

Title: A research domain criteria (RDoC)-guided dashboard to review psilocybin target domains: a systematic review

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Table S3. The RDoC-motivated grid for Psilocybin effects on RDoC domains

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
1	Varley et al. 2020[1] Turton et al., 2014[2] Roseaman et al., 2014[3] Tagliazucchi et al., 2013[4] Carhart-Harris et al., 2013 [5] <i>Parent study:</i> Robin L. Carhart-Harris et al., 2012[6]	Single-blind placebo-controlled study; the two sessions were separated by at least 7 days. Behavioral scans (autobiographical memory) started 7.5 min after infusion; the modified version of the 5D-ASC was taken prior to drug administration and 5- and 12-min post-infusion. Subjects underwent an anatomical MRI scan followed by two task-free functional MRI scans. Placebo and psilocybin were administered respectively in the first and the second task-free scans.	Psilocybin 2mg IV	15 volunteers with previous psychedelic use experience (10 men, 5 women) Mean age: 34.1±8.2 y/o	*5D-ASC (modified version with visual analogue scale (VAS)) ^a: psilocybin increased ^{se} the “sense of joy”.	*5D-ASC (modified version with visual analogue scale (VAS)) ^a: Psilocybin altered following scales related to NVS - o Increased ^{sif} “Fear of losing control”. - o Did not alter ^{ns} “I felt afraid” and “I felt suspicious and paranoid”	*5D-ASC (modified version with visual analogue scale (VAS)): Psilocybin altered ^{sa} the following items related to the cognitive systems: - o Sense of size /space - o Sense of time - o Perceptions: including visual, auditory perception and experiencing synesthesia *Participants described a sense of physical sensation ^{sa} including tingling, warmth, rushing, and altered proprioception. *Resting state networks: psilocybin altered ^{sa} the following parameters: - o Psilocybin increased within network functional connectivity in a number of network hubs related to cognitive domain ^a including: • Anteriorly loaded default mode network (aDMN) and Auditory network • aDMN and Dorsal attentional network • Visual and somatosensory networks • Etc (for more information please refer to Roseman et al. 2014[3]) - o Psilocybin increased the fractal dimension (a measure of signal diversity) of the BOLD time-series in the dorsal-attention network. - o Psilocybin altered spectral behavior (spectral scaling exponents) in dorsal attention and executive control networks.	*5D-ASC (modified version with visual analogue scale (VAS)) ^a: Psilocybin altered ^{sas} “sense of self” and “melting into the surroundings”		

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2	Smigielski et al., 2020[7]	Double blind, Placebo-controlled cross over design; two weeks between the two sessions. 5D-ASC was completed retrospectively 350-min post-intervention, verbal self-monitoring task using EEG was performed 75-min post-administration.	Psilocybin 0.230 mg /kg	17 healthy volunteers (9 men and 8 women) Mean age: 25.1 ±4.1 y/o	*5D-ASC: Psilocybin increased ^{se} item “blissful state”.	*5D-ASC: psilocybin had no effect ^{NS} on item “anxiety”.	*5D-ASC: Psilocybin increased ^{sa} following items related to the cognitive systems: o Complex imagery o Elementary imagery o Audiovisual synesthesia o Changed meaning of percepts	P300 to self-stimuli: the following measurements in p300 time frame indicate blunted self-processing ^{sas} : o Lower Euclidean distance (more similarities) between “self” and “other” datasets using multi-dimensional scaling (MDS) analysis o Topographical analysis of covariance (TANCOVA[8]) showed significant effects for “feeling of unity” from 5D-ASC (see below) during p300 time frame. o Psilocybin caused a lower cortical source density (CSDs) in supragenual anterior cingulate and right insular cortex *Self-monitoring task performance: Psilocybin disrupted ^{sas} differentiation of “self” voice from “others” voice. *5D-ASC: Psilocybin increased ^{sas} following items of 5D-ASC related to the social processes (perception and understanding of self): o Disembodiment o Experience of unity		
3	Preller et al. 2020 [9]	Randomized, double blind, placebo-controlled within subject cross over design; two weeks between the two sessions. 5D-ASC was completed retrospectively 360-	Psilocybin 0.2 mg/kg	23 healthy volunteers (12 men and 11 women) Mean age: 26.3±? y/o	*5D-ASC: Psilocybin increased ^{se} item “blissful state”.	* 5D-ASC: Psilocybin increased ^{sif} item “anxiety”	*5D-ASC: Psilocybin increased ^{sa} following items of 5D-ASC related to the cognitive systems: o Complex imagery o Elementary imagery o Audiovisual synesthesia o Changed meaning of percepts	*5D-ASC: Psilocybin increased ^{sas} following items of 5D-ASC related to the social processes (perception and understanding of self): o Disembodiment o Experience of unity		

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		min post-intervention. A short version of 5D-ASC was completed right after each resting-state brain scan, 20-, 40- and 70-min post-administration.					*Resting-state functional connectivity: psilocybin induced a time-dependent hyperconnectivity ^{sa} in the sensory network, especially in the bilateral occipital regions. The hyperconnectivity in the sensory regions was negatively associated ^m with the psilocybin-induced and baseline hypoconnectivity in the associative networks. i.e., strongest coupling in the sensory networks had strongest decoupling in the associative networks, and the lowest values in the hyperconnectivity areas had highest decoupling in the hypoconnected regions			
4	Mertens et al. 2020 [10] Stroud et al., 2018[11] Lyons & Carhart-Harris, 2018[12] Carhart-Harris et al., 2018 [13] (Roseman et al., 2018)[14] <i>Parent study:</i> Carhart-Harris et al., 2016 [15]	Open-label feasibility study to investigate short and long-term effect of two doses of psilocybin on treatment-resistant depression. Low and high dose of psilocybin were administered in the first and second session respectively. The two study sessions were separated by 7 days. SHAPS was assessed at baseline, 1-wk and 3-month post-intervention. STAI-trait was measured at baseline, 1-wk, 3-months and 6 months post-intervention. Prediction Of Future Life Events task (POFLE)[16] was performed at baseline and at 1-wk post-intervention. fMRI acquisition with emotional face paradigm took place at baseline and the day after the high-dose session. BDI and ruminative thinking	Psilocybin: Low dose: 10 mg High dose: 20 mg	20 patients with TRD (14 men and 6 women) Mean age: 44.1±11.0 y/o For the study of Stroud et al., 19 TRD patients (13 men and 6 women) Mean age: 44.7 ± 10.9; 16 healthy controls (11 men, 5 women) Mean age: 32.0±10.4 y/o <i>*NOTE the data of a subset of the participants were used for each of the included analysis. For more information, please refer to the study of interest.</i>	*SHAPS: psilocybin reduced^{le} the total score, 1 week, and 3 months post-intervention. This was interpreted as an improvement in anhedonia. *POFLE: Psilocybin significantly increased the accuracy of predicting life events and decreased pessimism bias^{le}. This decrease was markedly associated^{le} with decreases in depressive symptoms as measured by Beck's depression inventory (BDI)	STAI-trait: Psilocybin decreased STAI-trait scores at 1-wk, 3 months, and 6 months^{ldt} after administration		*Emotional faces task (happy, fearful, neutral): ○ Psilocybin decreased the reaction time (RT) to all emotional stimuli only in patients both post-treatment^{sasc} and in 1- month follow-up^{lasc}. ○ The reaction time was positively correlated^m with SHAPS scores i.e., faster RT ~lower SHAPS or improvement in anhedonia at both post-treatment and follow-up. ○ Psilocybin use was associated with following alterations^{sasc} in the resting-state networks: • Increased the functional connectivity between amygdala and visual areas^a during happy		

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		was measured at baseline and 1wk post-treatment.						and neutral face processing. • Increased the responses to fearful and happy faces in the right amygdala post-treatment. • There was a correlation^m between the increased amygdala reactivity to fearful faces and clinical improvements (as measured by BDI, QIDS) at 1-wk follow-up. • Increased the functional connectivity between vmPFC and areas ^a in left occipital and parietal lobes during face processing. These connectivity changes had a negative correlation^m with BDI score changes 1-wk post-treatment. • Decreased the functional connectivity between vmPFC and right amygdala during fearful and neutral face processing. Absolute connectivity between these		

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								areas had a positive association ^m with rumination scores 1-wk post-treatment.		
5	(Mason et al., 2020)[17]	Double-blind placebo-controlled parallel group design. Structural MRI were acquired (50 min post treatment), single-voxel proton MRS in the mPFC (65 min-post) and hippocampus (95 min-post), and resting state fMRI (102-min) post-administration. 5D-ASC and ego-dissolution inventory (EDI) were completed retrospectively 360-min post-administration.	Psilocybin 0.170 mg /kg	60 healthy volunteers (35 men and 25 women) with previous psychedelic use experience (not in the 3 months prior to the study) Mean age: Psilocybin group: 22.73± 2.9 y/o Placebo group: 23.20± 3.65 y/o	*5D-ASC: Psilocybin increased ^{se} item “blissful state”.	* 5D-ASC: Psilocybin increased ^{sif} item “anxiety”.	*5D-ASC: Psilocybin increased ^{sa} following items related to cognitive domain: o Visual restructuralization o Auditory alteration *Resting state networks: Psilocybin decreased ^{sa} within network functional connectivity in the following networks related to the cognitive systems: o Auditory network o Visual networks 1 & 2 ^a *5D-ASC: Psilocybin increased ^{sa} following items of 5D-ASC related to the cognitive systems: o Complex imagery o Elementary imagery o Audiovisual synesthesia o Changed meaning of percepts	*5D-ASC: Psilocybin increased ^{sas} following items of 5D-ASC related to the social processes (perception and understanding of self): o Disembodiment o Experience of unity *MRS ^a : results showed that lower and higher levels of glutamate in hippocampus are respectively associated ^m with higher scores in positive ego dissolution, and anxious ego dissolution subscales from 5D-ASC questionnaire (<i>this item can also be categorized in the PVS domain</i>). *EDI: compared to placebo, psilocybin significantly increased EDI ^{sas} scores.		
6	(Lewis et al., 2020)[18]	Randomized double-blind placebo-controlled study; at least 10 days between sessions; MRI acquisition took place 60-min post-administration	Psilocybin High dose: 0.215 mg /kg Low dose: 0.160 mg /kg	55 healthy volunteers (33 men, 22 women) 25.00 ±3.96 y/o	*MRI structural analysis ^a show a positive association ^m between item “blissfulness” from 5D-ASC questionnaire and the thickness of right rostral anterior cingulate cortex (rACC).			*MRI structural analysis ^a show a positive association ^m between item “unity” from 5D-ASC questionnaire and the thickness of rACC.		

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7	(Dudysová et al., 2020)[19] (Bravermanová et al., 2018)[20]	Double blind, Placebo-controlled cross over design; P300 and MMN paradigms were performed 100- and 125-min post-administration respectively. Polysomnography was performed 12h post-administration. APZ and HRS were completed 360-min post-administration.	Psilocybin 15-22 mg dose range	20 healthy (10 men, 10 women) Mean age 36.0 ± 8.1 y/o			P300: Psilocybin decreased ^{sa} P300 amplitude (auditory oddball task). This decrease was positively associated with the intensity of psychedelic state as measured by HRS questionnaire. Psilocybin had no effect ^{ns} on P300 latency. MMN: (single deviant auditory paradigm) Psilocybin did not affect ^{ns} MMN amplitude (known for early perceptual processing). N100: Psilocybin decreased ^{sa} N100 amplitude. *HRS: Psilocybin increased ^{sa} following subscale related to the cognitive systems: - o Cognition; This item was negatively associated ^m with P300 amplitude - o Perception - o Somaesthesia *APZ (revised version only containing three subscales): Psilocybin increased ^{sa} following items related to the cognitive systems: - o Visionary restructuralization; This item was negatively associated ^m with P300 amplitude	*HRS: Psilocybin increased “Volition” ^{sas} .	REM sleep: Psilocybin significantly prolonged ^{ssw} REM sleep latency and decreased REM duration (trending non-significant). Slow-wave activity (SWA): Psilocybin suppressed ^{ssw} SWA in the first sleep cycle. NREM: Psilocybin did not change ^{ns} NREM. Subjective sleep measures: psilocybin did not ^{ns} affect subjective total sleep time and sleep quality.	
8	(Carbonaro et al., 2020)[21] (Carbonaro et al., 2018)[22] <i>Parent study:</i> (Barrett et al., 2018)[23]	Double blind, placebo-controlled within subject, cross over within-subject design; comparison with dextromethorphan and inert placebo. 48h-1-wk interval between sessions. Participant rating scales were measured before and 60-, 120-, 180-, 240-, 300-, 360- and 480-min after capsule ingestion. Monitor rating scales were taken 10 min	Psilocybin 10, 20, 30 mg/70 kg Dextromethorphan (NMDA receptor antagonist, non-selective serotonin reuptake inhibitor and sigma-1 receptor agonist) 400mg/70kg	20 healthy with history of hallucinogen use Mean age: 28.5 ± ? y/o	*Monitor rating scale ^a: compared to dextromethorphan ^m (at 30 mg/kg) and placebo (all doses), psilocybin increased ^{se} item “joy/intense happiness” post-intervention. *5D-ASC: compared to dextromethorphan ^m (at 30 mg/kg) and placebo (all doses) ^m, psilocybin increased ^{se} item “blissful state”	* 5D-ASC: at 20 and 30 mg/70 kg, psilocybin increased ^{sif} item “anxiety” as measured retrospectively 7hrs post-intervention. *Monitor rating questionnaire ^a: There were no significant differences ^{ns} between psilocybin and placebo in “anxiety or fearfulness”. *Challenging Experience Questionnaire:	*5D-ASC: Compared to placebo, psilocybin increased ^{sa} following items of 5D-ASC questionnaire related to the cognitive systems as measured retrospectively 7hrs post-intervention: - o Complex imagery (all doses); significantly higher ^m than dextromethorphan at 20 and 30 mg/70 kg - o Elementary imagery (all doses) - o Changed meaning of percepts (all doses) - o Audiovisual synesthesia percepts (all doses) *HRS: Compared to placebo (all <u>doses</u>), psilocybin increased ^{sa} the following	*5D-ASC: Compared to placebo and dextromethorphan ^m, at 20 and 30 mg/70 kg, psilocybin significantly increased ^{sas} following items related to the social processes (perception and understanding of self), retrospectively 7hrs post-intervention: o Disembodiment; higher than placebo at 20 and 30 mg/70 kg and lower ^m than dextromethorphan at all doses.	*Monitor rating questionnaire ^a: - o There were no differences ^{ns} between Psilocybin and placebo in “Unresponsiveness to questions”. - o Psilocybin did not affect ^{ns} “drowsiness	*Psychomotor performance using the motor praxis task: psilocybin retarded ^{sim} the performance at doses 20 and 30 mg/kg.

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		before and 30-, 60-, 90-, 120-, 180-, 240-, 300-, and 360-min after intervention. 5D-ASC, HRS, and MEQ30 were completed 7hrs and 1-week post-administration. N-back test and word encoding were performed 3h post-administration and word recall was measured approximately 6h post-administration. Digit symbol substitution task (DSST) was taken at baseline, 2h and 4h post-intervention. Mini-mental status examination (MMSE) and Penn line orientation test (PLOT) were taken at 2h and 4h post-intervention respectively.			as measured retrospectively 7hrs post-intervention. *MEQ30: compared to dextromethorphan (at 20 and 30 mg/ 70 kg) ^m and placebo, (at all doses), <u>psilocybin increased</u> ^{se} “deeply felt positive mood” as measured retrospectively 7hrs post-intervention. *Classic drug abuse liability measures: Psilocybin increased ^{se} “euphoria” as measured retrospectively on the study day and 1-wk post-intervention. The scores were significantly higher ^m than that of dextromethorphan at 30mg/70 kg. *Participants’ ratings ^{a:} compared to placebo all doses of Psilocybin increased positive mood as measured by the relevant items (except for item “happy which was only increased at 20 and 30 mg/70kg) from the following questionnaires (as measured retrospectively on the study day and 1-wk post-intervention) - o 5D-ASC ^{se} - o SOCQ ^{se}	Compared to placebo, psilocybin increased ^{sif} “fear” and grief ^{sif}.	items related to the cognitive systems as measured 7hrs post-intervention: - o Cognition; higher than dextromethorphan at 20 and 30 mg/70 kg ^m. - o Perception; higher than dextromethorphan at 20 and 30 mg/70 kg ^m. - o Somaesthesia; lower ^m than dextromethorphan at 10 mg/70 kg. *MEQ30: Compared to placebo, <u>all doses of psilocybin increased</u> ^{sa} “transcendence of time and space” as measured retrospectively 7hrs after administration. At 10 mg/70 kg, psilocybin group had lower scores ^m than dextromethorphan. *Participants’ ratings ^{a:} - o During-session assessments: all doses of psilocybin increased ^{sa} “timelessness” and “visual effects” compared to placebo. Compared to dextromethorphan, psilocybin scores were lower ^m at 10 mg/70 kg for item “timelessness” and higher ^m at 20 and 30 mg/70 kg for item “visual effects”. - o Assessed retrospectively 7hrs post-intervention: compared to placebo, psilocybin increased ^{sa} “visual effects”. The scores were significantly higher ^m than dextromethorphan at 20 and 30 mg/70 kg. Executive functions: - o MMSE: psilocybin had no effect ^{NS} on this scale. - o DSST: At all doses, psilocybin administration led ^{si} to • Increased number of attempted trials • Reduced accuracy • Reduced substitution recall Memory outcome measures:	o Experience of unity; higher than placebo at all doses and higher than dextromethorphan at 30 mg/70kg ^m. *HRS: compared to placebo at 20 and 30 mg/70 kg, psilocybin increased “volition” ^{sas}, as measured retrospectively 7hrs post-intervention. At 10mg/70 kg, psilocybin group had lower scores than dextromethorphan. *Participants’ ratings ^{a:} all doses of psilocybin increased ^{sas} “Fusion of personal self into a larger whole” compared to placebo. Compared to dextromethorphan, psilocybin scores were lower at 10 mg/70 kg for this item. *Participants’ ratings ^{a:} Compared to Dextromethorphan ^m and placebo, <u>all doses of psilocybin increased</u> “positive social effects” as measured by the relevant items the following questionnaires (as measured on the study day and retrospectively 1-wk post-intervention) - o 5D-ASC ^{seo} - o HRS ^{seo}	/deep relaxation”. o At 30 mg/70 kg, psilocybin increased ^{sia} “restlessness/fidgety”.	

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					*Participants' ratings for preference for repeating the drug condition^a: Compared to placebo, all doses of psilocybin increased^{si} the scores for this item. At 20 and 30 mg/70 kg the scores were higher^m than that of dextromethorphan.		o Letter N back test: at all doses, psilocybin administration led^{si} to • Reduced discriminability • Reduced response bias • Increased response time o Episodic memory: Word recall: at all doses, psilocybin administration reduced^{si} correct recalls and sensitivity index. *Visual perception using PLOT psilocybin had no effect^{NS} on the accuracy of line orientation. *Participants' ratings^a: all doses of psilocybin increased^{sa} "numbness/tingling" compared to placebo.			
9	(Barrett et al., 2020b)[24]	Blinded placebo-controlled study; placebo and drug administration took place at 8 am noon of each study day. Resting state functional MRI acquisition took place 90-min after administration and MEQ30 was acquired immediately after each resting-state scan.	Psilocybin 10 mg/70 kg	15 healthy volunteers (10 men and 5 women) Mean age: 51.3±12.3 y/o	*MEQ30 : Psilocybin increased ^{se} "joy" measured immediately in scanner.		*Caudate signal (as isolated signal by small region confound correction technique): Psilocybin altered^{sa} the brain activity in the following manner: o Decreased the connectivity between left caudate and frontoparietal task control network (FPTC), right Caudate and auditory network, but, increased the connectivity between right Caudate and FPTC. *MEQ30: Psilocybin increased^{sa} item "Timelessness" measured immediately in the scanner.	*MEQ30 : Psilocybin increased ^{sas} item "fusion of your personal self into a larger whole" measured immediately in the scanner.		
10	(Barrett et al., 2020a)[25]	Open-label study. All measures were taken one day before, 1-wk and 1-month after psilocybin administration.	Psilocybin 25 mg/70 kg	12 healthy (5 men, 7 women) Mean age: 32.0±7.5 y/o	*DPES: Psilocybin increased^{le} following subscales related to PVS 1-wk and 1-month post-intervention: - o Joy - o Content - o Pride - o Amusement	PANAS negative & STAI-state anxiety: Decreased^{ldt} by psilocybin 1-wk and returned to the baseline 1-month post-intervention. STAI-trait: compared to baseline, psilocybin decreased^{ldt} the scores of this questionnaire 1-month post-intervention.		* Emotion recognition task^a 1-wk^{lasc} post-intervention, psilocybin decreased amygdala reactivity to all facial expressions, independent of valence, which returned back to baseline 1-month post-intervention. *DPES: Psilocybin increased^{leo}		

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						*POMS Psilocybin decreased ^{ldt} items “Tension”, and “total mood disturbances” 1-wk post-intervention, and returned to baseline 1-month post-intervention.		“Compassion” subscale 1-wk and 1-month post-intervention. *Emotional conflict Stroop task: in high conflict trials vs. low conflict trials, psilocybin increased ^{sasc} the BOLD signals in number of brain regions ^a including dorsolateral prefrontal cortex (DLPFC) and medial orbitofrontal cortex 1-wk post-administration.		
11	(Anderson et al., 2020)[26]	Open-label study; 8-10 group therapy sessions with one psilocybin-assisted therapy session. Changes of mean demoralization were assessed at baseline to end-of-treatment (week 3), and 3-months follow-up.	Psilocybin 0.3-0.36 mg/kg	18 participants (all men, older long-term AIDs survivors) Mean age: 59.2±4.4 y/o	*Demoralization scale [27]: Psilocybin reduced ^{le} demoralization as measured 1-2 weeks after first dose and lasted for 3 months (“88.9% and 66.7% of participants demonstrated at least a 2-point reduction in demoralization compared to baseline, and 50% and 33.3% demonstrated a 50% reduction in demoralization compared to baseline” after the second dosing.	*Inventory of Complicated Grief-Revised: psilocybin improved this scale ^{ldl} as measured at end-of-treatment and 3-months follow-up. STAI-trait: Psilocybin decreased STAI-trait scores as measured at end-of-treatment and 3-months follow-up ^{ldt}. STAI-state: psilocybin had no effect ^{ns} on STAI-state.				
12	(Agin-Liebes et al., 2020)[28] <i>Parent study:</i> (Ross et al., 2016)[29]	Double-blind placebo-controlled cross-over clinical trial; drug or placebo in conjunction with psychotherapy; 7-week interval between dosing sessions; STAI trait and state were taken at baseline, one day before, one day after the first and	Psilocybin 0.3 mg/kg single dose Placebo: niacin 250 mg	29 cancer patients diagnosed with depression and/or anxiety (11 men, 18 women) Mean age: 56.28±12.93 y/o	*Demoralization scale [27]: Psilocybin reduced ^{le} demoralization as measured 2 weeks after first dose and were shown to stay significantly lower than baseline at 26 weeks, 3.2, and 4.5	STAI-trait: Psilocybin decreased STAI-trait scores on day one ^{sdh}, week 7 ^{ldt} and were shown to stay significantly lower than baseline at 26 weeks, 3.2, and 4.5 years after administration as measured by within-	*MEQ30: Psilocybin altered ^{sa} the score of “transcendence of time and space” as measured <u>7hrs</u> after administration and retrospectively 26 weeks after administration.	*PEQ: High dose vs. low dose Psilocybin increased following items related to the social processes in the 6-month follow-up: - o Positive attitudes about self ^{les} - o Altruistic/positive social effects ^{leo}		

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		second dosing session, and 26 wks after the second session; demoralization scale, HAI, PEQ, and MEQ were measured at baseline, two weeks and six weeks after the first and second drug administrations, and 26 weeks (6.5 months) after the second drug administration. The long-term follow-up measures were 3.2 yrs and 4.5yrs after the second administration session of the parent study.		The long-term follow up participants: 14 of the parent study's patients [29]	years after the second dosing. *HAI [30]: Psilocybin decreased ^{le} HAI as measured 2-wks after first dose and were shown to stay significantly lower than baseline at 26 weeks, 3.2, and 4.5 years after the second dosing. *PEQ: Psilocybin increased ^{le} following items related to PVS at 2-wk and 6.5-month post-intervention timepoints: oPositive attitudes about life oPositive mood changes oPositive behavior changes *MEQ: Psilocybin increased "positive mood" as measured 7hrs ^{se} and 26 ^{le} weeks after administration	group and between group comparisons. STAI-state: Psilocybin decreased STAI-state scores measured on day one ^{sd} t, week 7 ^{ld} t and were shown to stay significantly lower than baseline at 26 weeks, 3.2, and 4.5 years after administration as shown by within-group and between group comparisons. *Death anxiety scale: Psilocybin decreased death anxiety scores were significantly lower ^{ld} t than baseline at 26 weeks, 3.2, and 4.5 years after administration.		*WHO brief-version questionnaire: compared to placebo psilocybin enhanced ^{lasc} "social relationships" 26-wks after the second dose.		
13	(Smigielski et al., 2019)[31]	Double-blind, placebo-controlled, between-subject in a 5-day meditation group retreat. Two retreats including two groups first with 16-member (8 placebo/8 psilocybin) & Second with 23-member (11 placebo/12	Psilocybin 0.315 mg/kg,	39 healthy meditators (23 men and 16 women) Mean age: placebo group 50.47 ±2.15 y/o psilocybin group 52.80 ±1.55 y/o	*5D-ASC Psilocybin increased ^{se} the item "blissful state". *M-scale Psilocybin significantly increased ^{se} "positive affect". *LCI-R scale	* 5D-ASC: psilocybin had no effect ^{NS} on item "anxiety ".	*5D-ASC Psilocybin increased ^{sa} following items related to the cognitive systems: o Complex imagery o Elementary imagery o Audiovisual synesthesia o Changed meaning of percept *M-scale Psilocybin significantly increased ^{sa} "time/spacelessness" subscale.	*LCI-R scale At 4-month follow up, psilocybin significantly increased "self-acceptance" ^{les} and "concern for others" ^{leo} . *5D-ASC: Psilocybin increased ^{sas} following items of 5D-ASC related to the social processes	*5D-ASC: Psilocybin increased ^{sia} "Vigilance reduction".	

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		psilocybin). Psilocybin or placebo were always administered on day 4 of the retreat. 5D-ASC and M-scale were taken 360-min post drug administration and LCI-R was completed at 4-month follow-up.			At 4-month follow up, psilocybin significantly increased ^{le} “Appreciation for life”, “Quest for meaning” & “sense of purpose”.			(perception and understanding of self): O Disembodiment O Experience of unity *M-scale Psilocybin significantly increased ^{sas} “unity”, “ego loss”.		
14	(Mason et al., 2019)[32]	Open-label study. Empathy task, satisfaction with life scale (SWLS) questionnaire, and measures of creative thinking were taken at baseline, the morning after and seven days after ingesting psilocybin. 5D-ASC questionnaire was completed retrospectively the morning after psilocybin intake.	Psilocybin 27.1 mg (average dosing)	55 healthy volunteers (29 men 26 women) Mean age: 34.8±8.9 y/o	*SWLS: psilocybin increased the scores of this questionnaire the morning after ^{se} . The effects lasted for 7 days ^{le} .		*5D-ASC (modified version with visual analogue scale (VAS)): Psilocybin altered ^{sa} the following items related to the cognitive systems: O Sense of size /space O Sense of time O Perceptions: including visual, auditory perception and experiencing synesthesia *Creative thinking ^a : O Divergent thinking: Psilocybin increased ^{se} the total number of associations and originality scores on the morning after psilocybin intake. O Convergent thinking: Psilocybin increased ^{le} the number of correct associations seven days after psilocybin intake.	*Multifaceted empathy task (MET): O Explicit emotional empathy (EE): Psilocybin increased ^{seo} average explicit EE which remained until the morning after the administration (N=50) these effects were valence-specific towards negative faces. O Implicit EE: Psilocybin increased ^{seo} average implicit EE which remained until the morning after the administration (N=50). This increase existed for both positive and negative valence stimuli. Only the implicit arousal to negative and not positive stimuli remained after 7 days ^{leo} (N=22). O There was a strong correlation ^m between implicit and explicit arousal to positive stimuli and participants’ reports of “life satisfaction” as measured 1 day and 7 days after administration.		

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
								o The treatment did not affect ^{NS} cognitive empathy subscale.		
15	(Nicholas et al., 2018)[33]	Open-label study with different doses of psilocybin. There was a minimum 4-wk interval between consecutive doses. PEQ was measured 30 days after the last dose. MEQ30 was measured after each psilocybin dosing session.	Psilocybin: First Dose: 0.3 mg/ kg (18.8-36.6 mg range) Second Dose: 0.45 mg/kg (27.1-54.0 mg range) Third dose: 0.60 mg/kg (36.3-59.2 mg range)	12 healthy (10 men, 2 women) Mean age: 41±? y/o (age range 24-61)	*PEQ: Psilocybin altered ^{le} following items related to PVS domain: o Positive attitudes about life were significantly higher than negative attitudes. This item was positively associated with MEQ total score. o Positive mood changes significantly higher than negative mood changes o Positive behavior changes were significantly higher than negative behavioral changes		*MEQ30: o There was a positive association ^m between the item “transcendence of time and space” and the area under the curve (AUC) acquired from the pharmacokinetic studies. o There was a positive association ^m between “transcendence of time and space” and MEQ30 total score. *5D-ASC (modified version with visual analogue scale (VAS)): Psilocybin caused “Unusual bodily sensations” ^{sa} .	*PEQ: Ratings for “altruistic/positive social effects” ^{leo} were higher than antisocial/negative social effects.		
16	(Grimm et al., 2018)[34] Kraehenmann et al. 2016[35] <i>Parent study:</i> (Kraehenmann et al., 2015)[36]	Randomized, double blind, cross-over, placebo-controlled design. Placebo or psilocybin were administered with a 2-wk interval. PANAS and STAI questionnaires were taken before and 210 min after drug intake. Scanning session was conducted 70 to 90-min post-intervention and a motor task was performed within the scanner. 5D-ASC was completed	Psilocybin 0.16 mg/kg	25 healthy (16 men, 9 women) Mean age: 24.20±3.42 y/o	PANAS: Psilocybin increased ^{se} positive affect. o Positive affect was negatively associated ^m with the reactivity of right amygdala to negative stimuli. *5D-ASC: Psilocybin increased ^{se} item “blissful state”.	PANAS: no effect ^{NS} STAI5-state: no effect ^{NS} * 5D-ASC: no effect ^{NS} on item “anxiety “	*5D-ASC: Psilocybin increased ^{sa} following items related to the cognitive systems: o Complex imagery o Elementary imagery o Audiovisual synesthesia o Changed meaning of percepts	*Amygdala reactivity task (modified version for amygdala reactivity task comprises of negative, neutral faces and shapes), psilocybin: o Reduced ^{sasc} the bilateral amygdala reactivity, considerably in right amygdala, to both negative and neutral pictures, which implies a non-valence-specific reduction in amygdala reactivity to emotional stimuli. o Reduced ^{sasc} the top-down connection	-	*Motor task ^a: there were no differences ^{NS} between psilocybin and placebo on the BOLD signals of the primary motor cortex.

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		retrospectively 360 post-intervention.						from amygdala to primary visual cortex (using dynamic causal modeling framework) - o Increased reaction time ^{sasc} for all the three conditions. - o No effect on accuracy ^{NS} *Event-related Emotion recognition task: Psilocybin altered ^{sasc} the following components: - o Reduced connectivity between left striatum to right amygdala during angry vs. neutral faces perception. - o Increased connectivity between amygdala and frontal lobe during happy vs neutral faces. The increased connection correlated with the less negative mood and STAI or self-rated depression scores. - o Increased reaction time ^{sasc} for all four conditions (angry, sad, happy and neutral faces). *5D-ASC: Psilocybin increased ^{sas} following items related to the social processes (perception and understanding of self): - o Disembodiment - o Experience of unity		

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
17	(Griffiths et al., 2018)[37]	Randomized double-blind study. Measures were separated by one month. Monitor ratings were assessed ten minutes before and 30-, 60-, 90-, 120-, 180-, 240-, 300-, and 360-min after capsule administration. 5D-ASC, MEQ30, and HRS were measured 7hrs after each dosing session. PEQ was assessed at 6-month follow-up.	Psilocybin was administered to three groups (N=25) as follows: 1. very low dose (1mg/70kg) +moderate spiritual/meditation: control group 2. High dose (20 and 30 mg/kg on first and second day with standard spiritual/meditation support 3. High dose (20 and 30 mg/kg in the first and second session) with high spiritual support	75 healthy volunteers (30 male, 45 female) Mean age: 42±? y/o	*Monitor rating questionnaire during the session *: Psilocybin increased ^{sf} “Anxiety or fearfulness” in high-dose groups. *MEQ30 [38]: Psilocybin increased ^{se} positive mood measured 7hrs after administration. *PEQ : high dose vs. low dose Psilocybin increased ^{le} following items related to PVS at 6-month follow-up: o Positive attitudes about life o Positive behavior changes Positive mood changes	*Monitor rating questionnaire *: Psilocybin increased ^{sf} “Anxiety or fearfulness” in high-dose groups.	*5D-ASC : both groups that received High doses of Psilocybin showed increases ^{sa} in the following items related to the cognitive systems measured 7hrs after administration: o Visual restructuralization o Auditory alteration *HRS : high doses of psilocybin increased ^{sa} following items related to the cognitive systems <u>measured 7hrs</u> after administration: o Cognition o Perception o Somaesthesia *MEQ30 : high dose vs low dose of Psilocybin altered ^{sa} the score of “transcendence of time and space” measured 7hrs after administration.	*PEQ : high dose vs. low dose psilocybin increased following items related to the social processes at 6-month follow-up: o Positive attitudes about self ^{les} o Altruistic/positive social effects ^{leo} *HRS : high doses of psilocybin increased ^{sas} “volition”. *Monitor rating questionnaire during the session *: high dose vs. low dose psilocybin increased ^{sia} “Physical discomfort”.		
18	(Gabay et al., 2018)[39]	Open label, within participant study. Participants attended two sessions. A drug-free session and an intervention session. Ultimatum game was performed 60-min post-intervention.	Psilocybin 2 mg IV	Twenty-three male participants with previous psychedelic use experience (analysis were eventually made on 19 participants) Mean age: 26.6±7.1 y/o	0			*Ultimatum game [40]: Psilocybin reduced ^{sea} the rejection of first-person and random-generated unfair offers.		

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
19	(Schartner et al., 2017; Muthukumaraswamy et al., 2013) [41,42]	Single-blind within-subject study. Two separate MEG sessions were carried out, placebo and psilocybin were administered in first and second session respectively. Psychometric tests were taken within 15 minutes after each scanning session.	Psilocybin 2mg IV	15 healthy volunteers (15 men) Mean age: 34.5 ±2.3 y/o		*5D-ASC (modified version with visual analogue scale (VAS)): Psilocybin altered ^{sa} the following items related to the cognitive systems: - o Sense of size /space; these scores have positive associations with measures of signal diversity ^m. - o Sense of time - o Perceptions: including visual, auditory perception and experiencing synesthesia - o Cognitive processes; this item was positively correlated ^m with decreases in PCC alpha-power from the resting-state MEG acquisitions. *MEG resting state-networks: psilocybin significantly decreased ^{sa} the spectral power of the bilateral beta-band-derived visual network.	*5D-ASC (modified version with visual analogue scale (VAS)): Psilocybin altered ^{sa} the following items related to the cognitive systems: - o Sense of size /space; these scores have positive associations with measures of signal diversity ^m. - o Sense of time - o Perceptions: including visual, auditory perception and experiencing synesthesia - o Cognitive processes; this item was positively correlated ^m with decreases in PCC alpha-power from the resting-state MEG acquisitions. *MEG resting state-networks: psilocybin significantly decreased ^{sa} the spectral power of the bilateral beta-band-derived visual network.	*5D-ASC (modified version with visual analogue scale (VAS)) ∴ Psilocybin altered ^{sas} the following items related to the social processes: - o Sense of self/ego; the scores of this item were positively correlated ^m with decreases in PCC alpha-power, the magnitude of the decreases in the PCC alpha power, and deep-layer pyramidal cell excitations from the resting-state MEG acquisitions. - o The scores of “Ego dissolution” had positive associations ^m with measures of signal diversity.		MEG resting state-networks: psilocybin significantly decreased ^{sim} the spectral power of the bilateral beta-band-derived motor network.
20	(Pokorny et al., 2017)[43]	Double-blind placebo-controlled within-subject study consisting of two sessions with 10 days interval. Multifaceted empathy task (MET) and moral dilemma test (MDT) were performed 160 min post-intervention. 5D-Asc was completed retrospectively 360 min after and PANAS before and 360-min after psilocybin administration.	Psilocybin 0.215 mg /kg	32 healthy volunteers (17 men, 15 women) Mean age: 26.72±5.34 y/o	PANAS: Psilocybin increased ^{se} positive affect item scores. *5D-ASC: Psilocybin increased ^{se} item “blissful state”.	* 5D-ASC: psilocybin had no effect ^{NS} on item “anxiety”. PANAS: psilocybin had no effect ^{NS} on negative affect.	*5D-ASC: Psilocybin increased ^{sa} following items of 5D-ASC related to cognitive systems: - o Complex imagery - o Elementary imagery - o Audiovisual synesthesia - o Changed meaning of percepts	*MET: Psilocybin increased the implicit ^{seo} and explicit ^{seo} emotional empathy. The treatment did not affect ^{NS} cognitive empathy subscale. Psilocybin-induced increase in implicit empathy was associated ^m with “change meaning of percept” from 5D-ASC. *MDT: psilocybin did not affect ^{NS} moral decision making *5D-ASC: Psilocybin increased ^{sas} following items of 5D-ASC related to the social processes		

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
								(perception and understanding of self): o Disembodiment o Experience of unity		
21	(Lewis et al., 2017)[44]	Randomized Placebo-controlled double-blind study. Two doses with at least 10-day interval. 5D-ASC was completed retrospectively 360-min after intake.	Psilocybin Low dose: 0.160 mg/kg High dose: 0.215 mg/kg	58 healthy volunteers (36 men, 22 women) Mean age: 25.00±4.16 y/o	*5D-ASC: compared to placebo, psilocybin increased ^{se} item “blissful state”.	* 5D-ASC: compared to placebo, psilocybin increased ^{sif} item “anxiety”.	*5D-ASC: compared to placebo, psilocybin increased ^{sa} following items of 5D-ASC related to the cognitive systems: o Complex imagery (high vs. low dose had a significantly more increase in this item) o Elementary imagery (high vs. low dose had a significantly more increase in this item) o Audiovisual synesthesia (high vs. low dose had a significantly more increase in this item) o Changed meaning of percepts	*5D-ASC: Psilocybin increased ^{sas} following items of 5D-ASC related to the social processes (perception and understanding of self): o Disembodiment (high vs. low dose had a significantly more increase in this item) o Experience of unity		
22	(Johnson et al., 2017)[45] (Garcia-Romeu et al., 2015)[46] <i>Parent study:</i> (Johnson et al., 2014)[47]	Open-label Study. Assessing Short-term and long-term effect (12-month follow-up) of psilocybin-facilitated smoking cessation program consisting of 4 weekly psychotherapy sessions (CBT, mindfulness training and guided imagery). Psilocybin was administered at weeks 5, namely (Target Quit Date; TQD) and 7 and week 13 (optional dosing). PEQ and Time-line follow-back data of self-reported	Week 5: psilocybin (20 mg/70 kg) Week 7: Psilocybin (30 mg/70 kg) Week 13: Optional psilocybin treatment (30 mg/70 kg)	15 psychiatrically healthy adult smokers (10 men, 5 women) Mean age: 51.0±10.5 y/o	*PEQ: Psilocybin altered ^{le} following items related to PVS domain: o Positive attitudes about life (as measured 1 week after each psilocybin session, and 12 months after psilocybin session 1) Positive attitudes about life were significantly higher than negative attitudes. o Positive mood changes were significantly higher than			*PEQ: one week after psilocybin sessions and 12 months after psilocybin session 1, the ratings for “altruistic/positive social effects” ^{leo} were higher than antisocial/negative social effects.		

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		daily smoking (TLFB) were taken at 10 weeks, 6 months, 12 months and approximately 30 months post-TQD. Smoking cessation measures including Smoking Abstinence Self-Efficacy (SASE), Questionnaire on Smoking Urges (QSU), and Wisconsin Smoking Withdrawal Scale scores (WSWS) were administered at baseline, weekly post-TQD until end of treatment (Excluding psilocybin session weeks), and at 6-month follow-up. Ratings of personal meaning and well-being were taken 1-wk and 15-wks post-TQD.			negative mood changes of the same period. - o Most of the participants stated having positive rather than negative behavioral changes. - o Item well-being was significantly higher in participants that quit smoking compared to the ones that continued smoking following the intervention^m. *TLFB: compared to baseline, psilocybin significantly reduced ^{le} the number of cigarette consumption at 10wks, 6 months, 12 months and 30 months post-TQD. There was a significant association ^m between change scores of TLFB and “personal meaning” and “well-being” ratings. *Smoking cessation outcomes: psilocybin altered ^{le} the following outcome measures related to PVS - o SASE: reduced temptation to smoke and increased confidence to					

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					abstain; there was a significant association ^m between SASE change scores and “personal meaning” and “well-being” ratings. o <i>QSU</i>: reduced craving to smoke. There was a positive correlation ^m between QSU and mean “states of consciousness” questionnaire. o <i>WSWS</i>: peaked at 1-wk post-TQD but significantly decreased through 6-month follow-up.					
23	(Preller et al., 2016)[48]	Double-blind placebo-controlled, within-subject study, cross-over, counter-balanced design. The two separate sessions were 10-days apart. Cyberball task was conducted 75 min post-intervention, and MRS scans were performed 50min before and after the Cyberball task. PANAS was assessed 75 min before and 360 min after intake. 5D-ASC was completed retrospectively 360 min after psilocybin ingestion.	Psilocybin 0.215 mg /kg	21 healthy participants (12 men, 9 women) Mean age: 26.48±4.76 y/o	PANAS: Psilocybin increased ^{se} positive affect subscale scores. *5D-ASC: Psilocybin increased ^{se} item “blissful state”.	* 5D-ASC: Psilocybin increased ^{sif} item “anxiety”. PANAS: psilocybin had no effect ^{NS} on negative affect.	*5D-ASC: Psilocybin increased ^{sa} following items of 5D-ASC related to the cognitive systems: - o Complex imagery - o Elementary imagery - o Audiovisual synesthesia - o Changed meaning of percepts	Cyberball task: - o Post-task questionnaire (PTQ): participants reported a reduced feeling ^{sea} of exclusion after psilocybin vs. placebo treatment - o Explicit exclusion conditions: compared to placebo, psilocybin reduced activation in the left middle frontal gyrus (MFG) and anterior midcingular cortex (aMCC)/dACC, areas associated with social exclusion processing - o Implicit exclusion conditions: compared to placebo, psilocybin		

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								reduced activation in the left middle frontal gyrus (MFG), anterior and posterior midcingular cortex (aMCC)/dACC & pMCC), and ventral anterior cingulate cortex (vACC) areas were associated with social exclusion processing. o Psilocybin-induced reduction in dACC activity was correlated ^m with the “sense of unity” in the 5D-ASC questionnaire (below). o Psilocybin-induced reduction in dACC activity was correlated ^m with decreased aspartate content measured by MRS. *5D-ASC: Psilocybin increased ^{sas} following items of 5D-ASC related to the social processes (perception and understanding of self): o Disembodiment o Experience of unity		
24	(Pokorny et al., 2016)[49]	Double-blind, placebo-controlled, within-subject design to investigate the role of 5-HT _{1A} and 5-HT _{2A} modulators on psychological effects of psilocybin. Four intervention combinations were separated by minimum of 2-week intervals. In the ergotamine group placebo or ergotamine	Psilocybin: 0.170 mg/kg Buspiron (5-HT_{1A} agonist): 20 mg Ergotamine (5-HT_{2A/1A} agonist): 3 mg	36 healthy volunteers Ergotamine group: 19 participants (10 men and 9 women) Mean age: 24.89±4.03 y/o Buspiron group: 17 participants (8 men and 9 women) Mean age: 23.82±3.70 y/o			*5D-ASC: o Compared to placebo, psilocybin increased ^{sa} “Visual restructuralization” subscale. Buspirone significantly reduced ^m psilocybin-induced VR changes, specifically, “elementary and complex visual hallucination” clusters and to a lesser extent “autobiographic memory recollection”, and “facilitated imagination”. Ergotamine had no effect ^m on psilocybin-induced VR. o Psilocybin had no effect ^{ns} on auditory alteration at this dose.			

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		administration was followed by placebo or Psilocybin intake. In the buspirone group, placebo or buspirone administration was followed by placebo or Psilocybin intake. 5D-ASC questionnaire was completed retrospectively 180 min post-intervention.								
25	(Griffiths et al., 2016)[50]	Randomized, double-blind cross-over clinical trial consisted of two separate sessions with a 5-wk interval. Monitor ratings were assessed ten minutes before and 30, 60, 90, 120, 180, 240, 300, and 360 min after capsule administration. 5D-ASC, MEQ30, and HRS were measured 7hrs after each dosing session. PEQ was completed 5-wks after the low and high dose session and retrospectively at 6-month follow-up. STAI and the Revised Life Orientation Test (LOT-R) questionnaires were assessed at baseline, 5-wks and 6-month after intervention.	Psilocybin Very low dose: 1 or 3 mg/70 kg: control group High dose: 22 or 30 mg/70 kg	51 cancer patients (25 men, 24 women) with life-threatening diagnosis and symptoms of anxiety and/or depression Mean age: 56.3±1.4 y/o	*MEQ30: Psilocybin increased ^{se} positive mood measured 7hrs after administration. *Monitor rating questionnaire ^a : high dose vs. low dose Psilocybin increased ^{se} “Joy/intense happiness”. *PEQ: high dose vs. low dose Psilocybin increased ^{le} following items related to PVS measured at 5-wks and 6-month follow-up: - o Positive attitudes about life - o Positive mood changes - o Positive behavior changes *LOT-R: high dose vs. low dose of psilocybin increased ^{se} the scores of LOT-R (optimism) as measured post-intervention.	STAI-trait: Psilocybin altered ^{sdt} STAI-trait in the following manner: - o Reduced scores after the second session where the order of administration was: low dose (first session), high dose (second session) - o Reduced the scores only after the first session where the order of administration was: high dose (first session), low dose (second session) STAI-state: Psilocybin altered ^{sdt} STAI-state in the following manner: - o Reduced scores after the second session where the order of administration was: low dose (first session), high dose (second session) - o The scores resulted from neither of the above dosing regimens remained low in the 6-month follow-up	*5D-ASC: high dose vs. low dose Psilocybin increased ^{sa} following items related to the cognitive systems 7hrs post-administration: - o Visual restructuralization - o Auditory alteration *HRS: high dose vs. low dose Psilocybin increased ^{sa} following items related to cognitive domain - o Cognition - o Perception - o Somaesthesia *Monitor rating questionnaire ^a : high dose vs. low dose Psilocybin increased ^{sa} “Visual effects with eyes open/close”. *MEQ30: high dose of Psilocybin altered ^{sa} the score of “transcendence of time and space “measured 7hrs after administration.	*PEQ: high dose vs. low dose Psilocybin increased following items related to social domain in 6-month follow-up: - o Positive attitudes about self^{les} - o Altruistic/positive social effects^{leo} *HRS: high dose vs. low dose Psilocybin increased ^{sas} “volition”. *Monitor rating questionnaire ^a : high dose vs. low dose Psilocybin increased ^{sia} “Unresponsiveness to questions”. - o Physical discomfort and restlessness	*5D-ASC: high dose vs. low dose Psilocybin increased ^{sia} “Vigilance reduction “ *Monitor rating questionnaire ^a : high dose vs. low dose psilocybin increased “spontaneous motor activity” ^{sim} o	

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
						*Monitor rating questionnaire ^a : Psilocybin increased ^{slf} “Anxiety or fearfulness”.				
26	(Lebedev et al., 2015)[51]	Within-subject, placebo-controlled counterbalance-order design. Psilocybin and placebo were administered in two separate sessions along with task-free fMRI acquisitions. Psychometric tests were taken shortly after each scanning session.	Psilocybin 2mg IV	15 healthy volunteers (13 men and 2 women) Mean age: 32.0±8.9 y/o				*5D-ASC (modified version with visual analogue scale (VAS)): the first principal component was derived from subjective measures, and was associated with “Ego-dissolution” phenomenon. This principal component was associated ^m with: - o Decreased connectivity between medial temporal lobe and high-level cortical regions - o Disintegration of salience network - o Reduced interhemispheric communication - o Lower diversity of executive network nodes at baseline - o Reduced connectivity of hippocampal formation with somatosensory, Frontoparietal, salience, and dorsolateral Prefrontal networks		
27	(Bogenschutz et al., 2015)[52]	Open-label within subject design together with motivational enhancement therapy (4 weeks), drug administration at week 4. Penn alcohol craving scale (PACS), Alcohol Abstinence Self-Efficacy (AASE), and POMS were taken at 4,5,8,9,12,24, 36 wks post-administration.	Psilocybin, First dose: 0.3 mg/kg (one participant) Second dose (optional): 0.3 mg/kg N=6 0.4 mg/kg, N=1	10 individuals with alcohol dependence (6 men and 4 women) Mean age: 40.1 ±10.3 y/o	*POMS: - o Item “vigor” was significantly higher^{le} than baseline (p<0.05) at week 24 post-intervention. - o No significant change^{ns} in positive moods subscales post-intervention.		*5D-ASC: Psilocybin increased ^{sa} “Auditory visual” scale.		*5D-ASC: Psilocybin increased ^{sia} “Vigilance reduction” post-intervention.	

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		5D-ASC, HRS, MEQ-30 were completed retrospectively 7hrs post-administration. Time-line follow-back data of self-reported daily alcohol consumption (TLFB) were taken at baseline and at each visit ^a during the 9 months following the intervention.			*PACS: compared to baseline psilocybin reduced ^{le} PACS at 8, 9, 12 and 36 wks post-intervention. the scores of PACS were inversely correlated ^m with total scores of 5D-ASC, MEQ and the item “intensity” from the HRS questionnaire. *AASE: compared to baseline, psilocybin increased ^{le} “confidence” 5wks post-intervention and decreased “temptation”. The scores of AASE were positively associated ^m with total scores of MEQ and item “intensity” from the HRS scale. TLFB: psilocybin reduced ^{le} the drinking days and heavy drinking days at the follow-up points.					
28	(Bernasconi et al., 2014)[53]	Randomized double-blind placebo-controlled design consisting of the two separate sessions with a minimum of 2-wks interval. 5D-ASC was completed retrospectively 360 min post-administration. Emotional face task with EEG acquisition was performed following psilocybin or placebo interventions.	Psilocybin 0.17 mg/kg	30 healthy (14 women, 16 men) Mean age: 25.0±10.6 y/o	*5D-ASC: Psilocybin increased ^{se} item “blissful state”.	* 5D-ASC: no effect ^{NS} on item “anxiety “.	*5D-ASC: Psilocybin increased ^{sa} following items of 5D-ASC questionnaire related to the cognitive systems: - o Complex imagery - o Elementary imagery - o Audiovisual synesthesia - o Changed meaning of percepts	*Emotional face task (happy, fearful, neutral) using source localization technique for EEG data showed that psilocybin altered ^{sasc} following components: - o Decreased activity in right fusiform gyrus, temporoparietal cortices, prefrontal areas, bilateral limbic areas for neutral and fearful faces - o Decreased activity in right lingual gyrus,		

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
								fusiform gyrus, middle-inferior occipital gyrus, bilateral limbic areas, temporoparietal cortices and prefrontal areas o N170: reduced response and shifted the latency towards 200ms. Independent of face valence. N170 is modulated by emotional (fearful and happy) vs. neutral faces. *5D-ASC: Psilocybin increased ^{sas} following items related to the social processes (perception and understanding of self): o Disembodiment o Experience of unity		
29	(Schmidt et al., 2013)[54] <i>Parent study:</i> (Schmidt et al., 2012) [55]	Randomized double-blind, cross-over, placebo-controlled design. Placebo and psilocybin were administered in two separate sessions with a minimum of 1-wk interval. 5D-ASC was completed retrospectively 360 min post-administration and emotional measures were taken 110 min post-intervention. Auditory “roving” oddball paradigm, and visual vigilance task were performed post-intervention.	Psilocybin 0.115 mg/kg	21 healthy volunteers (13 men and 8 women) Mean age: 23.00±2.22 y/o	*5D-ASC: psilocybin increased ^{se} item “blissful state”.	* 5D-ASC: psilocybin had no effect ^{NS} on item “anxiety”.	*5D-ASC: Psilocybin increased ^{sa} following items related to the cognitive systems: o Complex imagery o Elementary imagery o Changed meaning of percepts o Psilocybin did not affect ^{NS} “auditory alteration”. Auditory MMN ERP: psilocybin did not affect ^{NS} MMN’s amplitude nor its latency. Conversely, ketamine disrupted ^m the MMN over the frontal electrodes and caused a latency shift. There were no correlations between mean or separate MMNs and behavioral measures.	*Event-related Emotion recognition task ^a o Psilocybin reduced ^{sasc} N170 ERP component in fearful face condition. This modulation is more pronounced in the conscious compared to non-conscious processing. o Psilocybin had no effect ^{NS} on P100 amplitudes o Sensitivity indices: psilocybin reduced ^{sasc} the d’ values for fearful vs. neutral pictures, but had no effects ^{NS} on d’ values for happy vs. neutral pictures. *5D-ASC: Psilocybin increased ^{sas} following related to the social	Visual vigilance task: psilocybin significantly prolonged ^{sia} reaction times and reduced sensitivity indices.	

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
								processes (perception and understanding of self): o Disembodiment o Experience of unity		
30	(Kometer et al., 2013)[56]	Double blind, placebo-controlled, cross over design. Each subject received four intervention combinations separated by a minimum of a 2-wk interval: inert placebo or ketanserin (50 mg) (pretreatment) were followed by placebo or psilocybin after 1h. Modal object completion task (kanizsa) with EEG acquisition started 90 min and 5D-ASC questionnaire was completed retrospectively 360 min post-intervention.	Psilocybin 0.251 mg /kg Ketanserin 50 mg (5-HT2A receptor antagonist)	15 healthy (11 men and 4 women) Mean age: 26.60 ±4.25 y/o			Modal object completion task: • N170: Psilocybin decreased ^{sa} the N170 component after placebo but not after ketanserin ^m pretreatment. • The psilocybin-induced N170 decrease correlated ^m only with the psilocybin-induced increase in Visionary restructuralization from 5D-ASC questionnaire. o P100: Psilocybin altered ^{sa} the P100 in the following manner: • Psilocybin selectively increased P100 amplitudes over the medial but not the lateral, parieto-occipital ROIs. Medial parieto-occipital ROI were selectively decreased ^m by ketanserin pretreatment. The ketanserin-induced decrease was associated with a decrease in phase-lock index (PLI) during the 0-200 ms frame. • Psilocybin-induced increase in the medial P100 potential correlated ^m significantly with psilocybin-induced decrease in α power values in the parieto-occipital regions.			

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
							• *Object completion reaction time^a: psilocybin did not affect^{NS} reaction time in this task. ○ α power^a: Psilocybin altered^{sa} α-power in the following manner: • Psilocybin reduced α power over the right parieto-occipital regions after pretreatment with placebo and not with ketanserin^m. • Psilocybin reduced the pre-stimulus and subsequent stimulus induced α-power compared to baseline. ○ Error rates: psilocybin increased^{si} the error rates in Kanizsa stimuli. *5D-ASC (authors focused on visual perception alteration items for the purpose of their work): Psilocybin increased^{sa} “visual restructuralization”, which was blocked^m by ketanserin.			
31	Quednow et al., 2012[57]	Double-blind crossed, counter-balanced placebo-controlled, design; 4-week interval between test dates; startle measures were taken 60 min, Stroop task was performed 85 min and 5D-ASC was measured 125 min post-intervention	Psilocybin 260 µg/kg Ketanserin 40 mg (5-HT2A receptor antagonist)	16 healthy volunteers (13 men and 3 women) Mean age: 29.7 ±? y/o			PPI: ○ Psilocybin did not affect^{NS} startle amplitude and habituation. There was a reduction in startle reactivity^m in ketanserin groups. ○ Psilocybin decreased^{sa} %PPI (in the 30 ms condition). This effect was reversed by ksetanserin. ○ The change in PPI positively correlated^m with Visual restructuralization and oceanic boundless ness from the 5D-ASC questionnaire. Stroop task: ○ Psilocybin increased^{si} • Error rates in the conflict condition and reaction time in all conditions. Ketanserin reversed these effects. • Stroop interference and Stroop effect of the response latencies compared to ketanserin^m and placebo. • Enhanced facilitation in combination^m with ketanserin			

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
							*5D-ASC: Psilocybin increased ^{sa} "Visual restructuralization"			
32	(Kometer et al., 2012)[58]	Randomized, double blind, cross-over, placebo-controlled design. The 4 study days were separated by 1-2 wks intervals and consisted of psilocybin, placebo (Ketanserin), Placebo (inactive), Psilocybin + Ketanserin administration. Experiments started approximately 130 min and self-report questionnaires were completed 360 min post-intervention.	Psilocybin 0.215 mg/kg Ketanserin 50 mg (5-HT2A receptor antagonist)	17 healthy (11 men, 6 women) Mean age: 26.00±4.36 y/o	PANAS: compared with ketanserin ^m , psilocybin increased ^{se} positive affect subscale scores, which was reversed ^m by ketanserin. *5D-ASC: Psilocybin increased ^{se} item "blissful state", which was reversed ^m by ketanserin.	STAI-state: o No increase ^{NS} after placebo pre-treatment. o Increase ^m after pretreatment with ketanserin PANAS: Psilocybin did not increase ^{NS} negative affect subscale. * 5D-ASC: no effect ^{NS} on item "anxiety".	P300 & N2: Psilocybin increased ^{sa} P300 and decreased ^{sa} N2 components during emotional vs. Neutral stimuli, which indicates a general decrease in attentional resource allocation, more for negative and neutral vs. positive stimuli, and a shift towards positive stimuli processing. *5D-ASC: Psilocybin increased ^{sa} following items related to the cognitive systems: o Complex imagery o Elementary imagery o Audiovisual synesthesia o Changed meaning of percepts These effects were reversed ^m by ketanserin.	*Emotional recognition task ^{a:} Psilocybin significantly attenuated ^{sasc} the recognition of negative emotional stimuli, and biased to choose words with higher valences. These effects were inhibited ^m by ketanserin. *Emotional go/no go task ^{a:} Psilocybin increased ^{sasc} the reaction time to negative and neutral stimuli compared to positive stimuli, and increased error rates in a valence-dependent manner. Pretreatment with ketanserin did not affect ^m these changes. *5D-ASC: Psilocybin increased ^{sas} following items related to <u>social processes</u> (perception and understanding of self): o Disembodiment o Experience of unity These effects were reversed ^m by ketanserin.		
33	(R. L. Carhart-Harris et al., 2012)[59]	Placebo-controlled cross over study consisting of two scanning sessions separated with a minimum of 1-wk interval. Infusion of either placebo or psilocybin was performed during scanning. Subjective ratings were collected	Psilocybin 2 mg IV	10 healthy (9 male and 1 female) Mean age: 32.0±10.4 y/o			*fMRI during an autobiographical memory recollection ^{a:} (<i>participants were asked to re-experience a specific personal memory</i>): Psilocybin increased ^{sa} the activity in left occipital lobe, visual association region, mid-insula, primary and secondary auditory cortex, temporal pole, primary and secondary somatosensory cortex, superior parietal regions. Post-hoc analysis confirmed activation of sensory and visual clusters.			

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		immediately after the scanning session.					*Subjective ratings: the psilocybin group had higher ^{se} ratings of “memory vividness”, “emotional intensity”, “valence”, and “visual imagery” of the recollection experience. Memory vividness had a positive correlation ^m with subjective well-being.			
34	(Kometer et al., 2011)[60]	Cross-over randomized design. Experiment days were at least 2-wks apart. Modal object completion task (kanizsa) was performed 120 min post-intervention. 5D-ASC was completed retrospectively post-administration.	Psilocybin Low dose: 125 µg /kg High dose: 250 µg /kg	17 healthy volunteers (8 men and 9 women) Mean age: 28.8 ±3.5 y/o			Modal object completion task: - o N170: Psilocybin dose-dependently decreased^{sa} N170. This reduction was more pronounced in the Kanizsa vs. non-Kanizsa condition. - o P100 (modal object completion task): both low and high doses of Psilocybin increased^{sa} the amplitude of P100 over Occipital electrodes (O1/O2). - o *Object completion reaction time^a: psilocybin increased^{sa} reaction time in this task but did not alter error rates. *5D-ASC (authors mainly focused on visual perception alteration items for the purpose of their work): Psilocybin increased ^{sa} following items related to the cognitive systems: - o Visual restructuralization: both high and low dose increase VR - o Auditory alteration: compared to placebo, only high-dose increased AA.			

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
35	(Grob et al., 2011)[61]	Within-subject, double-blind, placebo-controlled study. Each subject received psilocybin and placebo on two different sessions several weeks apart. POMS and STAI were taken one day before, administration, at the end of each session, one day and 2wks after the session and at monthly intervals for 6 months. 5D-ASC was taken one day before and at the end of the experiment session.	Psilocybin 0.2 mg/kg	12 adults with advanced-stage cancer and anxiety (11 women, 1 man) Age range: 36-58 y/o	*5D-ASC: psilocybin increased ^{se} the following item clusters: - o Positive Mood - o Mania-like experience *POMS (short version: total mood disturbance score): compared to placebo, there was a trend toward reduction ^{le} after-psilocybin administration from 1-day before to 2wks post-administration.	STAI-trait anxiety score: there was a significant reduction ^{ldt} at 1 and 3-month point after second treatment session. STAI-state anxiety score: psilocybin had no significant effects ^{NS} on this scale.	*5D-ASC: Psilocybin increased ^{sa} the following item clusters related to the cognitive systems: - o Positive Derealization - o Altered Sense of Time - o Elementary Hallucination - o Visual Pseudohallucination - o Synesthesia - o Changed Meaning of Percept - o Facilitated Recollection and imagination^{se}	*5D-ASC: Psilocybin increased ^{sas} "Depersonalization".		
36	(Griffiths et al., 2011)[62]	Double-blind between-group, cross-over study consisting of five 8h sessions with 1-month intervals. Participants were randomized to receive psilocybin in ascending or descending order. Placebo was administered quasi-randomly. Monitor ratings were assessed ten minutes before and 30, 60, 90, 120, 180, 240, 300, and 360 min after capsule administration. APZ, MEQ30, and HRS were measured 7hrs after each dosing session. PEQ was completed 3-4 wks after each session and retrospectively at 14-month follow-up.	Psilocybin 5,10, 20, 30 mg/70 kg	18 participants (8 men, 10 women) hallucinogen naïve Mean age: 46 ±? y/o	* Monitor rating scale^a: Psilocybin increased ^{se} "Joy/intense happiness", in a dose-dependent manner, starting from 10 mg/70 kg. *MEQ30: psilocybin increased "deeply felt positive mood" in a dose-dependent manner starting from 5 mg/70kg as measured 7hrs ^{se} and 14 months ^{le} after administration. *PEQ: Psilocybin increased following items related to PVS in a dose-dependent manner, as measured in 1 and 14-month ^{le} follow-up (the latter was only measured for 20 and 30 mg/70 kg doses):	*Acute measure/Monitor ratings questionnaire: Psilocybin dose-dependently increased ^{sif} "Anxiety and fearfulness".	*HRS: Psilocybin increased ^{sa} the following items related to the cognitive systems, 7hrs after administration: - o Cognition - o Perception - o Somesthesia *APZ: Psilocybin increased ^{sa} "Visual restructuralization". *MEQ30: psilocybin increased ^{sa} "transcendence of time and space" in a dose-dependent manner starting from 5 mg/70kg as measured 7hrs and retrospectively 14 months after administration (measured only for 20 and 30 mg/70 kg doses).	*HRS: psilocybin increased Volition ^{sas} in a dose-dependent manner, starting from 5 mg/70 kg: *PEQ: Psilocybin increased following items related to the social processes in a dose-dependent manner, as measured in 1-month follow-up and 14-month retrospective testing (measured only for 20 and 30 mg/70 kg doses): - o Positive attitudes about self (all doses)^{les} - o Altruistic/positive social effects (all doses)^{leo} - o Negative attitudes about self (5 and 10 mg/70 kg)^{las}	*Monitor rating scale^a: - o Psilocybin increased^{sia} following items related to the arousal and regulatory systems in a dose-dependent manner, starting from 5 mg/70 kg: • Unresponsiveness to questions • Stimulation/arousal • restlessness/fidgety. - o Psilocybin did not affect^{NS} following items:	

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
					- o Positive attitudes about life (starting from 5 mg/70 kg) - o Positive mood changes (starting from 10 mg/70 kg) - o Positive behavior changes (starting from 10 mg/70 kg)				• Sleepiness/sedation • Sleep	
37	(Wackermann et al., 2008) [63] <i>Parent study:</i> (Wittmann et al., 2007)[64]	Double blind, Placebo-controlled within-subject design. The two sessions were separated by a 14-day interval. DRT task was performed before, 90 and 240 min after administration. 5D-ASC was completed retrospectively 110 min and AMRS was taken at baseline, 80- and 280 min post-intervention. The spatial span task was measured at baseline and, 100, and 360 min after the administration.	Psilocybin High dose: 0.250 mg /kg Low dose: 0.115 mg /kg Very low dose: 0.012 mg /kg	12 healthy volunteers (6 men and 6 women) Mean age: 26.8 ±3.6 y/o <i>For DRT paradigm:</i> 9 healthy participants were added to above study sample (5 men and 4 women)	*AMRS: psilocybin did not affect ^{NS} “heightened mood”.	*AMRS: psilocybin did not affect ^{NS} “anxiety”.	Spatial span task: high-dose psilocybin impaired ^{si} spatial span task as measured by span length. *5D-ASC: psilocybin dose-dependently increased ^{sa} following items related to the cognitive systems: - o Visual restructuralization - o Auditory alteration *DRT 2^a (result from both experiments from both studies (N=19): psilocybin increased ^{sa} parameter κ of the “dual klepsydra” model of internal time representation at 90 min of drug intake.		*AMRS: psilocybin increased ^{sia} “tiredness” and “dazed state”. *5D-ASC: Psilocybin increased ^{sia} “Vigilance reduction “	*Sensorimotor temporal synchronization: - o Psilocybin impaired ^{sim} following items related to sensorimotor domain: - o Individuals’ capacity to accurately reproduce interval lengths longer than 3 seconds, - o Synchronize a motor response (finger tap) to regular auditory beats with intervals longer than 2 seconds

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
										o Slowed down the personal tapping tempo (preferred tapping rate).
38	(Vollenweider et al., 2007)[65]	Double-blind, placebo-controlled, randomized, counterbalanced order. Subjects received graded dose of psilocybin in each of the four experiment days, which were separated by 4-wks interval. Startle measurement were 90- and 165-min post treatment, FAIR task assessment at baseline, 105, 180, and 360 min and 5D-ASC was completed at 125 and 200 min after treatment.	Psilocybin: 115, 215, and 315 mg/k)	16 subjects (9 women, 7 men) Mean age: 26.4 ±? y/o			PPI: Psilocybin dose-dependently decreased % PPI (in the 30 ms condition), increased ^{sa} % PPI (in the 120-2000 ms), and had no effect ^{ns} on startle reactivity or habituation. *FAIR: Psilocybin dose-dependently impaired ^{sl} “sustained attention”; this impairment was associated ^m with reduced PPI at only 30ms interstimulus interval (ISI). *5D-ACS: Psilocybin increased ^{sa} following items related to the cognitive systems: 1. Visionary Restructuralization scores: all doses 2. Auditory alteration: medium and high doses		*5D-ASC: All doses of Psilocybin increased ^{sia} “Vigilance reduction”	
39	(Carter et al., 2007)[66] <i>Parent study:</i> (Carter et al., 2005a)[67]	Double blind, Placebo-controlled design, consisting of four conditions which were separated by a 14-day interval: placebo,	Psilocybin 0.215 mg /kg Ketanserin 50 mg (5-HT2A	10 healthy volunteers (6 men, 4 women) Mean age: 26.0 ±2.3 y/o	*AMRS: psilocybin did not affect ^{ns} “general positive mood”. However, its co-administration ^m with ketanserin	*AMRS: Psilocybin did not affect ^{ns} “anxiety”.	*Binuclear rivalry: o Psilocybin (with and without ketanserin ^m pretreatment) increased ^{sa} the phase duration in the 60, 90 135 min post-treatment. This effect remained		*AMRS: psilocybin did not affect ^{ns} “general inactivity”. However, its co-	

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		ketanserin, psilocybin, ketanserin + psilocybin. Object tracking and spatial working memory tasks were taken at baseline, and 120 min post-intervention. Binocular rivalry was performed 45 min before and at 30, 60, 90, 135, 180, 240-, 300-, 360-, and 420-min post-intervention; 5D-ASC was completed retrospectively at 180 post psilocybin ingestion (after the 180-min binuclear rivalry test). AMRS was administered at baseline and post-administration (before binocular rivalry test).	receptor antagonist)	For cognitive tasks: 8 healthy volunteers (4 men 4 women) Mean age: 29.5 ±? y/o	resulted in increased scores.		after 180 min for psilocybin without Ketanserin pretreatment. - Psilocybin increased^{sa} the proportion of mixed percept at 90- and 240-min post intake. Psilocybin plus pretreatment with ketanserin^m led to a significant increase at 135 min. - The combination of psilocybin and ketanserin^m led to slower response times at 60-, 90-, 180-, and 300-min post intake. *Multiple-object Tracking^a Psilocybin reduced^{sl} attentional tracking performance. This decline was not diminished^m by Ketanserin pretreatment. *Spatial Working Memory^a: Administration of psilocybin or other compounds in different groups had no significant effect^{NS} on spatial working memory. *5D-ASC: Psilocybin increased^{sa} following items related to the cognitive systems, which were blocked^m by Ketanserin pretreatment: - Visual restructuralization - Auditory alteration		administration^m with ketanserin resulted in increased scores. *5D-ASC: Psilocybin increased^{sia} “Vigilance reduction”. This effect was not blocked^m by Ketanserin pretreatment.	
40	(Carter et al., 2005b)[68]	Double blind, Placebo-controlled within-subject design. Sessions were separated by a 14-day interval. Binuclear rivalry was tested at baseline, 90-, 180-, 270- and 360-min post-intervention, and 5D-ASC was measured at 120 min post psilocybin intake.	Psilocybin High dose: 0.250 mg /kg Low dose: 0.115 mg /kg Ketanserin 50 mg (5-HT2A receptor antagonist)	12 healthy volunteers (6 men, 6 women) Mean age: 26.8 ±3.6 y/o	5D-ASC: Psilocybin increased ^{se} “heightened mood”.		*Binuclear rivalry: both doses of psilocybin increased^{sa} the phase duration in the 90 min post-treatment. This effect remained after 180 min only for high dose. *5D-ASC: Psilocybin increased^{sa} following items related to the cognitive systems: - Visual restructuralization (Low and high doses) - Auditory alteration (only high dose)		*5D-ASC: Psilocybin increased ^{sia} “Vigilance reduction”	
41	(Hasler et al., 2004)[69]	Double-blind placebo-controlled cross-over design consisting of four different doses in each session, which were separated by a	Psilocybin Very low dose (VLD): 0.045mg/kg	8 healthy volunteers (4 men 4 women) Mean age: 29.5 ±? y/o	*AMRS: Psilocybin did not affect ^{NS} “general positive mood”.	*AMRS: Psilocybin did not affect ^{NS} “anxiety”.	*5D-ASC: Psilocybin increased^{sa} following items related to the cognitive systems: - Visual restructuralization (Mild and high doses) - Auditory alteration (high dose)		*5D-ASC: Psilocybin increased ^{sia} “Vigilance reduction “	

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		14-day interval. 5D-ASC was completed retrospectively at 150 and 300 min and FAIR was assessed 140 min after drug administration. AMRS was taken at baseline, 95-, 275 min and 24 hrs post-intervention.	Low dose: 0.115 mg/kg Medium dose: 0.215 mg/kg High dose: 0.315 mg/kg				*FAIR: mild and high doses of Psilocybin reduced ^{sl} following items which is interpreted as a lowered attentional resource allocation: - o Performance value - o Continuity value		*AMRS: at medium and high doses, psilocybin increased ^{sia} “General inactivity”	
42	(Carter et al., 2004)[70]	Double-blind, placebo-controlled consisting of two sessions separated by a 2-wk interval. Subjects were tested before and 120 min after drug administration.	Psilocybin: 0.215 mg/kg	9 healthy volunteers (five men, four women) Mean age: 27.1±2.6 y/o			*Forced choice local and global motion discrimination tasks ^a: Psilocybin altered ^{sl} the following parameters: - o Selectively impaired global but not local motion processing. - o Significantly reduced coherence sensitivity, but not contrast sensitivity.			
43	Umbricht et al., 2003 [71] <i>Parent study:</i> Umbricht et al., 2002[72]	Randomized Single-blind placebo-controlled, counterbalanced design consisting of two sessions separated by a 14-day interval. Measurements were taken at baseline and approximately 120 min post intake. APZ questionnaire (analog scale version) was filled in the evening after the study session.	Psilocybin 0.280 mg /kg	18 healthy volunteers (10 men and 8 women) Mean age: 25.1 ±4.3 y/o			Auditory N1 and P2 ERP: - o Psilocybin significantly reduced ^{sa} N1 amplitude but did not affect ^{NS} its' latency. - o Psilocybin had no effects ^{NS} on P2. Auditory MMN ERP: psilocybin had no effects ^{NS} on MMN amplitude nor on its latency. AX-CPT: Psilocybin significantly lowered ^{sl} the task performance only where contextual information was needed (BX errors).			
44	Gouzoulis-Mayfrank et al., 2002 [73] <i>Parent study:</i> Gouzoulis-Mayfrank, et al., 1999 [74] Gouzoulis-Mayfrank, 1999[75]	Double blind, pseudorandomized Placebo-controlled study. The study sessions were separated by 2-4 wk intervals. PET scans with [¹⁸ F] FDG were performed 110-120 min after the drug administration. STAI-X1, APZ, HRS and PANSS were measured before, and during the	Psilocybin 0.2 mg/kg	16 healthy volunteers (8 men and 8 women) Age range: 27-45 y/o		STAI-X1 state: There were no differences ^{NS} between placebo and psilocybin group. PET scan ^a: Psilocybin-induced alterations in the activations in the following regions were associated with anxiety measures as follows: o Psilocybin increased activity in the right cingulate cortex,	*HRS: Psilocybin increased ^{sa} following items related to the cognitive systems: - o Cognition - o Perception - o Somaesthesia *COVAT with predictive peripheral cues: Psilocybin significantly increased reaction times ^{sl} in most types of trials ^a , compared to the placebo group. *APZ: Psilocybin increased ^{sa} “Visionary restructuralization”	*HRS: Psilocybin increased “Volition” ^{sas} in a dose-dependent manner, starting from 5 mg/70 kg.		

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		drug administration. PANSS was additionally measured retrospectively 24 hours post-intervention. Covert orienting of attention task (COVAT) was administered one hour before and 75-95 after drug administration.				which was negatively associated ^m with anxiety as measured by STAI-X1[76] o Psilocybin decreased the activity of the left thalamus; this deactivation was associated ^m with anxiety (as measured by STAI-X1 and PANSS).				
45	(Vollenweider et al., 1999)[77]	Randomized placebo-controlled study consisting of two sessions separated by a 1-month interval. Questionnaires were taken 140 min post-intervention; PET scan with [¹¹ C] raclopride was performed 80 min after drug administration.	Psilocybin 0.25mg/kg				*APZ: Psilocybin increased ^{sa} “Visual restructuralization”.	*APZ: Psilocybin ^{sas} increased “depersonalization”; this increase was associated ^m with an increase in dopamine release in ventral striatum as measured by PET scan.		
46	(Vollenweider et al., 1998)[78]	Placebo-controlled within-subject design consisting of two experiments. Experiment 1: Three pretreatment groups: ketanserin group (placebo or 20 mg or 40 mg ketanserin), Haloperidol group (placebo or 0.021 mg IV Haloperidol), and Risperidone group (placebo or 0.5 mg or 1 mg Risperidone). Two treatment groups Psilocybin 0.25 mg/kg Or placebo. Experiment 2: pretreatment with either 40 mg ketanserin or placebo	Psilocybin: 0.25 mg/kg Risperidone (5HT2/D2 receptor antagonist): 0.5 and 1 mg Haloperidol (D2 receptor antagonist): 0.021 mg IV Ketanserin 20 and 40 mg (5-HT2A receptor antagonist)	Experiment 1: 15 healthy volunteers (8 men and 7 women) Mean age: 29.7 ±5.3 y/o Experiment 2: 10 healthy volunteers (5 men and 5 women) Mean age: 28.4 ±4.0 y/o			*DRT: Psilocybin increased ^{si} the reaction time in this spatial working memory task. Ketanserin ^m and risperidone ^m, but not haloperidol ^m, dose-dependently blocked the increase in reaction time on the DRT. *APZ: Psilocybin increased ^{sa} “Visionary restructuralization”, which was blocked by Ketanserin ^m and risperidone ^m in a dose-dependent manner. No effect was seen in the haloperidol ^m pretreatment group.			

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		treatment with either 0.25 mg/kg psilocybin or placebo. APZ and DRT were measured before and 80 min after administration.								
47	(Gouzoulis-Mayfrank et al., 1998)[79]	Double-blind placebo-controlled pseudorandomized design. Startle reflex was measured at baseline and 75-90 min after the administration.	Psilocybin 0.2 mg/kg (max 15 mg)	12 healthy (6 men, 6 women) Mean age: 32.9 ±? y/o			PPI and startle reflex (habituation): Psilocybin increased ⁹⁶ PPI while having no clear effect ^{NS} on habituation. These results were interpreted as enhanced sensorimotor gating (filtering of irrelevant information).			
48	(Vollenweider, 1997)[80]	Open-label placebo-controlled study. Three sessions with [¹⁸ F] FDG -PET scans were carried out at monthly intervals: a baseline PET scan and one with psilocybin. Subjects were aware that they are receiving a drug but were unaware which one. Psilocybin was administered 90 min prior the PET scan acquisition. EPI and APZ questionnaire were measured at baseline and immediately after each PET scan.	Psilocybin 15 mg for subjects <50 kg body weight and 20 mg PO for subjects >51 kg	15 healthy volunteers (8 men and 7 women) Mean age: 33.3 ±4.8			*APZ: Psilocybin increased ⁹⁸ “Visual restructuralization” subscale; the scores of this subscale were negatively associated ^m with the increase of the frontomedial-temporolateral metabolic ratio.	*Ego pathology Inventory (EPI): Psilocybin increased ⁹⁸ the global score in comparison to baseline. The psilocybin-induced changes in the absolute metabolic rates or metabolic ratios were associated ^m with the EPI in the following manner: - o The scores of “ego-identity” and “ego-demarcation” subscales were positively associated with the increase in absolute cerebral metabolic rates of Glucose (CMR-glu) in the right frontomedial cortex. - o The scores of “ego identity” were positively associated with the changes of frontomedial-anterior cingulate ratio in the left hemisphere and the frontomedial-temporomedial ratio in the right hemisphere - o The EPIglobal scores showed positive correlations with		

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
								CMRglu in the left frontolateral cortex, right frontomedial cortex, and right cingulate posterior cortex.		
49	(Spitzer et al., 1996)[81]	Double-blind, placebo-controlled study consisting of two sessions separated by 1-wk interval. Two versions of lexical decision tasks were performed alternatively by subjects before, and 50,150 and 220 min after drug intake.	Psilocybin 0.2 mg/kg	8 healthy men Mean age: 39.4 ±? y/o			*Direct and Indirect semantic priming test ^a: ○ Compared to placebo group, psilocybin increased ^{sa} indirect semantic priming. ○ No increase ^{NS} in error rates or direct semantic priming were observed under psilocybin condition.			
Animal studies										
50	(Meinhardt et al. , 2020) [82]	Placebo-controlled study in an alcohol deprivation effect (ADE) model to investigate the effect of three different psilocybin-dosing regimens on relapse-like alcohol consumption. The repeated dose regiment consisted of 5 dosing across three days. The high-dose regimen consisted of two high doses with 1-wk interval. The intermittent microdosing regimen consisting of twice per week for 4 wks.	Psilocybin IP The repeated-dose regimen: 1mg/kg The high-dose regimen: 2.5 mg or 10 mg/kg The intermittent microdosing regimen: 0.1 mg /kg	64 male and female Wistar rats	*ADE: ○ <i>Repeated dosing regimen:</i> compared to saline group, psilocybin significantly reduced relapse-like drinking ^{le} ○ <i>High-dose and microdose regimens:</i> psilocybin had no effect on relapse-like drinking ^{NS}.					*Locomotor activity during the test: psilocybin reduced ^{sim} the activity only in male rats 2h post-administration in the first experiment.
51	(Jones et al., 2020) [83] <i>Note: at the time of publication only the preprint version was available. The results were directly verified with the authors on 24th November 2021</i>	Placebo-controlled; post-acute and delayed psilocybin effect on mouse anxious and hedonic behavior after chronic corticosterone treatment;	Psilocybin: IP 0 ,0.3,1,3 mg/kg 21 days 0-80 µg/ml PO corticosterone	270 C57BL/6J male mice Mean age: 6-8 wks old	*NSF In the absence of corticosterone, psilocybin increased ^{se} the time in the feeding zone, while at 80 µg/ml, these substances	OFT: 4 hours and 7 days after corticosterone pretreatment, compared to mice treated with psilocybin, mice receiving Corticosterone+				*Locomotor activity by OFT paradigm: at 3 mg/kg, psilocybin increased ^{sa} the locomotor activity 10

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		measurements taken 4 hours, 2- and 7-days post-injection.	OR 28 days 0-50 µg/ml PO corticosterone		decreased ^m time in this zone. *SPT No significant effect ^{NS} for psilocybin on sugar preference.	psilocybin spent less time ^m in the center.				minutes post-administration. This effect was absent in the 4h post-intervention time point.
52	(Hibicke et al., 2020) [84]	Placebo-controlled study consisting of four groups, placebo, repeated-measure psilocybin (rPSI) and interval psilocybin (iPSI), and an additional psilocybin group (PSI). All psilocybin groups received the injection on day 0. Locomotor activity (LCA) and forced swim test (FST) were assessed in placebo and rPSI rats on days 7, 14, 21, 28, and 35 following a pre-exposure to FST on day 6. iPSI rats were pre-exposed to FST on day 34 and were tested on day 35. PSI rats were pre-exposed on day 6 and were tested on day 7. Elevated plus Maze (EPM) behaviors were assessed on day 41.	Psilocybin IP 1 mg/kg	24 male Wistar-Kyoto (WKY) rats	*FST: psilocybin altered following outcome measures related to PVS: o Immobility: reduced ^{le} immobility compared to the placebo group. rPSI rats were significantly less immobile than saline group 4 and 5 wks (days 28 and 35) post-administration. iPSI rats were also more mobile on day 35 post-intervention. This immobility reduction was due to significantly higher swimming and climbing. In the PSI group, mobility and swimming was significantly higher than placebo group; climbing was not significantly ^{NS} different.	Anxiety paradigms: *EPM: rPSI and PSI rats spent more time ^{ldt} in the open arm and less time in the closed arm than placebo group.				*Locomotor activity by OFT paradigm: No difference ^{NS} were observed between psilocybin and control group.
53	(Sakloth et al., 2019)[85]	Placebo-controlled study using intracranial self-stimulation (ICSS) paradigm in two test-blocks. First, the dose-effect test block consists of 6 naïve rats. Second the time-course study block that	Psilocybin IP 0.032, 0.1, 0.32 and 1 mg/kg	7 adult male Sprague-Dawley rats for the psilocybin group	*ICSS: o At doses lower than 1 mg/kg, psilocybin had a weak and inconsistent effect ^{slr} on ICSS facilitation across the tested					

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
		consisted 5 rats from the previous test block plus one naïve rat.			frequency range (2-2.2 log Hz). More accurately, 0.1 mg/kg facilitated ICSS at one frequency 30 min post-injection. o At 1 mg/kg psilocybin depressed ^{se} ICSS and lowered the number of total stimulations at 10 min and 30 min post-injection.					
54	(Jefsen et al., 2019)[86]	Placebo-controlled study. Four different experiments in two of which tests were taken 24 hours after single administration of the test drugs. One experiment was conducted 4 hours post-intervention and another was conducted 8 days after three administrations of the test drugs on subsequent days.	Psilocybin IP: 2 mg/kg, 3 mg/kg, 10 mg/kg Psilocin IP: 0.5 mg/kg, and 2 mg/kg	76 Flinders Sensitive Line (FSL) rat 71 Flinders Resistant Line (FRL) rat	*FST No effects ^{ns} of psilocybin or psilocin on immobility, struggling and swimming.					OFT: No effect ^{ns} of Psilocybin on locomotor activity of FSL rats
55	(Horsley et al., 2018)[87]	Placebo-controlled study. Three interventions in 6 days. long-lasting effects (48-hour period after final drug treatment) of sub-chronic dosing of hallucinogens	Psilocin 0.05 or 0.075 mg/kg	8 male Wistar rats		*EPM The low dose of psilocin seemed to produce mild anxiogenic ^{sif} effect and reduced open arm entries. The high-dose did not affect ^{ns} this parameter.				Locomotor activity: Psilocybin did not affect ^{ns} this parameter.
56	(Tylš et al., 2016) [88]	Placebo-controlled study consisting of two 30-minute test blocks. The effect of psilocybin and sex differences on locomotor activity and PPI using OFT PPI acoustic reflex paradigms.	Psilocin 0.25, 1 and 4 mg/kg IV 5-HT1A receptor antagonist (WAY100635): 1 mg/kg	8-12 adult male and female Wistar rats in each experimental group		*Qualitative behavior: psilocin reduced the following items related to NVS domain: o Rearing: psilocin reduced ^{sif} rearing. During the second block, this effect was only observed	PPI of the acoustic startle reaction: Psilocybin decreased ^{sa} PPI only in male rats and only at 1mg/kg dose. 5-HT _{2A} receptor antagonist (MDL100907) reversed ^m the disruptions caused by 0.25 mg/kg of psilocin.			*Locomotor activity: o OFT paradigm: Psilocin dose-dependentl y increased ^{sim} “immobility

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
			5-HT _{2A} receptor antagonist (MDL100907): 0.5 mg/kg 5-HT _{2B} receptor antagonist (SB215505): 1 mg/kg 5-HT _{2C} receptor antagonist (SB242084): 1 mg/kg			with doses ≥ 1.2 mg/kg				" and "flat body posture". o <i>Trajectory length</i> : at doses 1 and 4 mg/kg, psilocin induced a dose-dependent decrease ^{sim} in the locomotor activity in male and MD (metoestrus +dioestrus) female rats but not in PE (prooestrus + oestrus) female rats. o The psilocin-induced locomotion inhibition was reversed by 5-HT _{2C} antagonist (SB242084) ^m and by a 5-HT _{1A} antagonist (WAY100635) ^m
57	(Spain et al., 2015)[89]	Placebo-controlled study. Measurements were taken immediately post-administration.	Psilocin IV 2 mg/kg, 0.03 mg/kg,	30 Sprague–Dawley rats			*phMRI : Following 2 mg/kg psilocin, BOLD signal decreases ^{sa} in the visual system and limbic and olfactory areas.			*phMRI Following 2 mg/kg psilocin, BOLD signal decreases ^{sa} in somatosensory cortex BOLD signal CBF :

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
										Following 2 mg/kg psilocin altered^{sa} following parameters: - Initial increase in CBF in somatosensory cortex in long stimulation paradigm - Increase in CBF in somatosensory cortex in shorter stimulation with multiple frequencies at 10 Hz LFP: Psilocybin - Did not change^{NS} somatosensory cortex neuronal response following long stimulation paradigm - Decrease^{sa} in somatosensory cortex neuronal response at high frequencies in mixed paradigm

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
58	(Rambosek et al., 2014)[90]	Placebo-controlled study of the effects of psilocin on memory acquisition, retrieval and consolidation in rats. Measurements were taken for reinforced retrieval on day 5 after 4 days of drug treatment, 6 days after the last injection, re-acquisition was assessed, memory consolidation was measured on day 2 after receiving IP injection of drugs on day 1.	Psilocin SC injection, 1 and 4 mg/kg	24 Male Wistar Rats Mean age: 12-14 wks			*Carousel maze: Both doses of psilocin disrupted^{sl} memory acquisition in this task; the higher dose blocked the learning process in the additional session with only saline administration. *MWM - Only 4 mg/kg psilocin significantly impaired^{sl} reinforced retrieval Neither of the doses affected^{ns} memory consolidation when administered post-training. Thus, the Psilocin had no effect on memory consolidation			
59	(Catlow et al., 2013)[91]	Animal Experiment Placebo-controlled; effect of psilocybin on extinction of trace fear conditioning in 10 trials and on hippocampal neurogenesis 2wks post-intervention; in 10 trials three days post-intervention and on hippocampal neurogenesis 2wks post-intervention	Psilocybin: IP 0.1, 0.5, 1.0 and 1.5 mg/kg Ketanserin: 1.0 mg/kg (5-HT2A receptor antagonist) Saline	48 C57BL/6J male mice (n = 9–10/condition)		Fear Conditioning^a - Doses of 0.1 and 0.5 mg/kg Psilocybin facilitated the extinction^{sdt} of trace fear conditioning by trial 3; which was significantly faster than that in mice that received higher doses or saline. Low dose was associated with a trend toward an increase^{ldt} or no change in hippocampal neurogenesis. - Mice, receiving higher doses of 1.0 and 1.5 mg/kg of psilocybin and Ketanserin, exhibited no sign^{ns} of freezing-like behavior by trial 10. - Ketanserin and High dose of Psilocybin significantly reduced^m the				

Row	Study	Study characteristics	Intervention	Study Sample	Positive valence systems (PVS)	Negative valence systems (NVS)	Cognitive systems	Social processes	Arousal and regulatory systems	Sensorimotor systems
						hippocampal neurogenesis.				
60	(Halberstadt et al., 2011)[92]	placebo-controlled study on the effects of psilocybin on locomotor activity and exploratory behavior using behavioral monitoring paradigm (BMP) [93] in two 30-minute test blocks.	Psilocin 0.3, 0.6, 1.2, 2.4, 4.8 mg/kg Selective 5-HT _{1A} antagonist (WAY-100635): 0.5 mg/kg Selective 5-HT _{2c} antagonist (SB-242084) 3 mg/kg	Male C57BL/6J mice N=103 5-HT2A wild-type (WT) mice N=20 5-HT2A knockout (KO) mice N=19		*BMP, center duration: psilocin reduced the following items related to NVS domain: o Center duration: Psilocin reduced center duration ^{sif} at doses ≥ 1.2 mg/kg during the first test block and at 4.8 mg/kg during the second block; this effect was blocked ^m by WAY-100635 o Rearing: During the first text block, all doses of psilocin reduced ^{sif} rearing. During the second block, this effect was only observed with doses ≥ 1.2 mg/kg o Holepoking: at doses ≥ 1.2 mg/kg, psilocin reduced ^{sif} holepoking only during the first test block; this effect was blocked ^m by WAY-100635				*BMP: psilocin decreased ^{sim} following items related to sensorimotor systems only at dose 4.8 mg/kg and during the second block: o Locomotor activity this effect was blocked by WAY-100635 o Spatial d coefficient this effect was blocked by SB-242084
61	(Fantegrossi et al., 2004)[94]	Placebo-controlled study on the reinforcing effect of psilocybin using a self-administration behavioral paradigm ^a	Psilocybin at doses 0.00003, 0.0001, 0.0003 and 0.001 mg/kg	4 adult rhesus monkeys (3 male and 1 female) with extensive self-administration histories	*Self-administration behavioral paradigm: None of the doses of ^{ns} psilocybin caused a significantly higher response rate Compared to saline.					

a: Readers are invited to refer to the article for more details about the study paradigm. 5D-ASC: five dimensional altered states of consciousness questionnaire. AMRS: adjective mood rating scale. APZ: (German word for) Altered states of consciousness. AX-CPT: stands for AX continuous performance task. BDI: Beck depression inventory. CBF: Cerebral blood flow. DPES: Dispositional positive emotion scale. DRT: Delayed response task (working memory). DRT (2): Duration response task. EDI: Ego dissolution inventory. EPM: Elevated plus maze. ERP: Event related potential. FAIR: Frankfurt attention inventory. FST: Forced swimming test. fMRI: functional magnetic resonance imaging. H: hour. HAI: hopelessness and illness scale. HRS: Hallucinogen rating scale. Hrs: hours. IP: Intraperitoneal injection. IV: intravenous. Kg: kilogram. LCIR- S: Life Change Inventory. LFP: Local field potential. M-scale /MEQ: mystical-type experiences questionnaire. MEQ30: 30-item Mystical experience questionnaire. Mg: milligram. MRI: Magnetic resonance imaging. MRS:

Magnetic resonance spectroscopy. MWM: Morris Water Maze. NSF: Novelty suppressed feeding test. OFT: Open-field test. PANAS: positive and negative affect schedule. PANSS: The positive and negative syndrome scale. PEQ: Persisting Effect Questionnaire sought information about changes in attitudes, moods, behavior, and spiritual experience. PO: per oral. POMS: Profile of mood states. PPI: Pre-pulse inhibition. (phMRI): Pharmacological magnetic resonance imaging. QIDS: Quick inventory of depressive symptomatology. REM: Rapid eye movement. TRD: treatment-resistant depression. SC: Subcutaneous. SOCQ: State of consciousness questionnaire. SHAPS: Snaith-Hamilton pleasure scale. STAI-trait: State-Trait Anxiety Inventory. SPT: Sugar preference test. SWA: Slow-wave activity. Wks: weeks. Y/o: years old.

Outcome measures were labeled by an indicator according to table S2. And are as follows: leo: long-term effect on enhancement in "perception & understanding of others". las: long-term effect on alteration in "perception & understanding of self", lasc: long-term effect on alteration in "social communication". les: long-term effect on Enhancement in "perception & understanding of self". ldt: Long-term decrease in the "sustained threat" subdomain. le: long-term enhancement. m: miscellaneous. sa: short-term alteration. sea: short-term effect on enhancement in "affiliation and attachment". sim: short-term impairment in "motor actions". seo: short-term effect on enhancement in "perception & understanding of others". sas: short-term effects on alteration in "perception & understanding of self". sasc: short-term alteration in "social communication". se: short-term enhancement. sdt: short-term decrease in the "sustained threat" subdomain. si: short-term impairment, sif: short-term increase of "fear".ssw: short-term alteration in "sleep-wakefulness. sir: short-term Increase in reward seeking, ns: non-significant changes. sil: short-term Increase in "loss" subdomain. m: Miscellaneous. sia: short-term Impaired "arousal". PVS: Positive valence systems. NVS: Negative valence systems. Cog.sys: Cognitive systems. Soc.pro: Social processes. A & R sys: Arousal and regulatory systems. SM sys: sensorimotor systems. *NOTES: The administration of the pharmacological agents was per oral unless otherwise indicated*

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