



A transdiagnostic meta-analysis of acute augmentations to psychological therapy

In the format provided by the authors and unedited

Supplemental Materials

1. Supplementary Methods

1.1. Search terms

The databases Medline (via Ovid), Embase (via Ovid) and PsycInfo (via Ebscohost) were searched from inception to February 2nd 2021 ([initial search](#)) and then again from inception until 25 May 2022 ([updated search](#)), using the search terms below. Results were limited to English language papers. In addition, the ClinicalTrials.gov website was searched for grey literature, using the modified search terms below.

Medline via Ovid

("cognitive processing" OR "narrative exposure therapy" OR "prolonged exposure therapy" OR "virtual reality exposure therapy" OR "cognitive behavioural therapy" OR "cognitive behavioral therapy" OR CBT OR "eye movement desensiti*" OR EMDR OR "psychodynamic psychotherapy" OR "interpersonal psychotherapy" OR "mindfulness" OR "acceptance and commitment therapy" OR "attention training" OR "dialectical behavioural therapy" OR "dialectical behavioral therapy" OR "animal assisted" OR "animal-assisted" OR "cognitive analytical therapy" OR "imagery psychotherapy" OR psychotherapy OR "Cognitive therapy" OR "behavioural activation" OR "behavioral activation" OR "behaviour therapy" OR "behavior therapy" OR "cognitive analytic therapy" OR "cognitive behaviour therapy" OR "cognitive behavior therapy" OR "dialectical behaviour therapy" OR "dialectical behavior therapy" OR ACT OR "exposure therapy").ti,ab,kw. OR Cognitive Behavioral Therapy/ OR Narrative Therapy/ OR Eye Movement Desensitization Reprocessing/ OR psychotherapy/ or imagery, psychotherapy/ or interpersonal psychotherapy/ or psychotherapy, psychodynamic/ OR mindfulness/ OR "Acceptance and Commitment Therapy"/ OR animal assisted therapy/ OR behavior therapy/ OR dialectical behavior therapy/

AND

(psychiatric OR "mood disorder*" OR depress* OR dysphori* OR dysthymi* OR bipolar OR mania OR manic OR schiz* OR psychosis OR psychotic OR delusional OR paranoid OR anxiety OR "post traumatic stress disorder" OR PTSD OR "posttraumatic stress disorder*" OR "post-traumatic stress disorder*" OR "acute stress disorder*" OR agoraphobia OR phobia OR panic OR "obsessive compulsive" OR OCD OR hoarding OR "eating disorder*" OR anorexi* OR bulimi* OR "binge eating" OR "body dysmorphi*" OR "personality disorder*" OR borderline OR antisocial OR narcissistic OR histrionic OR somatoform OR somatic OR "substance use disorder*" OR "substance abuse" OR "substance dependence" OR addiction OR dependen* OR "oppositional defiant" OR "intermittent explosive" OR "sexual dysfunction" OR "dissociative disorder" OR Hypomania).ti,ab,kw. OR exp mental disorders/

AND

(augment* OR enhanc* OR adjunct* OR conjunct* OR amplify OR assist* OR supplement* OR combin*).ti,ab,kw.

AND

("clinical trial*" OR "controlled trial*" OR "Controlled Before-After Studies" OR "Pilot Projects" OR "feasibility trial*" OR "exploratory trial*").ti,ab,kw. OR exp Clinical Trials/ OR Controlled Before-After Studies/ OR Pilot Projects/

Embase via Ovid

("cognitive processing" OR "narrative exposure therapy" OR "prolonged exposure therapy" OR "virtual reality exposure therapy" OR "cognitive behavioural therapy" OR "cognitive behavioral therapy" OR CBT OR "eye movement desensiti*" OR EMDR OR "psychodynamic psychotherapy" OR "interpersonal psychotherapy" OR mindfulness OR "acceptance and commitment therapy" OR "attention training" OR "dialectical behavioural therapy" OR "dialectical behavioral therapy" OR "animal assisted" OR "animal-assisted" OR "cognitive analytical therapy" OR "imagery psychotherapy" OR psychotherapy OR "Cognitive therapy" OR "behavioural activation" OR "behavioral activation" OR "behaviour therapy" OR "behavior therapy" OR "cognitive analytic therapy" OR "cognitive behaviour therapy" OR "cognitive behavior therapy" OR "dialectical behaviour therapy" OR "dialectical behavior therapy" OR ACT OR "exposure therapy").ti,ab,kw. OR Cognitive Behavioral Therapy/ or Narrative Therapy/ OR Eye Movement Desensitization Reprocessing/ OR psychotherapy/ or imagery, psychotherapy/ or interpersonal psychotherapy/ or psychotherapy, psychodynamic/ OR mindfulness/ OR "Acceptance and Commitment Therapy"/ OR animal assisted therapy/ OR cognitive therapy/ OR behaviour therapy/ OR exposure therapy/

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PsycInfo via Ebscohost

TI ("cognitive processing" OR "narrative exposure therapy" OR "prolonged exposure therapy" OR "virtual reality exposure therapy" OR "cognitive behavioural therapy" OR

“cognitive behavioral therapy” OR CBT OR “eye movement desensiti*” OR EMDR OR
“psychodynamic psychotherapy” OR “interpersonal psychotherapy” OR “mindfulness” OR
“acceptance and commitment therapy” OR “attention training” OR “dialectical behavioural
therapy” OR “dialectical behavioral therapy” OR “animal assisted” OR “animal-assisted”
OR “cognitive analytical therapy” OR “imagery psychotherapy” OR “psychotherapy” OR
“Cognitive therapy” OR “behavioural activation” OR “behavioral activation” OR
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OR “dialectical behavior therapy” OR ACT OR “exposure therapy”) OR AB (“cognitive
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“behaviour therapy” OR “behavior therapy” OR “cognitive analytic therapy” OR “cognitive
behaviour therapy” OR “cognitive behavior therapy” OR “dialectical behaviour therapy”
OR “dialectical behavior therapy” OR ACT OR “exposure therapy”) OR DE “Cognitive
Processing Therapy” OR DE “Narrative Therapy” OR DE “Exposure Therapy” OR DE “Eye
Movement Desensitization Therapy” OR DE “Psychodynamic Psychotherapy” OR DE
“Interpersonal Psychotherapy” OR DE “Mindfulness” OR DE “Animal Assisted Therapy”
OR DE “Psychotherapy” OR DE “Cognitive Therapy” OR DE “Behavioral Activation
System” OR DE “Behavior Therapy” OR DE “Cognitive Behavior Therapy” OR DE
“Dialectical Behavior Therapy” OR DE “Exposure Therapy”

AND

TI (psychiatric OR “mood disorder*” OR depress* OR dysphori* OR dysthymi* OR bipolar OR
mania OR manic OR schiz* OR psychosis OR psychotic OR delusional OR paranoid OR
anxiety OR “post traumatic stress disorder” OR PTSD OR “posttraumatic stress disorder*” OR
“post-traumatic stress disorder*” OR “acute stress disorder*” OR agoraphobia OR phobia OR
panic OR “obsessive compulsive” OR OCD OR hoarding OR “eating disorder*” OR anorexi*
OR bulimi* OR “binge eating” OR “body dysmorphi*” OR “personality disorder*” OR
borderline OR antisocial OR narcissistic OR histrionic OR somatoform OR somatic OR
“substance use disorder*” OR “substance abuse” OR “substance dependence” OR addiction OR
dependen* OR “oppositional defiant” OR “intermittent explosive” OR “sexual dysfunction” OR
“dissociative disorder” OR Hypomania) OR AB (psychiatric OR “mood disorder*” OR
depress* OR dysphori* OR dysthymi* OR bipolar OR mania OR manic OR schiz* OR
psychosis OR psychotic OR delusional OR paranoid OR anxiety OR “post traumatic stress
disorder” OR PTSD OR “posttraumatic stress disorder*” OR “post-traumatic stress disorder*”
OR “acute stress disorder*” OR agoraphobia OR phobia OR panic OR “obsessive compulsive”
OR OCD OR hoarding OR “eating disorder*” OR anorexi* OR bulimi* OR “binge eating” OR
“body dysmorphi*” OR “personality disorder*” OR borderline OR antisocial OR narcissistic
OR histrionic OR somatoform OR somatic OR “substance use disorder*” OR “substance abuse”
OR “substance dependence” OR addiction OR dependen* OR “oppositional defiant” OR

"intermittent explosive" OR "sexual dysfunction" OR "dissociative disorder" OR Hypomania) OR DE "Mental Disorders" OR DE "Affective Disorders" OR DE "Anxiety Disorders" OR DE "Autism Spectrum Disorders" OR DE "Bipolar Disorder" OR DE "Borderline States" OR DE "Chronic Mental Illness" OR DE "Dissociative Disorders" OR DE "Eating Disorders" OR DE "Gender Dysphoria" OR DE "Mental Disorders due to General Medical Conditions" OR DE "Neurocognitive Disorders" OR DE "Neurodevelopmental Disorders" OR DE "Neurosis" OR DE "Paraphilias" OR DE "Personality Disorders" OR DE "Psychosis" OR DE "Serious Mental Illness" OR DE "Sleep Wake Disorders" OR DE "Somatoform Disorders" OR DE "Stress and Trauma Related Disorders" OR DE "Substance Related and Addictive Disorders" OR DE "Thought Disturbances" OR DE "Hypomania"

AND

TI (augment* OR enhanc* OR adjunct* OR conjunct* OR amplify OR assist* OR supplement* OR combin*) OR AB (augment* OR enhanc* OR adjunct* OR conjunct* OR amplify OR assist* OR supplement* OR combin*)

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TI ("clinical trial*" OR "controlled trial*" OR "Controlled Before-After Studies" OR "Pilot Projects" OR "feasibility trial*" OR "exploratory trial*") OR AB ("clinical trial*" OR "controlled trial*" OR "Controlled Before-After Studies" OR "Pilot Projects" OR "feasibility trial*" OR "exploratory trial*") OR DE "Clinical Trials" OR DE "Randomized Controlled Trials"

ClinicalTrials.gov

(Psychiatric disorder*) AND (behavioral OR pharmacological OR somatic) AND (psychological therapy)

2. Supplementary Results

2.1. Database search results

Supplemental Table S1. Studies identified by database in each search

Database	Results	New results (updated May 2022)
Medline via Ovid	4923	767
Embase via Ovid	10175	1373
PsycInfo via Ebscohost	2908	443
ClinicalTrials.gov	341	46

Total results prior to deduplication: 17347

Unique results after deduplication: 12458

New total results May 2022: 2629

Unique results after deduplication May 2022: 1984

Supplemental Table S2. Characteristics of studies included in the meta-analysis

Authors (year of publication)	Mental health measure (assessment)	HiTOP dimension	N	Mean (SD) age (1) Augmentation (2) Control group	Gender (% female)	(1) Augmentation group(s) & (2) Control group	Type of augmentation	Duration
Acheson et al. (2015) ³⁸	Arachnophobia (FSQ)	Fear	23	(1) 33.3 (4.01) (2) 26.77 (2.67)	82.6	(1) Exposure therapy + Oxytocin (2) Exposure therapy + Placebo	Pharmacological	Single session
Alladin & Alibhai (2007) ³⁹	Depression (BDI-II)	Distress	84	(1) 35.67 (11.40) (2) 33.67 (9.87)	57.1	(1) CBT + Hypnosis (2) CBT	Psychological/cognitive	16 weeks
Andersson et al. (2015) ⁴⁰	OCD (Y-BOCS)	Fear	128	(1) 34.64 (12.42) (2) 34.88 (12.22)	58	(1) ICBT + D-cycloserine (2) ICBT + Placebo	Pharmacological	12 weeks
Arntz et al. (2007) ⁴¹	PTSD (PSS-SR)	Distress	67	(1) 35.29 (11.29) (2) 35.41 (12.73)	65.7	(1) Imaginal exposure + Imagery rescripting (2) Imaginal exposure	Psychological/cognitive	10 weeks
Aust et al. (2022) ⁴²	Depression (MADRS)	Distress	95	(1) 42.7 (12.7) (2) 39.0 (14.8)	60.1	(1) CBT + tDCS (2) CBT + Sham tDCS	Somatic	6 weeks
Baker et al. (2020) ¹⁵	Panic Disorder (PDSS)	Fear	23	*32.4 (1.53)	43.5	(1) CBT + Attention Bias Modification Task (2) CBT + Sham task	Psychological/cognitive	6 weeks
Bischoff et al. (2018) ²⁴	Panic Disorder with agoraphobia (HAM-A)	Fear	77	(1) 37.2 (10) (2) 36.2 (10.1)	63.6	(1) CBT + Moderate-intensity exercise (2) CBT + Low-intensity exercise	Somatic	7 weeks
Bouso et al. (2008) ⁴³	PTSD (SSSPTSD)	Distress	5	(1) 36.67 (2) 33	100	(1) Psychotherapy + MDMA (2) Psychotherapy + Placebo	Pharmacological	Not reported
Brooks et al. (2021) ⁴⁴	Depression or anxiety + cognitive decline (FCC)	-	26	(1) 68.2 (5.9) (2) 69.2 (4.6)	46.2	(1) Mindfulness-based stress reduction + tDCS (2) Mindfulness-based stress reduction + Sham	Somatic	10 weeks
Bryant et al. (2005) ⁴⁵	Acute stress disorder (IES)	Distress	63	(1) 32.97 (7.70) (2) 33.09 (12.45)	Not reported	(1) CBT + Hypnosis (2) CBT	Psychological/cognitive	5 weeks
Bryant et al. (2008) ⁴⁶	PTSD (CAPS)	Distress	118	(1) 34.85 (10.99) (2) 39.98 (13.36)	Not reported	(1) Exposure therapy + IE/IVE & IE/IVE/CR (2) Exposure therapy + IE & IVE	Psychological/cognitive	8 weeks
Buchanan et al. (2021) ⁴⁷	Social functioning in schizophrenia (BSFS)	Thought disorder	62	(1) 42.8 (8.7) (2) 40.7 (10.2)	38.7	(1) CBSST + Oxytocin (2) CBSST + Placebo	Pharmacological	24 weeks
Burton et al. (2019) ⁴⁸	PTSD (PCL-M)	Distress	20	(1) 48 (15) (2) 46 (13)	20	(1) Psychotherapy + Equine-assistance (2) Psychotherapy	Other	6 weeks
Cesa et al. (2013) ⁴⁹	Binge eating disorder (BSS)	-	66	(1) 32.9 (8.8) (2) 31.02 (7.22)	100	(1) CBT + VR-enhanced CBT (2) CBT	Psychological/cognitive	6 weeks
Chien et al. (2015) ²⁵	Depression (PSQI)	Distress	89	(1) 28.15 (10.66) (2) 28.95 (11.55)	5.6	(1) Cognitive behavioural intervention + Breathing relaxation exercise (2) No therapy or augmentation	Somatic	4 weeks
Cobb et al. (2021) ¹⁹	Phobia (BAT)	Fear	49	*21.41 (7.12)	71	(1) Exposure therapy + tDCS (2) Exposure therapy + Sham tDCS	Somatic	Single session
Coffey et al. (2016) ⁵⁰	PTSD (IES-R)	Distress	126	(1) 34.4 (11.32) (2) 33.84 (10.44)	43.5	(1) Prolonged exposure + Motivational enhancement therapy (2) Prolonged exposure + Relaxation session	Psychological/cognitive	5 to 8 weeks
Contalbrigo et al. (2017) ⁵¹	Substance use disorder (SCL-90-R)	Substance abuse	22	(1) 35.5 (13.83) (2) 42.9 (9.1)	0	(1) Psychotherapy + Dog assistance (2) Psychotherapy	Other	6 months
Craske et al. (2019) ⁵²	Social anxiety (SCR to public speaking onset)	Fear	60	(1) 25.99 (10.27) (2) 23.05 (8.58)	67.5	(1) Exposure therapy + Scopolamine (0.5mg) (2) Exposure therapy + Placebo	Pharmacological	Not reported
Danforth et al. (2018) ⁵³	Social anxiety (LSAS)	Fear	12	(1) 32.8 (10.4) (2) 28.3 (3.8)	16.7	(1) Psychotherapy + MDMA (2) Psychotherapy + Placebo	Pharmacological	Not reported

Davis et al. (2014) ⁵⁴	Schizophrenia (Social-cognition composite score)	Thought disorder	22	(1) 42.8 (9.1) (2) 37 (10.8)	0	(1) Social cognitive skills training + Oxytocin (2) Social cognitive skills training + Placebo	Pharmacological	6 weeks
Davis et al. (2017) ⁵⁵	Social anxiety (LSAS)	Fear	73	(1) 26.88 (6.99) (2) 24.98 (7.73)	68	(1) Exposure therapy + Power posing (2) Exposure therapy + Submissive posing & no posing	Other	1 week
Davis et al. (2021) ⁵⁶	MDD (GRID-HAMD)	Distress	24	(1) 43.6 (13) (2) 35.2 (9.9)	66.7	(1) Psychotherapy + Psilocybin (2) Wait list (no therapy or augmentation)	Pharmacological	8 weeks
De Kleine et al. (2012) ⁵⁷	PTSD (CAPS)	Distress	67	(1) 36.27 (11.56) (2) 40.26 (11.05)	80.6	(1) Prolonged exposure + D-cycloserine (2) Prolonged exposure + Placebo	Pharmacological	Not reported
de Leeuw et al. (2017) ⁵⁸	OCD (Y-BOCS)	Fear	39	(1) 38.1 (14.2) (2) 32.2 (8.9)	Not reported	(1) Exposure therapy + D-cycloserine (2) Exposure therapy + Placebo	Pharmacological	7 weeks
De Quervain et al. (2011) ⁵⁹	Acrophobia (AQ)	Fear	40	(1) 42.8 (2.4) (2) 40.2 (2.6)	45	(1) VRET + Cortisol (2) VRET + Placebo	Pharmacological	2 weeks
Difede et al. (2014) ⁶⁰	PTSD (CAPS)	Distress	25	(1) 47.77 (11.92) (2) 43.75 (8.72)	24	(1) VRET + D-cycloserine (2) VRET + Placebo	Pharmacological	12 weeks
Diminich et al. (2020) ⁶¹	Delusions (PSYRATS-D)	Thought disorder	58	(1) 44.60 (13.3) (2) 45.55 (12.0)	39.7	(1) CBT + D-cycloserine (2) CBT + Placebo	Pharmacological	12 weeks
Falkenstein et al. (2022) ¹⁶	OCRDs (TBI, interpretation)	Fear	31	(1) 30.36 (8.44) (2) 27.25 (3.77)	50	(1) IRT + CBM-I (2) IRT + Psychoeducation	Psychological/cognitive	~4 weeks
Fayaz Feyzi et al. (2022) ⁶²	Methamphetamine use disorder (OCDUS)	Substance abuse	27	(1) 34 (6.7) (2) 37 (7)	0	(1) Matrix Model psychotherapy + tDCS (2) Matrix Model psychotherapy + Sham tDCS	Somatic	12 weeks
Feng et al. (2019) ⁶³	PTSD (CAPS)	Distress	120	(1) 40.9 (12.7) (2) 41 (12.8)	69.2	(1) CBT + Transcutaneous electrical acupoint stimulation (2) CBT + Simulated TEAS	Somatic	12 weeks
Flanagan et al. (2018) ⁶⁴	PTSD (CAPS)	Distress	17	(1) 41.63 (14.58) (2) 45.78 (15.09)	17.7	(1) Prolonged exposure + Oxytocin (2) Prolonged exposure + Placebo	Pharmacological	10 weeks
Foa et al. (2005) ⁶⁵	PTSD (PSS-I)	Distress	153	Not reported	100	(1) Prolonged exposure + Cognitive restructuring (2) Prolonged exposure	Psychological/cognitive	12 weeks
Fryml et al. (2019) ²¹	PTSD (CAPS)	Distress	8	(1) 27 (2.1) (2) 30 (2.6)	12.5	(1) Exposure therapy + rTMS (2) Exposure therapy + Sham rTMS	Somatic	5 weeks
Guastella et al. (2008) ⁶⁶	Social anxiety (SPAI)	Fear	56	*35.48 (11.35)	43	(1) Exposure therapy + D-cycloserine (2) Exposure therapy + Placebo	Pharmacological	5 weeks
Guastella et al. (2009) ⁶⁷	Social anxiety (SPAI)	Fear	25	*42.28 (11.27)	0	(1) Exposure therapy + Oxytocin (2) Exposure therapy + Placebo	Pharmacological	5 weeks
Harb et al. (2019) ⁶⁸	PTSD (NFQ)	Distress	78	(1) 37 (9.9) (2) 37.2 (10.1)	13.9	(1) CBT-I + Imagery rescripting (2) CBT-I	Psychological/cognitive	6 weeks
Harvey et al. (2016) ⁶⁹	MDD (IDS-SR)	Distress	42	(1) 43.92 (9.98) (2) 44.65 (12.17)	60.4	(1) Cognitive therapy + Memory support (2) Cognitive therapy	Psychological/cognitive	14 weeks
Hofmann et al. (2006) ⁷⁰	Social anxiety (SPAI)	Fear	23	(1) 30.08 (7.56) (2) 36.53 (22.04)	33.3	(1) Exposure therapy + D-cycloserine (2) Exposure therapy + Placebo	Pharmacological	5 weeks
Hofmann et al. (2013) ⁷¹	Social anxiety (SPD-S)	Fear	169	(1) 34.6 (2) 30.5	43.2	(1) CBT + D-cycloserine (2) CBT + Placebo	Pharmacological	12 weeks
Hofmeijer-Sevink et al. (2017) ⁷²	Panic disorder with agoraphobia (Mobility Inventory, alone subscale)	Fear	57	(1) 33.95 (10) (2) 38.3 (11.4)	59.6	(1) Exposure with response prevention + D-cycloserine (2) Exposure with response prevention + Placebo	Pharmacological	12 weeks
Hutschemaekers et al. (2021) ⁷³	Social anxiety disorder (SUDS)	Fear	54	(1) 22.61 (4.12) (2) 24.00 (6.85)	100	(1) Exposure therapy + Testosterone (2) Exposure therapy + Placebo	Pharmacological	Twice over month

Isserles et al. (2021) ⁷⁴	PTSD (CAPS)	Distress	125	(1) 44.8 (13.19) (2) 43.7 (12.25)	66.4	(1) Exposure (ultrabrief SDI) + DTMS (2) Exposure (ultrabrief SDI) + Sham DTMS	Somatic	4 weeks
Isserles et al. (2013) ²²	PTSD (CAPS)	Distress	18	(1) 49 (12.5) (2) 40.4 (10.5)	16.7	(1) Exposure therapy + DTMS (2) Exposure therapy + Sham DTMS	Somatic	4 weeks
Janse et al. (2020) ⁷⁵	Somatoform, mood, and/or anxiety disorder (SCL-90-R, GSI)	-	368	(1) 40.4 (11.9) (2) 42.6 (12.3)	57.9	(1) CBT + High-intensity progress monitoring (feedback) (2) CBT + Low-intensity feedback monitoring	Psychological/cognitive	33 weeks
Kamboj et al. (2012) ⁷⁶	Nicotine dependence (VAS)	Substance abuse	32	(1) 30 (9.37) (2) 32.31 (10.64)	31.2	(1) Exposure/response prevention + D-cycloserine (2) Exposure/response prevention + Placebo	Pharmacological	Two sessions
Kozel et al. (2018) ²³	PTSD (CAPS)	Distress	61	(1) 34.06 (7.56) (2) 32.93 (6.04)	Not reported	(1) Cognitive processing therapy + rTMS (2) Cognitive processing therapy + Sham rTMS	Somatic	12 weeks
Krupitsky et al. (2002) ⁷⁷	Heroin dependence (VAS, craving)	Substance abuse	70	(1) 23 (4.4) (2) 21.6 (3)	21.4	(1) Psychotherapy + Ketamine (2mg) (2) Psychotherapy + Ketamine (0.2mg)	Pharmacological	Single session
Kushner et al. (2007) ⁷⁸	OCD (Y-BOCS)	Fear	25	Not reported	Not reported	(1) Exposure/ritual prevention therapy + D-cycloserine (2) Exposure/ritual prevention therapy + Placebo	Pharmacological	5 weeks
Kwee et al. (2022) ⁷⁹	Panic disorder with agoraphobia or social anxiety (Fear Questionnaire)	Fear	80	(1) 34.9 (9.3) (2) 38.3 (11.3)	40	(1) Exposure therapy + Cannabidiol (2) Exposure therapy + Placebo	Pharmacological	8 weeks
Lancaster et al. (2020) ⁸⁰	Fear of spiders or snakes (BAT-T, step no.)	Fear	166	(1) 19.51 (2.20) (2) 19.27 (1.46)	80	(1) Exposure therapy + Pre-extinction fear memory reactivation & deepened extinction (2) Exposure therapy	Psychological/cognitive	1 day
Lass-Hennemann & Michael (2014) ⁸¹	Spider phobia (BAT)	Fear	60	(1) 23.33 (1.12) (2) 25.87 (1.06)	100	(1) Exposure therapy + High endogenous cortisol levels (morning) (2) Exposure therapy + Low endogenous cortisol (evening)	Somatic	Single session
Lazarov et al. (2018) ¹⁴	Social anxiety (LSAS)	Fear	50	(1) 33.60 (5.14) (2) 35.54 (10.62)	36	(1) CBGT + Attention bias modification (2) CBGT + Placebo	Psychological/cognitive	18 weeks
Lee et al. (2020) ⁸²	MDD (Patient recall task)	Distress	42	(1) 42.18 (8.10) (2) 45.25 (12.02)	54.8	(1) Cognitive therapy + Memory support (2) Cognitive therapy	Psychological/cognitive	14 weeks
Lehrner et al. (2021) ⁸³	PTSD (CAPS)	Distress	60	(1) 36.07 (8.07) (2) 34.63 (7.68)	90	(1) Prolonged exposure + Hydrocortisone (2) Prolonged exposure + Placebo	Pharmacological	12 weeks
Leuchter et al. (2022) ⁸⁴	Depression (FSQ)	Distress	17	(1) 21.1 (2.3) (2) 21.1 (3.8)	64.7	(1) Exposure therapy + rTMS (vmPFC) (2) Exposure therapy + vertex rTMS	Somatic	3 sessions over 2 weeks
Litz et al. (2012) ⁸⁵	PTSD (CAPS)	Distress	26	(1) 32.77 (9.85) (2) 31.62 (9.10)	0	(1) Exposure therapy + D-cycloserine (2) Exposure therapy + Placebo	Pharmacological	6 weeks
Maples-Keller et al. (2017) ⁸⁶	Fear of flying (FFI)	Fear	89	(1) 43.4 (11.32) (2) 40.8 (12)	79.8	(1) VRET + Reactivation cue (2) VRET + Neutral cue	Psychological/cognitive	8 weeks
Marker et al. (2020) ⁸⁷	Anxiety, OCD and/or PTSD (ADIS-5, CSR)	Fear	36	(1) 41.56 (12.89) (2) 40.61 (17.61)	55.6	(1) CBT + Motivational interviewing (2) CBT + Psychoeducation	Psychological/cognitive	12 weeks
McEvoy et al. (2020) ⁹	Social anxiety (SIAS)	Fear	105	(1) 30.14 (12.79) (2) 27.06 (9.71)	49.5	(1) CBT + Imagery-enhanced CBT (2) CBT + Verbally-based CBT	Psychological/cognitive	12 weeks
Meyer et al. (2010) ⁸⁸	OCD (Y-BOCS)	Fear	93	*38.6 (12.5)	75.3	(1) CBGT + Motivational interviewing and thought mapping (2) CBGT	Psychological/cognitive	12 weeks
Meyer et al. (2022) ⁸⁹	Depression (HAM-D)	Distress	10	(1) 46 (range 35-59)	90	(1) Online CBT + Moderate-intensity exercise (ActiveCBT)	Somatic	8 weeks

Meyerbroeker et al. (2012) ⁹⁰	Fear of flying (FAM)	Fear	45	(2) 44 (range 19-51) Not reported	Not reported	(2) Online CBT + Usual activities before therapy (CalmCBT) (1) Virtual reality exposure therapy + Yohimbine Hydrochloride (2) Virtual reality exposure therapy + Placebo	Pharmacological	4 weeks
Meyerbröker et al. (2018) ⁹¹	Fear of flying (FAM)	Fear	54	*36.6 (12.1)	55	(1) VRET + Yohimbine Hydrochloride & propranolol (2) VRET + Placebo	Pharmacological	Not reported
Mithoefer et al. (2011) ⁹²	PTSD (CAPS)	Distress	20	(1) 40.2 (7.6) (2) 40.8 (7)	85	(1) Psychotherapy + MDMA (2) Psychotherapy + Placebo	Pharmacological	Not reported
Mithoefer et al. (2018) ⁹³	PTSD (CAPS)	Distress	26	(1) 36.43 (10.66) (2) 39.2 (9.7)	27	(1) Psychotherapy + MDMA (75 or 125mg) (2) Psychotherapy + MDMA (30mg)	Pharmacological	Not reported
Morissette et al. (2008) ⁹⁴	Social anxiety (SUDS)	Fear	8	*27.5 (range 22-34)	Not reported	(1) Exposure therapy + Alprazolam & propranolol (2) Exposure therapy + Placebo or no pill	Pharmacological	Two sessions
Moshier & Otto (2017) ⁹⁵	MDD (BDI-II)	Distress	34	(1) 36.3 (14.4) (2) 34.38 (15.4)	52	(1) BATD + CCT (Cognitive Control Training) (2) BATD + PVT	Psychological/cognitive	4 weeks
Nations et al. (2012) ⁹⁶	Panic disorder (PDSS)	Fear	37	(1) 35.09 (9.76) (2) 32.4 (11.2)	67.5	(1) CBT + Org 25935 (Glycine transporter inhibitor; 4mg or 12mg) (2) CBT + Placebo	Pharmacological	6 weeks
Nejati et al. (2017) ²⁰	Major depression (BDI-II)	Distress	11	*19.40 (1.96)	Not reported	(1) STPP + tDCS (2) STPP	Somatic	5 weeks
Nicholas et al. (2022) ⁹⁷	Comorbid PTSD and substance use disorder (AUDIT)	Substance abuse	90	(1) 44.18 (13.10) (2) 38.53 (10.64)	64.6	(1) Trauma-focused therapy + MDMA (2) Trauma-focused therapy + Placebo	Pharmacological	3-4 weeks
Nord et al. (2019) ¹⁸	Major depression (HAM-D)	Distress	39	(1) 35.60 (12.91) (2) 31.05 (8.17)	51.3	(1) CBT + tDCS (2) CBT + Sham tDCS	Somatic	8 weeks
Oehen et al. (2013) ⁹⁸	PTSD (CAPS)	Distress	12	(1) 42.1 (12.8) (2) 40 (6.2)	83	(1) Psychotherapy + MDMA (125mg) (2) Psychotherapy + MDMA (25mg)	Pharmacological	Not reported
Ot'Alora G et al. (2018) ⁹⁹	PTSD (CAPS)	Distress	28	(1) 42.55 (13.36) (2) 40 (11.7)	67.9	(1) Psychotherapy + MDMA (125mg and 100mg) (2) Psychotherapy + MDMA (40mg)	Pharmacological	Not reported
Otto et al. (2010) ¹⁰⁰	Panic disorder (PDSS)	Fear	27	*35 (11)	50	(1) CBT + D-cycloserine (2) CBT + Placebo	Pharmacological	5 weeks
Pace-Schott et al. (2018) ¹⁰¹	Social anxiety (LSAS)	Fear	31	(1) 27.24 (6.79) (2) 24.60 (5.49)	56.3	(1) Exposure therapy + Nap (2) Exposure therapy + Wake	Somatic	5 weeks
Powers et al. (2009) ¹⁰²	Claustrophobia (BAT, peak fear)	Fear	24	*24.45 (8.65)	79	(1) Exposure therapy + Yohimbine hydrochloride (2) Exposure therapy + Placebo	Pharmacological	Not reported
Pyrkosch et al. (2018) ¹⁰³	Agoraphobia (PAS)	Fear	69	(1) 34.11 (10.37) (2) 40.86 (12.94)	65.8	(1) CBT + D-cycloserine (2) CBT + Placebo	Pharmacological	12 weeks
Raeder et al. (2019) ¹⁰⁴	Spider phobia (FSQ)	Fear	43	(1) 22.7 (4.21) (2) 22.57 (3.78)	76.7	(1) Exposure therapy + Cortisol (2) Exposure therapy + Placebo	Pharmacological	Single session
Reinecke et al. (2020) ¹⁰⁵	Panic disorder (Faces dot probe task)	Fear	31	(1) 42.1 (16.7) (2) 41.9 (13.7)	75.8	(1) Exposure therapy + D-cycloserine (2) Exposure therapy + Placebo	Pharmacological	Single session
Reitmaier et al. (2022) ¹⁰⁶	Spider phobia (FSQ)	Fear	53	*24.14 (6.00)	9.6	(1) VRET + Rhythmic eye movements (2) VRET	Psychological/cognitive	Single session
Rodebaugh et al. (2013) ¹⁰⁷	Social anxiety (SUDS)	Fear	34	(1) 49 (2) 38	67	(1) Exposure therapy + D-cycloserine (2) Exposure therapy + Placebo	Pharmacological	2 weeks
Ross et al. (2016) ¹⁰⁸	Anxiety and depression (HADS)	-	26	(1) 52 (15.03) (2) 60.27 (9.45)	62	(1) Psychotherapy + Psilocybin (2) Psychotherapy + Niacin	Pharmacological	Not reported

Ross et al. (2021) ¹⁰⁹	Anxiety or adjustment disorder due to cancer (Suicidal Ideation [item 9 of the BDI & BSI])	Distress	11	(1) 57.5 (7.5) (2) 63.6 (5.3)	63.6	(1) Preparatory and post-integrative psychotherapy + Psilocybin (2) Preparatory and post-integrative psychotherapy + Niacin	Pharmacological	Single session
Rubin et al. (2022) ¹¹⁰	Social anxiety disorder (PRPSA)	Fear	21	(1) 25.90 (15.42) (2) 19.20 (1.23)	61.9	(1) VRET + Attention guidance tracking (2) VRET	Psychological/cognitive	Single session
Santa Ana et al. (2015) ¹¹¹	Cocaine dependence (Craving rating)	Substance abuse	47	(1) 49.2 (8.8) (2) 44.4 (8.7)	14.9	(1) Cue exposure therapy + D-cycloserine (2) Cue exposure therapy + Placebo	Pharmacological	Not reported
Sherman et al. (2017) ¹¹²	Cannabis dependence (TLFB)	Substance abuse	15	*25.5 (7.6)	37.5	(1) Motivational enhancement therapy + Oxytocin (2) Motivational enhancement therapy + Placebo	Pharmacological	4 weeks
Shiban et al. (2017) ²⁶	Aviophobia (FFS)	Fear	29	(1) 34.3 (9.81) (2) 43 (9.96)	82.8	(1) VRET + Diaphragmatic breathing (2) VRET	Somatic	2 weeks
Siegmund et al. (2011) ¹¹³	Panic disorder (PAS)	Fear	39	(1) 37.85 (11.3) (2) 37.32 (13)	46.2	(1) CBT + D-cycloserine (2) CBT	Pharmacological	Not reported
Simpson et al. (2010) ¹¹⁴	OCD (Y-BOCS)	Fear	30	(1) 40.7 (11.1) (2) 39.1 (15.7)	47	(1) Exposure and response prevention + Motivational interviewing (2) Exposure and response prevention	Psychological/cognitive	8 weeks
Sippel et al. (2020) ¹¹⁵	PTSD (PCL-5)	Distress	17	(1) 41.63 (14.58) (2) 45.78 (15.09)	17.6	(1) Prolonged exposure + Oxytocin (2) Prolonged exposure + Placebo	Pharmacological	10 weeks
Smits et al. (2006) ¹¹⁶	Social anxiety (LSAS)	Fear	68	(1) 22.99 (7.55) (2) 20.42 (4.43)	57	(1) Exposure therapy + Videotape feedback (2) Exposure therapy + No feedback	Psychological/cognitive	1 week
Smits et al. (2014) ¹¹⁷	Social anxiety (LSAS)	Fear	40	(1) 35.50 (14.02) (2) 38.70 (12.08)	35	(1) Exposure therapy + Yohimbine hydrochloride (2) Exposure therapy + Placebo	Pharmacological	5 weeks
Smits et al. (2020a) ¹¹⁸	Social anxiety (LSAS)	Fear	152	(1) 29.39 (9.61) (2) 28.76 (11.81)	55.3	(1) Exposure therapy + D-cycloserine (2) Exposure therapy + Placebo	Pharmacological	5 weeks
Smits et al. (2020b) ¹¹⁹	Nicotine dependence (ASI-3)	Substance abuse	53	(1) 35.19 (12.37) (2) 36.64 (12.85)	69.1	(1) Exposure therapy + D-cycloserine (2) Exposure therapy + Placebo	Pharmacological	7 weeks
Soravia et al. (2014) ¹²⁰	Spider phobia (FSQ)	Fear	22	(1) 33.1 (2.9) (2) 30.5 (3.7)	77.3	(1) Exposure therapy + Cortisol (2) Exposure therapy + Placebo	Pharmacological	2 weeks
Soucy et al. (2021) ¹²¹	Generalised anxiety (GAD-7)	Distress	434	(1) 37.80 (12.98) (2) 37.55 (12.88)	74.9	(1) iCBT + Motivational interviewing (2) iCBT	Psychological/cognitive	25 weeks
Stuedte-Schmiedgen et al. (2021) ¹²²	Arachnophobia (SAS)	Fear	33	(1) 25.12 (7.98) (2) 24.25 (6.13)	78.8	(1) CBT (exposure-based) + Hydrocortisone (2) CBT (exposure-based) + Placebo	Pharmacological	Single session
Storch et al. (2007) ¹²³	OCD (Y-BOCS)	Fear	24	(1) 32 (9.4) (2) 25.9 (9.7)	50	(1) Exposure and response prevention therapy + D-cycloserine (2) Exposure and response prevention therapy + Placebo	Pharmacological	12 weeks
Tart et al. (2013) ¹²⁴	Acrophobia (BAT)	Fear	29	(1) 29.33 (14.67) (2) 37.71 (16.81)	Not reported	(1) VRET + D-cycloserine (2) VRET + Placebo	Pharmacological	2 weeks
Thierrée et al. (2021) ¹²⁵	PTSD (CAPS)	Distress	38	(1) 31.3 (10.0) (2) 33.5 (11.1)	65.8	(1) Exposure therapy (trauma script) + rTMS (hi-freq; 110% motor threshold) (2) Exposure therapy (trauma script) + rTMS (low-freq; 70% motor threshold)	Somatic	>2 weeks (8 sessions)
Tuerk et al. (2018) ¹²⁶	PTSD (Trauma-cued heart-rate reactivity)	Distress	26	(1) 34.6 (5.5) (2) 29.9 (6.7)	0	(1) Prolonged exposure + Yohimbine hydrochloride (2) Prolonged exposure + Placebo	Pharmacological	15 weeks
Vermes et al. (2020) ¹²⁷	PTSD (SCR)	Distress	42	(1) 34.7 (9.81) (2) 37.4 (11)	90.5	(1) Imaginal exposure + Trauma retrieval (2) Imaginal exposure + Neutral retrieval	Psychological/cognitive	1 week
Weingarden et al. (2019) ¹²⁸	Body dysmorphic disorder (BDD-YBOCS)	-	26	(1) 23.92 (5.74) (2) 29.07 (11.04)	65.4	(1) CBT + D-cycloserine (2) CBT + Placebo	Pharmacological	10 weeks

Wilhelm et al. (2008) ¹²⁹	OCD (Y-BOCS)	Fear	23	(1) 40 (13.4) (2) 38.2 (13)	Not reported	(1) Behaviour therapy + D-cycloserine (2) Behaviour therapy + Placebo	Pharmacological	5 weeks
Witkiewitz et al. (2019) ¹⁷	Alcohol use disorder (TLFB [drinks per drinking day])	Substance abuse	84	(1) 51.43 (14.19) (2) 53.35 (11.41)	40.5	(1) Mindfulness-based relapse prevention + tDCS (2) Mindfulness-based relapse prevention + Sham tDCS	Somatic	8 weeks
Wolfson et al. (2020) ¹³⁰	Anxiety (STAI)	Fear	18	(1) 55.5 (7) (2) 53.2 (10.5)	77.8	(1) Psychotherapy + MDMA (2) Psychotherapy + Placebo	Pharmacological	Not reported
Zoellner et al. (2017) ¹³¹	PTSD (PSS-I)	Distress	31	*37.5 (12.4)	71.4	(1) Imaginal exposure + Methylene blue (2) Imaginal exposure + Placebo	Pharmacological	1 week

* indicates the average age between both groups; N: Sample Size; SD: Standard Deviation; PHARM: Pharmacological Augmentations; PSYC: Psychological/Cognitive Augmentations; SOM: Somatic Interventions.

Mental health dimensions and assessment measures: ADIS-5, CSR: Anxiety and Related Disorders Interview Schedule for DSM-5, Clinician Severity Rating; AQ: Acrophobia Questionnaire; ASI-3: Anxiety Sensitivity Index; AUDIT: Alcohol Use Disorders Identification Test; BAT: Behavioural Approach Task; BDD: Body Dysmorphic Disorder; BDD-YBOCS: Body Dysmorphic Disorder Modification Of The Yale-Brown Obsessive-Compulsive Scale ; BDI: Beck Depression Inventory; BSFS: Birchwood Social Functioning Scale; BSI: Brief Symptom Inventory; BSS: Body Satisfaction Scale; CAPS: Clinically Administered Post-Traumatic Stress Disorder Scale; FAM: Flight Anxiety Modality Questionnaire; FCC: Fluid Cognitive Composite; FFI: Fear Of Flying Inventory; FFS: Fear Of Flying Scale; FSQ: Fear Of Spiders Questionnaire; GAD-7: Generalised Anxiety Disorder Assessment; GSI: Global Severity Index; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; IDS-SR: Inventory Of Depressive Symptomatology – Self-Report; IES-R: Impact Of Event Scale – Revised; LSAS: Liebowitz Social Anxiety Scale; MADRS: Montgomery–Åsberg Depression Rating Scale; MDD: Major Depressive Disorder; MI: Mobility Inventory; NFQ: Nightmare Frequency Questionnaire; OCD: Obsessive Compulsive Disorder; OCDUS: Obsessive-Compulsive Drug Use Scale; PAS: Panic And Agoraphobia Scale; PCL-5: Post-Traumatic Stress Disorder Checklist for DSM-5; PCL-M: Post-Traumatic Stress Disorder Checklist – Military; PDSS: Panic Disorder Severity Scale; PRPSA: Personal Report of Public Speaking Apprehension; PSQI: Pittsburgh Sleep Quality Index; PSS-I: Post-Traumatic Symptom Scale – Interview; PSS-SR: Post-Traumatic Stress Disorder Symptom Scale – Self Report Version; PSYRATS-D: Psychotic Symptom Rating Scale (delusion subscale); PTSD: Post-Traumatic Stress Disorder; SAS: Spider Anxiety Screening; SCL-90-R: Symptom Checklist – 90 – Revised; SCR: Skin Conductance Response; SIAS: Social Interaction Anxiety Scale; SPAI: Social Phobia And Anxiety Inventory; SSSPTSD: Severity Of Symptoms Scale For Post-Traumatic Stress Disorder; SUDS: Subjective Units Of Distress Scale; TBI: Target Bias Index; TLFB: Timeline Followback; VAS: Visual Analogue Scale; Y-BOCS: Yale-Brown Obsessive-Compulsive Scale.

Psychological therapies, augmentation and control groups: ABM: Attention Bias Modification; BATD: Behavioural Activation Therapy For Depression; CBGT: Cognitive Behavioural Group Therapy; CBI: Cognitive Behavioural Intervention; CBM-I: Cognitive Bias Modification for Interpretation; CBSST: Cognitive Behavioural Social Skills Training; CBT: Cognitive Behavioural Therapy; CBT-I: Cognitive Behavioural Therapy For Insomnia; CCT: Cognitive Control Training; CPT: Cognitive Processing Therapy CR: Cognitive Restructuring; ERP: Exposure And Response Prevention; DTMS: Deep Transcranial Magnetic Stimulation; ICBT: Internet Cognitive Behavioural Therapy; IE: Imaginal Exposure; IVE: In Vivo Exposure; MET: Motivational Enhancement Therapy; MBRP: Mindfulness Based Relapse Prevention; MDMA: 3,4-Methylenedioxy methamphetamine; PVT: Peripheral Vision Training; rTMS: Repetitive Transcranial Magnetic Stimulation; STPP: Short-Term Psychoanalytic Psychotherapy; tDCS: Transcranial Direct Current Stimulation; TEAS: Transcutaneous Electrical Acupuncture Stimulation; VR: Virtual Reality; VRET: Virtual Reality Exposure Therapy; YOH: Yohimbine Hydrochloride.

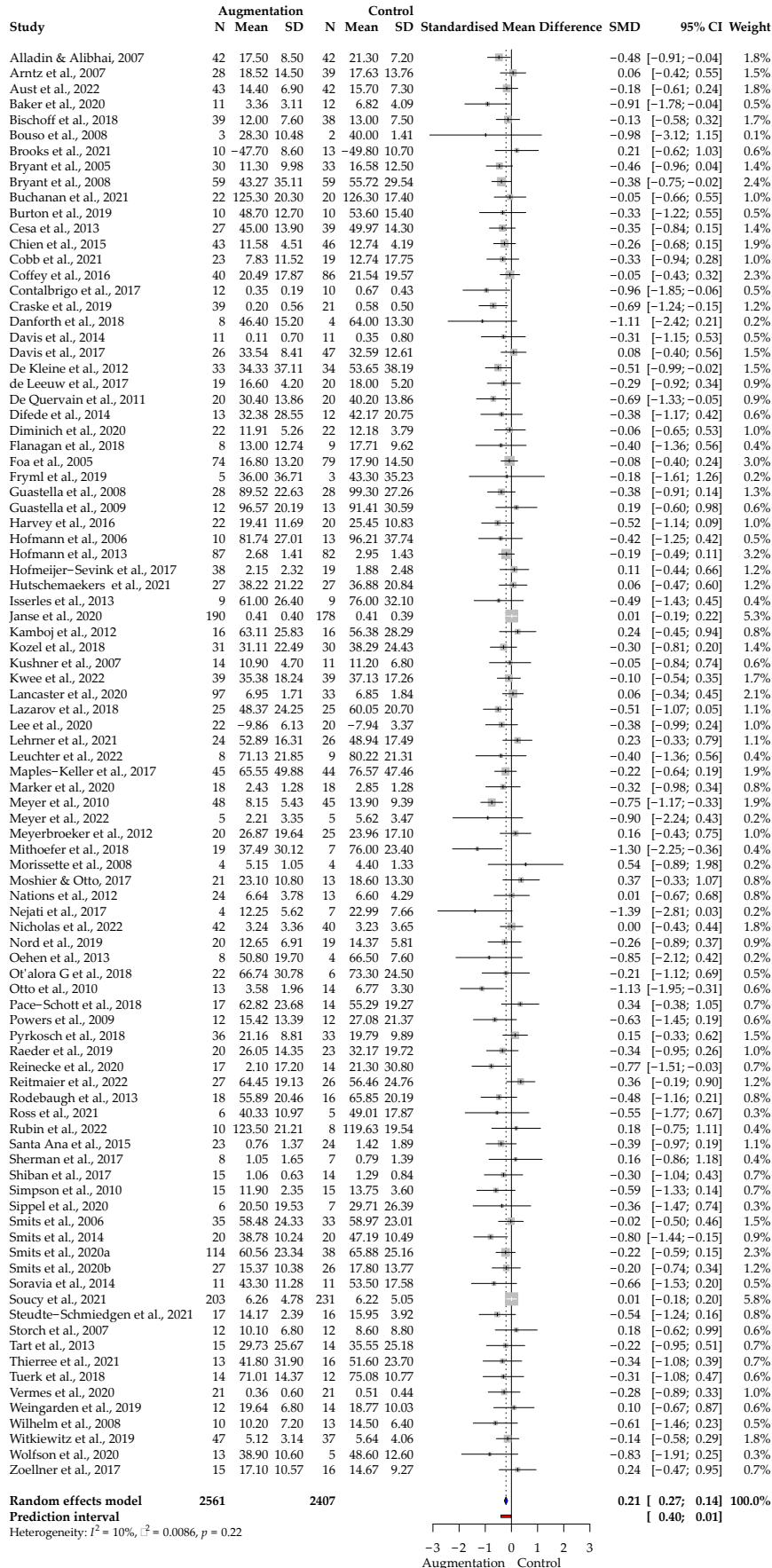
2.2. Outlier analyses

Supplemental Table S3. Studies defined as outliers (confidence intervals not overlapping with the confidence intervals of the pooled effect).

Authors (year of publication)	Mental health measure (assessment)	Mean (SD) age (1) Augmentation (2) Control group	Gender (% female)	(1) Augmentation group(s) & (2) Control group	Type of augmentation	Duration
Acheson et al. (2015) ¹	Arachnophobia (FSQ)	(1) 33.3 (4.01) (2) 26.77 (2.67)	82.6	(1) Exposure therapy + Oxytocin (2) Exposure therapy + Placebo	Pharmacological	Single session
Andersson et al. (2015) ²	OCD (Y-BOCS)	(1) 34.64 (12.42) (2) 34.88 (12.22)	58	(1) ICBT + D-cycloserine (2) ICBT + Placebo	Pharmacological	12 weeks
Davis et al. (2021) ³	MDD (GRID-HAMD)	(1) 43.6 (13) (2) 35.2 (9.9)	66.7	(1) Psychotherapy + Psilocybin (2) Wait list (no therapy or augmentation)	Pharmacological	8 weeks
Falkenstein et al. (2022) ⁴	OCRDs (TBI interpretation)	(1) 30.36 (8.44) (2) 27.25 (3.77)	50	(1) IRT + CBM-I (2) IRT + Psychoeducation	Psychological/ cognitive	~4 weeks
Fayaz et al. (2022) ⁵	Methamphetamine use disorder (OCDUS)	(1) 34 (6.7) (2) 37 (7)	0	(1) Matrix Model psychotherapy + tDCS (2) Matrix Model psychotherapy + Sham tDCS	Somatic	12 weeks
Feng et al. (2019) ⁶	PTSD (CAPS)	(1) 40.9 (12.7) (2) 41 (12.8)	69.2	(1) CBT + Transcutaneous electrical acupoint stimulation (2) CBT + Simulated TEAS	Somatic	12 weeks
Harb et al. (2019) ⁷	PTSD (NFQ)	(1) 37 (9.9) (2) 37.2 (10.1)	13.9	(1) CBT-I + Imagery rescripting (2) CBT-I	Psychological /cognitive	6 weeks
Isserles et al. (2021) ⁸	PTSD (CAPS)	(1) 44.8 (13.19) (2) 43.7 (12.25)	66.4	(1) Exposure (ultrabrief SDI) + DTMS (2) Exposure (ultrabrief SDI) + Sham DTMS	Somatic	4 weeks
Krupitsky et al. (2002) ⁹	Heroin dependence (VAS, craving)	(1) 23 (4.4) (2) 21.6 (3)	21.4	(1) Psychotherapy + Ketamine (2mg) (2) Psychotherapy + Ketamine (0.2mg)	Pharmacological	Single session
Lass-Hennemann & Michael (2014) ¹⁰	Spider phobia (BAT)	(1) 23.33 (1.12) (2) 25.87 (1.06)	100	(1) Exposure therapy + High endogenous cortisol levels (morning) (2) Exposure therapy + Low endogenous cortisol (evening)	Somatic	Single session
Litz et al. (2012) ¹¹	PTSD (CAPS)	(1) 32.77 (9.85) (2) 31.62 (9.10)	0	(1) Exposure therapy + D-cycloserine (2) Exposure therapy + Placebo	Pharmacological	6 weeks
McEvoy et al. (2020) ¹²	Social anxiety (SIAS)	(1) 30.14 (12.79) (2) 27.06 (9.71)	49.5	(1) CBT + Imagery-enhanced CBT (2) CBT + Verbally-based CBT	Psychological/ cognitive	12 weeks
Meyerbröker et al. (2018) ¹³	Fear of flying (FAM)	*36.6 (12.1)	55	(1) VRET + Yohimbine Hydrochloride & propranolol (2) VRET + Placebo	Pharmacological	Not reported
Mithoefer et al. (2011) ¹⁴	PTSD (CAPS)	(1) 40.2 (7.6) (2) 40.8 (7)	85	(1) Psychotherapy + MDMA (2) Psychotherapy + Placebo	Pharmacological	Not reported
Ross et al. (2016) ¹⁵	Anxiety and depression (HADS)	(1) 52 (15.03) (2) 60.27 (9.45)	62	(1) Psychotherapy + Psilocybin (2) Psychotherapy + Niacin	Pharmacological	Not reported
Siegmund et al. (2011) ¹⁶	Panic disorder (PAS)	(1) 37.85 (11.3) (2) 37.32 (13)	46.2	(1) CBT + D-cycloserine (2) CBT	Pharmacological	Not reported

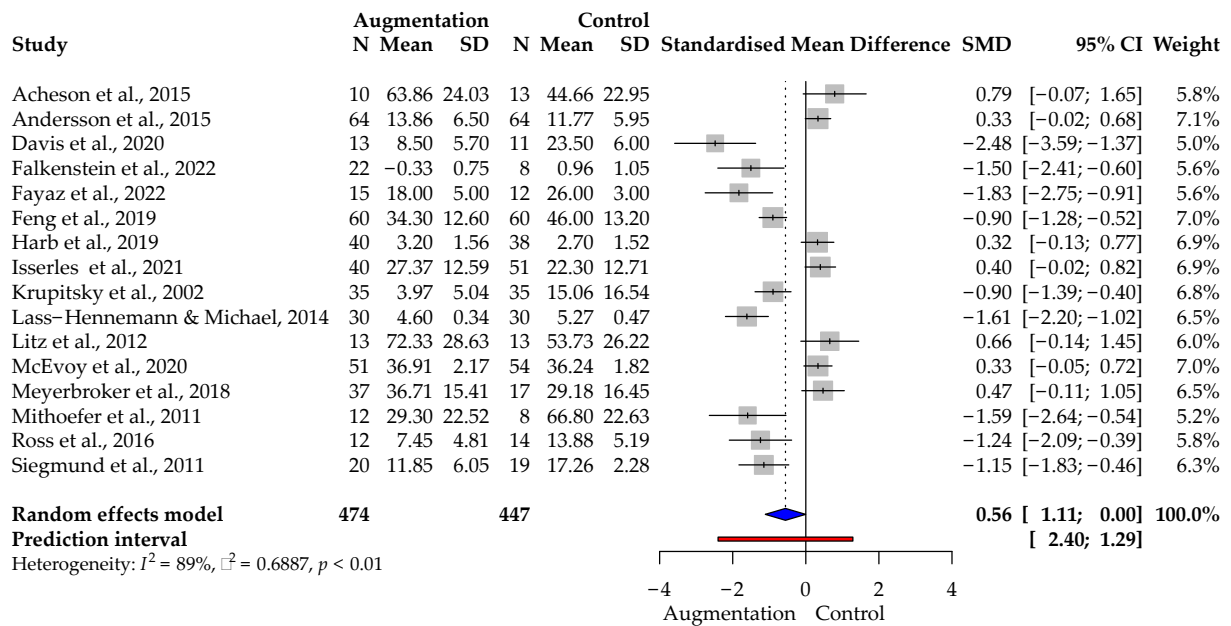
Supplemental Figure S1. Results from random effect meta-analysis excluding outliers.

Main effect ($k = 92$ studies): Hedges' $g = -0.21$, 95% CI = $(-0.27, -0.14)$; $p < 0.0001$.



Supplemental Figure S2. Random effects meta-analysis results including only outliers. Main effect ($k = 16$ studies):






Hedges' $g = -0.56$, 95% CI = (-1.11, -0.00); $p = 0.0489$.



2.3. Risk of bias assessment

Supplemental Table S4. Risk of bias assessment. Studies marked according to the Cochrane Risk of Bias Tool. Green indicates low risk of bias on the specified index, yellow indicates unclear risk of bias on the specified index, and red indicates high risk of bias on the specified index. Selective reporting was not assessed due to our meta-analysis focus on specified (mental health) outcome criteria.

Authors (year of publication)	Mental health measure (assessment)	Random sequence generation	Allocation concealment	Blinding (participants/personnel)	Blinding outcome assessment*	Incomplete outcome data (attrition)
Acheson et al. (2015) ¹	Arachnophobia (FSQ)	Green	Yellow	Green	Green	Green
Alladin & Alibhai (2007) ¹⁷	Depression (BDI-II)	Green	Yellow	Red	Green	Red
Andersson et al. (2015) ²	OCD (Y-BOCS)	Green	Green	Green	Green	Green
Arntz et al. (2007) ¹⁸	PTSD (PSS-SR)	Yellow	Red	Red	Green	Red
Aust et al. (2022) ¹⁹	Depression (MADRS)	Green	Green	Green	Green	Red
Baker et al. (2020) ²⁰	Panic Disorder (PDSS)	Green	Yellow	Green	Green	Green
Bischoff et al. (2018) ²¹	Panic Disorder with agoraphobia (HAM-A)	Green	Yellow	Red	Green	Green
Bouso et al. (2008) ²²	PTSD (SSSPTSD)	Green	Yellow	Green	Green	Green
Brooks et al. (2021) ²³	Depression or anxiety + cognitive decline (FCC)	Green	Yellow	Green	Green	Red
Bryant et al. (2005) ²⁴	Acute stress disorder (IES)	Green	Red	Red	Green	Red
Bryant et al. (2008) ²⁵	PTSD (CAPS)	Green	Green	Green	Green	Red

Buchanan et al. (2021) ²⁶	Social functioning in schizophrenia (BSFS)					
Burton et al. (2019) ²⁷	PTSD (PCL-M)					
Cesa et al. (2013) ²⁸	Binge eating disorder (BSS)					
Chien et al. (2015) ²⁹	Depression (PSQI)					
Cobb et al. (2021) ³⁰	Phobia (BAT)					
Coffey et al. (2016) ³¹	PTSD (IES-R)					
Contalbrigo et al. (2017) ³²	Substance use disorder (SCL-90-R)					
Craske et al. (2019) ³³	Social anxiety (SCR to public speaking onset)					
Danforth et al. (2018) ³⁴	Social anxiety (LSAS)					
Davis et al. (2014) ³⁵	Schizophrenia (Social-cognition composite score)					
Davis et al. (2017) ³⁶	Social anxiety (LSAS)					
Davis et al. (2021) ³	MDD (GRID-HAMD)					
De Kleine et al. (2012) ³⁷	PTSD (CAPS)					
de Leeuw et al. (2017) ³⁸	OCD (Y-BOCS)					
De Quervain et al. (2011) ³⁹	Acrophobia (AQ)					
Difede et al. (2014) ⁴⁰	PTSD (CAPS)					
Diminich et al. (2020) ⁴¹	Delusions (PSYRATS-D)					
Falkenstein et al. (2022) ⁴	OCRDs (TBI, interpretation)					
Fayaz Feyzi et al. (2022) ⁵	Methamphetamine use disorder (OCDUS)					
Feng et al. (2019) ⁶	PTSD (CAPS)					
Flanagan et al. (2018) ⁴²	PTSD (CAPS)					
Foa et al. (2005) ⁴³	PTSD (PSS-I)					
Fryml et al. (2019) ⁴⁴	PTSD (CAPS)					
Guastella et al. (2008) ⁴⁵	Social anxiety (SPAI)					
Guastella et al. (2009) ⁴⁶	Social anxiety (SPAI)					
Harb et al. (2019) ⁷	PTSD (NFQ)					
Harvey et al. (2016) ⁴⁷	MDD (IDS-SR)					
Hofmann et al. (2006) ⁴⁸	Social anxiety (SPAI)					
Hofmann et al. (2013) ⁴⁹	Social anxiety (SPD-S)					
Hofmeijer-Sevink et al. (2017) ⁵⁰	Panic disorder with agoraphobia (Mobility Inventory, alone subscale)					
Hutschemaekers et al. (2021) ⁵¹	Social anxiety disorder (SUDS)					
Isserles et al. (2021) ⁸	PTSD (CAPS)					
Isserles et al. (2013) ⁵²	PTSD (CAPS)					

Otto et al. (2010) ⁷⁷	Panic disorder (PDSS)	Green		
Pace-Schott et al. (2018) ⁷⁸	Social anxiety (LSAS)	Yellow	Green	Yellow
Powers et al. (2009) ⁷⁹	Claustrophobia (BAT, peak fear)	Green	Yellow	Green
Pyrkosch et al. (2018) ⁸⁰	Agoraphobia (PAS)	Green		
Raeder et al. (2019) ⁸¹	Spider phobia (FSQ)	Yellow	Green	Yellow
Reinecke et al. (2020) ⁸²	Panic disorder (Faces dot probe task)	Green		
Reitmaier et al. (2022) ⁸³	Spider phobia (FSQ)	Yellow	Red	Green
Rodebaugh et al. (2013) ⁸⁴	Social anxiety (SUDS)	Green		Red
Ross et al. (2016) ¹⁵	Anxiety and depression (HADS)	Green		Yellow
Ross et al. (2021) ⁸⁵	Anxiety or adjustment disorder due to cancer (Suicidal Ideation [item 9 of the BDI & BSI])	Yellow	Green	Red
Rubin et al. (2022) ⁸⁶	Social anxiety disorder (PRPSA)	Green	Red	
Santa Ana et al. (2015) ⁸⁷	Cocaine dependence (Craving rating)	Green		Yellow
Sherman et al. (2017) ⁸⁸	Cannabis dependence (TLFB)	Yellow		Green
Shiban et al. (2017) ⁸⁹	Aviophobia (FFS)	Yellow		Green
Siegmund et al. (2011) ¹⁶	Panic disorder (PAS)	Green		
Simpson et al. (2010) ⁹⁰	OCD (Y-BOCS)	Yellow	Red	Green
Sippel et al. (2020) ⁹¹	PTSD (PCL-5)	Yellow	Green	Red
Smits et al. (2006) ⁹²	Social anxiety (LSAS)	Yellow	Red	Yellow
Smits et al. (2014) ⁹³	Social anxiety (LSAS)	Green	Yellow	Green
Smits et al. (2020a) ⁹⁴	Social anxiety (LSAS)	Green		
Smits et al. (2020b) ⁹⁵	Nicotine dependence (ASI-3)	Green		
Soravia et al. (2014) ⁹⁶	Spider phobia (FSQ)	Green		Red
Soucy et al. (2021) ⁹⁷	Generalised anxiety (GAD-7)	Green	Yellow	Red
Stuedte-Schmiedgen et al. (2021) ⁹⁸	Arachnophobia (SAS)	Green		Red
Storch et al. (2007) ⁹⁹	OCD (Y-BOCS)	Yellow	Green	Red
Tart et al. (2013) ¹⁰⁰	Acrophobia (BAT)	Green	Yellow	Green
Thierrée et al. (2021) ¹⁰¹	PTSD (CAPS)	Green	Yellow	Red
Tuerk et al. (2018) ¹⁰²	PTSD (Trauma-cued heart-rate reactivity)	Green		Yellow
Vermes et al. (2020) ¹⁰³	PTSD (SCR)	Yellow	Red	Yellow
Weingarden et al. (2019) ¹⁰⁴	Body dysmorphic disorder (BDD-YBOCS)	Yellow	Green	Red
Wilhelm et al. (2008) ¹⁰⁵	OCD (Y-BOCS)	Green		

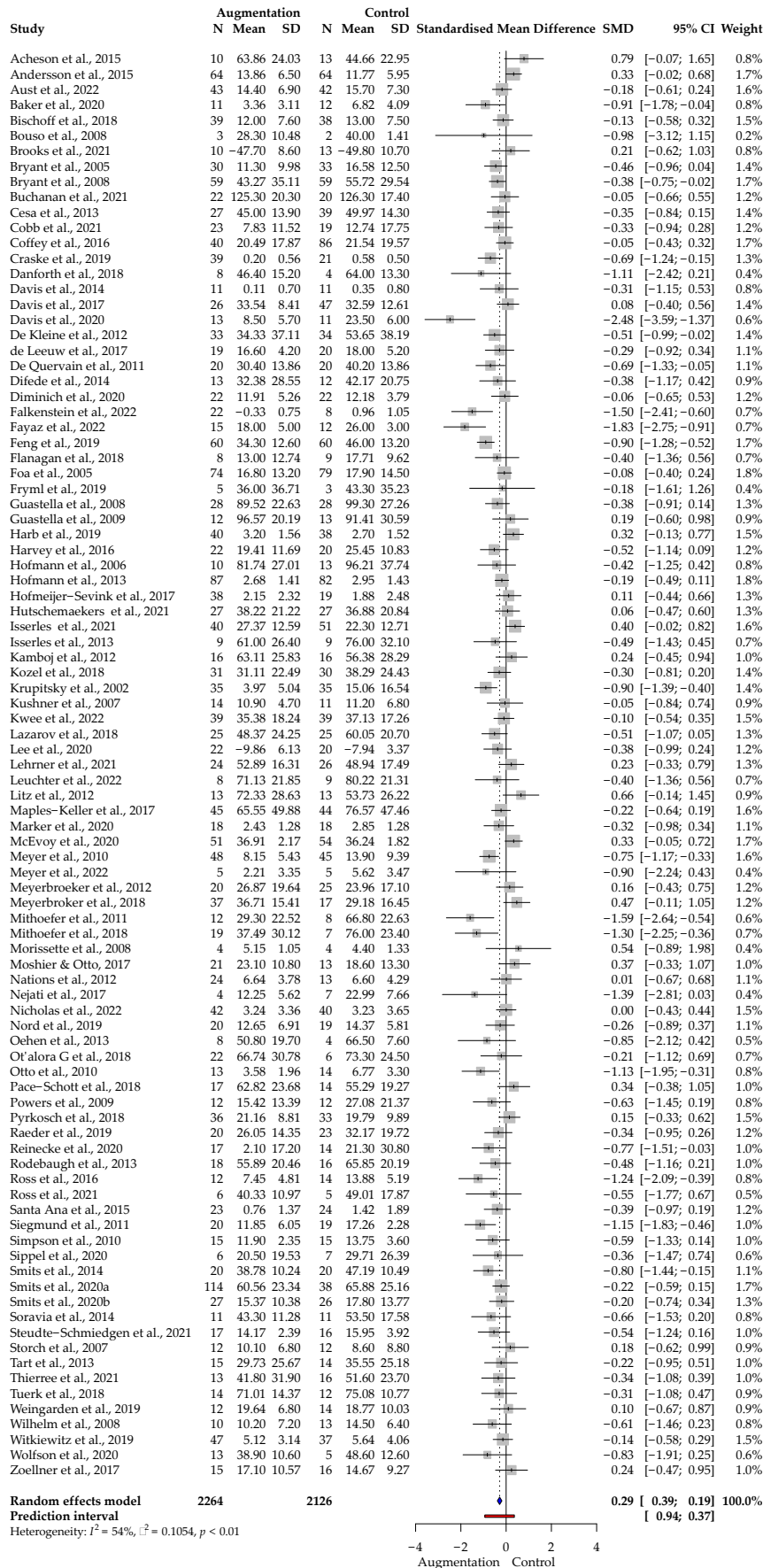
Witkiewitz et al. (2019) ¹⁰⁶	Alcohol use disorder (TLFB [drinks per drinking day])			
Wolfson et al. (2020) ¹⁰⁷	Anxiety (STAI)			
Zoellner et al. (2017) ¹⁰⁸	PTSD (PSS-I)			

*The fifteen studies coloured red or yellow in this category were labelled 'high risk' due to the importance of blinding of outcome assessment for our meta-analysis; these were excluded in our follow-up analysis in the main text (see 'Risk of bias analysis').

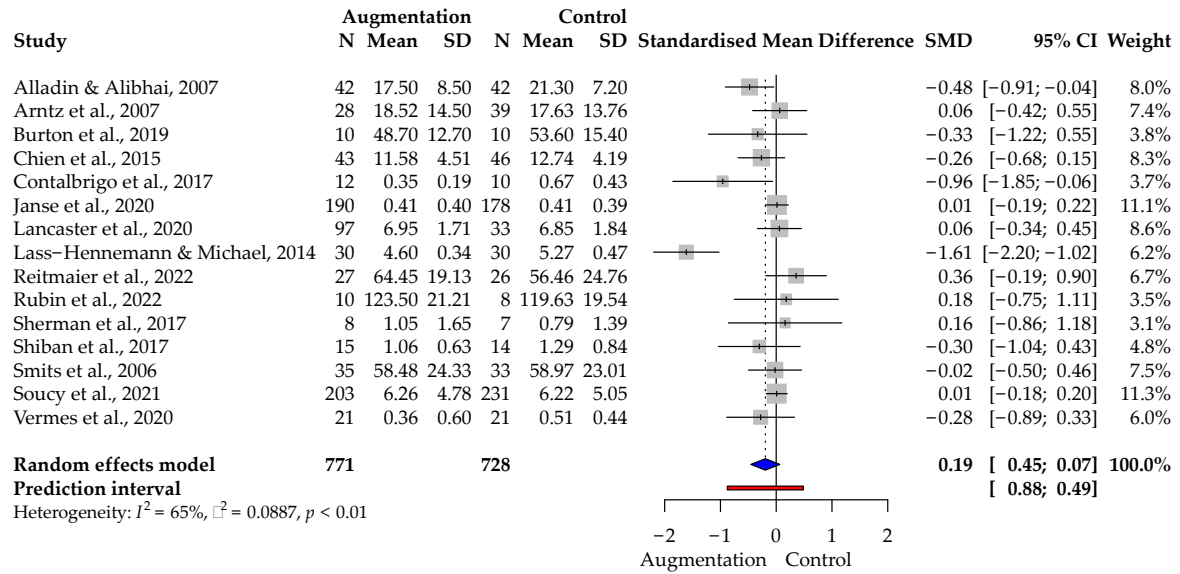
Mental health dimensions and assessment measures: ADIS-5, CSR: Anxiety and Related Disorders Interview Schedule for DSM-5, Clinician Severity Rating; AQ: Acrophobia Questionnaire; ASI-3: Anxiety Sensitivity Index; AUDIT: Alcohol Use Disorders Identification Test; BAT: Behavioural Approach Task; BDD: Body Dysmorphic Disorder; BDD-YBOCS: Body Dysmorphic Disorder Modification Of The Yale-Brown Obsessive-Compulsive Scale ; BDI: Beck Depression Inventory; BSFS: Birchwood Social Functioning Scale; BSI: Brief Symptom Inventory; BSS: Body Satisfaction Scale; CAPS: Clinically Administered Post-Traumatic Stress Disorder Scale; FAM: Flight Anxiety Modality Questionnaire; FCC: Fluid Cognitive Composite; FFI: Fear Of Flying Inventory; FFS: Fear Of Flying Scale; FSQ: Fear Of Spiders Questionnaire; GAD-7: Generalised Anxiety Disorder Assessment; GSI: Global Severity Index; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; IDS-SR: Inventory Of Depressive Symptomatology – Self-Report; IES-R: Impact Of Event Scale – Revised; LSAS: Liebowitz Social Anxiety Scale; MADRS: Montgomery–Åsberg Depression Rating Scale; MDD: Major Depressive Disorder; MI: Mobility Inventory; NFQ: Nightmare Frequency Questionnaire; OCD: Obsessive Compulsive Disorder; OCDUS: Obsessive-Compulsive Drug Use Scale; PAS: Panic And Agoraphobia Scale; PCL-5: Post-Traumatic Stress Disorder Checklist for DSM-5; PCL-M: Post-Traumatic Stress Disorder Checklist – Military; PDSS: Panic Disorder Severity Scale; PRPSA: Personal Report of Public Speaking Apprehension; PSQI: Pittsburgh Sleep Quality Index; PSS-I: Post-Traumatic Symptom Scale – Interview; PSS-SR: Post-Traumatic Stress Disorder Symptom Scale – Self Report Version; PSYRATS-D: Psychotic Symptom Rating Scale (delusion subscale); PTSD: Post-Traumatic Stress Disorder; SAS: Spider Anxiety Screening; SCL-90-R: Symptom Checklist – 90 – Revised; SCR: Skin Conductance Response; SIAS: Social Interaction Anxiety Scale; SPAI: Social Phobia And Anxiety Inventory; SSSPTSD: Severity Of Symptoms Scale For Post-Traumatic Stress Disorder; SUDS: Subjective Units Of Distress Scale; TBI: Target Bias Index; TLFB: Timeline Followback; VAS: Visual Analogue Scale; Y-BOCS: Yale-Brown Obsessive-Compulsive Scale.

Psychological therapies, augmentation and control groups: ABM: Attention Bias Modification; BATD: Behavioural Activation Therapy For Depression; CBGT: Cognitive Behavioural Group Therapy; CBI: Cognitive Behavioural Intervention; CBM-I: Cognitive Bias Modification for Interpretation; CBSST: Cognitive Behavioural Social Skills Training; CBT: Cognitive Behavioural Therapy; CBT-I: Cognitive Behavioural Therapy For Insomnia; CCT: Cognitive Control Training; CPT: Cognitive Processing Therapy CR: Cognitive Restructuring; ERP: Exposure And Response Prevention; DTMS: Deep Transcranial Magnetic Stimulation; ICBT: Internet Cognitive Behavioural Therapy; IE: Imaginal Exposure; IVE: In Vivo Exposure; MET: Motivational Enhancement Therapy; MBRP: Mindfulness Based Relapse Prevention; MDMA: 3,4-Methylenedioxymethamphetamine; PVT: Peripheral Vision Training; rTMS: Repetitive Transcranial Magnetic Stimulation; STPP: Short-Term Psychoanalytic Psychotherapy; tDCS: Transcranial Direct Current Stimulation; TEAS: Transcutaneous Electrical Acupuncture Stimulation; VR: Virtual Reality; VRET: Virtual Reality Exposure Therapy; YOH: Yohimbine Hydrochloride.

Supplementary Figure S3. Random effects meta-analysis results excluding studies with high risk of bias. Main effect ($k = 93$ studies): Hedges' $g = -0.29$, 95% CI = $(-0.39, -0.19)$; $p < 0.0001$.

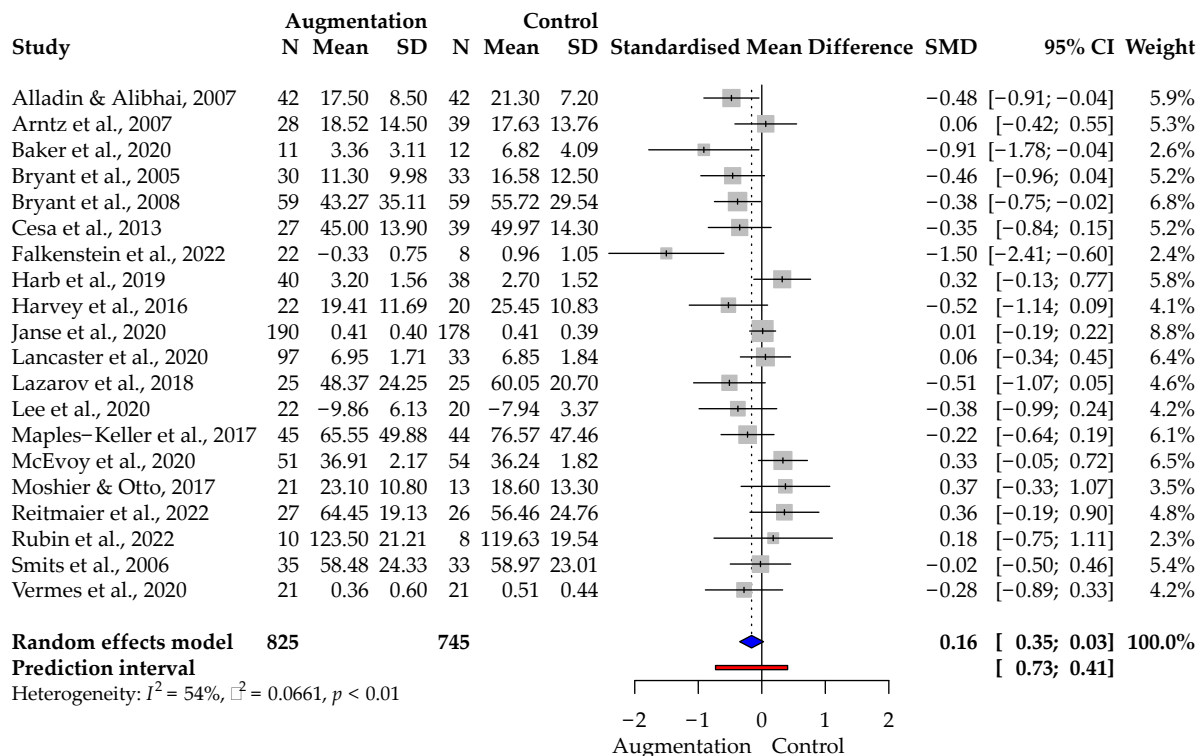


Supplementary Figure S4. Random effects meta-analysis results including only studies with high risk of bias. Main effect ($k = 15$ studies): Hedges' $g = -0.19$, 95% CI = $(-0.45, 0.07)$; $p = 0.1314$.

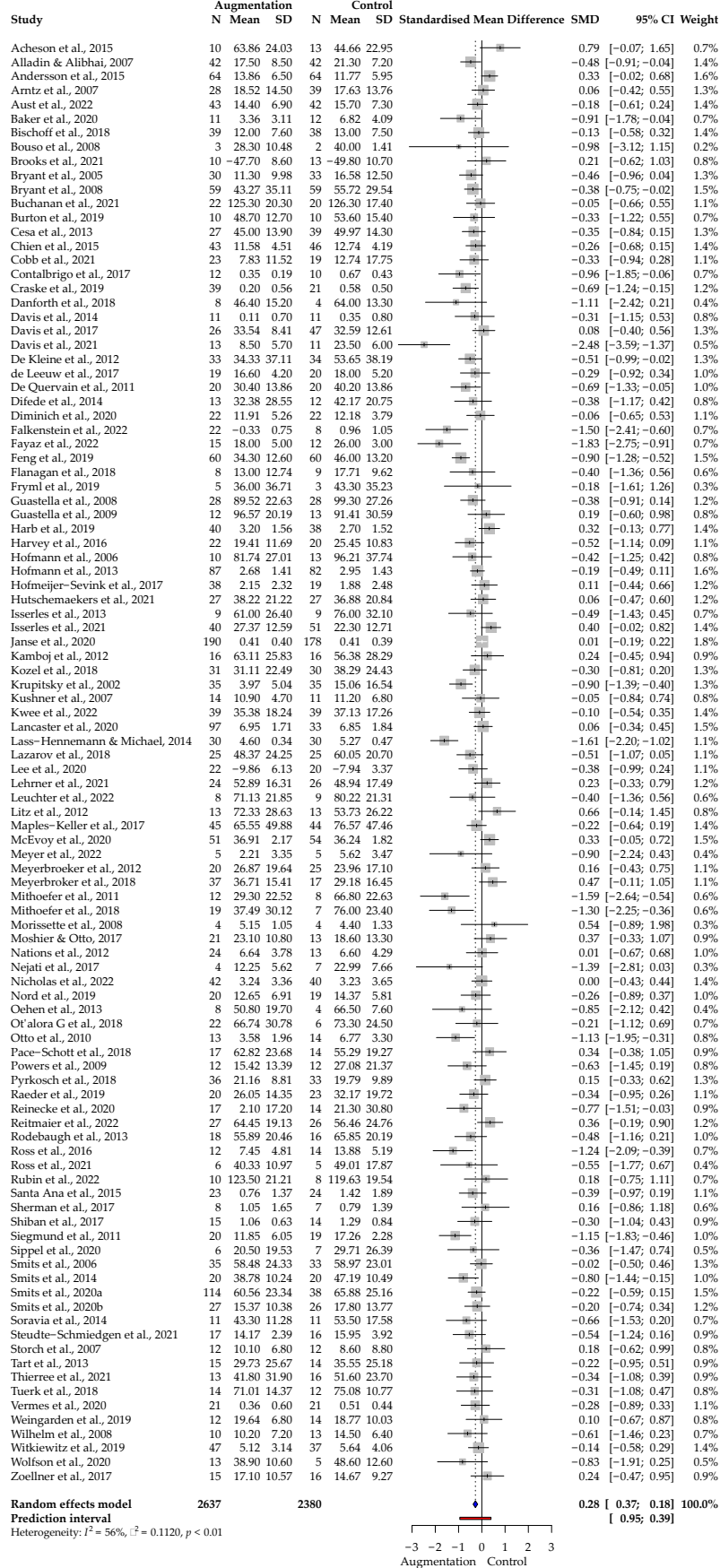


2.4. Results excluding psychological therapy combinations

Supplemental Figure S5. Psychological sub-study random effects meta-analysis results excluding six studies^{31,43,64,65,90,97} identified as being “combinations” of psychotherapies rather than psychotherapy augmented with a psychological intervention. Main effect ($k = 20$ studies): Hedges' $g = -0.16$, 95% CI = $(-0.35, 0.03)$; $p = 0.0886$.

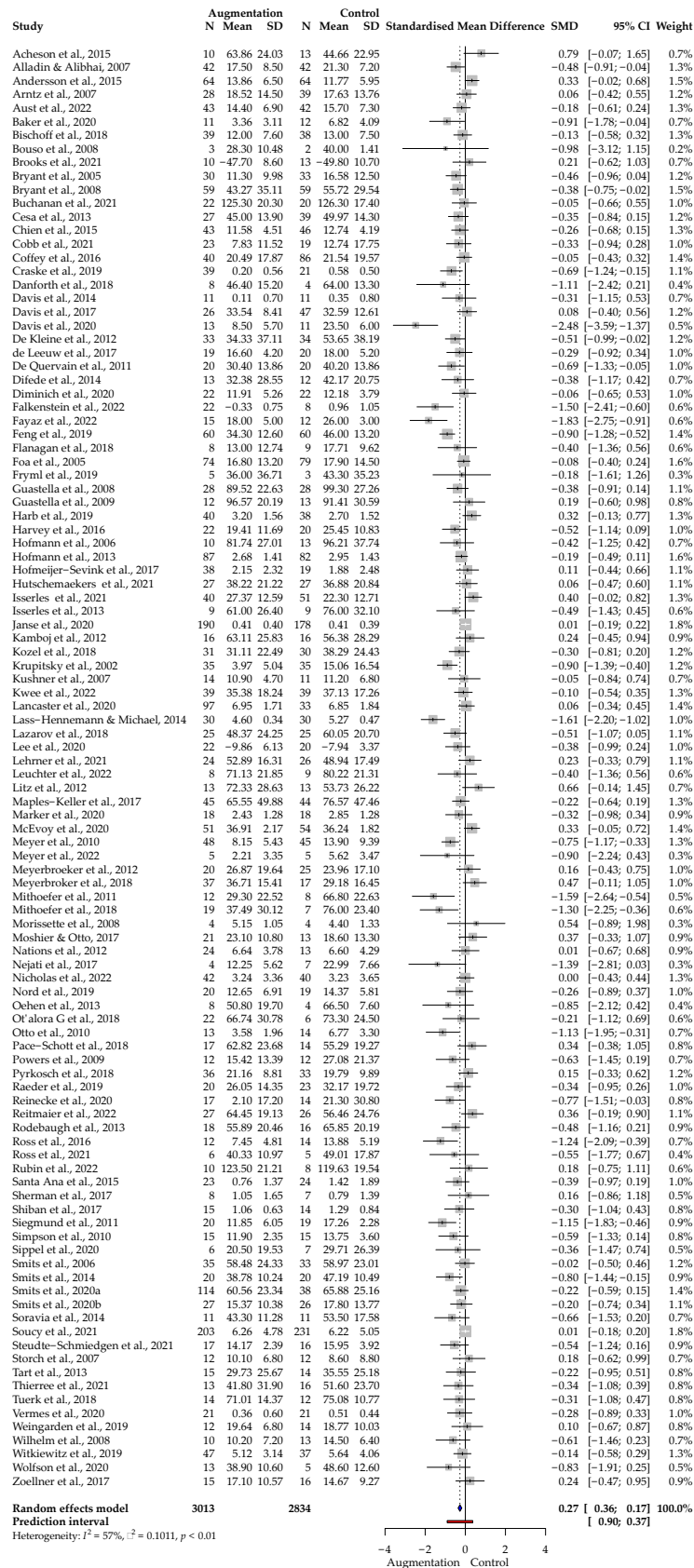


Supplemental Figure S6. Random effects meta-analysis results excluding the six psychological combination studies. Main effect ($k = 102$ studies): Hedges' $g = -0.28$, 95% CI = $(-0.37, -0.18)$; $p < 0.0001$.



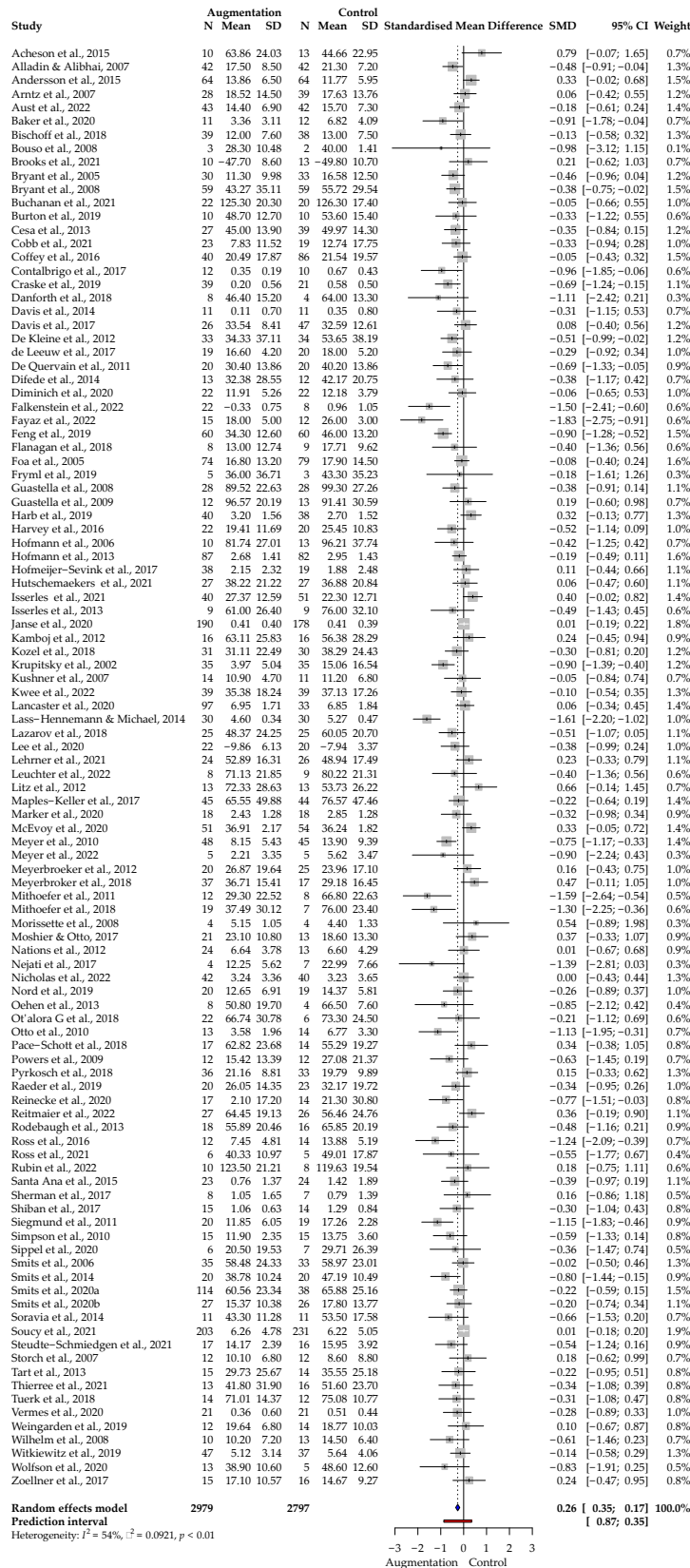
2.5. Results excluding non-randomised studies

Supplemental Figure S7. Random effects meta-analysis results excluding two non-randomised studies^{27,32}. Main effect ($k = 106$ studies): Hedges' $g = -0.27$, 95% CI = $(-0.36, -0.17)$; $p < 0.0001$.



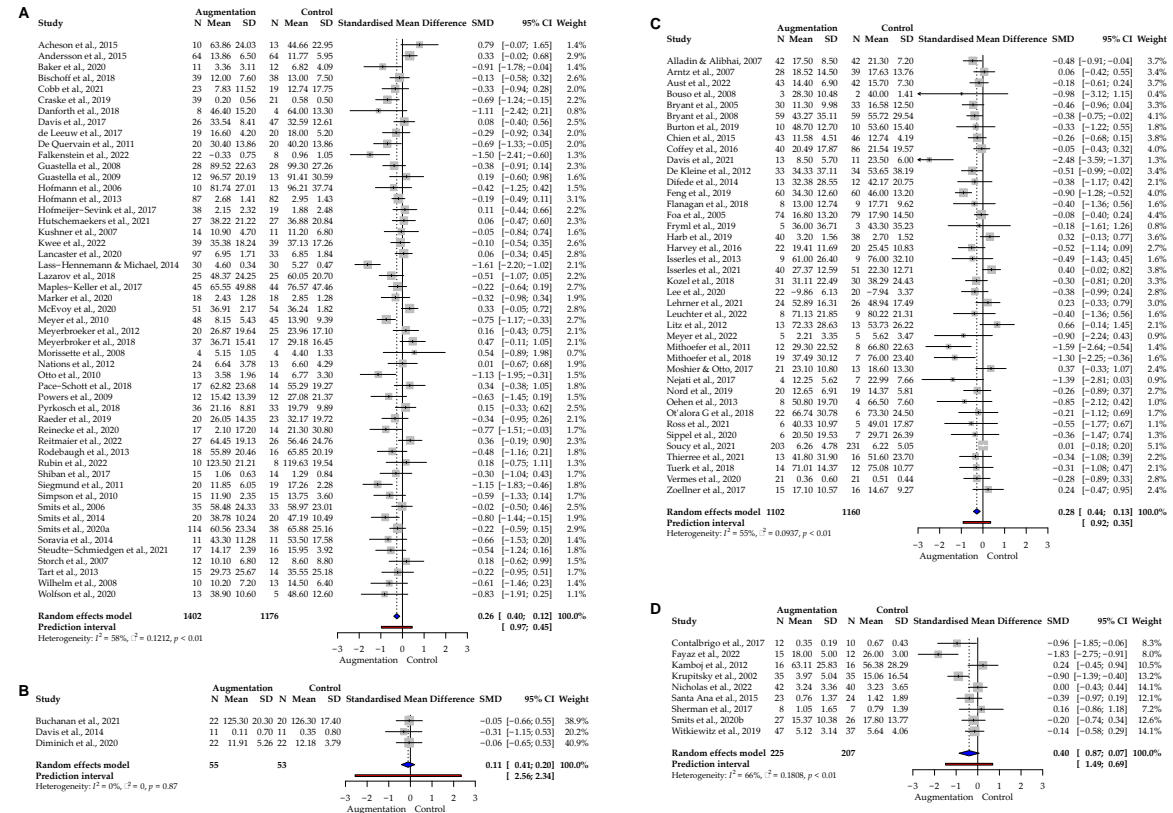
2.6. Results excluding studies with non-therapeutic controls

Supplemental Figure S8. Random effects meta-analysis results excluding two studies in which the control group did not receive psychological therapy (either waitlist³ or occupational therapy²⁹). Main effect ($k = 106$ studies): Hedges' $g = -0.27$, 95% CI = $(-0.36, -0.17)$; $p < 0.0001$.



2.7. Analyses stratified by HiTOP dimensions (excludes five studies)

Supplemental Figure S9. Sub-study Random effects meta-analysis results for the HiTOP dimensions of (A) Fear, (B) Thought disorder, (C) Distress and (D) Substance abuse.

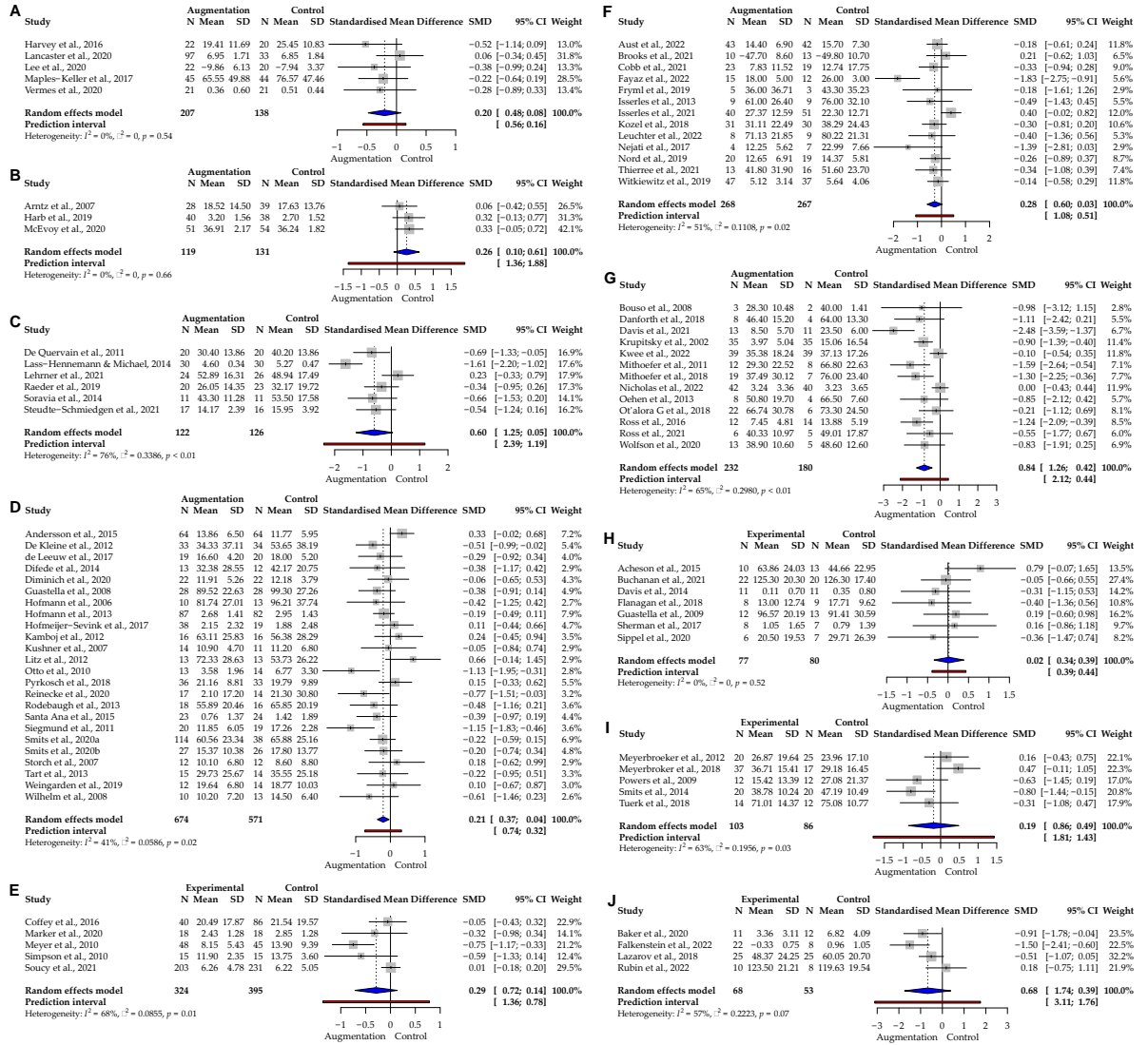


Supplementary Table S5. Main effects for each of the HiTOP dimensions (excluding five studies^{15,23,28,53,104} which did not fit any of them) from a random effects meta-analysis

HiTOP dimension	No. studies	Hedges' <i>g</i>	95% CI	<i>p</i>
Fear	51	-0.26	(-0.40, -0.12)	0.0004
Distress	40	-0.28	(-0.44, -0.13)	0.0008
Substance abuse	9	-0.40	(-0.87, 0.065)	0.083
Thought disorder	3	-0.11	(-0.41, 0.20)	0.28

2.8. Analyses stratified by specific augmentation (> 3 studies per category; excludes 22 studies)

Supplemental Figure S10. Sub-study random effects meta-analysis results for augmentation categories including more than three studies. These were (A) memory (e.g., memory support; trauma retrieval), (B) imagery (e.g., imagery rescripting; imagery-enhanced CBT), (C) cortisol, (D) D-cycloserine, (E) motivational (e.g., motivational interviewing), (F) brain stimulation (e.g., rTMS, tDCS), (G) psychotropic (e.g., MDMA, psilocybin, ketamine, or cannabidiol), (H) oxytocin, (I) yohimbine, and (J) bias modification (e.g., cognitive bias or attentional bias modifications) augmentations.



Supplementary Table S6. Main effects for each of the specific augmentation categories (excluding 22 studies which did not fit into groups larger than three) from a random effects meta-analysis

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