Striatal dopamine correlates brain activation in precuneus and thalamus: a PET-fMRI study

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INTRODUCTION: Dopamine (DA) is implicated in the modulation of attention[1] but its specific role is not well understood. Here we assessed the relationship between DA markers [DA D2 receptors (D2R) and transporters (DAT)] in the striatum and brain activation during a parametric visual attention (VA) task[2] (measured with BOLD-fMRI) in healthy controls. We hypothesized that D2R and DAT in the striatum would correlate with activation in regions included in the executive and arousal attentional networks.

METHODS: Fourteen healthy non-smoking and right-handed men (age: 36±5 years, education: 16±2 years) participated in the study. Subjects underwent two different PET scans with [^{11}C]raclopride and [^{11}C]cocaine (4-10 mCi; 20 min half-life) to measure D2R and DAT availability in the brain, respectively. PET images were collected in 3D mode with 4.5 mm isotropic spatial resolution. ROIs analyses were used to calculate the availability of D2R and DAT in the striatum. After the PET session, BOLD-fMRI signals were measured in a 4-Tesla MRI scanner using a single-shot gradient-echo EPI sequence (TE/TR = 20/1600 ms, 4 mm slice thickness, 1-mm gap, 35 coronal slices, 64x64 matrix size, 231 time points) while the subjects performed a set of VA tasks involving visual tracking of 2-, 3-, and 4 out of 10 identical moving balls[2]. The fMRI time series were motion corrected, spatially normalized to the Talairach frame (3×3×3 mm^3 voxel size), and smoothed (8-mm Gaussian). Activation maps were calculated for each subject and task using the general lineal model in SPM2. These BOLD maps were entered into SPM2 multiple regression (random-effects) analyses to identify brain regions showing statistically significant linear correlations between the DA markers and BOLD-fMRI signals; complementary ROI analyses were carried out to validate the SPM results using a customized IDL code.

RESULTS: Across subjects, D2R and DAT availability in the striatum were 3.42 ± 0.05 and 1.80 ± 0.03, respectively (Fig 1). Performance accuracy on the VA task (>86%) was similar for 2- and 3-balls but significantly lower for 4-balls compared to 2- or 3-balls ($p < 0.011$), reflecting the increased attention load of the tasks. The VA tasks caused bilateral activation in parietal (including precuneus, BA7), occipital, and prefrontal cortices, thalamus, and the cerebellum ($p_{corr} < 0.001$, cluster-level corrected for multiple comparisons; Fig 3A). Increased attention load (from 2-balls to 4-balls) increased brain activation bilaterally in the thalamus ($p_{corr} < 0.001$; Fig 2B). D2R and DAT availability in caudate and putamen correlated positively BOLD-fMRI responses in precuneus (BA 7) and thalamus ($p_{corr} < 0.05$; Figs 2C-D, and 3). Negative correlations between D2R and DAT availability in striatum and BOLD signals in the brain were not statistically significant. Subjects (N=7) with high DAT availability in the striatum had higher cortical BOLD-fMRI responses (ROI analyses; $p < 0.001$, ANOVA; Fig 4) and lower accuracy during the more demanding task (4-balls) than those with low DAT availability in striatum ($p < 0.05$; Fig 5).

CONCLUSIONS: The posterior parietal cortex (precuneus; BA 7) is thought to play an important role in orienting attention and the thalamus is essential for the alerting component of attention[3]. Increased DAT and D2R availability in striatum were associated with higher activation of the precuneus (BA 7) and the thalamus. Thus, this study suggests that the DA mesostriatal pathways facilitate attention by modualting the activation of regions in the alerting and orienting pathways of attention.

REFERENCES: 1- Nieoullon (2002). Prog Neurobiol **67**: 53-83; 2- Tomasi (2004). Neuroimage **23**:1414-1421; 3- Fan (2005) Neuroimage **26**:471-479.

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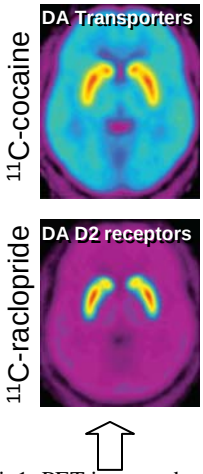


Fig1: PET images showing the uptake of 11C radiotracers in the striatum.

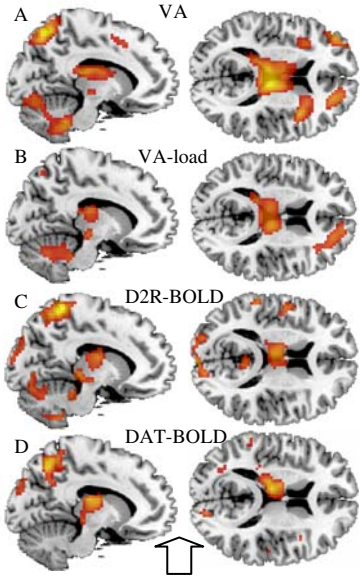
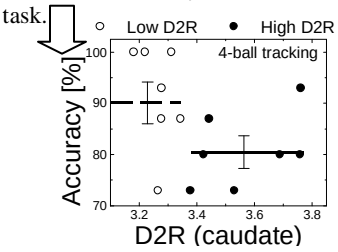


Fig2: BOLD-fMRI activation produced by the visual attention (VA) task (A), and brain areas increasingly recruited with increased VA load (B). C-D: correlation of fMRI signals and striatal DA markers (D2R and DAT) across subject (N=14).

Fig5: Subjects with high striatal D2R availability have lower accuracy on the more demanding task.



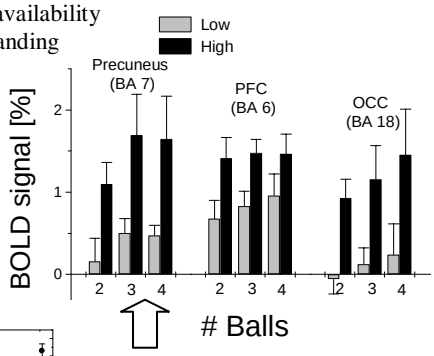


Fig4: Cortical BOLD-fMRI signals were lower for subjects with low DAT availability in caudate (gray; N=7) than for those with high DAT availability in caudate (black; N=7).

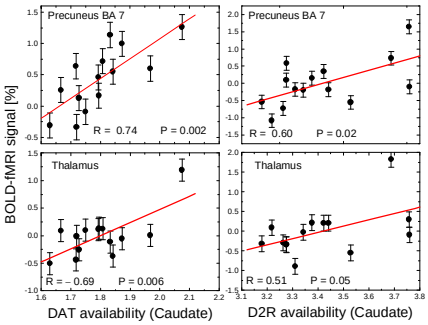


Fig3: Linear correlation analyses between DA markers in the caudate and BOLD signals in the parietal cortex and the thalamus.