

**Table S2. Functional neuroimaging studies (conducted during 2000-2010) comparing PFC activity during direct drug administration in addicted individuals and healthy controls.**

	Subjects	Abstinence length	Amount/procedure	PFC results	PFC correlations with drug use
<b>Cocaine</b>					
Volkow, Wang et al. 2003	23 S	Active users	FDG 4 days PL or MPH (iv .5 mg/kg) expected vs. not	<b>Dr&gt;PL expected</b> ↑ L ACC, ↓ B MedFG, B subcallosal gyrus, B ACC, B subgyral, R INS <b>Dr unexpected &gt; PL expected</b> ↑ L IFG, ↓ B MedFG, B rectal gyrus, B subcallosal gyrus, B ACC, B INS <b>Dr unexpected &gt; D expected</b> ↑ L OFC 47	NS
Kufahl, Li et al. 2005	10 S	12 hours	fMRI 1 day (10 min) Saline or cocaine (iv 20 mg/70 kg, 30 sec)	<b>Dr&gt;PL</b> ↓ B subcallosal gyrus 25, ↓ R posterior OFC 47, ↑ R DLPFC 46, ↑ R INS 43, ↑ L anterior OFC 11, ↑ L mOFC 11,13, ↑ R frontopolar 10	NR
Kufahl, Li et al. 2008	13 S	12 hours	fMRI 2 days Saline or cocaine (iv 20 mg/70 kg) expected vs. not	<b>Dr&gt;PL expected</b> ↑ L mOFC 11,13,14, ↑ L frontopolar 10, ↓ R mOFC/subcallosal gyrus 11,13,25, ↑ L ACC 24,32, ↑ L DLPFC 9, ↑ L INS 13, ↓ R ACC 24, ↑ L MidFG 6 <b>Dr&gt;PL unexpected</b> ↑ L mOFC 10,11, ↑ L frontopolar 10, ↑ L ACC 24, ↑ L MedFG, ↑ L DLPFC 9,46 <b>Dr unexpected &lt; D expected</b> L OFC 47, 47/12, ↑ L frontopolar 10, L ACC 24, 10, ↓ R caudal OFC <b>Dr unexpected &gt; D expected</b> ↓ L OFC 47	NR
Garavan, Kaufman et al. 2008	13 S	36 hours	fMRI (go/no-go) 1 day Saline or cocaine (iv 40 mg/70 kg)	<b>Dr&gt;PL T&gt;BL</b> ↑ R MidFG 46, 9, ↑ R INS ↑ inhibition	NR
Adinoff, Devous et al. 2010	23 S 22 C	27 days	SPECT 3 days Saline, physostigmine (iv 1.93 mg/h then 0.816), or scopolamine (iv 0.315 mg/70 kg)	<b>S&lt;C Dr&gt;PL</b> ↓ R DLPFC, ↓ R INS	NS

	Subjects	Abstinence length	Amount/procedure	PFC results	PFC correlations with drug use
Ersche, Bullmore et al. 2010	18 S 18 C	9 hours	fMRI (Stroop) 3 days Saline, amisulpride (oral 400 mg) or pramipexole (oral 0.5 mg) D, N	<b>S&gt;C D&gt;N</b> ↑ L vPFC (& R cerebellum) ↑ Interference RT	<b>Reaction time (+)</b> D>N L vPFC (& cerebellum)
Goldstein, Woicik et al. 2010	13 S 14 C	6 days	fMRI (emotional Stroop) 2 days PL or MPH (oral 20 mg) D, N	<b>Dr&gt;PL T&gt;BL</b> (driven by S) ↑ rvACC 32, ↑ L dACC 24 <b>Dr&lt;PL T&gt;BL (S)</b> R SFG 8 <b>Interaction</b> C Med/SFG 8,9	<b>Accuracy (+)</b> Dr>PL T>BL B mOFC, MedFG 10,32, R dACC 24 <b>Drug use (-)</b> MPH T>BL L MedFG/DLPFC 9, M dACC 32 <b>Drug use (+)</b> PL T>BL L MedFG/DLPFC 8,6,9
Li, Morgan et al. 2010	10 S 36 C	8 days	fMRI (SSRT) 2 days Saline or MPH (iv 0.5 mg/kg)	<b>Dr&gt;PL T&gt;N</b> NS for PFC ↓ SSRT	<b>SSRT (+)</b> Dr>PL T>N L MidFG <b>SSRT (-)</b> Dr>PL T>N L vmPFC 25
Volkow, Wang et al. 2010	24 S	2 days	FDG 4 days PL or MPH (oral 20 mg) D, N	<b>Dr&lt;PL D&lt;N</b> ↓ L OFC 47	<b>Craving (-)</b> PL L SFG 8/9 <b>Craving (+)</b> Dr B OFC 11/47, INS
<b>Nicotine</b>					
Zubieta, Heitzeg et al. 2005	19 S	12 hours	H <sub>2</sub> <sup>15</sup> O 1 day Low vs. 2 average cigarettes (1.01 mg nicotine, 9.5 mg tar)	<b>Dr 1<sup>st</sup>&gt;BL</b> ↓ L dACC 32/24, mOFC 25 <b>Dr 1<sup>st</sup>&gt;N</b> ↓ L rvACC/PFC 10/25/32 <b>Dr 2<sup>nd</sup>&gt;N</b>	<b>Craving (+)</b> Dr 1 <sup>st</sup> >BL L dACC

	Subjects	Abstinence length	Amount/procedure	PFC results	PFC correlations with drug use
				↓ L rvACC/PFC 9/10/25/32	
<b>Heroin</b>					
Sell, Morris et al. 2000	10 S	Daily users	H <sub>2</sub> <sup>15</sup> O 2 days PL or heroin (iv 20 mg) watching D or N videos	NS	<b>Urge (+)</b> ↑ L IFG 47, ↑ R OFC 11, ↑ L INS 47

S subjects, fMRI functional magnetic resonance imaging, FDG positron emission tomography with [<sup>18</sup>F]fluorodeoxyglucose, H<sub>2</sub><sup>15</sup>O positron emission tomography with H<sub>2</sub><sup>15</sup>O for cerebral blood flow, SPECT single photon emission-computed tomography for cerebral blood flow, iv intravenous administration, PL placebo, MPH methylphenidate, D drug cue or stimulus (within respective category), Dr actual drug, N neutral, BL baseline, T Task, SSRT stop signal reaction time task, RT reaction time

NR not reported, NA not applicable, NS not significant

ACC anterior cingulate cortex, dACC dorsal ACC, pgACC perigenual ACC, rACC rostral ACC, scACC subcallosal ACC, vACC ventral ACC, FC frontal cortex, aFC anterior FC, mFC middle FC, IFC inferior FC, PFC prefrontal cortex, mPFC medial PFC, dmPFC dorsomedial PFC, vmPFC ventromedial PFC, DLPFC dorsolateral PFC, vlPFC ventrolateral PFC, IFG inferior frontal gyrus, OFC orbitofrontal cortex, mOFC medial OFC, MedFG medial frontal gyrus, MidFG middle frontal gyrus, SFG superior frontal gyrus, INS insula, SMA supplementary motor area

(+) positive correlation, (-) negative correlation

R right, L left, B bilateral, C central

If available: ↑ increase/activation/hyperactivation, ↓ decrease/deactivation/hypoactivation, Brodmann Areas are noted by numbers

**References**

- Adinoff, B., M. D. Devous, Sr., M. J. Williams, S. E. Best, T. S. Harris, A. Minhajuddin, T. Zielinski and M. Cullum (2010). "Altered Neural Cholinergic Receptor Systems in Cocaine-Addicted Subjects." *Neuropsychopharmacology* **35**(7):1485-99.
- Ersche, K. D., E. T. Bullmore, K. J. Craig, S. S. Shabbir, S. Abbott, U. Muller, C. Ooi, J. Suckling, A. Barnes, B. J. Sahakian, E. V. Merlo-Pich and T. W. Robbins (2010). "Influence of compulsivity of drug abuse on dopaminergic modulation of attentional bias in stimulant dependence." *Arch Gen Psychiatry* **67**(6): 632-44.
- Garavan, H., J. N. Kaufman and R. Hester (2008). "Acute effects of cocaine on the neurobiology of cognitive control." *Philos Trans R Soc Lond B Biol Sci* **363**(1507): 3267-76.
- Goldstein, R. Z., P. A. Woicik, T. Maloney, D. Tomasi, N. Alia-Klein, J. Shan, J. Honorio Carrillo, D. Samaras, R. Wang, F. Telang, G.-J. Wang and N. D. Volkow (2010). "Oral methylphenidate normalizes cingulate activity in cocaine addiction during a salient cognitive task." *Proc Natl Acad Sci U S A* **107**(38):16667-72.
- Kufahl, P., Z. Li, R. Risinger, C. Rainey, L. Piacentine, G. Wu, A. Bloom, Z. Yang and S. J. Li (2008). "Expectation modulates human brain responses to acute cocaine: a functional magnetic resonance imaging study." *Biol Psychiatry* **63**(2): 222-30.
- Kufahl, P. R., Z. Li, R. C. Risinger, C. J. Rainey, G. Wu, A. S. Bloom and S. J. Li (2005). "Neural responses to acute cocaine administration in the human brain detected by fMRI." *Neuroimage* **28**(4): 904-14.
- Li, C. S., P. T. Morgan, D. Matuskey, O. Abdelghany, X. Luo, J. L. Chang, B. J. Rounsaville, Y. S. Ding and R. T. Malison (2010). "Biological markers of the effects of intravenous methylphenidate on improving inhibitory control in cocaine-dependent patients." *Proc Natl Acad Sci U S A* **107**(32):14455-9.
- Sell, L. A., J. S. Morris, J. Bearn, R. S. Frackowiak, K. J. Friston and R. J. Dolan (2000). "Neural responses associated with cue evoked emotional states and heroin in opiate addicts." *Drug Alcohol Depend* **60**(2): 207-16.
- Volkow, N. D., G. J. Wang, Y. Ma, J. S. Fowler, W. Zhu, L. Maynard, F. Telang, P. Vaska, Y. S. Ding, C. Wong and J. M. Swanson (2003). "Expectation Enhances the Regional Brain Metabolic and the Reinforcing Effects of Stimulants in Cocaine Abusers." *J Neurosci* **23**(36): 11461-11468.
- Volkow, N. D., G. J. Wang, D. Tomasi, F. Telang, J. S. Fowler, K. Pradhan, M. Jayne, J. Logan, R. Z. Goldstein, N. Alia-Klein and C. Wong (2010). "Methylphenidate attenuates limbic brain inhibition after cocaine-cues exposure in cocaine abusers." *PLoS ONE* **5**(7): e11509.
- Zubieta, J. K., M. M. Heitzeg, Y. Xu, R. A. Koeppe, L. Ni, S. Guthrie and E. F. Domino (2005). "Regional cerebral blood flow responses to smoking in tobacco smokers after overnight abstinence." *Am J Psychiatry* **162**(3): 567-77.