

### Latent organization of dopamine D2 receptors

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# Introduction

Relatively little work has attempted to characterize crossregional organization of the dopamine system in living humans. Typical univariate statistical analysis of PET data limits estimation of the organization of latent spatial features due to shared variability across regions of the brain. These latent features reveal greater insight on the organization of co-varying regions which may reflect unique transcriptomes of dopamine signaling.

## Conclusions

We identified latent spatial covariance of DA receptors and suggest other neuromodulatory systems may be intrinsically organized. Age-related associations revealed relatively preserved integrity of mesolimbic components, non-linear associations in dorsal striatal and thalamocortical circuits, and strengthened integrity in a midbrain-hippocampal circuit, suggesting that age differentially impacts the intrinsic organization of dopamine circuits and may account for relative preservation of affective and motivational function across the adult life span.

# Methods

N = 158, ages 18-81 (M = 36.8, SD = 19), 85 females underwent a PET scan with the high-affinity D2/3R tracer, [18F]fallypride across 4 study samples collected at Vanderbilt University between 2006 and 2017.

#### Independent Component Analysis



Binding potential maps were concatenated and fed into FSL MELODIC software to estimate 20 dimensions.

Using the alleninf toolbox (https://github.com/chrisgorgo/ Gene Expression Analysis alleninf), we used random effects analysis to identify the



# Results

From 20 components, 8 were discarded as noise. 12 components below explained 59% of variance.



mean slope between gene expression values from 6 tissue samples in standard space and ICA components of interest.

We tested spatial correlations with ICA maps for D2-like receptor sub-types (DRD2, DRD3, and DRD4) and a marker of DA synthesis (TH).



**Example microarray gene expression** for DRD2 across 6 tissue samples

#### Individual Differences Analysis

We explored linear and nonlinear associations between individual differences in age and ICA loading scores on component maps showing significant associations with gene expression.



# DRD3 Gene Expression and Fallypride Component Maps 0.20

IC 2	IC 3	IC 4		16.6	IC 8
DRD2	DRD2		DRD2		
DRD3		N/A	DRD3		N/A
TH	TH			TH	





Above & Below: Violin plots depict correlation values between Z-transformed ICA maps and gene expression across 6 tissue samples.









Above: Regression plots depict association between ICA loading scores and age. Associations suggest differences in the covariance structure of the IC map, not the raw receptor availability.

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