Development of Corticostriatal Connectivity During Adolescence Supports A Dorsal-Ventral Gradient of the Human Striatum

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Background

- Adolescents undergo pronounced changes in neurodevelopment, including increased development of striatal pathways linked to reward-driven behaviors[1].
- Seminal work in animal neuroscience suggests that ventral (VS) and dorsal (DS) subdivisions of the striatum are topographically organized: the VS is connected to brain areas involved with reward processing, while the DS is connected to areas implicated in higher-order cognition[2].
- The functional development of this topographic organization of the striatum, and how it changes during adolescence, is poorly understood.
- The present work examined longitudinal changes in resting-state functional connectivity (FC) of DS and VS to address this gap.

Participants & Methods

A. Longitudinal Design

Participants aged 11.6 – 25.70 underwent 6-minute long resting fMRI scans. Participants were followed every 2-3 years for four assessment waves (8-years total), yielding 339 data points.

Participant Demographics

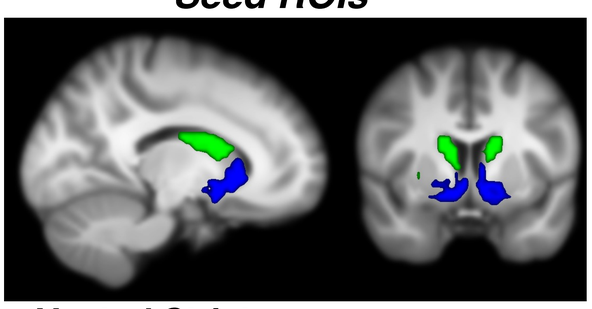
Resting Data	Baseline (*n* = 116)	T2 (*n* = 39)	T3 (*n* = 100)	T4 (*n* = 84)
Age Range	11.63 – 25.70	14.40 - 26.98	15.84 - 29.42	18.04 -32.28
Age	18.51 (3.85)	19.80 (3.16)	21.89 (3.92)	23.46 (3.77)
Female (n %)	92 (54.76%)	45 (56.96%)	62 (53.0 %)	56 (54.36%)
Ethnicity (%)				
White	89.7 %	95.7 %	90.2 %	91.0 %
Black	1.1 %	0 %	1.1 %	1.3 %
Hispanic	1.1 %	2.2 %	2.2 %	2.6 %
Asian	2.2 %	2.2 %	2.2 %	2.6 %
Other†	5.4 %	0 %	4.3 %	2.6 %
Parental Education	15.95 (2.55)	16.56 (2.49)	16.27 (2.84)	15.97 (2.36)
Average FD	0.128 (.05)	0.133 (.03)	0.122 (.04)	0.120 (.06)

Note. Baseline denotes year 0 of present study. T2 denotes study year 2, T3 denotes study year 4, and T4 denotes study year 6. All values are presented using Mean (Standard Deviation [SD]) unless otherwise noted.
† Includes individuals with multiple racial identities

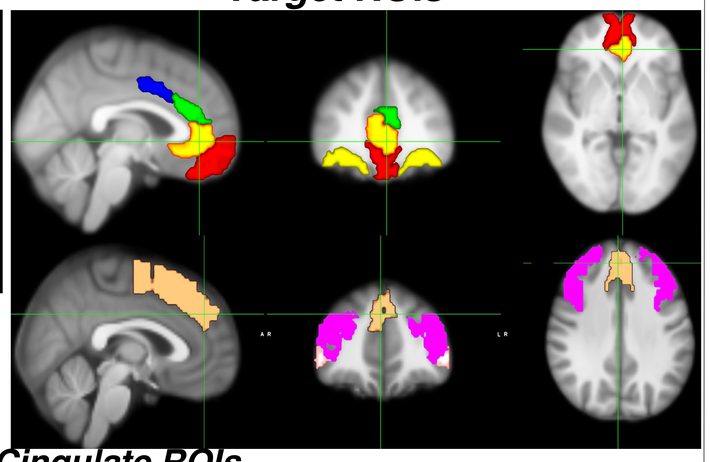
B. MRI Processing

fMRI data was denoised using ICA-AROMA, and global signal regression was applied to filter out white matter and CSF. We also applied high pass temporal filtering (100s cutoff); registered participants to MNI-152 2mm space via MPRAGE scan transforms.

Seed ROIs



Target ROIs



Ventral Striatum

The ventral striatum seed consisted of the nucleus accumbens (Nac), and ventral aspects of the putamen **(VS; blue).**

Dorsal Striatum

The dorsal striatum consisted of dorsal spects of the caudate nucleus and putamen (**DS; green).**

Cingulate ROIs

Subgenual cingulate (**sgCG; yellow and red**), anterior cingulate (**antcing; green**), caudal dorsal cingulate (**cdCG; blue**).

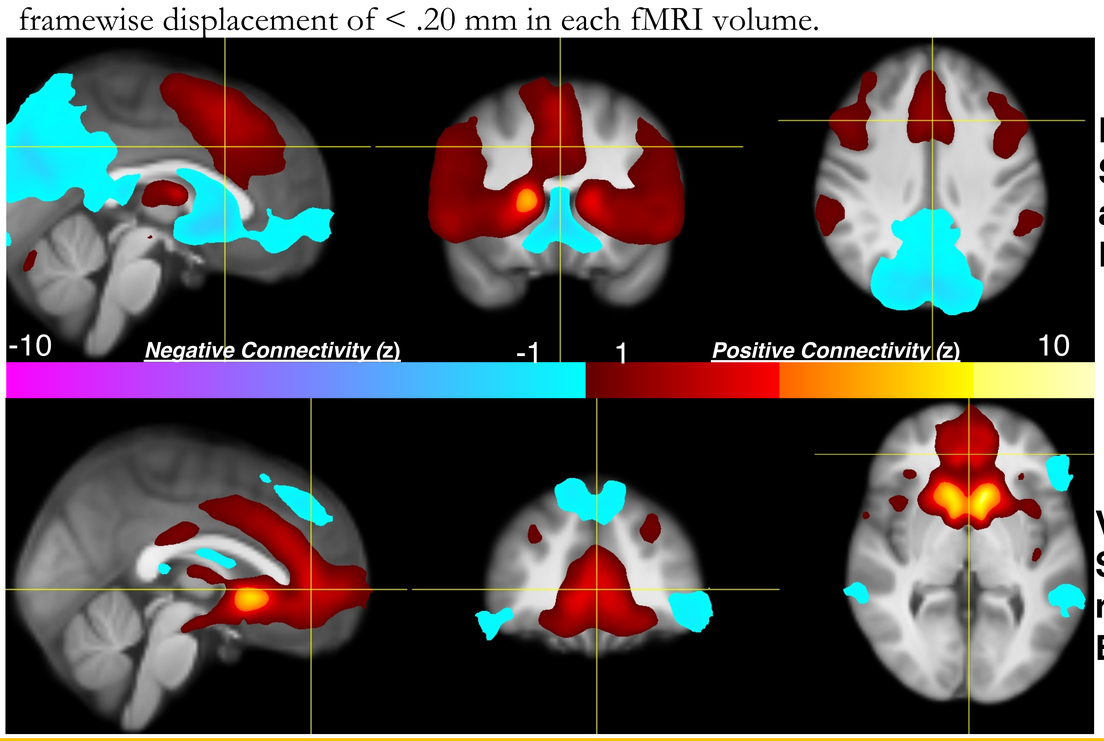
Prefrontal ROIs

Medial orbitofrontal cortex (**mOFC; red**); lateral aspects of OFC (**latOFC; yellow**); dorsal medial prefrontal (**dmPFC; tan**); ventrolateral PFC (**vlPFC; pink.** dorsolateral prefrontal (**dlPFC; purple**).

C. rsMRI Connectivity Maps

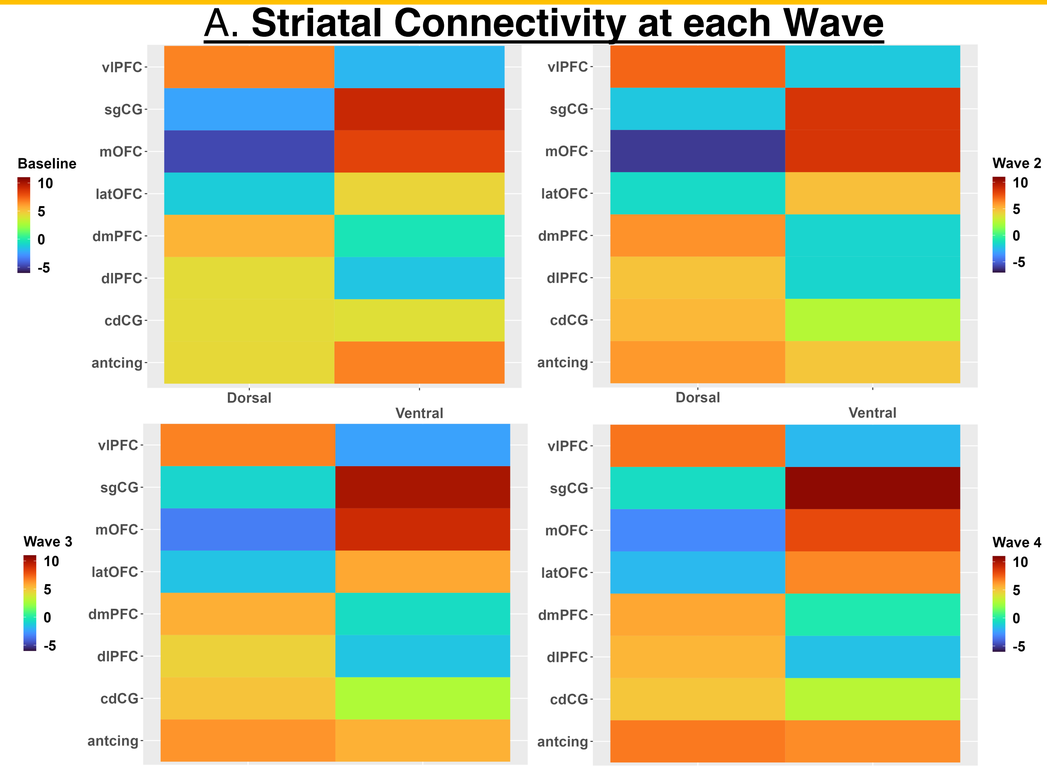
We employed a seed-based approach. Seed (i.e., VS and DS) and target ROIs were selected from the Brainnetome Atlas[3]. Target ROIs were selected using specific areas of prefrontal cortex shown to anatomically project to VS and DS in both humans, and nonhuman primates[2].

Connectivity values were extracted using dual regression in FSL[4]. Data sets were included if they had average framewise displacement of < .50 mm and at least 4 minutes of data with framewise displacement of < .20 mm in each fMRI volume.



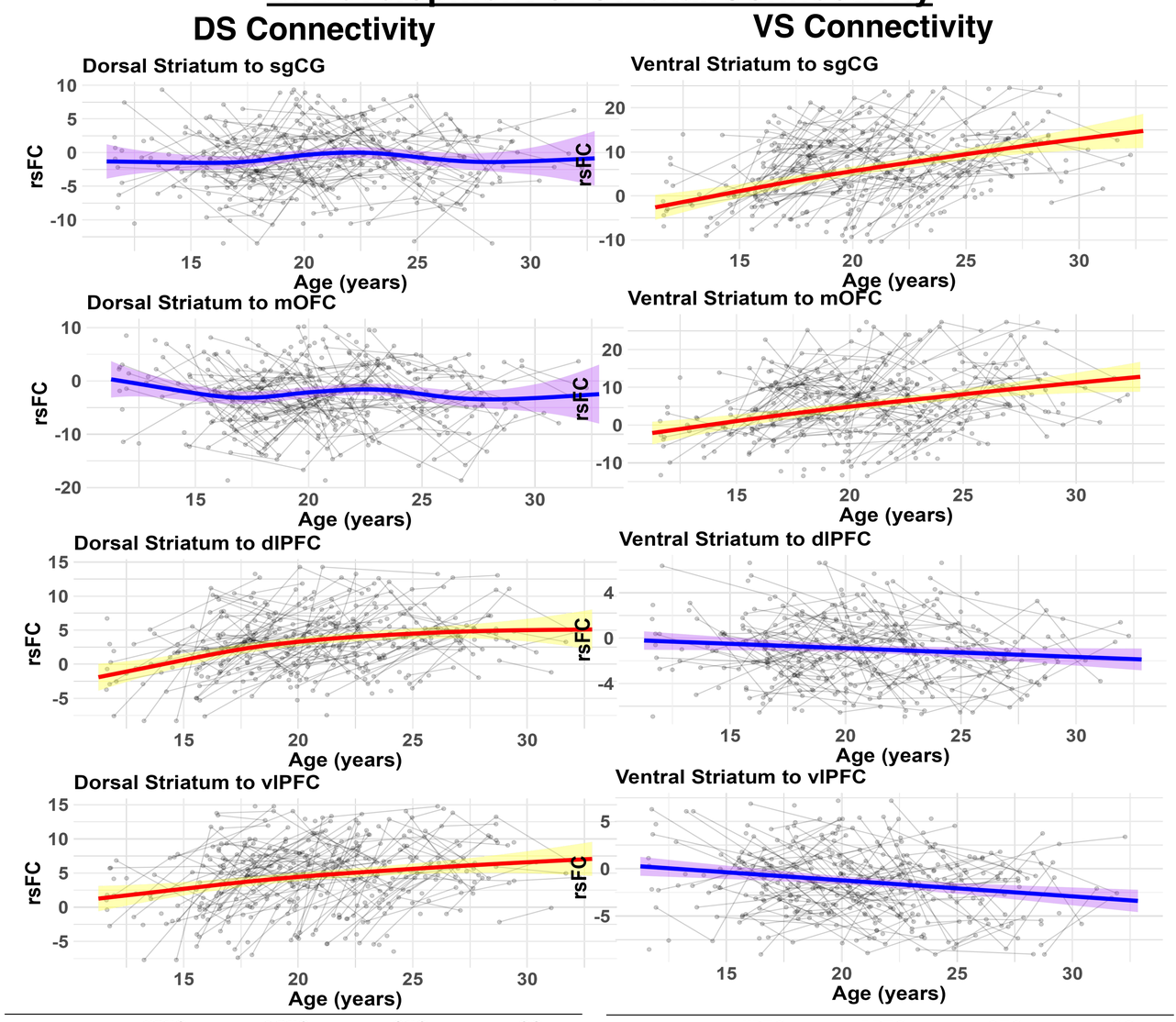
Results

A. Striatal Connectivity at each Wave



- Across each wave, VS showed strong positive connectivity with reward areas mOFC, sgCG, as well as latOFC. In contrast, VS showed weak connectivity with areas implicated in higher order processing (e.g, **dlPFC, vlPFC**).
- DS demonstrated the inverse connectivity pattern, exhibiting strong positive connectivity with **dlPFC, vlPFC, dmPFC, and cdCG**, and weak connectivity with reward areas (e.g., **mOFC, sgCG).**

B. Development of Striatal Connectivity



	dlPFC		vLPFC		mOFC		sgCG	
Component	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*
Model Intercept	3.1	<0.001	4.5	<0.001	-2.3	<0.001	-0.77	0.005
Age Smooth		<0.001		<0.001		0.14		0.15
Random Int. Smooth		<0.001		0.6		<0.001		<0.001
RMSE	3.28		4.89		4.86		3.82	
Sigma	5.03		7.51		7.45		5.86	
Deviance Exp.	0.435		0.051		0.313		0.317	
No. Obs.	339		339		339		339	

	dlPFC		vLPFC		mOFC		sgCG	
Component	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*	*Beta*	*p*
Model Intercept	-1.0	<0.001	-1.4	<0.001	5.3	<0.001	6.1	<0.001
Age Smooth		0.046		<0.001		<0.001		<0.001
Random Int. Smooth		<0.001		<0.001		<0.001		<0.001
RMSE	2.19		2.55		6.17		5.45	
Sigma	3.37		3.91		9.47		8.37	
Deviance Exp.	0.411		0.490		0.491		0.512	
No. Obs.	339		339		339		339	

- **General additive mixture models (GAMS)** revealed that VS connectivity with ROIs implicated in reward processing (e.g., **mOFC**) steadily increased from childhood to adulthood, whereas VS FC between ROIs associated with higher-order cognition (e.g**.,dlPFC)** steadily decreased over this same period.
- In contrast, DS connectivity with areas implicated in higher order cognition increased more rapidly during adolescence, stabilizing in early adulthood; DS connectivity with reward ROIs did not change as a function of development.

Discussion

- Our findings suggest that the development of frontostriatal connectivity follows a ventral-to-dorsal gradient where VS and DS pathways exhibit functional segregation that increases during adolescence.
- Both VS and DS functional connectivity increased with the anterior cingulate, consistent with a conceptualization of this area as a connectional hub linking aspects of reward and cognitive control.
- Taken together, these results concur with a ventral-dorsal divide of striatal connectivity, aligning anatomically defined striatal projections in nonhuman primates to functional connectivity derived using human neuroimaging.
- Future work will examine the functional and personality correlates of striatal connectivity changes during adolescence.

References

1. Porter, J.N, *et al.* (2015). *Developmental Cog. Neuroscience*
2. Haber, SN (2016) *Dialogues in Clin. Neuroscience*
3. Fan, L., *et al.* (2016). *Cerebral Cortex.*
4. Jenkinson, M., *et al.* (2012). *Neuroimage*

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