Pathway-Specific Dopamine Abnormalities in Schizophrenia

Supplemental Information

Supplemental Methods

Criteria for the Range and Source of Literature to Review

To collect data papers to include in this review, a literature search was performed in August 2015 in PubMed with the specifiers: “dopamine” [Title] and “schizophrenia” [Title], and filters “Humans” and “English”. This yielded roughly 800 papers. Of these, we only included molecular imaging studies of dopamine in schizophrenia that used highly rigorous quantitative methods and experimental designs. We avoided dopamine-D_2 receptor studies that included participants currently on antipsychotic treatment. When studies reported aggregation or reanalysis of previously published datasets, the study with the larger cohort was included.

Table S1. PET and SPECT imaging findings of the dopamine system in schizophrenia

Publication	Tracer/ Challenge	Measure	Sample	Results by Brain Region:																						Reported Correlates / Notes	Meta-Analysis Inclusion
				Striatum	LST	AST	SMST	Caudate	Putamen	Thalamus	G. Pallidus	Hippocampus	Amygdala	Entorhinal	ACC	PCC	Uncus	DLPFC	MPFC	OFC	Insula	Temporal	Parietal	Occipital	Midbrain		
Studies of Dopamine (DA) synthesis in SZ																											
Reith *et al.*, 1994 (1)	$[^{18}F]$DOPA	K_i^{Cortex}	5 chronic SZ (4 Rx-naïve + 1 Rx-free) > 13 HC	Ý				Ý	Ý																	Û between SZ and group of patients with temporal epilepsy with psychosis. Û between HC and group of patients with temporal epilepsy without psychosis. -In SZ, mean illness duration was 14 +/- 9 years; and the 1 Rx-free had not received antipsychotics in >3 years.	(2, 3)
Dao-Castellana *et al.*, 1997 (4)	$[^{18}F]$DOPA	$K_i^{Occipital}$	6 chronic SZ (2 Rx-naïve, 4 Rx-free) > 7 HC					Û	Û																	-K_i variances in caudate and putamen were greater in SZ. -Not correlated with PANSS	(2, 3)
Hietala *et al.*, 1995 (5), 1999 (6)	$[^{18}F]$DOPA	$K_i^{Occipital}$	10 SZ (Rx-naïve) > 13 HC	Ý				Ý*	Ý																	*Ý in SZ for left caudate was significant; right was not. -Asymmetry in caudate K_i was seen in HC, but not SZ. -STR K_i correlated with PANSS positive symptoms. -Left STR K_i negatively correlated with depressive symptoms (by PANSS). -In putamen, K_i highest in paranoid subtype, especially in paranoid patient experiencing florid persecutory AH during scan. -In patient with catatonia, striatal K_i was lower than HC (5).	(2, 3)
Lindstrom *et al.*, 1999 (7)	$[^{11}C]$L-DOPA	$K_i^{Occipital}$	12 SZ (10 Rx-naïve + 2 Rx-free) > 10 HC	Ý				Ý	Ý									Û	Ý			Û				-Trend for hemispheric lateralization in HC, but not SZ.	(2, 3, 8)
Meyer-Lindenberg *et al.*, 2002 (9)	$[^{18}F]$DOPA	$K_i^{Occipital}$	6 SZ (Rx-free) > 6 HC	Ý																						-Negative correlation with working memory (Wisconsin card sort) task-related activation (rCBF) in right DLPFC in SZ, but not in HC.	(2, 3)
McGowan *et al.*, 2004 (10)	$[^{18}F]$DOPA	$K_i^{Occipital}$	16 SZ (on Rx) > 12 HC	Ý	Ý	Û									Û				Û							-K_i in ACC correlated with performance on Stroop color-word test in both SZ and HC. -Semantic-category word production (by FAS cluster scores) did not correlate with LST K_i in SZ, but did in HC.	(2)
Kumakura *et al.*, 2007 (11)	$[^{18}F]$DOPA	K	8 SZ (3 Rx-naïve + Rx-free) > 15 HC	Ý	Ý			Ý	Ý				Ý												Ý	-K is "K_{in}^{app}" corrected for K_{loss}, using cerebellum as reference. -In all VOIs of SZ, K was 20-50% greater and K_{loss} was 75-90% greater than in HC. -For all VOIs, no significant group differences in K_{in}^{app}. -Significant negative correlation between V_d in bilateral amygdala and PANSS positive score (*r= -0.775; p=0.024*). -No significant correlations with PANSS negative scores.	(2, 3, 8)
Nozaki *et al.*, 2009 (12)	$[^{11}C]$L-DOPA	$K_i^{Occipital}$	18 SZ (14 Rx-naïve + 4 Rx-free) > 20 HC					Ý	Û	Û				Û	Û			Û				Û				Ý in SZ in left caudate only. -K_i in thalamus correlated with PANSS total score. -K_i in right temporal cortex correlated with PANSS positive score.	(2, 3, 8)

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Howes *et al.*, 2009 (13)	[^{18}F]DOPA	K_i^{cer}	7 SZ (4 Rx-naïve + 3 Rx-free) > 12 HC	Ý	Û	Ý	Û																			-In Sz, K_i in STR did not correlate with PANSS, CAARMS, HAM-D or HAM-A scores. -Also, in 24 CHR>HC, K_i in AST was Ý, and intermediate compared to SZ>HC. (See extension of UHR cohort in Howes et al., 2011 (14, 15) and Egerton et al., 2013 (16) below).	(2, 3)
Howes *et al.*, 2013 (17)	[^{18}F]DOPA	K_i^{cer}	29 SZ (5 Rx-naïve + 8 Rx-free + 16 on-Rx) > 29 HC	Ý*	Ý	Ý	Ý																		Ý**	*Ý in STR even when restricted to 13 Rx-free SZ > 29 HC, and Ý in STR when contrasted 16 SZ on-Rx > HC. **Ý in SN even when restricted to 13 Rx-free SZ > 29 HC, however Û in SN when contrasted SZ on-Rx > HC. -Nigral K_i^{cer} was proportional to STR K_i^{cer} in HC, but not in SZ. -In SZ, nigral uptake was proportional to symptom severity.	-
Demjaha *et al.*, 2012 (18)	[^{18}F]DOPA	K_i^{cer}	12 Rx-resistant SZ > 12 HC	Û	Û	Û	Û																			-All SZ pts were on antipsychotic Rx (on-Rx).	-
			12 Rx-responsive SZ > 12 HC	Ý	Û	Ý	Û																				
			12 Rx-responsive SZ > 12 Rx-resistant SZ	Ý	Ý	Ý	Û																				
Howes *et al.*, 2012 (2)	Meta-analysis of Striatal DA synthesis, Endogenous DA and DA release studies		17 studies					Û	Ý																	-231 SZ and 251 HC -Sample overlaps with that of Fusar-Poli et al., 2013b (3).	
Fusar-Poli *et al.*, 2013b (3)	Meta-analysis of Striatal DA synthesis studies		11 studies	Ý				Ý	Ý																	-113 SZ and 131 HC -In STR: SZ>HC by average of 14% (*Hedges' g=0.867, p<0.001*) and was significantly Ý'd in *all* studies with acutely psychotic pts. -In caudate: SZ>HC with Hedges' g=0.569, p=0.005. -In putamen: SZ>HC with Hedges' g=0.643, p=0.021. -SZ sample included groups with varied mixes of Rx-free & on-Rx pts. -Not moderated by pts' age, illness duration, psychotic symptoms, antipsychotic exposure, or gender. -Sample overlaps with that of Howes et al., 2012 (2).	
Studies of DA synthesis in Clinical High Risk (CHR, UHR)																											
Howes *et al.*, 2009 (13)	[^{18}F]DOPA	K_i^{cer}	24 UHR > 12 HC ("1st cohort")	Ý	Û	Ý	Û																			-Compared to 7 SZ>HC (same study, listed above, effect size=1.25), for 24 UHR>HC, K_i in AST was also Ý, and intermediate (effect size=0.75). -In UHR, K_i in STR correlated with severity of psychopathology (CAARMS & PANSS scores) and neuropsychological impairment (poor verbal fluency performance), but not with severity of anxiety or depressive symptoms (HAM-A and HAM-D scores). Similar CAARMS & PANSS score correlations were observed for K_i in AST and SMST, but not for LST.	(2, 3)
Howes *et al.*, 2011 (14, 15)	[^{18}F]DOPA	K_i^{cer}	9 UHR-transitioned > 29 HC	Ý	Û	Ý	Û																			-In UHR-transitioned (*i.e.* UHR who transitioned to psychosis within 2 years after scan) > HC, effect size was 1.18 in STR and 1.24 in AST. -For 15 UHR-non-transitioned > 29 HC, Û in K_i^{cer} in STR or any subregions.	-

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				Striatum	LST	AST	SMST	Caudate	Putamen	Thalamus	G. Pallidus	Hippocampus	Amygdala	Entorhinal	ACC	PCC	Uncus	DLPFC	MPFC	OFC	Insula	Temporal	Parietal	Occipital	Midbrain		
Howes *et al.*, 2011 (14, 15)	$[^{18}F]$DOPA	K_i^{cer}	9 UHR-transitioned > 15 UHR-non-transitioned	Ý	Û	Ý	Û																			-Ý ΔK_i^{cer} in SMST in UHR-transitioned (compared to UHR-non-transitioned) and remained significant after excluding 2 UHR-transitioned pts who were antipsychotic-treated before the 2nd scan.	-
Egerton *et al.*, 2013 (16)	$[^{18}F]$DOPA	K_i^{cer}	26 UHR > 20 HC ("2nd cohort")	Ý	Û	Ý	Û																			-In UHR, no correlates with prodromal symptoms severity (CAARMS total score) or SZ symptoms (PANSS total score).	-
			50 UHR > 32 HC (Combined cohorts from (16) and (13))	Ý	Û	Ý	Ý																			In overlapping sample of 18 unmedicated UHR > 18 HC examined by Roiser et al., 2013 (19): In UHR, K_i^{cer} in AST was negatively correlated with fMRI-measured hippocampal responses to irrelevant stimulus features (*I.e.* Aberrant neural reward prediction signals). Whereas, these were positively correlated in HC.	-
Allen *et al.*, 2012 (20)	$[^{18}F]$DOPA	K_i^{cer}	5 UHR-transitioned > 16 UHR-non-transitioned																						Ý	-2-year follow-up: 5/21 transitioned to psychosis. -Small sample size and 1 UHR who transitioned and 2 UHR who did not transition were getting antipsychotics at low doses (<1.5 mg haloperidol equivalents/day) or other medications. -Midbrain ROI also included pons. -Sample overlaps and extends that of Howes et al., 2011 (14, 15).	-
Studies of Endogenous DA in SZ																										(Also see meta-analysis (2) above)	
Abi-Dargham *et al.*, 2000 (21)	$[^{123}I]$IBZM/ α-MPT	ΔBP_{ND}	18 SZ (8 Rx-naïve + 10 Rx-free) > 18 HC	Ý																						Ý baseline synaptic DA in striatum predicted reduction of positive-symptoms with antipsychotic. -In SZ, 8 first-episode Rx-naïve and 10 Rx-free, previously-treated pts with chronic SZ experiencing illness exacerbation.	(2)
Abi-Dargham *et al.*, 2009 (22)	$[^{123}I]$IBZM/ α-MPT	ΔBP_{ND}	6 SZ (Rx-naïve) > 8 HC	Ý																						-In Rx-naïve SZ, ΔBP_{ND} in response to depletion correlated with ΔBP_{ND} in response to amph-challenge.	(2)
	$[^{123}I]$IBZM/ Amph	ΔBP_{ND}		Ý																							
Kegeles *et al.*, 2010 (23)	$[^{11}C]$Rac/ α-MPT	ΔBP_{ND}	18 SZ (6 Rx-naïve + 12 Rx-free) > 18 HC	Û	Û	Ý	Û																			-Within AST, Ý was specific to rostral caudate. -In SZ, Ý in LST inversely correlated with severity of baseline negative symptoms.	(2)
Studies of DA Release in SZ																										(Also see meta-analysis (2) above)	
Laruelle *et al.*, 1996 (24)	$[^{123}I]$IBZM/ Amph	ΔBP_{ND}	15 SZ (Rx-free) > 15 HC	Ý																						-In SZ, greater STR ΔBP_{ND} variance (*ratio=3.85, p<0.02*) -In SZ, STR ΔBP_{ND} correlated with transient amph-induced worsening of positive, but not negative symptoms (PANSS). Û between SZ and HC in amph-induced behavioral activation scores (by AIRS).	(2)
Breier *et al.*, 1997 (25)	$[^{11}C]$Rac/ Amph	ΔBP_{ND}	11 SZ (6 Rx-naïve + 5 Rx-free) > 12 HC	Ý																						Û between STR ΔBP_{ND} in Rx-naïve and Rx-free. -STR ΔBP_{ND} correlated with ΔBPRS scores in SZ; not in HC.	(2)
Abi-Dargham *et al.*, 1998 (26)	$[^{123}I]$IBZM/ Amph	ΔBP_{ND}	15 SZ (2 Rx-naïve + 13 Rx-free) > 15 HC	Ý																						-In SZ, STR ΔBP_{ND} correlated with Ý transient amph-induced positive symptoms, but not with Δ in negative symptoms.	(2)

Publication	Tracer/ Challenge	Measure	Sample	Striatum	LST	AST	SMST	Caudate	Putamen	Thalamus	G. Pallidus	Hippocampus	Amygdala	Entorhinal	ACC	PCC	Uncus	DLPFC	MPFC	OFC	Insula	Temporal	Parietal	Occipital	Midbrain	Reported Correlates / Notes	Meta-Analysis Inclusion
				Results by Brain Region:																							
Laruelle *et al.*, 1999 (27)	[^{123}I]IBZM/ Amph	ΔBP_{ND}	34 SZ (7 Rx-naïve + 27 Rx-free) > 26 HC (sample extended from (24))	Ý																						-In SZ, STR ΔBP_{ND} correlated with amph-induced Ý in positive symptoms (by PANSS). -Severity of negative symptoms at baseline predicted amph-induced improvement in negative symptoms (by PANSS), but did not predict ΔBP_{ND}. - STR ΔBP_{ND} correlated with amph-induced improvement in negative symptoms, but was likely driven by 2 pts.	(2)
Pogarell *et al.*, 2012 (28)	[^{123}I]IBZM/ Amph	ΔBP_{ND}	8 SZ (Rx-free x7 days) > 7 HC	Ý																						-Trends for STR ΔBP_{ND} association with symptoms in SZ; small sample size	-
Mizrahi *et al.*, 2012 (29)	[^{11}C]PHNO/ Stress	ΔBP_{ND}	10 SZ (Rx-naive) > 12 HC	Ý	Û	Ý	Ý																			-Also compared with 12 CHR: Ý AST ΔBP_{ND} in CHR and SZ, compared to HC; while Û between CHR and SZ.	-
Slifstein *et al.*, 2015 (30)	[^{11}C]FLB457/ Amph	ΔBP_{ND}	20 SZ (6 Rx-naïve and 14 Rx-free) > 21 HC							ß		ß	ß	ß	ß	ß	ß	ß	ß	ß	ß	ß	ß	ß	ß	-In both SZ and HC, ΔBP_{ND} in DLPFC correlated with working memory-related BOLD activation of DLPFC.	-
Studies of DA Release in SZ or CHR with Substance use																											
Thompson *et al.*, 2013 (31)	[^{11}C]Rac/ Amph	ΔBP_{ND}	11 SZ+SubsDep > 15 HC	ß	Û	ß	ß																			-In SZ participants, ΔBP_{ND} in pre-DCA and LST associated with change in positive symptoms (PANSS) after amph. -All were unmedicated and substance-free. 2 were Rx-naïve.	-
Mizrahi *et al.*, 2014 (32)	[^{11}C]PHNO/ Stress	ΔBP_{ND}	12 CHR+Cannabis (CHR-CU) > 12 CHR	ß	ß	ß	ß				Û														Û	-Stress decreased BP_{ND} in CHR; whereas stress increased BP_{ND} in CHR-CU.	-
Studies of Vesicular monoamine transporter-2 (VMAT2) in SZ																											
Taylor *et al.*, 2000 (33)	[^{11}C]DTBZ	BP_{ND}	12 SZ (on-Rx) > 12 matched HC	Û	Û	Û	Û	Û	Û	Û														Û			-
Zubieta *et al.*, 2001 (34)	[^{11}C]DTBZ	BP_{ND}	12 SZ (on-Rx) > 15 matched HC							Û															Ý	-Also contrasted with group of 15 euthymic pts with bipolar I disorder with history of psychotic features, which had Ý BP_{ND} in thalamus and ventral midbrain	-
Studies of Dopamine transporter (DAT) in SZ																											
Laruelle *et al.*, 2000 (35)	[^{123}I]β-CIT	BP_{ND}	24 SZ (4 Rx-free >2 wks, 4 Rx-free <2 wks, and 16 on-Rx) > 22 HC	Û																						-DAT levels did not correlate with amph-induced DA release (measured in same cohort using [^{123}I]IBZM).	(2, 36)
Arakawa *et al.*, 2009 (37)	[^{11}C]PE2I	BP_{ND}	8 SZ (6 Rx-Naïve + 2 Rx-Free) > 12 HC	Û				Û	Û	Ý															Û	-In SZ, BP_{ND} in thalamus correlated with total, positive and negative PANSS scores.	(2, 36)
Howes *et al.*, 2012 (2)	Meta-analysis of Striatal DAT studies		11 studies	Û				Û	Û																	-152 SZ and 132 H (*d=-0.34, p=0.10).* -Significant sample overlaps with that in Fusar-Poli et al., 2013a (36).	
Fusar-Poli *et al.*, 2013a (36)	Meta-analysis of Striatal DAT studies		13 studies	Û				Û	Û																	-202 SZ and 147 HC (Hedges' g=-0.244, p=0.269). -Significant sample overlaps with that in Howes et al., 2012 (2). -SZ sample was mixed with pts on-Rx, Rx-naïve, and Rx-free.	
Studies of Dopamine-$D_{2/3}$ receptor ($D_{2/3}$) availability in SZ																											

Publication	Tracer/ Challenge	Measure	Sample	Striatum	LST	AST	SMST	Caudate	Putamen	Thalamus	G. Pallidus	Hippocampus	Amygdala	Entorhinal	ACC	PCC	Uncus	DLPFC	MPFC	OFC	Insula	Temporal	Parietal	Occipital	Midbrain	Reported Correlates / Notes	Meta-Analysis Inclusion
Howes *et al.*, 2012 (2)	Meta-analysis of Striatal $D_{2/3}$ availability studies		22 studies	Ý*				Û	Ý*																	337 SZ and 324 HC For striatum (22 studies): Ý* in SZ (effect size *d=0.26, p=0.049*) *Small and inconsistent finding, differences only significant in studies with pts who had received butyrophenone radiotracers. Also, was not significant when included only those studies with Rx-naïve patients. For striatum (14 studies that used a benzamide tracer): SZÛ HC (*d=0.13, p=0.44)*. For caudate (8 studies): SZÛ HC (*d=0.37, p=0.12*). For putamen (8 studies): Ý in SZ (*d=0.51, p=0.007*), although this included studies irrespective of radiotracer used.	
Kambeitz *et al.*, 2014 (8)	Meta-analyses of studies of Extrastriatal $D_{2/3}$ availability		Thalamus: 8 studies Temporal: 6 studies Substantia Nigra (SN): 5 studies							Û												Û			Û	-For Thalamus: 138 SZ and 126 HC (8 studies), *d*=-0.32, p=0.07. -For Temporal Cortex: 84 SZ and 86 HC (6 studies), d=-0.23, p=0.1. -For SN, 61 SZ and 72 HC (5 studies), d= 0.04, p= 0.9. Also no effect when excluded the one study of Rx-naïve SZ.	
Nakajima *et al.*, 2015 (38)	$[^{11}C]$Rac	BP_{ND}	10 SZ(age50[+]) > 10 HC(age48[+])	Û	Û		Û	Û	Û																	-No correlations with PANSS total or subscale scores. -Of 10 SZ, 4 were Rx-naïve; all were Rx-free>3mo and no exposures to depot antipsychotic Rx. -In SZ, no difference in BP_{ND} between Rx-naïve and Rx-free, although subgroups were not sex-matched.	-
Slifstein *et al.*, 2015 (30)	$[^{11}C]$FLB457	BP_{ND}	20 SZ (6 Rx-naïve + 14 Rx-free) > 21 HC							Û		Û	Û	Û	Û	Û	Û	Û	Û	Û	Û	Û	Û	Û		-Within SZ, BP_{ND} in Rx-Naïve > Rx-Free.	-
Studies of Dopamine-D_1 receptor (D_1) availability in SZ																											
Okubo *et al.*, 1997 (39)	$[^{11}C]$SCH23390	BP_{ND}	17 SZ (10 Rx-Naïve, 7 Rx-Free>2wks) > 18 HC	Û														ß								ß related to severity of negative symptoms (BPRS) and poor performance in Wisconsin Card Sort Test.	-
Karlsson *et al.*, 2002 (40)	$[^{11}C]$SCH23390	BP	10 SZ (Rx-Naïve, first episode) > 10 HC					Û	Û							Û			Û		Û		Û			-B_{max} in right frontal cortex associated with negative symptoms (BPRS).	-
Abi-Dargham *et al.*, 2002 (41)	$[^{11}C]$NNC112	BP	16 SZ (7 Rx-Naïve, 9 Rx-free) > 16 HC		Û	Û	Û			Û		Û	Û	Û	Û			Ý	Û	Û		Û	Û	Û		Ý BP in DLPFC correlated with working memory deficits (n-back) in SZ and HC. Rx-naïve were in 1st episode and Rx-free were chronic pts Entorhinal ROI was "parahippocampal gyrus"	-
Abi-Dargham *et al.*, 2012 (42)	$[^{11}C]$NNC112	BP_{ND} and BP_p	12 SZ (Rx-Naïve) > 24 HC		Û	Û	Û											Ý	Ý	Ý						Ý in cortical ROIs in Rx-naïve SZ, but not Rx-free. Rx-free interval was associated with cortical BP_p	-
			13 SZ (Rx-Free) > 24 HC		Û	Û	Û											Û	Û	Û						-Did not replicate first cohort's (41) association with working memory deficits.	-
Study of D_1 availability in Schizotypal Personality Disorder																											
Thompson *et al.*, 2014 (43)	$[^{11}C]$NNC112	BP_{ND} and BP_F	18 Schizotypal personality disorder (SPD) > 21 HC		Û	Û	Û											ß	Û	Û						-BP_F and BP_P in MPFC negatively related to PASAT (paced auditory serial addition test) performance, but BP was not related to 2-back performance. -SPD were all unmedicated. -Trends of Ý BP_F and BP_{ND} for SPD in LST, but no other striatal subregions. Also trend for Ý BP_F for SPD in whole striatum, but not BP_{ND}.	-

Note: "Ý" indicates that the measure is significantly higher in SZ, compared to HC. In all cases, this refers to the dopamine-related interpretation of the measure. For BP_{ND}, Ý indicates binding potential in SZ is higher than in HC. For ΔBP_{ND}, Ý indicates greater displacement (i.e. greater change in BP_{ND} with challenge, compared to baseline) in SZ than in

HC. For K_i^{cer}, Ý denotes higher uptake ratio (i.e. greater DA synthesis and storage capacity) in SZ than in HC. "ß" indicates significantly lower, and "Û " indicates no significant group difference.

Abbreviations: Participants (pts); Healthy control participants (HC); Participants with schizophrenia (SZ); Participants with schizophrenia and comorbid substance dependence (SZ+SubsDep); Participants at ultra-high risk for psychosis (UHR) or clinical high risk for schizophrenia (CHR), as determined using clinical high risk criteria for psychosis (44); Taking antipsychotic medication at time of study (on-Rx); Antipsychotic-naïve (Rx-naïve); Antipsychotic-free >3 weeks, unless otherwise noted (Rx-free); Schizotypal personality disorder (SPD); Dopamine (DA); Dopamine-D_1 receptor (D_1); Dopamine-D_2 receptor (D_2); Dopamine-D_2 and -D_3 receptors ($D_{2/3}$); Vesicular monoamine transporter, type 2 (VMAT2); Dopamine transporter (DAT); [^{11}C]Raclopride ([^{11}C]Rac); Binding potential (BP); Binding potential relative to non-displaceable compartment (BP_{ND}); Percent change in binding potential (ΔBP_{ND}); Influx rate constant (K_i) and, when concentration in a reference region (such as cerebellum, cortex, or occipital cortex) is used as the input for the plasma concentration (K_i^{cer}, K_i^{Cortex} or $K_i^{Occipital}$, respectively); Amphetamine (Amph); Region of interest (ROI); Voxel of interest (VOI); Striatum (STR); Limbic striatum (LST); Associative striatum (AST); Sensorimotor striatum (SMST); Precommissural dorsal caudate (Pre-DCA); Globus pallidus (G. Pallidus); Anterior cingulate cortex (ACC); Posterior cingulate cortex (PCC); Dorsolateral prefrontal cortex (DLPFC); Medial prefrontal cortex (MPFC); Orbitofrontal cortex (OFC); Substantia nigra (SN); Ventral tegmental area (VTA); Comprehensive Assessment of At-Risk Mental States (CAARMS); Positive And Negative Syndrome Scale (PANSS); Brief Psychiatric Rating Scale (BPRS); Amphetamine Interview Rating Scale (AIRS); Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A).

Supplemental References

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