

**Supplementary online information S1 (Table).**

This table is a summary of the fMRI and PET studies in drug-addicted individuals vs. healthy control subjects conducted during 2000-2010 (articles published in 2011 have not been methodically reviewed), which were used to create **Figure 2**. Studies are divided by the neuropsychological process and type of drug studied. Number of subjects included, abstinence length, task and analyses, are provided in addition to main results. For our main search, we used PubMed, probing for all articles since 2000 that included the following terms: [(substance OR drug) AND (abus\* OR addict\* OR dependen\*)] AND [(prefrontal OR orbitofrontal OR ventromedial OR anterior cingulate) AND (cortex)] AND [(fMRI OR functional magnetic resonance imaging) OR (PET OR positron emission tomography)] (\*designates search of all possible word endings). This search resulted in 295 manuscripts that were reviewed for inclusion. Excluded from the current review are articles that did not include a control group (unless when not necessary or feasible, such as when studying the effects of acute drug administration, abstinence, treatment, or relapse), studies where methodological concerns precluded deriving definitive conclusions [those without a control task or well defined baseline condition, those that were underpowered (N<10 in each group; also, within the reviewed studies, analyses pertaining to subgroups of N<10 subjects are not reviewed)], and those that lacked explicit group comparisons or had technical difficulties. Other excluded studies are non-English articles, reviews, or studies where focus was not on drug addiction or abuse.

**Functional neuroimaging studies (conducted during 2000-2010) in drug addicted individuals, included in Figure 2**

	Subjects	Abstinence	Task	Coordinates	PFC results	Correlations
<b>ATTENTION</b>						
<b>Nicotine</b>						
Musso, Bettermann et al. 2007	15 S 12 C	1 hour	fMRI visual oddball	AFNI, talairach	S<C T>BL ↑ L mPFC 6	Use duration (-) B mPFC 6
<b>Cocaine</b>						
Tomasi, Goldstein et al. 2007	14 S 14 C	6 S ≤72 hours 8 S >30 days	fMRI visual ball-tracking	SPM2, MNI	S>C T>BL ↓ CL rACC 32, ↓ CL ACC 24, ↑ B MidFG 6, ↑ R MidFG 9	
<b>WORKING MEMORY</b>						
<b>Alcohol</b>						
Vollstadt-Klein, Hermann et al. 2010	11 S 12 C	NR	fMRI spatial WM	SPM5, MNI	S>C T>N ↑ L dACC 9	
<b>Cocaine</b>						
Tomasi, Goldstein et al. 2007	16 S 16 C	8 S ≤72 hours 8 S >4 days	fMRI verbal n-back	SPM2, MNI	S>C T>BL ↑ L MidFG 9, ↑ L & CL MidFG 6, ↑	

					CL SFG 8, ↓ CL ACC 24	
<b>Nicotine</b>						
Sutherland, Ross et al. 2010	20 S 27 C	3 hours	fMRI attention switching verbal WM	AFNI, talairach	<b>S&gt;C T&gt;BL</b> ↑ R mesial FC 8/6, ↑ B ant PFC 10/46	
<b>DECISION MAKING</b>						
<b>Methamphetamine</b>						
Paulus, Hozack et al. 2002	10 S 10 C	22 days	fMRI 2-choice prediction	AFNI, talairach	<b>S&lt;C T&gt;N</b> ↑ R IFG 44, ↑ L MidFG 46, ↑ L MidFG 9/10, ↑ B MedFG 10, ↑ R OFC 11	
Paulus, Hozack et al. 2003	14 S 14 C	25 days	fMRI 2-choice prediction	AFNI, talairach		<b>Use duration (-)</b> L MidFG 9, ACC 32 <b>Sobriety duration (+)</b> L MedFG 8
Paulus, Lovero et al. 2008	12 S 12 C	48 hours	fMRI 2-choice prediction	AFNI, talairach	<b>S&gt;C T&gt;BL</b> ↑ L MidFG 10 (20 & 50% errors), ↑ R MidFG 10 (20% errors)	
Monterosso, Ainslie et al. 2007	10 S 13 C	5-7 days	fMRI delay discounting	FSL, MNI	<b>S&lt;C T&gt;N</b> ↑ L DLPFC 9, ↑ R vIPFC/DLPFC 46, ↑ L vIPFC/INS 46, ↑ ACC/SMA 32	
<b>Cocaine</b>						
Bolla, Eldreth et al. 2003	13 S 13 C	≥25 days	H <sub>2</sub> <sup>15</sup> O IGT	SPM99, talairach		<b>Use amount (-)</b> L OFC 11
<b>Any dependence</b>						
Ersche, Fletcher et al. 2005	15 Samp 15 Sopi 15 ex 15 C	S: urine positive ex: 10 years	H <sub>2</sub> <sup>15</sup> O Cambridge Risk Task	SPM2, talairach	<b>S&lt;C T&gt;N</b> ↑ R DLPFC 9/46 <b>S&gt;C T&gt;N</b> ↑ L OFC 11	
Tanabe, Thompson et al. 2007	16 S 18 Sg 14 C	≥2 months	fMRI IGT	SPM2, MNI	<b>S&lt;C T&gt;N</b> ↑ R mPFC 25/11, ↑ R frontopolar 10	
<b>INHIBITORY CONTROL</b>						
<b>Methamphetamine</b>						
Leland, Arce et al. 2008	19 S 19 C	34 days	fMRI go/no-go	AFNI, talairach		<b>False alarm rate (-)</b> L vACC 32

Salo, Ursu et al. 2009	12 S 16 C	4 months	fMRI Stroop	SPM5, MNI	<b>S&lt;C T&gt;N</b> ↑ R SFG 6	
<b>Cocaine</b>						
Bolla, Ernst et al. 2004	13 S 13 C	~23 days	H <sub>2</sub> <sup>15</sup> O Stroop	SPM99, MNI		<b>Use amount (-)</b> R rACC 24
Li, Huang et al. 2008	15 S 15 C	≥2 weeks	fMRI stop signal RT	SPM2, MNI	<b>S&lt;C T&gt;N</b> ↑ L pgACC 32/24	<b>Stop signal RT (-)</b> dmPFC 8
<b>Marijuana</b>						
Tapert, Schweinsburg et al. 2007	16 S 17 C	58 days	fMRI go/no-go	AFNI, talairach		<b>Use duration (-)</b> R DLPFC 10, 46
<b>MDMA</b>						
Roberts and Garavan 2010	20 S 20 C	16 days	fMRI go/no-go	AFNI, talairach	<b>S&gt;C T&gt;BL</b> ↑ R MidFG/IFG 46,10, ↑ R MidFG 9,8,6, ↑ L MedFG 10	
<b>Alcohol</b>						
Heitzeg, Nigg et al. 2010	21 S+fh 20 C+fh 20 C	NR	fMRI go/no-go	SPM2, MNI (& FSL)	<b>S&gt;C T&gt;N</b> ↑ B OFC 10, ↑ L mPFC 9, ↑ L dmPFC 8	
<b>Heroin</b>						
Yucel, Lubman et al. 2007	24 S 24 C	Morning opiate dose	fMRI interference	FSL, talairach		<b>Errors (+)</b> dACC 32 (C not S)
<b>Nicotine</b>						
Kozink, Kollins et al. 2010	15 S	S: as usual A: 24 hours	fMRI go/no-go	SPM5, MNI	<b>A&gt;S T&gt;BL</b> ↑ R IFC 9	
<b>EMOTION</b>						
<b>Alcohol</b>						
Heitzeg, Nigg et al. 2008	11 S 11 C	NR	fMRI press for words: P, U, N	SPM2, MNI	<b>S&lt;C U/P&gt;N</b> ↑ R OFC 11 <b>S&lt;C U&gt;N</b> ↑ L OFC 11 <b>S&gt;C P&gt;N</b> ↑ R dmPFC BA 8/9/10	
<b>MOTIVATION</b>						
<b>Cocaine</b>						
Goldstein, Alia-Klein et al. 2007	16 S 13 C	5 days	fMRI money for go/no-go	SPM99, MNI	<b>S&lt;C T&gt;N</b> ↑ L OFC 47, 13	

Goldstein, Alia-Klein et al. 2009	17 S 17 C	5 days	fMRI money for drug Stroop	SPM2, MNI	<b>S&lt;C T&gt;BL</b> ↑ R dACC 32 <b>S&gt;C T&lt;BL</b> ↓ L rvACC/mOFC 10,11 <b>S&gt;C T&gt;BL</b> ↑ L DLPFC 6,8, ↑ L dmPFC 6	<b>Current use frequency (-)</b> L dACC 24 <b>Task-induced craving (+)</b> L rvACC 10
<b>Nicotine</b>						
Buhler, Vollstadt-Klein et al. 2010	21 S 21 C	36 hours vs. as usual	fMRI instrumental motivation	SPM5, MNI	<b>S&lt;C Money&gt;Cigarette</b> ↑ L ACC 24,32, ↑ R SFG 9,10	
<b>CUES</b>						
Miyake, Okamoto et al. 2010	36 S 12 C	NR	fMRI select most negative or neutral words: Bd, N, U	SPM5, MNI	<b>S&gt;C Bd&gt;N</b> ↑ L vmPFC 9	
Reuter, Raedler et al. 2005	12 S 12 C	NR	fMRI guessing task W, L	SPM2, MNI		<b>Gambling severity (-)</b> L vmPFC 32
Filbey, Claus et al. 2008	37 S	24 hours	fMRI preferred taste D, N	FSL, talairach		<b>Alcohol use severity (+)</b> B OFC 11, 47, vmPFC 24, 10
McClernon, Kozink et al. 2009	18 S	24 hours vs. as usual	fMRI passive picture viewing D, N	SPM5, MNI		<b>Nicotine craving (+)</b> R SFG 6,10, R ACC 32
Zhang, Salmeron et al. 2011	22 S 22 C	≥2 hours	ASL passive picture viewing : D, N	AFNI, talairach	<b>S&gt;C D&gt;N</b> ↑ B dmPFC, ↑ R DLPFC, ↑ B dACC, ↑ B rACC	<b>Lifetime drug use (+)</b> rACC <b>Lifetime drug use (-)</b> DLPFC
<b>MECHANISMS</b>						
<b>Dopamine/Norepinephrine</b>						
Volkow, Wang et al. 2005	21 S 15 C	14 days	FDG + Raclopride PL, iv MPH	SPM99, MNI	<b>S&lt;C PL&gt;MPH</b> ↑ R mOFC 25,11	
Goldstein, Woicek et al. 2011	13 S 14 C	6 days	fMRI (emotional Stroop) 2 days PL or MPH (oral 20 mg) D, N	SPM2, MNI	<b>Dr&gt;PL T&gt;BL</b> (driven by S) ↑ rvACC 32, ↑ L dACC 24	<b>Accuracy (+)</b> B mOFC/MedFG 10,32, R dACC 24 <b>Drug use (-)</b> M dACC 32
Li, Morgan et al. 2010	10 S	8 days	fMRI SSRT	SPM8, MNI		<b>SSRT (+)</b>

	36 C		PL, iv MPH			L MidFG 8 <b>SSRT (-)</b> L vmPFC 25
<b>Opioid</b>						
Gorelick, Kim et al. 2005	17 S 16 C	1. ~24 hours 2. ~1 week 3. ~12 weeks	Carfentanil ( $\mu$ )	SPM2, MNI		<b>Craving (+)</b> 1. L ACC 24, L FC 9 2. L FC 10 <b>Use frequency (+)</b> 1. R ACC 32, R FC 9
Ghitza, Preston et al. 2010	Cocaine 25 S	NR (17 urine positive)	Carfentanil ( $\mu$ )	SPM2, MNI		<b>Drug use (+)</b> R MidFG 8, L MedFG 10 <b>Abstinence (-)</b> L medFG 6, L MidFG 9, L ACC 24, R MidFG 46
<b>Cholinergic</b>						
Adinoff, Devous et al. 2010	23 S 22 C	27 days	SPECT 3 days Saline, physostigmine (iv >0.816 mg/h), or scopolamine (iv 0.315 mg/70 kg)	SPM2, MNI	<b>S&lt;C Dr&gt;PL</b> ↓ R DLPFC 10	

C controls, S subjects, Sg gamblers, Samp amphetamine users, Sopi opiate users, ex past users, +fh with family history of alcohol use disorders  
 fMRI functional magnetic resonance imaging, FDG positron emission tomography (PET) with [<sup>18</sup>F]fluorodeoxyglucose for glucose metabolism, H<sub>2</sub><sup>15</sup>O PET for blood flow, SPECT single photon emission-computed tomography for cerebral blood flow, WM working memory, IGT Iowa gambling task, RT reaction time, PL placebo, MPH methylphenidate, iv intravenous administration, DV distribution volume, SERT serotonin transporter  
 MNI Montreal Neurological Institute, SPM Statistical Parametric Mapping, FSL FMRIB (fMRI of the Brain) Software Library, AFNI Analysis of Functional Neuroimages software package  
 D drug (within respective category), Dr Drug, T Task, N neutral, P pleasant, U unpleasant, W win, L loss, BL baseline  
 ACC anterior cingulate cortex, dACC dorsal ACC, ifgACC infragenual 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, vIPFC 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, CL central  
 If available: ↑ increase/activation/hyperactivation, ↓ decrease/deactivation/hypoactivation

Subject column is in italics if groups are matched on 2 of the following: age, sex, race, education

Where not provided, xyz coordinates were converted to the Talairach space for Brodmann area identification (regions where nearest grey matter did not include a PFC Brodmann Area were excluded)

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