Supplementary Online Content

Capuron L, Pagnoni G, Drake DF, Woolwine BJ, Spivey JR, Crowe RJ, Votaw JR, Goodman MM, Miller AH. Dopaminergic mechanisms of reduced basal ganglia responses to hedonic reward during interferon alfa administration. *Arch Gen Psychiatry*. 2012. doi: 10.1001/archgenpsychiatry.2011.2094.

eAppendix 1. fMRI Methods

eAppendix 2. F-DOPA Methods

eFigure 1. Fluorodopa F 18 (^{18}F-dopa) uptake before and during interferon alfa administration in ventral striatal regions identified in the functional magnetic resonance imaging (fMRI) hedonic reward task. Patients with chronic hepatitis C virus were administered ^{18}F-dopa followed by positron emission tomography before (visit 1) and after 4 to 6 weeks of interferon alfa treatment (visit 2). A, The ^{18}F-dopa uptake (Ki [1/min]) was measured using the Patlak method (see the "Methods" section) in the ventral striatal regions used as the regions of interest (ROIs) in the fMRI study (Figure 1A). Significant increases in ^{18}F-dopa uptake were found during interferon alfa administration compared with baseline in right, left, and bilateral ventral striatum ($P<$ .02, $P<.005$, and $P<.01$, respectively). B, Effective dopamine turnover (EDT) was calculated by the method of Sossi et al[36] (see the "Methods" section) in ventral striatal regions used as the ROIs in the fMRI study (Figure 1A). Significant decreases in EDT were found during interferon alfa administration compared with baseline in right, left, and bilateral ventral striatum ($P<.02$, $P<.001$, and $P<.002$, respectively).

eFigure 2. Regional differences in fluorodopa F 18 (^{18}F-dopa) uptake after interferon alfa administration. The ^{18}F-dopa uptake (Ki [1/min]) was measured using the Patlak

method (see the “Methods” section) before and during interferon alfa treatment. A paired-difference image (post-pre) was generated yielding 2 clusters (434 and 282 voxels for left and right striatum, respectively) (p threshold = 0.010; k threshold = 250 voxels). Marked overlap was found with the ventral striatal regions of interest from the functional magnetic resonance imaging study (see Figure 1A). The color bar represents the range of uptake values (Ki [1/min]) from 0 to 7.

eReference.

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. fMRI Methods

Detailed fMRI analyses: For each subject, the three EPI runs were slice-time corrected and aligned via rigid body transformation to a common reference EPI volume to correct for head motion. The anatomical volume was co-registered to the EPI reference volume and then spatially normalized to Talairach-Tournoux standard stereotaxic brain space. The same transformation was used to warp all functional volumes to standard space. Each volume was smoothed with a 4mm FWHM Gaussian kernel and then intensity-normalized to a percent change relative to the run's temporal mean on a voxel-wise basis.

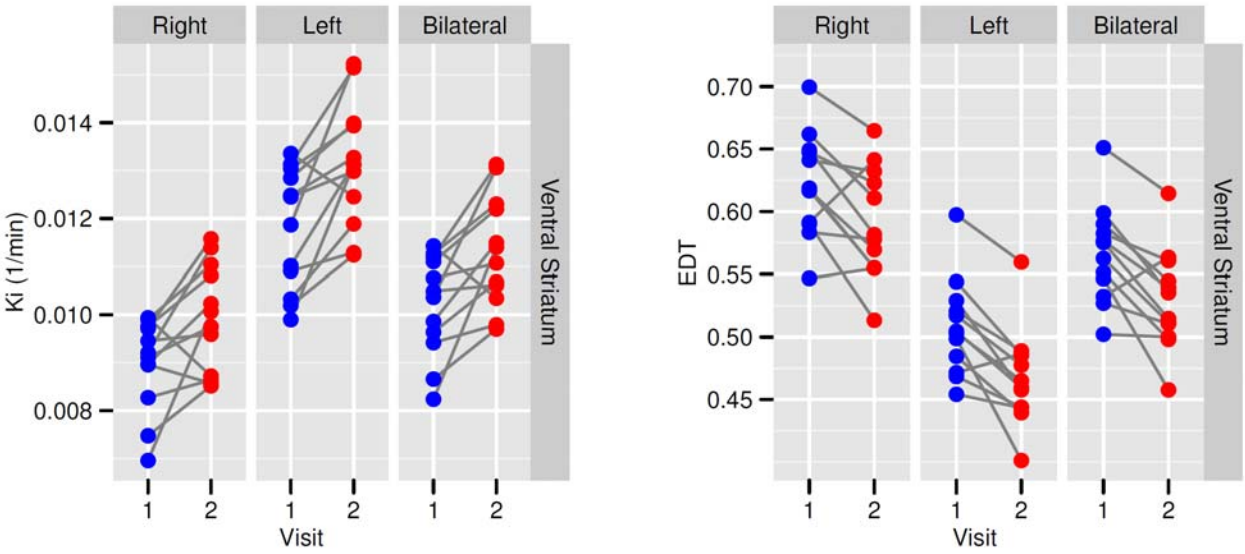
Task-related activation maps were computed for each subject using AFNI's Restricted Maximum Likelihood procedure that minimizes the temporal auto-correlation of the scans prior to ordinary least squares model fit.[1] The model matrix was block-diagonal, one block per run. Each block contained (a) a baseline model of four Legendre polynomials (degree zero to three) plus six motion parameters, to account for signal drifts and head motion residual confounds, and (b) two task regressors modeling the trials when a red card (Win) and a black card (Lose) were selected respectively, obtained by convolving the corresponding stimulus timing vectors with a standard hemodynamic gamma function. General linear tests were used to compute the Win-Lose contrast combined over all three runs.

eAppendix 2. F-DOPA Methods

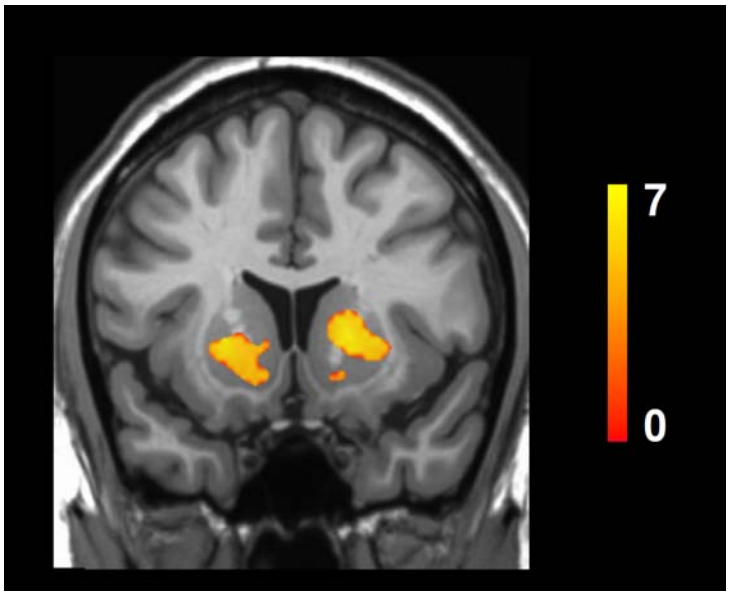
Detailed FDOPA analyses: Two subjects were scanned before and during interferon alfa in a Siemens ECAT 921 tomograph; the remaining ten were scanned in a Siemens High Resolution Research Tomograph (HRRT). ECAT scans were reconstructed at 2.574 mm x 2.574 mm with 3.375 mm slices; HRRT scans were reconstructed at 1.219mm in all three dimensions. For image reconstruction the ECAT scanner uses traditional filtered backprojection with a ramp filter, while the HRRT scanner uses Poisson OSEM (Ordered Subset Expectation Maximization) with 6 iterations, 16 subsets, and 4mm Gaussian filter.

Scans were corrected for attenuation and decay, and re-sampled to 2 mm (after smoothing HRRT scans by 7 mm FWHM to match smoothness of ECAT scans). Rigid-body (6-parameter) transformations were used to compensate for subject motion, aligning each frame to frame 12. The final five frames were then averaged to form a reference image. The reference images from each subject's scans before and during treatment were used to co-register the two scans, again using rigid-body transformations. The co-registered reference images were averaged, and, via SPM5 (http://www.fil.ion.ucl.ac.uk/spm/), spatially normalized to an MNI-space FDOPA template (courtesy of Andreas Meyer-Lindenberg, University of Heidelberg, Mannheim, Germany). The resulting nonlinear transform was applied to all frames of co-registered runs.

eFigure 1.



eFigure 2.



eReference

Cox RW. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. *Comput Biomed Res.* 1996;29(3):162-173.