

Table 1:

Summary of Brain Recovery in In Human Substance-Using Samples. Studies are sorted by imaging measure, drug type and by the increasing duration of abstinence (at the final neuroimaging scan).

GM and WM							
van Bolk et al. (2013)	T1 HC: n=55 SUD: n=49 T2 HC: n=20 SUD: n=49	3T MRI: T1- weighted MPRAGE ROI (anterior frontal gyrus, cingulate gyrus, insula, parietal and temporal lobes, cerebellum, and hippocampus); total WM	T1: 1 day T2: 2 weeks	p<0.05; whole-brain FWE-corrected	SUD at T1 vs. HC at T1 ↓ GM volume: middle and inferior frontal gyrus, cingulate and precentral gyrus, insula, precuneus, superior parietal lobule, middle temporal gyrus, and cerebellum SUD at T2 vs. HC at T2 Not reported	HC NS SUD ↑ GM volume: cingulate gyrus, insula, temporal gyrus, precuneus, parietal lobule, and cerebellum	
Kuhn et al. (2014)	T1 HC: n=32 SUD: n=42 T2 HC: n=32 SUD: n=42	3T MRI: T1- weighted MPRAGE ROI (hippocampal subfields)	T1: ~ 9 days T2: 2 weeks	p<0.017; Bonferroni corrected for 3 ROIs	SUD at T1 vs. HC at T1 ↓ GM volume: hippocampus (subfield CA2+3) SUD at T2 vs. HC at T2 NS	HC NS SUD ↑ GM volume: hippocampus (subfield xCA2+3)	
Wojc et al. (2016)	T1 HC: n=20 SUD: n=49 T2 HC: n=20 SUD: n=49	3T MRI: T1- weighted MPRAGE ROI in subcortical regions (volume: hippocampus, amygdala, caudate, putamen, pallidum, nucleus accumbens); cortical thickness; surface area in cortical areas	T1: 1 day T2: 2 weeks	Subcortical regions: p<0.05 Cortical thickness and surface area: cluster-wise correction with Monte Carlo simulations (vertex-wise threshold p< 0.05, 5,000 iterations)	SUD at T1 vs. HC at T1 ↓ GM volume: hippocampus v. amygdala, putamen, and nucleus accumbens ↓ Cortical thickness: medial OFC, middle frontal, superior frontal, and inferior frontal lobe, inferior parietal lobe, fusiform, inferior temporal and lateral occipital lobe Surface area: NS SUD at T2 vs. HC at T2 ↓ GM volume: hippocampus, amygdala, putamen, and nucleus accumbens ↓ Cortical thickness: middle frontal, superior frontal, and inferior frontal lobe, inferior parietal lobe, fusiform, inferior temporal and lateral occipital lobe Surface area: NS	HC NS SUD ↑ Cortical thickness: medial OFC, middle frontal, superior frontal, rostral ACC, cuneus, and inferior parietal and lateral occipital regions; ↑in global sulci > gyri	
Bach et al. (2020)	T1 HC: n=74 SUD: n=62 T2 HC: N/A SUD: n=62	3T MRI: T1- weighted MPRAGE Whole-brain volume and cortical thickness	T1: ~12 days T2: 27 days	p<0.05; FWE-corrected	SUD at T1 vs. HC at T1 ↓ GM volume: superior, inferior and middle frontal gyrus, posterior cingulate gyrus, insula, fusiform gyrus, hippocampus, amygdala, thalamus, putamen, precuneus, and cuneus ↓ cortical thickness: superior frontal cortex, rostral middle frontal cortex, caudal middle frontal cortex and medial and lateral OFC, superior parietal cortex, occipital cortex, precuneus, cuneus, lingual and fusiform cortex SUD at T2 vs. HC at T1 ↓ GM volume: posterior cingulate gyrus, insula, fusiform gyrus, hippocampus, thalamus, and precuneus ↓ cortical thickness: superior parietal cortex, occipital cortex, and precuneus	HC N/A SUD ↑ GM volume: middle and inferior frontal gyri, middle cingulate gyrus, insula, supramarginal gyrus, and precuneus ↑ cortical thickness: superior frontal cortex, rostral middle frontal cortex, lateral OFC, insula, and lateral occipital cortex	
Durazzo et al. (2017)	T1 HC: n=33 SUD: n=82 T2 HC: N/A SUD: n=42	1.5T MRI: T1- weighted MPRAGE ROI (frontal, parietal, temporal, occipital lobes GM and WM)	T1: 1 week T2: 4 weeks	p < .024	SUD at T1 vs. HC at T1 ↓ GM volume: DLPFC, parietal, temporal, and occipital SUD at T2 vs. HC at T1 ↓ GM volume: frontal, parietal, and occipital	HC N/A SUD ↑ GM volume: frontal	
Durazzo and Meyerhoff (2020)	T1 HC: n=33 SUD: n=78 T2 HC: N/A SUD: 24	1.5T MRI: T1- weighted MPRAGE ROI (DLPFC, OFC, ACC, precentral gyri, and insula)	T1: 1 week T2: 4 weeks	p<0.05; corrected	SUD at T1 vs. HC at T1 ↓ GM volume: rostral ACC, medial OFC, insula and total frontal cortex SUD at T2 vs. HC at T1 ↓ GM volume: rostral ACC and insula	HC N/A SUD NS	
Gazdzinski et al. (2008)	T1 HC: 14 SUD: n=24 (13smokers, 11 non-smokers) T2 HC: N/A SUD: n=24	1.5T MRI: T1- weighted MPRAGE ROI (hippocampus)	T1: 1 week T2: 1 month	p<0.05; uncorrected	SUD at T1 vs. HC at T1 NS SUD at T2 vs. HC at T1 NS	HC N/A SUD ↑ GM volume: hippocampus (in both smokers and non-smokers)	
Mon et al. (2013)	T1 HC: n=17 (not genotyped) SUD: n=41 (26 Val/Val BDNF; 15 Val/Met BDNF) T2 HC: n=17 SUD: n=41	1.5T MRI: T1- weighted MPRAGE ROI (GM major lobes and subcortical regions: thalamus, lenticular nuclei, caudate, brainstem, and cerebellum; WM major lobes)	T1: 1 week T2: 5 weeks	p≤0.027 and p≤0.017 respectively for cortical and subcortical regions	Not reported	HC NS SUD Val/Val BDNF carriers ↑ GM volume: frontal, parietal, and temporal lobes, and thalamus ↓ GM volume: caudate Val/Met BDNF carriers ↑ GM volume: cerebellum, temporal lobe ↑ WM volume: frontal lobe, parietal, and temporal lobes (at trend level)	
Dominko et al. (2011)	T1 HC: n=66 SUD: n=50 T2 HC: N/A SUD: n=14	1.5T MRI: T1- weighted MPRAGE Global GM, WM, and ROI (cingulate gyrus, OFC, insula, thalamus, amygdala, and hippocampus)	T1: 5 weeks T2: 4 months	p<0.05 (FWE)	SUD at T1 vs. HC at T1 ↓ GM volume: anterior and middle cingulate gyrus, insula, superior temporal gyrus, parahippocampal gyrus, amygdala, SUD at T2 vs. HC at T1 N/A	HC N/A SUD ↑ total GM and WM volume ↑ GM volume: OFC, cingulate gyrus, and insula	
Sheer et al. (1994)	T1 HC: n=N/A SUD: n=24 T2 HC: N/A SUD: n=15	1.5T MRI: Protondensity and T2weighted scans (Total GM and WM)	T1: 1 month T2: 4 months	p<0.05	N/A	HC N/A SUD ↑ total WM volume	
Hoefler et al. (2014)	T1 HC: n=35 (not genotyped) SUD: n=84 (subst: 26 Val/Val BDNF; 15 Val/Met BDNF) T2 HC: n=N/A SUD: n=121 T3 HC: 16 SUD: n=37	1.5 T MRI: T1- weighted MPRAGE ROI: hippocampus	T1: 1 week T2: 3 months T3: 3 months	p<0.05 (uncorrected)	SUD at T1 vs. HC at T1 ↓ GM volume: hippocampus SUD at T2 vs. HC at T3 ↓ GM volume: hippocampus SUD at T2 vs. HC at T3 ↓ GM volume: hippocampus	HC NS SUD ↑ GM at trend level: hippocampus (between T1 and T2) in Val/Val carriers No effect of smoking	
Gazdzinski et al. (2007)	T1 HC: n=18 SUD: n=47 T2 HC: n=8 SUD: n=17	1.5T MRI: T1- weighted MPRAGE Whole-brain (GM; WM)	T1: ~1 week T2: 7 months	p<0.05; uncorrected	SUD at T1 vs. HC at T1 ↓ GM and WM volume: DLPFC, GM: temporal region SUD at T2 vs. HC at T2 Not reported	HC NS SUD ↑ GM volume: OFC and parietal lobes	
Durazzo et al. (2015)	T1 HC: n=32 SUD: n=82 (46smokers, 36 non-smokers) T2 HC: N/A SUD: n=82 T3 HC: n=15 SUD: n=36	1.5T MRI: T1- weighted MPRAGE ROI (GM: frontal, parietal, temporal, occipital lobes, thalamus, caudate, lenticular nucleus, and cerebellum; WM: frontal, parietal, temporal, occipital lobes)	T1: 1 week T2: 5 weeks T3: 7.5 months	p<0.05; uncorrected	SUD at T1 vs. HC at T1 ↓ GM volume: frontal and parietal lobes, thalamus, and lenticular nucleus (in smokers + non-smokers) SUD at T2 vs. HC at T1 ↓ GM volume: frontal and parietal lobes, thalamus, and lenticular nucleus (in smokers + non-smokers) SUD at T3 vs. HC at T1 ↓ GM volume: frontal and parietal lobes, thalamus, and lenticular nucleus (in smokers + non-smokers)	HC NS SUD ↑ GM volume: frontal and parietal lobes and thalamus, and cerebellum (T2>T1)>(T3>T1) frontal, parietal, occipital lobes, thalamus, caudate, and cerebellum (T3>T2) frontal and parietal lobes, thalamus, and cerebellum (T2>T3>T1) ↑ WM volume: parietal, temporal, and occipital lobes (T2>T3)	
Zou et al. (2018)	T1 HC: n=17 SUD: n=65 T2 HC: N/A SUD: n=82 T3 HC: n=17 SUD: n=36	1.5T MRI: T1- weighted MPRAGE ROI (DLPFC, OFC, ACC, insula, amygdala, and hippocampus)	T1: 1 week T2: 7.5 months	p<0.023; modified Bonferroni correction	SUD at T1 vs. HC at T1 ↓ GM volume: DLPFC, ACC, insula (at trend level), and hippocampus SUD at T2 vs. HC at T1 ↓ GM volume: DLPFC, ACC, insula (at trend level), and hippocampus SUD at T3 vs. HC at T3 ↓ GM volume: hippocampus	HC NS SUD ↑ GM volume: DLPFC, OFC, insula, and hippocampus (T2>T1)>(T3>T1) DLPFC, OFC, ACC, insula, and hippocampus (T3>T2) DLPFC, OFC, and insula (T3>T2>>T1)	
Gazdzinski et al. (2005)	T1 HC: n=17 SUD: n=18 T2 HC: N/A SUD: n=23 T3 HC: n=17 SUD: n=7	1.5T MRI: T1- weighted MPRAGE Whole-brain	T1: 1 week T2: 1 month T3: 6–12 months for SUD; 2 years for HC	p<0.05; uncorrected	SUD at T1 vs. HC at T1 Not reported SUD at T2 vs. HC at T3 Not reported	HC NS SUD ↑ total GM volume (T1-T2<<T2<T3)	
Hefterbaum et al. (1995)	T1 HC: n=58 SUD: n=58 T2 HC: n=58 SUD: n=58 T3 HC: n=11 SUD: n=19	1.5T MRI: T1- weighted Spin Echo ROI (anterior and posterior cortical GM and WM volume, basal ganglia, thalamus, and subcortical WM)	T1: ~12 days T2: 1 month T3: up to 12 months (~130 days)	p<0.05; uncorrected	SUD at T1 vs. HC at T1 ↓ GM and WM volume: anterior and posterior cortical regions ↓ GM volume: thalamus SUD at T2 VS. HC at T2 ↓ GM and WM volume: anterior and posterior cortical regions ↓ GM volume: thalamus SUD at T3 vs. HC at T1 ↓ WM volume: anterior and posterior cortical regions	HC NS SUD ↑ GM volume: anterior cortical regions (at trend level) (T2>T1)	
DTI							
Gazdzinski et al. (2010)	T1 HC: n=22 SUD: n=36 (20smokers, 16 non-smokers) T2 HC: 22 SUD: n=21 (11smokers, 10 non-smokers)	1.5T MRI: DTI single-shot doubleechoed spincho echo-planar imaging sequence ROI (frontal, temporal, parietal and occipital white matter)	T1: ~4.5 days T2: 1 month (SUD) T2: 1 year (HC)	p<0.05; uncorrected	SUD at T1 vs. HC at T1 ↓ MD: frontal, temporal and parietal white matter in non-smokers ↑ MD: frontal white matter insmokers SUD at T2 vs. HC at T2 NS	HC NS SUD ↑ FA: temporal white matter ↑ MD: mean diffusivity in frontal, temporal, parietal, and occipital in non-smokers and ↑ WM volume in frontal and temporal lobes in smokers	
Althosoon et al. (2014)	T1 HC: n=15 SUD: n=15 T2 HC: n=15 SUD: n=15	1.5T MRI: DTI single-shot, stimulated-echo sequence with spiral acquisition ROI (genu and body of corpus collosum)	T1: 2 weeks T2: 1 year	p<0.05; uncorrected	SUD at T1 vs. HC at T1 ↓ FA & RD SUD at T2 vs. HC at T2 NS	HC NS SUD ↑ FA, ↓ RD: Genu and body of the corpus collosum	
Hefterbaum et al. (2014)	T1 HC: n=56 SUD: n=47 T2 HC: n=56 SUD: n=27	1.5T MRI: DTI single shot spincho, echo-planar diffusion-weighted sequence ROI: 27 ROIs (21 bilateral and 6 midline regions) were examined	T1: 47 weeks (mean) T2: 1–8 years (325.5 ± 391.9 weeks)	p<0.001; tice	SUD at T1 vs. HC at T1 Not reported SUD at T2 vs. HC at T2 ↓ FA	HC ↓ FA SUD ↑ FA: 20 out of 27 ROIs including corpus collosum, the fornix, corona radiata	
Cocaine							
GM							
Parvaz et al. (2016)	T1 HC: n=12 SUD: n=19 T2 HC: n=12 SUD: n=19	4T MRI: T1- weighted 3DMDEFT Whole-brain	T1: ~3 weeks T2: 6 months	p<0.005; uncorrected >50 contiguous voxels	SUD at T1 vs. HC at T1 Not reported SUD at T2 vs. HC at T2 Not reported	HC NS SUD ↑ GM volume: IFG, vmPFC, OFC	
Methamphetamine							
GM							
Buan et al. (2018)	T1 HC: n=27 SUD: n=19 T2 HC: N/A SUD: n=29	3T MRI: T1- weighted scan (sequence not reported) Whole-brain	T1: 6 months T2: 12 months	p<0.05 (FWE); >500 contiguous voxels	SUD at T1 vs. HC at T1 ↓ GM volume: precentral gyrus, fusiform gyrus, caudate, and cerebellum SUD at T2 vs. HC at T2 Not reported	HC N/A SUD ↑ GM volume: cerebellum ↓ GM volume: cingulate gyrus	
DTI							
Zhuang et al. (2016)	T1 HC: n=19 SUD: n=20 T2 HC: N/A SUD: n=19	3T MRI: single-shot EPI DWI Whole-brain + ROI (based on group differences)	T1: 6 months T2: 13 months	p<0.05; uncorrected	SUD at T1 vs. HC at T1 ↓ FA and ↑ RD : internal capsule and superior corona radiata ↑ MD: internal capsule SUD at T2 vs. HC at T1 Not reported	HC N/A SUD ↓ FA: internal capsule and superior corona radiata	
Heroin							
GM							
Wang et al. (2012b)	T1 HC: n=19 SUD: n=20 T2 HC: N/A SUD: n=20	1.5T MRI: T1- weighted scan (sequence not reported) Whole-brain	T1: 3 days T2: 1 month	p<0.001; uncorrected, >100 clusters	SUD at T1 vs. HC at T1 ↓ GM volume: superior and middle frontal gyrus, posterior cingulate, and inferior occipital gyrus SUD at T2 vs. HC at T1 ↓ GM volume: middle frontal gyrus, posterior cingulate, and inferior occipital gyrus	HC N/A SUD NS	
DTI							
Wang et al. (2013)	T1 HC: n=20 SUD: n=20 T2 HC: N/A SUD: n=20	1.5T MRI: DTI (sequence not reported) Whole-brain	T1: 3 days T2: 1 month	< 0.001; uncorrected, >15 voxels	SUD at T1 vs. HC at T1 ↓ FA: frontal gyrus and cingulate gyrus SUD at T2 vs. HC at T1 NS	HC N/A SUD NS	
(B) FUNCTIONAL STUDIES							
Study	Sample (at each time point)	Imaging Modality / Whole brain analysis or a priori ROI assessed	Task or Stim uli	Abstinence Length (at each scan)	Statistical Threshold for Longitudinal Changes	Crosssectional Results (SUD vs. HC)	Within-Group Longitudinal Changes
Alcohol							
Mon et al. (2009)	T1 HC: n=28 SUD: n=58 T2 HC: n=13 SUD: n=41 (22 cigarette smokers, 19 non-smokers)	Perfusion MRI (ASL): Frontal and Parietal GM	Rest: Eyes closed	T1: 6 days T2: 34 days	p<0.05	SUD at T1 vs. HC at T1 ↓ Cerebral blood flow: Frontal and parietal GM SUD at T2 vs. HC at T1 ↓ Cerebral blood flow: Parietal GM Non-smokers NS ↑ Cerebral blood flow: Frontal and parietal GM	HC NS SUD NS Non-smokers ↑ Cerebral blood flow: Frontal and parietal GM Smokers NS
Durazzo et al. (2010)	T1 HC: 28 SUD: n=57 T2 HC: N/A SUD: n=41 SUD labeled as Abs or Rel based on a 12 months clinical follow-up	Perfusion MRI (ASL): Frontal and parietal GM	N/A	T1: 7 ± 3 days T2: 35 ± 11 days	p<0.05	SUD-Abs at T1 vs. SUDRel at T1 vs. HC at T1 ↓ Cerebral blood flow in Rel compared to both Abs and HC: Frontal and parietal GM SUD-Abs at T2 vs. SUDRel at T2 vs. HC at T1 ↓ Cerebral blood flow in Rel compared to both Abs and HC: Frontal GM	HC N/A SUD NS
Colrain et al. (2012)	T1 HC: N/A SUD: n=15 T2 HC: N/A SUD: n=15	EEG (Sleep evoked potentials): FP1, FP2, Fz, FCz, Cz, CPz, Pz	Auditory stimuli	T1: 165 days T2: 394 days	p<0.05	N/A	HC N/A SUD ↑ N550 and ↑ P900 amplitudes: Frontal electrodes
Nicotine							
James et al. (2009)	T1 HC: N/A SUD: n=13 T2 HC: N/A SUD: n=13	Task fMRI: Whole-brain	Cue reactivity (smokingrelated versus neutral pictures)	T1: prequit T2: 52 ± 11 days	P<0.005	N/A	HC N/A SUD ↑ BOLD activation (smoking vs. neutral pictures): Frontal cortex (BA 5, 9, 44, 46), ACC (BA 24, 32), PCC (BA 31), temporal cortex (BA 22, 41, 42), parietal cortex (BA 1, 2, 4, 7, 40), and caudate. ↓ BOLD activation (smoking vs. neutral pictures): hippocampus
Cocaine							
Rajoldi et al. (2016)	T1 HC: n=28 SUD: n=29 T2 HC: n=28 SUD: n=29	Task fMRI: Whole-brain and ROI (VS)	MID task (reward and loss anticipation; N, reward and loss outcome)	T1: 2 months T2: 5 months	p< 0.05 (FWE)	N/A	HC ↓ BOLD activation (reward outcome): Ventromedial PFC extending to ACC SUD ↑ BOLD activation (reward anticipation): Precuneus, posterior cingulate extending to culmen, midbrain, thalamus extending to striatal regions
Moelet et al. (2012)	T1 HC: n=13 SUD: n=15 T2 HC: N/A SUD: n=15	Task fMRI: Whole brain	Drug Stroop task (drug and neutral words)	T1: ~3 weeks T2: 6 months	p<0.05 (cluster-corrected); >15 contiguous voxels	SUD at T1 vs. HC at T1 ↓ BOLD activation: Midbrain SUD at T2 vs. HC at T1 NS	HC N/A SUD ↑ BOLD activation: Midbrain and thalamus
Alger et al. (1998)	T1 HC: N/A SUD: n=17 T2 HC: N/A SUD: n=17 T3 HC: N/A SUD: n=17	Quantitative EEG: frontal absolute and relative power, asymmetry and coherence: delta frequency band	Rest: Eyes closed	T1: ~5–10 days (3.2±2.4 days) T2: 1 month T3: 6 months	p<0.05	N/A</	