the anterior/posterior and medial/lateral axis of the hippocampus and surrounding cortex.



Conclusions

Although the ROI analyses revealed a lack of an age effect on hippocampal D2R in general, there were:

- **relatively greater age-related declines in the anterior-superior and posterior-inferior portions of the hippocampus** approximately consistent with the location of CA1
- **shallower declines in superior compared to inferior MTL cortical subregions**

The **relative preservation of hippocampal D2R suggest a potential preservation of dopamine influence within the MTL**. Despite declines in episodic memory that occur with age, the influence of dopamine on these processes may remain largely intact. This may prove important for decisions that require episodic memory of past experiences.

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