Introduction
Dopamine has been hypothesized to provide the basis for the interaction between motivation and cognition. However, there is no evidence for this hypothesis in humans. In the present genetic imaging study, we sought to determine the role of dopamine in the component processes of reward, and its consequences for cognitive flexibility.

Experimental Paradigm
We employed a task-switch design with reward cues preceding each trial and feedback following each manual response (Fig. 1).

In MRI scanner (3 Tesla):

- high > low reward during reward cues
- high > low reward during task cues
- switch > repeat targets
- positive > negative feedback

Genotyping
- took into account inter-individual variation in the dopamine transporter gene (DAT1, SLC6A3)
- 11 participants homozygous for the 10-repeat allele (10R) and 9 9-repeat allele (9R) carriers
- 9R allele = decreased DAT1 expression
- also tested for (structural) differences in striatal volumes between the genotype groups (not significant)
- corrected for the effects of variation in the catechol-O-methyltransferase (COMT) gene

Behavioral Results

- reward x DAT1 only on switch trials, not on repeat trials (Fig. 2)

Conclusions
- Medial-lateral gradient for reward processing in ventral striatum depending on task phase
- Region-specific dissociation between the effects of DAT1 on striatal activity depending on task phase
- Striatal dopamine potentiates cognitive flexibility as a function of preparatory reward

**Fig 1.** Task-switching design with reward manipulation

**Fig 2.** Error rates for high rewarded and low rewarded targets in 10R homozygotes (DAT 10/10) and 9R carriers (DAT 9/10) on switch trials and repeat trials.

**Fig 3.** Reward anticipation (high > low reward during both reward and task cues) and reward receipt (positive > negative feedback) in ventral striatum (voxel-level cut-off at P < .001, uncorrected).

**Fig 4.** Anatomical ROI analyses showing opposing effects of DAT1 genotype on reward anticipation during reward cues in caudate nucleus (red) and on reward receipt during feedback in putamen (blue).

**Fig 5.** Dopamine-dependent motivation-cognition interaction in the left caudate nucleus (left panel) revealed by anatomical ROI analysis (right panel).

**Fig 3.** Reward anticipation (high > low reward during both reward and task cues) and reward receipt (positive > negative feedback) in ventral striatum (voxel-level cut-off at P < .001, uncorrected).

- Statistical threshold of P < 0.05 cluster level corrected for multiple comparisons over the whole brain
- Medial-lateral gradient of reward effect in ventral striatum from nucleus accumbens to ventrolateral putamen as a function of task phase (Fig. 3)

**Fig 4.** Anatomical ROI analyses showing opposing effects of DAT1 genotype on reward anticipation during reward cues in caudate nucleus (red) and on reward receipt during feedback in putamen (blue).

**Fig 5.** Dopamine-dependent motivation-cognition interaction in the left caudate nucleus (left panel) revealed by anatomical ROI analysis (right panel).

- DAT1 x reward x switching in the striatum (Fig. 5, left)
- 9R carriers > 10R homozygotes: reward anticipation in the caudate nucleus during reward cues
- 9R carriers < 10R homozygotes: reward receipt in the putamen during feedback
- no DAT1 effect during task cues