Table 1. Summary of included PET studies from 1997-2022

Published PET Study	Drug Administered	Method of Analysis	Type of Imaging	Time Elapsed Between Drug and/or Placebo Administration and Scan	Principal Findings
Vollenweider et al (1997)	Psilocybin	ROIs chosen from Talairach coordinate system	^{18}F-FDG PET, an isotope of glucose	Baseline scan, then scan with radiotracer administered 90 minutes after drug ingestion, with a month between each session	Increase in cerebral glucose metabolism in frontomedial, frontotemporal, temporomedial and anterior cingulate cortices and thalamus. This demonstrates a hyper frontal pattern.

Vollenweider et al (1999)	Psilocybin	ROIs with high tracer activity in cerebellum and striatum	^{11}[C]-Raclopride PET, a D_2R antagonist	Radiotracer and scan administered 80 minutes after drug (and placebo) ingestion, with one month between each session	Binding decreased at D_2 receptor in striatum. Psilocybin has direct effect on endogenous dopamine release.
Gouzoulis-Mayfrank et al (1999)	Psilocybin	ROIs of whole brain	^{18}[F]-FDG PET, a glucose isotope Word activation task	Scans started 110-120 minutes after drug or placebo ingestion, repeated 2-4 weeks later with activation or control task	Increase in glucose metabolism at right frontotemporal regions and anterior cingulate cortex. Decrease in glucose metabolism in right thalamus and left precentral region.

Hasler et al (2009)	Psilocybin	Distribution volume in whole brain	^{18}[F]-Altanserin PET, a 5-HT_{2A}R antagonist	Radiotracer and scan administered 75 min after drug (and placebo) administration, with two weeks between each session	Psilocybin competed for receptor occupancy in frontomedial regions, the insula and anterior cingulate cortex.
Madsen et al (2019)	Psilocybin	Simplified reference tissue model and ROIs	^{11}[C]-Cimbi-36 PET, a 5-HT_{2A}R agonist	Scan started one hour after drug (and placebo) administration, with a week between each session	Dose-dependent occupancy of 5-HT_{2A} receptors in neocortex. High interindividual variability in dose response curves, correlated with psilocin concentration level.

[a]McCulloch et al (2022) *Data from Madsen et al. (2020)*	Psilocybin	Neocortical and cerebellar ROIs	^{11}[C]-Cimbi-36 PET, a 5-HT$_{2A}$R agonist	Scan at baseline and 1 week after drug administration	Change in binding of 5-HT$_{2A}$ receptor from baseline to one week after psilocybin reflective of resting state changes at 3 months in executive control network.
Sondegaard et al (2022)	Psilocybin	Linear regression model using ROI binding potentials	^{11}[C]-Cimbi-36 PET, a 5-HT$_{2A}$R agonist	Scan at baseline then for 120 min after tracer injected	Negative association between mindfulness at 3 months and right amygdala 5-HT$_{2A}$ receptor binding.

Notes: [a]This manuscript includes both PET and fMRI analyses in its experimental design. The word activation task (Gouzoulis-Mayfrank et al., 1999) involved a control task (repeating stimulus word) and activation task (associating one word to every stimulus) during the PET scan.

Table 2. Summary of included functional MRI studies from 2012-2023

Published fMRI Study	Drug Administered	Method of Analysis	Type of Imaging	Time Elapsed Between Drug and/or Placebo Administration and Scan	Principal Findings
Carhart-Harris et al (2012)	Psilocybin	Ventromedial PFC ROI	Resting-state fMRI Eyes closed	Scan started 6 min before drug (and placebo) administration, with one week between each session	Decreased coupling between posterior cingulate cortex and medial PFC, decreases in medial PFC, ventral posterior cingulate cortex, putamen and subthalamic nuclei. Reduced resting state functional connectivity in the

					anterior cingulate cortex and medial PFC.
Carhart-Harris et al (2013) *Data from Carhart-Harris et al (2012)*	Psilocybin	Independent component analysis of DMN	Resting-state fMRI Eyes closed	Scan started 6 min before drug (and placebo) administration, with one week between each session	Increased connectivity between DMN and task positive network, and between thalamus and task positive network.
Tagliazucchi et al (2014) *Data from Carhart-Harris et al (2012)*	Psilocybin	Voxel-wise distribution	Resting-state fMRI Eyes closed	Scan started 6 min before drug (and placebo) administration, with one week between each session	Increased signaling variation in hippocampi and anterior cingulate cortex. Decrease signaling in executive control and attention network.

Kraehenmann et al (2014)	Psilocybin	General linear model and ROIs of amygdala	Task-based fMRI Amygdala reactivity task	Scans started 70 to 90 min after drug (and placebo) administration, with two weeks between each session	Decrease in right amygdala activation after exposure to negative and neutral facial expressions.
Roseman et al (2014) *Data from Carhart-Harris et al (2012)*	Psilocybin	Independent component analysis of whole brain	Resting-state fMRI Eyes closed	Scan started 6 min before drug (and placebo) administration, with one week between each session	Decreased coupling between visual and sensorimotor network. Increased coupling between network resting state networks.

Kraehenmann et al (2015) *Data from Kraehenmann et al (2014)*	Psilocybin	Dynamic causal modeling and network ROIs	Task-based fMRI Amygdala reactivity task	Scans started 70 to 90 min after drug (and placebo) administration, with two weeks between each session	Decreased connectivity between amygdala and primary visual cortex (area V1), preventing processing of negative visual stimulus.
Lebedev et al (2015)	Psilocybin	Clustering coefficients of whole brain ROIs	Resting-state fMRI Eyes closed	Scan started 6 minutes before drug (and placebo) administration	Decreased FC between medial temporal lobe and parietal lobes. Decreased integrity of salience network and inter-hemispheric connectivity. These decreases corresponded to ego-dissolution.

Preller et al (2016)	Psilocybin	Small-volume correction of ROIs	Task-based fMRI Cyberball task	Scan and task started 75 min after drug administration	Decreased neural response in the dorsal anterior cingulate cortex and middle frontal gyrus.
Carhart-Harris et al (2016)	LSD	Seed-based analysis and independent component analysis	Resting-state fMRI Eyes closed	Scan performed 70 min after drug (and placebo) administration with two weeks between each session	Increased resting-state FC between primary visual cortex and (sub)cortical regions, between parahippocampus and dorsal medial PFC, between ventromedial PFC, caudate and inferior frontal gyrus. Decreased resting-state FC between parahippocampus and retrosplenial cortex and posterior cingulate cortex.

Tagliazucchi et al (2016) *Data from Carhart-Harris et al (2016)*	LSD	Functional connectivity density of ROIs	Resting-state fMRI Eyes closed	Scan performed 70 min after drug (and placebo) administration with two weeks between each session	Increased global connections between thalamus and primary sensory cortex. Increased coupling between association and sensory networks. Increased global FC in areas with high 5-HT_{2A} receptor density.
Müller et al (2017)	LSD	ROI-to-ROI and ROI-to-voxel of whole brain	Resting-state fMRI Eyes closed	Scan started 2.5h after drug (and placebo) administration, with a week between each session	Increased functional connectivity between thalamus, right fusiform gyrus and insula. Overall increased connectivity of thalamus and striatum.

					Explains intense sensory and visual effects.
Mueller et al (2017)	LSD	ROI-based voxel clusters	Task-based fMRI Facial expression task	Scan started 2.5h after drug or placebo administration, with one week between each session	Decreased response in left amygdala and right medial PFC during fearful faces (fear stimulus). Increased subjective effects linked to decreased amygdala response.
Grimm et al (2018) *Data from Kraehenmann et al (2014)*	Psilocybin	Seed-to-voxel connectivity	Task-based fMRI Amygdala reactivity task	Scans started 70 to 90 min after drug or placebo administration, with two weeks between each session	Decreased connectivity between right amygdala and left striatum (angry face) and between amygdala and frontal pole decreased.

Preller et al (2018)	LSD	ROI-to-ROI global brain connectivity	Resting-state fMRI Eyes closed	Scan started 75 and 300 min after drug or placebo administration	Increased connectivity from thalamus to posterior cingulate cortex. Decreased connectivity from ventral striatum to thalamus. Both dependent on 5-HT_{2A} receptor activation.
Barrett et al (2020)	Psilocybin	Independent component analysis of claustrum	Resting-state fMRI Eyes closed	Scans started 90 min after drug (and placebo) administration, both on same day	Decreased connectivity between right claustrum and DMN. Increased connectivity of right claustrum-fronto-parietal task network. Decreased connectivity of left claustrum-fronto-parietal task network.

					Significant effect of 5-HT_{2A} receptor signaling on claustrum function.
Barrett et al (2020)	Psilocybin	ROI analysis of amygdala, anterior cingulate cortex	Resting-state and task-based fMRI Emotion conflict, recognition, and discrimination task	First scan one day before drug administration then follow-up scans one week and one month after	Decreased emotional response in left anterior cingulate cortex, right and left amygdala up to one month later.
Bershad et al (2020)	LSD	Seed based ROI of amygdala	Resting-state fMRI	Scans started 90 min after drug (and placebo) administration, with one week	Decreased connectivity from amygdala and bilateral postcentral gyrus and superior temporal gyrus. Increased connections from amygdala to right angular

				between each session	gyrus, middle frontal gyrus and cerebellum. Increased connectivity of thalamus to cerebellum.
Preller et al (2020)	Psilocybin	Voxel-based global brain connectivity	Resting-state fMRI Eyes closed	Scans started 20, 40, and 70 min after drug (and placebo) administration, with two weeks between each session	Reduction in connectivity at associative regions. Increase in connectivity at sensory regions. 5-HT_{1A}R expressed baseline readout indicates response.
Mason et al (2020)	Psilocybin	Independent component analysis of	Resting-state fMRI Eyes open, focused on cross	Scan started 102 min after drug or placebo administration	Overall increase of between-network functional connectivity. Increased connectivity between the

		resting-state networks			DMN and the frontoparietal network and salience networks.
Madsen et al (2021)	Psilocybin	Region-based network pairs	Resting-state fMRI Eyes closed	Baseline scan performed, then 40, 80, 130, 300 min after drug administration	5-HT_{2A} receptor agonism induces desynchrony of executive control and attention networks, that connect to other networks in the brain. Plasma psilocin level negatively correlated with level of network integrity.
[a]McCulloch et al (2022)	Psilocybin	ROI network	Resting-state fMRI Eyes closed	First scan at baseline, then 1 week and 3 months after drug administration	Decrease in executive control network FC at 1 week reflective of subjective personality changes at 3 months.

Gaddis et al (2022)	Psilocybin	Independent component analysis of thalamus	Resting-state fMRI Eyes closed	First scan at baseline, second scan 2-4 months later, starting 90 min after drug (and placebo) administration	Overall decrease in connectivity between thalamocortical pathway and visual and default mode networks.
Avram et al (2022) *Data from Holze et al (2020)*	LSD	Seed-based correlation analysis of thalamus	Resting-state fMRI Eyes closed	Scan began 2.5 hours after drug or placebo administration	Increased thalamic self-inhibition between left auditory cortex and right lingual cortex and connectivity between right lingual gyrus and thalamus. Decreased self-inhibition in right postcentral cortex.

					Decreased effective connectivity between left auditory cortex, right postcentral cortex and thalamus.
Moujaes et al (2023) *Data from Preller et al (2018)*	LSD	ROI-to-ROI connectivity matrices	Resting-state fMRI Eyes closed	Scan started 75 and 300 min after drug or placebo administration	Increased connectivity in frontoparietal, somato-motor, right lingual, primary visual and dorsal attention networks, and inferior temporal gyrus. Decreased connectivity in salience, auditory and default mode networks and inferior temporal gyrus.

Moujaes et al (2023) *Data from Preller et al (2020)*	Psilocybin	Voxel-based global brain connectivity	Resting-state fMRI Eyes closed	Scans began 20, 40, 70 min after drug (and placebo) administration, with two weeks between each session	Increased FC between dorsal attention, primary visual and auditory networks, superior lateral occipital cortex and superior temporal gyrus. Decreased connectivity in DMN, frontoparietal network, superior temporal gyrus, auditory, salience networks and cerebellum and primary and secondary visual networks.
Pizzi et al (2023) *Data from Carhart-Harris et al (2016)*	LSD	Voxel-based z scores of intrinsic connectivity	Resting-state fMRI Eyes closed	Scan began 2 hours after drug (and placebo) administration, at	Increased FC in DMN and attention networks that correspond to high density of 5-HT_{2A} receptors.

				least two weeks between each session	Decreased FC in limbic regions that correspond to high density of 5-HT_{1A} receptors.
Bedford et al (2023) *Data from Müller et al (2018), Dolder et al (2016)*	LSD	Whole brain network of all ROIs	Resting-state fMRI Eyes closed	Scan started 121-200 min after drug (and placebo) administration, one week apart	Increased interregional connectivity and reduced local connectivity in occipital and subcortical regions. Direction of connectivity was changed upon drug administration.
Timmermann et al (2023)	DMT	Voxel-based connectivity matrix	Resting-state fMRI Eyes closed	Scan starts 8 minutes prior to drug (and placebo) administration, with two weeks	Decreased integrity of connections within global and language-associated networks. Decreased segregation in frontoparietal, salience and default mode networks.

		between each session	Increase in global FC in frontoparietal, salience, default mode networks. Hyper-connectivity of association pole and overall global FC increase.

Notes: [a]This manuscript includes both PET and fMRI analyses in its experimental design. The amygdala reactivity task (Kraehenmann et al., 2014, 2015) involves exposing the participant to a negative or neutral picture and having them select from two others, the image that best matches. The Cyberball task (Preller et al., 2016) involves the participant playing a video game that models social exclusion. The facial expression task (Mueller et al., 2017) involves exposing the participant to 10 different facial affects that demonstrate 50 or 100% fearful or neutral expression, and having the participant categorize the faces by gender. The amygdala reactivity task (Grimm et al., 2018) involves asking the participant to categorize an angry, happy, or neutral expression as 'emotional' or 'neutral' as quickly as possible. The emotional tasks (Barrett et al., 2020) involve matching one of two images at the bottom of a screen to a fearful or angry image in the center, identifying happy, sad, fearful, angry or neutral facial expressions, and identifying valence of facial expressions with emotional words. LSD= lysergic acid diethylamide; DMT= N, N-Dimethyltryptamine; DMN: default mode network; PFC= prefrontal cortex; FC= functional connectivity.

Table 3. Summary of Study Design, Drug Information and Demographics in PET Studies

Published PET Study	Psychedelic Administered	Study Design	Total N Female N	Dose Amount (mg/kg)	Method of Administration (IV, Oral)	Psychedelic-naïve/ Handedness
Vollenweider et al (1997)	Psilocybin	Open label without control group	N=10 Female N=2	15-20mg	oral	Treatment-naïve status not provided/ Handedness not considered
Vollenweider et al (1999)	Psilocybin	Randomized, single-blind, placebo-controlled cross over	N=7 Female N=0	0.25mg/kg	oral	Treatment-naïve status not provided/ Handedness not considered

Gouzoulis-Mayfrank et al (1999)	Psilocybin	Randomized, double-blind, placebo-controlled, cross over	N=32 Female N=11	0.2mg/kg	oral	Treatment-naïve status not provided/ Handedness not considered
Hasler et al (2009)	Psilocybin	Within-subjects, placebo-controlled	N=11 Female N=0	215µg/kg	oral	Treatment-naïve status not provided/ Handedness not considered
Madsen et al (2019)	Psilocybin	Single-blinded	N=8 Female N=3	3-30mg	oral	Not naïve/ Handedness not considered
[a]McCulloch et al (2021)	Psilocybin	Single-blinded	N=10 Female N=4	0.2-0.3mg/kg	oral	Naïve/ Handedness not considered

Sondergaard et al (2022)	Psilocybin	Randomized, double-blind placebo-controlled design	N=32 [b]Female N=17	0.21mg/kg or 0.31mg/kg	oral	Treatment-naïve status not provided/ Handedness not considered

Notes: [a]This manuscript includes both PET and fMRI analyses in its experimental design. [b]This value is taken from total psilocybin interventions, N=46. Mostly naïve: some participants had previous use of psychedelics, creating a mix of naïve and non-naïve individuals; Not naïve: participants had previous use of psychedelics, but not within three months of study date.

Table 4. Summary of Study Design, Drug Information and Demographics in fMRI Studies

Published fMRI Study	Psychedelic Administered	Study Design	Total N Female N	Dose Amount (mg/kg, mg, or µg)	Method of Administration (IV, Oral)	Psychedelic-naïve/ Handedness
Carhart-Harris et al (2012)	Psilocybin	Within-subjects placebo-controlled	N=15 Female N=2	2mg	IV	Not naïve/ Handedness not considered
Carhart-Harris et al (2013)	Psilocybin	Within-subjects placebo-controlled	N=15 Female N=2	2mg	IV	Not naïve/ Handedness not considered
Tagliazucchi et al (2014)	Psilocybin	Within-subjects placebo-controlled	N=15 Female N=2	2mg	IV	Not naïve/ Handedness not considered

Kraehenmann et al (2014)	Psilocybin	Randomized, double-blind, placebo-controlled, cross over	N= 25 Female N=9	0.16mg/kg	oral	Mostly naïve/ Right-handed
Roseman et al (2014)	Psilocybin	Within-subjects placebo-controlled	N=15 Female N=2	2mg	IV	Not naïve/ Handedness not considered
Kraehenmann et al (2015)	Psilocybin	Randomized, double-blind, placebo-controlled, cross over	N= 25 Female N=9	0.16mg/kg	oral	Mostly naïve/ Right-handed
Lebedev et al (2015)	Psilocybin	Within-subjects, counterbalanced-order, placebo-controlled	N= 15 Female N=2	2mg	IV	Not naïve/ Handedness not considered
Preller et al (2016)	Psilocybin	Randomized, double-blind counterbalanced cross-over	N=21 Female N=9	0.215mg/kg	oral	Treatment-naïve status not provided/ Right-handed

Carhart-Harris et al (2016)	LSD	Within-subjects, placebo-controlled counterbalanced	N=15 Female N=4	75µg	IV	Not naïve/ Handedness not considered
Tagliazucchi et al (2016)	LSD	Within-subjects, placebo-controlled counterbalanced	N=15 Female N=4	75µg	IV	Not naïve/ Handedness not considered
Müller et al (2017)	LSD	Randomized, placebo-controlled, double-blind crossover design with placebo	N=20 Female N=10	100µg	oral	Mostly naïve/ Right-handed
Mueller et al (2017)	LSD	Randomized, placebo-controlled, double-blind crossover design with placebo	N=20 Female N=11	100µg	oral	Mostly naïve/ Right-handed

Grimm et al (2018)	Psilocybin	Randomized, double-blind placebo-controlled design	N=18 Female N=6	0.16mg/kg	oral	Mostly naïve/ Right-handed
Preller et al (2018)	LSD	Double-blinded, randomized, crossover design, placebo-controlled	N=24 Female N=5	100µg	oral	Mostly naïve/ Right-handed
Barrett et al (2020)	Psilocybin	Single-blinded, placebo-controlled	N=15 Female N=5	10mg/70kg	oral	Not naïve/ Handedness not considered
Barrett et al (2020)	Psilocybin	Open-label, within-subjects, longitudinal	N=12 Female N=7	25mg/70kg	oral	Not naïve/ Right-handed
Bershad et al (2020)	LSD	Within-subject, double-blind design with placebo	N=20 Female N=10	13µg	oral	Not naïve/ Right-handed

Preller et al (2020)	Psilocybin	Double-blinded, randomized, placebo-controlled crossover design	N=23 Female N=11	0.2mg/kg	oral	Mostly naïve/ Handedness not considered
Mason et al (2020)	Psilocybin	Double-blind, placebo-controlled, parallel-group design	N=60 Female N=25	0.17mg/kg	oral	Not naïve/ Handedness not considered
Madsen et al (2021)	Psilocybin	Single-blind design with placebo	N=15 Female N=6	0.2mg/kg (N=4) 0.3mg/kg (N=11)	oral	Mostly naïve/ Handedness not considered
[a]McCulloch et al (2021)	Psilocybin	Within-subjects, single-blinded	N=10 Female N=4	0.2mg/kg (N=4) 0.3mg/kg (N=6)	oral	Naïve/ Handedness not considered

Gaddis et al (2022)	Psilocybin	Randomized, double-blind placebo-controlled design	N=18 Female N=5	10mg/70kg	oral	Mostly naïve/ Handedness not considered
Avram et al (2023)	LSD	Double-blind placebo-controlled crossover design	N=25 Female N=12	100µg	oral	Mostly naïve/ Handedness not considered
Moujaes et al (2023)	LSD	Randomized, placebo-controlled, double-blind crossover design with placebo	N=24 Female N=6	100µg	oral	Mostly naïve/ Right-handed
Moujaes et al (2023)	Psilocybin	Double-blinded, randomized, placebo-controlled crossover design	N=23 Female N=10	0.2mg/kg	oral	Mostly naïve/ Handedness not considered
Pizzi et al (2023)	LSD	Randomized, placebo-controlled, double-	N=15	75µg	IV	Mostly naïve/ Right-handed

		blind crossover design with placebo	Female N=4			
Bedford et al (2023)	LSD	Randomized, placebo-controlled, double-blind crossover design	N=45 Female N=23	100µg	oral	Mostly naïve/ Handedness not considered
Timmermann et al (2023)	DMT	Single-blind, placebo-controlled, counter-balanced design	N=20 Female N=7	20mg	IV	Not naïve/ Handedness not considered

Notes: [a]This manuscript includes both PET and fMRI analyses in its experimental design. LSD: lysergic acid diethylamide; DMT: N,N-dimethyltryptamine; IV: intravenous; Mostly naïve: some participants had previous use of psychedelics, creating a mix of naïve and non-naïve individuals; Not naïve: participants had previous use of psychedelics, but not within three months of study date.