Transdiagnostic MRI markers of psychopathology following traumatic brain injury: a systematic review and network meta-analysis protocol

Alexia Samiotis, Amelia J Hicks, Jennie Ponsford, Gershon Spitz

ABSTRACT

Introduction Psychopathology following traumatic brain injury (TBI) is a common and debilitating consequence that is often associated with reduced functional and psychosocial outcomes. There is a lack of evidence regarding the neural underpinnings of psychopathology following TBI, and whether there may be transdiagnostic neural markers that are shared across traditional psychiatric diagnoses. The aim of this systematic review and meta-analysis is to examine the association of MRI-derived markers of brain structure and function with both transdiagnostic and specific psychopathology following moderate–severe TBI.

Methods and analysis A systematic literature search of Embase (1974–2022), Ovid MEDLINE (1946–2022) and PsycINFO (1806–2022) will be conducted. Publications in English that investigate MRI correlates of psychopathology characterised by formal diagnoses or symptoms of psychopathology in closed moderate–severe TBI populations over 16 years of age will be included. Publications will be excluded that: (a) evaluate non-MRI neuroimaging techniques (CT, positron emission tomography, magnetencephalography, electroencephalogram); (b) comprise primarily a paediatric cohort; (c) comprise primarily penetrating TBI. Eligible studies will be assessed against a modified Joanna Briggs Institute Critical Appraisal Instrument and data will be extracted by two independent reviewers. A descriptive analysis of MRI findings will be provided based on qualitative synthesis of data extracted. Quantitative analyses will include a meta-analysis and a network meta-analysis where there are sufficient data available.

Ethics and dissemination Ethics approval is not required for the present study as there will be no original data collected. We intend to disseminate the results through publication to a high-quality peer-reviewed journal and conference presentations on completion.

PROSPERO registration number CRD42022358358.

INTRODUCTION

Traumatic brain injury (TBI) is a major cause of death, disability and economic burden worldwide. TBI is defined as an alteration to brain function, or the presence of brain pathology caused by an extraneous force to the head. Closed-head injuries are the most common form of TBI among civilians and occur due to a blunt impact, such as from traffic accidents, falls and sporting-related injuries. These injuries are highly heterogeneous and occur across a spectrum of severity from mild to severe based typically on duration of loss of consciousness, depth of coma and duration of post-traumatic amnesia (PTA). Following a TBI, individuals often experience a range of physical, neurological, cognitive, behavioural, functional and psychological sequelae. Psychological sequelae are often the most persistent and disabling in the long term, particularly for those with moderate–severe injuries.

Psychopathology following TBI is both highly prevalent and poorly understood. Approximately 60% of individuals with a moderate–severe injury are diagnosed with a psychiatric disorder within the first year post-injury. Up to 56% of individuals develop a novel psychiatric disorder within the first 5 years. A significant proportion of individuals have a chronic vulnerability to psychopathology; novel diagnoses were
shown up to 30 years post-injury. The most common psychological conditions post-TBI include mood disorders (43%) and anxiety disorders (21%), followed by substance use disorders (11.8%). A significant proportion of individuals also present with a range of symptoms related to emotional distress, which, although disabling, do not meet criteria for a formal diagnosis. Despite the prevalence of psychopathology after TBI, psychological conditions are cited as the most unmet need in TBI rehabilitation. Therefore, a better understanding of psychopathology after TBI is required. A wide range of factors have been explored in previous literature to understand psychological outcome, such as premorbid psychiatric history, socioeconomic status, educational attainment, level of early rehabilitation and psychological adjustment to a life-changing event. There is also a preliminary but growing body of research investigating whether neural correlates may help to understand the mechanisms involved in psychopathology after TBI.

Neuroimaging techniques have been employed to better understand the biological mechanisms underpinning TBI-related psychopathology. MRI is the most commonly used neuroradiological technique to assess altered brain structure and function. Previous systematic reviews have attempted to integrate MRI findings from studies within TBI populations. These investigations, however, focus on specific disorders. Reviews of depressive disorders, anxiety disorders, obsessive-compulsive disorders and post-traumatic stress disorder (PTSD) showed that regional associations found within individual studies could not be reliably synthesised.

The lack of consensus on reliable neuroimaging markers of psychopathology after TBI may reflect the significant heterogeneity of injury after TBI, but also could be attributed to limitations of categorical psychopathology. For example, mixed neurobiological findings may arise due to the heterogeneity of symptoms within diagnostic groups. This means that two individuals presenting with the same diagnosis could theoretically have no overlapping symptoms. Therefore, different neural substrates could be associated with clusters of symptoms within the same diagnoses, with some preliminary evidence of biologically driven subgroups in depression and PTSD in non-TBI populations. Another issue with the categorical system is the high comorbidity across diagnostic groups, which suggests that a shared neurobiological substrate may be implicated across diagnostic groups. To better understand the neural underpinnings of psychopathology and overcome the shortcomings of categorical classification systems, research in clinical populations has taken a transdiagnostic approach. This approach has been used to assess the mechanisms of a general factor of psychopathology (p-factor). Reviews in adult populations found preliminary evidence for transdiagnostic neural substrates of general psychopathology, and showed that there is difficulty dissociating disorder-specific brain regions or networks. For example, reductions in cortical volume converge on the ventromedial prefrontal cortex, medial orbitofrontal cortex, inferior temporal, dorsal, anterior cingulate, and the insula in major depressive disorder, schizophrenia, bipolar disorder, and anxiety disorders, demonstrating a significant shared diathesis of Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnoses. To date, these transdiagnostic neural substrates have not been examined within a review of psychopathology after TBI.

Rationale
The neuroscientific literature to date has not identified consistent markers of psychopathology after closed moderate–severe TBI. Inconsistent findings may be due to reliance on categorical classifications of psychopathology and the limited MRI evidence reported to date.

Objectives
The objective of the systematic review and meta-analysis is to identify and appraise all studies of MRI markers (structure, microstructure and function) of psychopathology following a closed moderate–severe TBI in adults. We aim to synthesise both shared and distinct neural mechanisms to understand whether transdiagnostic MRI markers exist for psychopathology after TBI.

METHODS
This protocol follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2015 statement and has been registered at the PROSPERO International Prospective Register of Systematic Reviews of the University of York (CRD4202358358).

Eligibility criteria
Types of studies
All relevant published observational studies (including cohort and case–control studies), regardless of sample size, that use MRI to examine brain morphometry (ie, volume, thickness), white matter microstructure or functional MRI (fMRI) in at least one area of psychopathology will be included. We will include randomised controlled trials or intervention studies that use MRI to examine brain morphometry, microstructure or function in the context of psychopathology at baseline. The following study types will be excluded from this review: methodological papers, editorials and opinion pieces, qualitative research, individual case reports, and secondary studies such as narrative reviews, systematic reviews and meta-analyses.

Types of participants
The eligible population will comprise people aged 16 years and over, of any gender, with a medically confirmed or self-reported diagnosis of moderate or severe closed-head TBI (including complicated mild TBI), as well as any of the following psychiatric conditions: depressive disorders, bipolar disorders, anxiety disorders, PTSD, acute stress disorder, adjustment disorders, obsessive-compulsive disorders, somatoform disorders, eating disorders, specific phobias, panic disorders, generalised anxiety disorders, and agoraphobia.
disorders, substance use disorders, schizophrenia spectrum and psychotic disorders and personality disorders, or reporting any symptoms of psychopathology.

We will include studies with mixed paediatric and adult populations where the sample consists of at least 80% of people over 16 years or results are presented separately for adults. We will include studies with populations of mixed TBI and other acquired brain injuries where more than 80% of the sample have a TBI or results are presented separately for the TBI group. Severity of TBI will be discerned by medical or self-reports of loss of consciousness of greater than at least 10 min or other associated clinical features (ie, Glasgow Coma Scale (GCS) <13; PTA >24 hours; positive neuroimaging) as well as structured interview tools (eg, Ohio State University TBI Identification Method) or questionnaires completed by a clinician or the individual.

Diagnoses which have been made using standardised diagnostic criteria such as the DSM, Third Edition (DSM-III), DSM-III-R, DSM-IV, DSM-5, and International Classification of Disease, 10th Revision (ICD-10) and ICD-11 will be included. We will also include psychopathology captured by self-rating scales such as the Depression Anxiety Stress Scales and the Hospital Anxiety and Depression Scale. Participants with pre-existing psychiatric histories prior to their TBI, as well as those who exhibit psychopathology in more than one area, will be considered eligible. Reports of psychopathology that are made by the participant or clinician will be accepted; however, reports by other proxies (ie, carer, family member) will be excluded.

Comparators
The current review will include studies both with and without a control group.

Outcome measures
The primary outcomes of the included studies should be structural or functional brain alterations of patients with TBI with at least one psychological condition or symptoms in one area of psychopathology. For each study, we plan to obtain information on whole brain and regional-specific measures of the following:
1. Structure: cortical and subcortical grey matter density, thickness, area or volume.
2. White matter microstructure/integrity: fractional anisotropy, mean diffusivity, axial diffusivity and radial diffusivity.
3. Function: voxel and region level task-based activation and fMRI based on blood-oxygen-level-dependent signal. Brain network architecture based on resting-state fMRI.

Other measures of brain morphometry, white matter microstructure and function will also be considered. For example, we will include diffusion MRI studies that use neurite orientation dispersion and density imaging: neurite density index, orientation dispersion index, free water fraction. We will also include fMRI studies that use regional homogeneity and amplitude of low-frequency fluctuation.

Search strategy and data management

Search strategy
An electronic systematic search will be conducted across the Embase (1974–2022), Ovid MEDLINE (1946–2022) and PsycINFO (1806–2022) databases in collaboration with an information specialist. The search strategy will include Medical Subject Headings terms, as well as free text, joined with appropriate Boolean operators. The selected search terms are broad, with high sensitivity for identification of relevant studies. All studies in English and published between the above dates and October 2022 will be eligible. A full search strategy for MEDLINE has been provided as an example in online supplemental materials 1. The search was conducted in November 2022.

Data management
All citations will be imported into Covidence (https://www.covidence.org) where all review data will be stored and managed.

Data acquisition and analysis

Selection process
After duplicates are removed, the titles and abstracts of articles will be independently reviewed by three reviewers (AS, GS and AJH) to assess eligibility for inclusion in this review. Eligible citations will be retrieved in full and assessed by two independent reviewers (AS and GS), with disagreement adjudicated by AJH and JP. Where necessary, additional information will be sought from study authors to determine eligibility. Throughout the study selection process, reviewers will not be blinded to the journal titles, study authors or their institutions. Study selection was completed in February 2023.

Data extraction
Two independent reviewers (AS and GS) will doubly extract data using a customised data extraction tool based on the standardised tool from the Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information. The following information will be retrieved and extracted from each record. Data extraction was completed in April 2023.

► Basic study identifying information: title, first author, year of publication and country.
► Details of methodology: design (case–control, cohort), participants, sample size, definition/measurement of TBI, TBI severity (mild, moderate or severe), TBI occurrence (single or multiple), demographic characteristics (mean age, time post-injury, handedness, ethnicity and education), population (civilian, military, sport), type of imaging modality (structural MRI/fMRI), power of the MRI magnetic field (0.35, 0.5, 1.5, 3 Tesla or 7 Tesla), metric used (eg, thickness, fractional anisotropy), rest/active condition (fMRI), brain segmentation process (manual, automatic),

psychopathology outcome measure, data analysis strategies.

- Results/key findings: anatomical locations (x, y, z) based on peak Montreal Neurological Institute or Talairach coordinates, cluster size and statistical threshold (Z-statistics, t-statistics, uncorrected p values) of regions of interest (ROIs) analyses that are conducted in the studies; morphological statistics from significant ROIs (eg, volume, thickness); diffusion tensor imaging (DTI) parameters from significant ROIs; maximum activation of the significant ROIs; the value of clinical characteristics (mean and SD of psychological rating scale scores); and the correlations between imaging data and clinical data.

Any missing information or questions about the above data will be obtained by directly contacting the authors. If no clarification is provided after 4 weeks, the study will be included in the final analysis with the missing information marked.

Outcomes and prioritisation

The primary outcomes are MRI markers of psychopathology which may include brain structure, microstructure and function, and these will be prioritised based on technique and psychopathology category. We will prioritise cortical and subcortical structural findings as well as white matter integrity based on DTI. Next, we will focus on cortical and subcortical functional activation patterns based on fMRI. We will categorise data by (a) transdiagnostic patterns of brain alterations and (b) specific psychopathology-related brain alterations. We will capture pre-injury psychopathology where data are available (eg, number of studies, study similarities) and analyse the impact on post-injury psychopathology and neural correlates.

Quality assessment

There are no standard tools for quality appraisal of neuroimaging studies. Therefore, we have devised a customised quality assessment checklist adapted from pre-existing tools: the Joanna Briggs’s Institute Critical Appraisal Tools for cohort studies and for case–control studies, tools used in pre-existing neuroimaging systemic reviews, and the Committee on Best Practices in Data Analysis Sharing in Neuroimaging MRI (http://www.humanbrainmapping.org). This tool has been included in online supplemental materials for reference. Two reviewers (AS and GS) will independently score the included articles against the checklist and study quality will be defined as high (>8 criteria met), medium (5–8) or low (<5) for category 1 and high (>5 criteria met), medium (3–5) or low (<3) for category 2.

Data synthesis

Data extracted from studies will be summarised in a table, including basic study identifying information, details of methodology and results. A qualitative review of the structural and functional brain correlates will be performed and synthesised into a detailed narrative of findings. First, we will present a narrative synthesis of neural correlates which are identified as common to multiple domains of psychopathology, structured by neuroimaging modality (structural MRI, DTI, fMRI). Next, findings will be integrated by domain of psychopathology (eg, depressive disorders, anxiety disorders), structured by neuroimaging modality. Data synthesis is expected to be complete by late August 2023.

Meta-analysis

If there are a sufficient number of comparative studies available (ie, at least two) that analyse a domain of psychopathology using a similar methodology, then we will use meta-analysis. Where there are enough appropriate studies available, we will use a balanced coverage of all information that is actually available. Where feasible, we will first obtain separate effect sizes for each study. Next, we will estimate Hedge’s g for whole brain and ROI measurements including volumetric, morphometric, white matter integrity and activation results. We will use a random-effects model to pool the effect sizes. Meta-regression analyses will consider the following potential covariates: sample size, mean age, % of females, methodological quality scores, year of publication, years post-injury and GCS score/duration of PTA. Where data are sparse, we will use a beta-binomial model for meta-analysis (see Mathes and Kuss, 2018). We will use R studio, R packages ‘meta’ and ‘metasens’ following the guide outlined in Balduzzi et al. Coordinate-based meta-analyses with permutation of subject images may be considered if a sufficient number of studies are available.

Heterogeneity will be assessed using prediction intervals (generated from the t-statistic) where there are a sufficient number of studies or minimal heterogeneity across pooled studies, and from the I² statistic.

Network meta-analysis

We will conduct a network meta-analysis where there is sufficient number of comparative studies available and sufficient similarity across study characteristics. We will employ the ‘netmeta’ package in R for a frequentist approach to synthesising biological data across studies. The aim of our network meta-analysis will be to understand commonalities between brain structure and function across different psychopathologies in TBI studies. We will visualise associations across studies using a network plot, where each node is reflective of a particular psychopathology (eg, depressive disorders and associated symptomatology), the node size relative to the number of studies included and the edges between nodes relative to the number of pairwise comparisons. Hedge’s g will be used to understand the brain structure and function differences between psychopathology classifications.

Meta-bias(es)

We will assess for the possibility of small-study effects and publication bias in our meta-analysis by inspecting...
funnel plot asymmetry and Egger’s test (p<0.1), following Balduzzi et al.49

Confidence in cumulative evidence
The quality of evidence for primary outcomes will be assessed using the Grading of Recommendations Assessment, Development and Evaluation guidelines.34

Patient and public involvement
There are currently no plans to involve patients or the public in the design, conduct, reporting or dissemination of our systematic review.

Ethics and dissemination
Ethics approval is not required for the present study as there will be no original data collected. We intend to disseminate the results through publication to a high-quality peer-reviewed journal and conference presentations on completion.

Strengths and limitations of the study protocol
The present review uses a transdiagnostic approach to investigate the possibility that shared neural substrates converge across the TBI literature more reliably than psychopathology-specific substrates. Our prospective systematic review and meta-analysis will synthesise both distinct and shared neural mechanisms of psychopathology across neuroimaging studies in moderate–severe TBI. This in turn will provide a greater understanding of biological mechanisms which may contribute to the expression of psychopathology after a TBI. There are several limitations of our study protocol which might be potential sources of bias in our prospective systematic review and meta-analysis. The current search strategy is limited to English language studies, which could present a language bias. We will exclude all studies which do not use MRI, which could limit the clinical utility of our findings, given other imaging modalities are more readily used in practice. However, currently in research, MRI studies are the most commonly used modality and our prospective systematic review and meta-analysis will focus a streamlined view on MRI-based studies.

Acknowledgements
Our information specialist, Farhad Shokraneh, for his contribution in design of the search strategies and collaboration with the search.

Contributors
AS—conceptualisation, methodology, writing (original draft) and writing (review and editing). AJH—conceptualisation, methodology, supervision and writing (review and editing). JSP—conceptualisation, funding acquisition, methodology, project administration, supervision and writing (review and editing). GS—conceptualisation, methodology, project administration, supervision and writing (review and editing).

Funding
The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests
None declared.

Patient and public involvement
Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication
Not required.

Provenance and peer review
Not commissioned; externally peer reviewed.

Supplemental material
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Online Supplementary Materials I

Full Search Strategies for Databases

Title
Transdiagnostic MRI Markers of Psychopathology following Traumatic Brain Injury: A Systematic Review and Meta-Analysis Protocol

Registration ID: CRD42022358358 (PROSPERO)
A. Embase

Database: Embase <1974 to 2022 October>

1  *Acquired Brain Injury/ OR *Brain Concussion/ OR *Brain Contusion/ OR *Brain Damage/ OR *Brain Hematoma/ OR *Brain Hemorrhage/ OR *Brain Injury/ OR *Diffuse Axonal Injury/ OR *Diffuse Brain Injury/ OR exp *Diffuse Brain Injury/ OR *Head Injury/ OR *Skull Fracture/ OR *Subarachnoid Hemorrhage/ OR *Subdural Hematoma/ OR *Traumatic Brain Injury/ OR (Traumatic OR Posttrauma* OR Brain Arachnoid Haemorrhage* OR Brain Arachnoid Hemorrhage* OR Brain Bleeding* OR Brain Bruise* OR Brain Contus* OR Brain Damage* OR Brain Haemorrhage* OR Brain Hemorrhage* OR Brain Injur* OR Brain Lesion* OR Brain System Trauma* OR Brain Trauma* OR Brain Vascular Injur* OR Brain Vascular Trauma* OR Broken Skull* OR Cerebral Bleeding OR Cerebral Concuss* OR Cerebral Contus* OR Cerebral Damage* OR Cerebral Haemorrhage* OR Cerebral Haemorrhage* OR Cerebral Injur* OR Cerebral Lesion* OR Cerebral Trauma* OR Cerebrocranial Injur* OR Cerebrocranial Trauma* OR Cerebrovascular Trauma* OR Cerebrum Haemorrhage* OR Cerebrum Hemorrhage* OR Cerebrum Lesion* OR Commotio* OR Concuss* OR DAI OR DAI OR Damaged Brain* OR Depressed Cranium* OR Depressed Skull* OR Diffuse Axonal Injur* OR Diffuse Brain Injury* OR Diffuse Hemorrhage* OR Fracture Skull* OR Fractured Cranial Bone* OR Fractured Cranium* OR Fractured skull* OR Frontal Region Trauma* OR Haemisphere Injur* OR Haemisphere Lesion* OR Head Bruis* OR Head Contus* OR Head Injur* OR Head Trauma* OR Head Wound* OR Hemisphere Injur* OR Hemisphere Lesion* OR Interhemispheric Haematoma* OR Interhemispheric Hematoma* OR Intracerebral Bleeding* OR Intracerebral Haemorrhage* OR Intracerebral Haemorrhage* OR Intracerebral Haematoma* OR Intracerebral Hemorrhage* OR Intracranial Bleding* OR Intracranial Epidural Haematoma* OR Intracranial Epidural Hematoma* OR Intracranial Haematoma* OR Intracranial Haemorrhage* OR Intracranial Hemorrhage* OR Intracranial Lesion* OR Intracranial Trauma* OR Intraventricular Haemorrhage* OR Intraventricular Hemorrhage* OR Midbrain Haemorrhage* OR Midbrain Hemorrhage* OR mTBI OR mTBIs OR Nervous System Injur* OR Nervous System Trauma* OR Neuroinjur* OR Neuro-Injur* OR Neurologic Damage* OR Neurotrauma* OR Occipital Region Trauma* OR Occipital Trauma* OR Parietal Region Trauma* OR Skull Depressed Fracture* OR Skull Fracture* OR Skull Frontobasal Fracture* Skullbase Fracture* OR Subarachnoid Bleeding* OR Subarachnoid Haematomat* OR Subarachnoid Haemorrhage* OR Subarachnoid Haemorrhagia* OR Subarachnoid Hemorrhage* OR Subarachnoid Hemorrhage* OR Subarachnoid Hemorhagia* OR Subarachnoidal Bleeding* OR Subarachnoidal Haemorrhage* OR Subarachnoidal Hemorrhage* OR Subdural Bleeding* OR Subdural Haematoma* OR Subdural Haemorrhage* OR Subdural Hemorrhage* OR Subepidural Haematoma* OR Subepidural Hematoma* OR Temporal Region Trauma* OR TBI OR TBI).

2  *Mental Disease/ OR exp *Mood Disorder/ OR *Affective Neurosis/ OR *Affective Psychosis/ OR *Blunted Affect/ OR exp *Depression/ OR *Major Affective Disorder/ OR exp *Mania/ OR *Minor
Insanity OR Mental Abnormalit\* OR Mental Change* OR Mental Confusion* OR Mental Defect* OR Mental Disorder* OR Mental Disturbance* OR Mental Illness* OR Mental Insufficiency OR Mental Symptom* OR Mentally Ill OR Neuropsychiatric Disease* OR Neuropsychiatric Disorder* OR Psychiatric Diagnosis OR Psychiatric Diseases* OR Psychiatric Disorder* OR Psychiatric Illness* OR Psychiatric Symptom* OR Psychiatric Disease* OR Psychic Disorder* OR Psychic Disturbance* OR Psychologic Disorder* OR Psychologic Disturbance* OR Psychological Disorder* OR Psychological Disturbance* OR Psychopatholog* OR Psycho-Patholog* OR Mood Disorder* OR Mood Disturbance* OR Affective Disorder* OR Affective Disturbance* OR Affective Illness* OR Cyclothymi* OR Depress* OR Melancholia* OR Paraphrenia* OR Dysthymi* OR Premenstrual Dysphoric Disorder* OR Premenstrual Dysphoric Syndrome* OR Psychosis OR Psychoses OR Psychotic OR Blunted Affect OR Flat Affect OR Schizo* OR Mania* OR Manic OR Bipolar OR Mental Fatigue OR Hypomani* OR Anxi* OR Anxious* OR Neurotic OR Neurosis OR Neuroses OR Mourning Syndrome OR Obsess* OR Compuls* OR OCD OR Hoarding OR Panic OR Phobic OR Phobia* OR Effort Syndrome OR Psychoneurosis* OR Anankastic Personalit* OR Stress* OR Catastrophiz* OR Catastrophes* OR Distress* OR Koro* OR Psychasthenia* OR Repetitive Behaviour* OR Repetitive Behavior* OR Trichotillomania* OR Hair Pulling OR PTSD OR Posttraumatic Psychotic Syndrome OR Posttraumatic Syndrome OR Moral Injur* OR Posttraumatic Stress* OR Post-Traumatic Stress* OR Traumatic Stress OR Shell Shock OR Complex Trauma OR DESMOS OR "Disorders of Extreme Stress Not Otherwise Specified" OR Adjustment Disorder* OR Adjustment Reaction* OR Anniversary Reaction* OR Reactive Depression* OR Reactive Disorder* OR Transient Situational Disorder* OR Transient Situational Disturbance* OR Amputee Identity Disorder* OR Apotemnophilia* OR Astasia-Abasia OR BIID OR Bodily Distress Disorder* OR Bodily Distress Disorders OR Body Dysmorphic Disorder* OR Body Image Disfunction* OR Body Image Disorder* OR Body Integrity Disorder* OR Body Integrity Identity Disorder* OR Briquet Syndrome* OR Cardiophobia* OR Conversion Disorder* OR Conversion Hysteri* OR Conversion Reaction* OR Conversion Syndrome* OR Da Costa Syndrome* OR Dyssmorphophobia OR Factitious Disorder* OR Foreign Limb Syndrome* OR Functional Heart Complaint* OR Functional Movement Disorder* OR Functional Neurologic Symptom Disorder* OR Functional Neurological Disorder* OR Functional Neurological Symptom Disorder* OR Ganser Syndrome OR Globus OR Hospital Addiction Syndrome* OR Hypochondria* OR Hysteria OR Hysteric* OR Medically Unexplained Syndrome* OR Munchausen Syndrome OR Munchhausen Syndrome OR Neurasthenia OR Neurocirculation Asthenia OR Neurocirculatory Asthenia OR Neurocirculatory Dystonia OR Neurodermatitis OR Neurogenic Heart OR "Pain Disorder" OR Pseudocyesis OR Pseudopsychosis OR Psychalg* OR Psychogenic Amaurosis OR Psychogenic Amblyopia OR Psychogenic Blindness OR Psychogenic Nonepileptic Seizure* OR Psychogenic Non-Epileptic Seizure* OR Psychogenic Pain OR Psychogenic Seizure* OR Psychogenic Vision OR Psychogenic Visual OR Psychophyslogic Disorder* OR Psychosomatic Blindness OR Psychosomatic Disorder* OR Soldier Heart OR Somatic Symptom Disorder* OR Somatization* OR Somatisation* OR Somatoform Disorder* OR Somatoform Pain* OR Xenomelia* OR Feeding
Disorder* OR Feeding Disorder OR Eating Disorder* OR Appetite Disorder* OR Disordered Eating OR Eating Pathology OR Pathologic Eating OR Pathologic Feeding OR Pathological Eating OR Pathological Feeding OR Anorexia Nervosa* OR Avoidant Restrictive Food Intake Disorder OR Binge-Eating Disorder OR Bulimia* OR Diabulimia* OR Food Addiction* OR Compulsive Eating OR Night Eating Syndrome* OR Orthorexia OR Pica OR Rumination Syndrome* OR Merycism OR Ruminating Disorder* OR ARFID OR Emotional Eating OR Food Aversion OR Food Refusal OR Muscle Dysmorphia OR Purging Disorder* OR Addict* OR Alcohol Abuse* OR Alcohol Amnes* OR Alcohol Depend* OR Alcohol Induced Amnes* OR Alcohol Induced Disorder* OR Alcohol Induced Dysmnesi* OR Alcohol Induced Korsakoff Syndrome* OR Alcohol Induced Persisting Amnestic Disorder* OR Alcohol Problem* OR Alcohol Related Disorder* OR Alcohol Related Seizure* OR Alcohol Syndrome* OR "Alcohol Use Disorder*" OR Alcoholic* OR Alcoholism OR Amphetamine Abuse* OR Amphetamine Depend* OR Amphetamine Related Disorder* OR "Amphetamine Use Disorder*" OR Angel Dust Abuse* OR Benzodiazepine Depend* OR Binge Alcohol* OR Binge Drink* OR Cannabinoid Abuse* OR Cannabinoid Depend* OR Cannabidiol Related Disorder* OR Chemical Depend* OR Cocaine Abuse* OR Cocaine Depend* OR Cocaine Related Disorder* OR Delirium Tremens OR Dipsomani* OR Drug Abuse* OR Drug Bombing OR Drug Craving OR Drug Depend* OR Drug Facilitation* OR Drug Habituation* OR Drug Misuse* OR Drug Overdose* OR Drug Parachuting OR Drug Physical Depend* OR Drug Psychoses OR Drug Related Craving OR "Drug Use Disorder*" OR Drugs Craving OR Drunkenness* OR Ethanol Abuse* OR Ethanol Depend* OR Hashish Abuse* OR Heroin Abuse* OR Heroin Depend* OR Heroin Smoking* OR Heroinism OR Inhalant Abuse* OR Marihuana Abuse* OR Marijuana Abuse* OR Marijuana Depend* OR Marijuana Related Disorder* OR "Marijuana Use*" OR Medication Misuse* OR Medicine Misuse* OR Methamphetamine Depend* OR Morphine Abuse* OR Morphine Depend* OR Narcotic Abuse* OR Narcotic Depend* OR Narcotic Related Disorder* OR Narcotism OR Nicotine Abuse* OR Nicotine Depend* OR "Nicotine Use Disorder*" OR Nicotinism OR Opiate Abuse* OR Opiate Alkaloid Depend* OR Opiate Crisis OR Opiate Depend* OR Opiate Epidemic* OR Opiate Overdose* OR Opioid Abuse* OR Opioid Crisis OR Opioid Depend* OR Opioid Epidemic* OR Opioid Misuse* OR Opioid Overdose* OR Opioid Related Disorder* OR "Opioid Use Disorder*" OR Opioids Crisis OR Opioids Depend* OR Opioids Epidemic* OR Opium Abuse* OR Opium Depend* OR Opium Epidemic* OR Opium Smoking OR "Opium Use*" OR PCP Abuse* OR PCP Depend* OR Phencyclidine Abuse* OR Phencyclidine Depend* OR Phencyclidine Related Disorder* OR Physical Depend* OR "Polydrug Use*" OR Substance Abuse* OR Substance Craving OR Substance Depend* OR Substance Induced Psychoses OR Substance Related Disorder* OR "Substance Use*" OR Tobacco Abuse* OR Tobacco Depend* OR "Tobacco Use Disorder*" OR Tobaccoism OR Toxic Psychoses OR Toxicomani* OR Parano* OR Delus* OR Psychogenic Parasites* OR Capgras Syndrome* OR Hebephreni* OR Hallucinosis OR Hallucinat* OR Anankastic Personalit* OR Antisocial Behavior* OR Antisocial Behaviour* OR Antisocial Personalit* OR Anti-Social Personalit* OR "As If Personality*" OR "As If
Personalities* OR Asthenic Personality* OR Avoidant Personality* OR Borderline OR Character Deviation* OR Character Disorder* OR Character Disturbance* OR Character Problem* OR Dependent Personality* OR Diogenes Syndrome OR Dissociative Identity Disorder* OR Dual Personality* OR Dyssocial Behavior* OR Dyssocial Behaviour* OR Histrionic Personality* OR Impulse-Ridden Personality* OR Inadequate Personality* OR Masochist* OR Multiple Identity Disorder* OR Multiple Personality* OR Narcism OR Narcissism OR Narcissistic OR Neuropsychopath* OR Passive-Aggressive Personality* OR Personality Change OR Personality Disorder* OR Personality Disturbance* OR Psychological Dependence* OR Psychopath* OR Sadist* OR Sadomasochist* OR "Self Love" OR Senile Squalor Syndrome OR Social Behavior Disorder* OR Social Breakdown Syndrome OR Social Disease* OR Social Pathology* OR Sociopath*).ti,ab.

3 exp Nuclear Magnetic Resonance Imaging/ OR exp Neuroimaging/ OR Brain Imaging/ OR Connectome/ OR "Cortical Thickness (Brain)"/ OR Neuroradiology/ OR exp Brain Radiography/ OR Diffusion Weighted Imaging/ OR Diffusion Tensor Imaging/ OR Fluid-Attenuated Inversion Recovery Imaging/ OR Anisotropy/ OR "Fractional Anisotropy"/ OR Diffusivity/ OR Axial Diffusivity/ OR Radial Diffusivity/ OR Mean Diffusivity/ OR Gray Matter/ OR White Matter/ OR Voxel Based Morphometry/ OR Cortical Thickness (Brain)/ OR (Magnetic Resonance OR MRI OR MRIs OR MR Imaging* OR NMR OR MR Tomography* OR Zeugmatography* OR Chemical Shift Imaging* OR Magnetization Transfer OR Proton Spin Tomography* OR IMRI OR Spin Echo* OR Diffusion Imaging* OR Diffusion Tensor* OR DTI OR Tractography* OR Diffusion Weighted* OR Echo Planar OR Echoplanar OR Neuroimaging* OR (Brain adj Imaging*) OR Brain Mapping OR Stereotaxic Atlas OR Functional Cerebral Localization? OR Connectome* OR Connectivity Map OR Connectivity Matrix OR Cortical Thickness OR Cortex Thickness OR Grey Matter Thickness OR Neuroradiology* OR DWI OR Fluid-Attenuated Inversion Recovery OR FLAIR OR GRE OR Gradient Recalled Echo* OR Gradient Echo* OR Cortical Thinning OR Subcortical Thickness OR Anisotropy* OR Anisotrophy* OR Diffusivity* OR Diffusion Rate* OR Gray Matter* OR Grey Matter* OR Voxel Based Morphometry* OR VBM).ti,ab.

4 and 1-3

6 Human/ OR Normal Human/ OR Human Cell/
7 5 and 6
8 5 not 7
9 4 not 8
10 limit 9 to embase
11 limit 10 to no language specified
12 limit 10 to English language
13 11 OR 12

**B. MEDLINE**

Database: Ovid MEDLINE(R) ALL <1946 to October, 2022>
Brain Concussion/ OR Brain Contusion/ OR Brain Damage, Chronic/ OR Brain Injuries, Traumatic/ OR Brain Injuries/ OR Brain Injury, Chronic/ OR Brain Stem Hemorrhage, Traumatic/ OR Cerebral Hemorrhage, Traumatic/ OR Cerebral Hemorrhage/ OR Cerebrovascular Trauma/ OR Diffuse Axonal Injury/ OR exp Brain Hemorrhage, Traumatic/ OR exp Brain Injuries, Diffuse/ OR exp Hematoma, Subdural/ OR exp Intracranial Hemorrhages/ OR Head Injuries, Closed/ OR Head Injuries, Penetrating/ OR Hematoma, Epidural, Cranial/ OR Hematoma, Subdural, Acute/ OR Hematoma, Subdural, Chronic/ OR Hematoma, Subdural, Intracranial/ OR Intracranial Hemorrhage, Traumatic/ OR Skull Fractures/ OR Subarachnoid Hemorrhage, Traumatic/ OR Subarachnoid Hemorrhage/ OR Trauma, Nervous System/ OR (Traumatic OR Posttrauma* OR Brain Arachnoid Haemorrhage* OR Brain Arachnoid Hemorrhage* OR Brain Bleeding* OR Brain Bruise* OR Brain Contus* OR Brain Damage* OR Brain Haemorrhage* OR Brain Hemorrhage* OR Brain Injur* OR Brain Lesion* OR Brain System Trauma* OR Brain Trauma* OR Brain Vascular Injur* OR Brain Vascular Trauma* OR Broken Skull* OR Cerebral Bleeding OR Cerebral Concuss* OR Cerebral Contus* OR Cerebral Damage* OR Cerebral Hemorrhage* OR Cerebral Injur* OR Cerebral Lesion* OR Cerebral Trauma* OR Cerebrocranial Injur* OR Cerebrocranial Trauma* OR Cerebrovascular Trauma* OR Cerebrum Haemorrhage* OR Cerebrum Hemorrhage* OR Cerebrum Lesion* OR Commotio* OR Concuss* OR DAI OR DAIls OR Damaged Brain* OR Depressed Cranium* OR Depressed Skull* OR Diffuse Axonal Injur* OR Forebrain Lesion* OR Fracture Skull* OR Fractured Cranial Bone* OR Fractured Cranium* OR Fractured Skull* OR Frontal Region Trauma* OR Haemisphere Injur* OR Haemisphere Lesion* OR Head Bruis* OR Head Contus* OR Head Injur* OR Head Trauma* OR Head Wound* OR Hemisphere Injur* OR Hemisphere Lesion* OR Interhemispheric Haematoma* OR Interhemispheric Hematoma* OR Intracerebral Bleeding* OR Intracerebral Haematoma* OR Intracerebral Haemorrhage* OR Intracerebral Hematoma* OR Intracerebral Hemorrhage* OR Intracerebral Trauma* OR Intracortical Haemorrhage* OR Intracortical Hemorrhage* OR Intracranial Bleeding* OR Intracranial Epidural Haematoma* OR Intracranial Epidural Hematoma* OR Intracranial Epidural Hemorrhage* OR Intracranial Haemorrhage* OR Intracranial Haemorrhage* OR Intracranial Lesion* OR Intracranial Lesion* OR Intracranial Lesion* OR Intracranial Trauma* OR Intracranial Trauma* OR Intracranial Hemorrhage* OR Intracranial Hemorrhage* OR Intracranial Hemorrhage* OR Midbrain Haemorrhage* OR Midbrain Hemorrhage* OR mTBI OR mTBls OR Nervous System Injur* OR Nervous System Trauma* OR Neuroinjur* OR Neuro-Injur* OR Neurologic Damage* OR Neurotrauma* OR Occipital Region Trauma* OR Occipital Trauma* OR Parietal Region Trauma* OR Skull Depressed Fracture* OR Skull Fracture* OR Skull Frontobasal Fracture* Skullbase Fracture* OR Subarachnoid Bleeding* OR Subarachnoid Haematoma* OR Subarachnoid Haemorrhage* OR Subarachnoid Haemorrhagia* OR Subarachnoid Hematoma* OR Subarachnoid Hemorrhage* OR Subarachnoid Hemorrhagia* OR Subarachnoidal Bleeding* OR Subarachnoidal Haemorrhage* OR Subarachnoidal Hemorrhage* OR Subdural Bleeding* OR Subdural Haematoma* OR Subdural Haemorrhage* OR Subdural Hematoma* OR Subdural Hemorrhage* OR Subependymal Haematoma* OR Subependymal Hematoma* OR Temporal Region Trauma* OR TBI OR TBls).ti,ab.
2 Psychopathology/ OR Mental Disorders/ OR exp Mood Disorders/ OR Cyclothymic Disorder/ OR exp Depressive Disorder/ OR Depressive Disorder, Major/ OR Depressive Disorder, Treatment-Resistant/ OR Dysthymic Disorder/ OR Premenstrual Dysphoric Disorder/ OR Seasonal Affective Disorder/ OR Mental Fatigue/ OR exp Anxiety Disorders/ OR Anxiety, Separation/ OR Neurocirculatory Asthenia/ OR Neurotic Disorders/ OR exp Obsessive-Compulsive Disorder/ OR Hoarding Disorder/ OR Panic Disorder/ OR exp Phobic Disorders/ OR Phobia, Social/ OR Stress Disorders, Post-Traumatic/ OR Adjustment Disorders/ OR exp Somatoform Disorders/ OR Body Dysmorphic Disorders/ OR Body Integrity Identity Disorder/ OR Conversion Disorder/ OR Factitious Disorders/ OR Munchhausen Syndrome/ OR “Munchhausen Syndrome by Proxy”/ OR Hypochondriasis/ OR Neurasthenia/ OR exp “Feeding and Eating Disorders”/ OR Anorexia Nervosa/ OR Avoidant Restrictive Food Intake Disorder/ OR Binge-Eating Disorder/ OR Bulimia Nervosa/ OR Diabulimia/ OR Food Addiction/ OR Night Eating Syndrome/ OR Orthorexia Nervosa/ OR Pica/ OR Rumination Syndrome/ OR exp Substance-Related Disorders/ OR exp Alcohol Amnestic Disorder/ OR Alcohol-Induced Disorders/ OR Alcohol-Induced Disorders, Nervous System/ OR Alcoholism/ OR Alcohol-Related Disorders/ OR Amphetamine-Related Disorders/ OR Binge Drinking/ OR Cocaine-Related Disorders/ OR Drug Overdose/ OR Heroin Dependence/ OR Inhaling Abuse/ OR Marijuana Abuse/ OR “Marijuana Use”/ OR Morphine Dependence/ OR Narcotic-Related Disorders/ OR Opiate Overdose/ OR exp Opioid-Related Disorders/ OR Opium Dependence/ OR Phencyclidine Abuse/ OR Psychoses, Alcoholic/ OR Psychoses, Substance-Induced/ OR Substance Abuse, Intravenous/ OR Substance Abuse, Oral/ OR “Tobacco Use Disorder”/ OR “Schizophrenia Spectrum and Other Psychotic Disorders”/ OR Schizotypal Personality Disorder/ OR exp Schizophrenia/ OR Schizophrenia, Catatonic/ OR Schizophrenia, Disorganized/ OR Schizophrenia, Paranoid/ OR Schizophrenia, Treatment-Resistant/ OR Shared Paranoid Disorder/ OR Affective Disorders, Psychotic/ OR Capgras Syndrome/ OR Delusional Parasitosis/ OR Paranoid Disorders/ OR Psychotic Disorders/ OR Psychoses, Substance-Induced/ OR Psychoses, Alcoholic/ OR exp Personality Disorders/ OR Antisocial Personality Disorder/ OR Borderline Personality Disorder/ OR Compulsive Personality Disorder/ OR Dependent Personality Disorder/ OR exp Histrionic Personality Disorder/ OR Hysteria/ OR Paranoid Personality Disorder/ OR Passive-Aggressive Personality Disorder/ OR Schizoid Personality Disorder/ OR Schizotypal Personality Disorder/ OR Dissociative Identity Disorder/ OR (Abnormal Mental State* OR Behavior Disorder* OR Diseased Mental State* OR Disordered Mental State* OR Disturbed Mental State* OR Insanity OR Mental Abnormality* OR Mental Change* OR Mental Confusion* OR Mental Defect* OR Mental Disorder* OR Mental Disturbance* OR Mental Illness* OR Mental Insufficiency OR Mental Symptom* OR Mentally Ill OR Neuropsychiatric Disease* OR Neuropsychiatric Disorder* OR Psychiatric Diagnosis OR Psychiatric Disease* OR Psychiatric Disorder* OR Psychiatric Illness* OR Psychiatric Symptom* OR Psychotic Disease* OR Psychic Disorder* OR Psychic Disturbance* OR Psychologic Disorder* OR Psychologic Disturbance* OR Psychological Disorder* OR Psychological Disturbance* OR Psychopathology* OR
Psycho-Patholog* OR Mood Disorder* OR Mood Disturbance* OR Affective Disorder* OR Affective Disturbance* OR Affective Illness* OR Cyclothym* OR Depress* OR Melancholia* OR Paraphrenia* OR Dysthym* OR Premenstrual Dysphoric Disorder* OR Premenstrual Dysphoric Syndrome* OR Psychosis OR Psychoses OR Psychotic OR Blunted Affect OR Flat Affect OR Schizo* OR Mania* OR Manic OR Bipolar OR Mental Fatigue OR Hypomani* OR Anxi* OR Astheni* OR Neurotic OR Neurosis OR Neuroses OR Mourning Syndrome OR Obsess* OR Compuls* OR OCD OR Hoarding OR Panic OR Phobic OR Phobia* OR Effort Syndrome OR Psychoneurosis* OR Anankastic Personality* OR Stress* OR Catastrophiz* OR Catastrophis* OR Distress* OR Koro* OR Psychasthenia* OR Repetitive Behaviour* OR Repetitive Behavior* OR Trichotillomania* OR Hair Pulling OR PTSD OR Posttraumatic Psychic Syndrome OR Posttraumatic Syndrome OR Moral Injur* OR Posttraumatic Stress* OR Post-Traumatic Stress* OR Traumatic Stress OR Shell Shock OR Complex Trauma OR DESNOS OR "Disorders of Extreme Stress Not Otherwise Specified" OR Adjustment Disorder* OR Adjustment Reaction* OR Anniversary Reaction* OR Reactive Depression* OR Reactive Disorder* OR Transient Situational Disorder* OR Transient Situational Disturbance* OR Amputee Identity Disorder* OR Apotemnophilia* OR Astasia-Abasia OR BID OR Bodily Distress Disorder* OR Bodily Distress Disorders OR Body Dysmorphic Disorder* OR Body Image Disfunction* OR Body Image Disorder* OR Body Integrity Disorder* OR Body Integrity Identity Disorder* OR Briquet Syndrome* OR Cardiophobia* OR Conversion Disorder* OR Conversion Hysteri* OR Conversion Reaction* OR Conversion Syndrome* OR Da Costa Syndrome* OR Dysmorphophobia OR Factitious Disorder* OR Foreign Limb Syndrome* OR Functional Heart Complaint* OR Functional Movement Disorder* OR Functional Neurologic Symptom Disorder* OR Functional Neurological Disorder* OR Functional Neurological Symptom Disorder* OR Ganser Syndrome OR Globus OR Hospital Addiction Syndrome* OR Hypochondria* OR Hysteria OR Hysteric* OR Medically Unexplained Syndrome* OR Munchausen Syndrome OR Munchhausen Syndrome OR Neurasthenia OR Neurocirculation Asthenia OR Neurocirculatory Asthenia OR Neurocirculatory Dystonia OR Neurodermatitis OR Neurogenic Heart OR "Pain Disorder* OR Pseudocyesis OR Pseudopsychosis OR Psychalg* OR Psychogenic Amaurosis OR Psychogenic Amblyopia OR Psychogenic Blindness OR Psychogenic Nonepileptic Seizure* OR Psychogenic Non-Epileptic Seizure* OR Psychogenic Pain OR Psychogenic Seizure* OR Psychogenic Vision OR Psychogenic Visual OR Psychophysiological Disorder* OR Psychosomatic Blindness OR Psychosomatic Disorder* OR Soldier Heart OR Somatic Symptom Disorder* OR Somatization* OR Somatisation* OR Somatoform Disorder* OR Somatoform Pain* OR Xenomelia* OR Feeding Disorder* OR Feeding Disorder OR Eating Disorder* OR Appetite Disorder* OR Disordered Eating OR Eating Pathology OR Pathologic Eating OR Pathologic Feeding OR Pathological Eating OR Pathological Feeding OR Anorexia Nervosa* OR Avoidant Restrictive Food Intake Disorder OR Binge-Eating Disorder OR Bulimia* OR Diabulimia* OR Food Addiction* OR Compulsive Eating OR Night Eating Syndrome* OR Orthorexia OR Pica OR Rumination Syndrome* OR Merycism OR Rumination Disorder* OR ARFID OR Emotional Eating OR Food Aversion OR Food Refusal OR Muscle Dysmorphia OR Purging Disorder* OR Trichophag* OR
Hyperphag* OR Polyphag* OR Addict* OR Alcohol Abuse* OR Alcohol Amnes* OR Alcohol Depend* OR Alcohol Induced Amnes* OR Alcohol Induced Disorder* OR Alcohol Induced Dysmnesi* OR Alcohol Induced Korsakoff Syndrome* OR Alcohol Induced Persisting Amnestic Disorder* OR Alcohol Problem* OR Alcohol Related Disorder* OR Alcohol Related Seizure* OR Alcohol Syndrome* OR "Alcohol Use Disorder***" OR Alcoholic* OR Alcoholism OR Amphetamine Abuse* OR Amphetamine Depend* OR Amphetamine Related Disorder* OR "Amphetamine Use Disorder***" OR Angel Dust Abuse* OR Benzodiazepine Depend* OR Binge Alcohol* OR Binge Drink* OR Cannabis Abuse* OR Cannabis Depend* OR Cannabis Related Disorder* OR Chemical Depend* OR Cocaine Abuse* OR Cocaine Depend* OR Cocaine Related Disorder* OR Delirium Tremens OR Dipsomani* OR Drug Abuse* OR Drug Bombing OR Drug Craving OR Drug Depend* OR Drug Facilitation* OR Drug Habituation* OR Drug Misuse* OR Drug Overdose* OR Drug Parachuting OR Drug Physical Depend* OR Drug Psychoses OR Drug Related Craving OR "Drug Use Disorder***" OR Drugs Craving OR Drunkenness* OR Ethanol Abuse* OR Ethanol Depend* OR Hashish Abuse* OR Heroin Depend* OR Heroin Depend* OR Heroin Smoking* OR Heroinism OR Inhalant Abuse* OR Marihuana Abuse* OR Marijuana Abuse* OR Marijuana Depend* OR Marijuana Related Disorder* OR "Marijuana Use***" OR Medication Misuse* OR Medicine Misuse* OR Methamphetamine Depend* OR Morphone Abuse* OR Morphone Depend* OR Narcotic Abuse* OR Narcotic Depend* OR Narcotic Related Disorder* OR Narcotism OR Nicotine Abuse* OR Nicotine Depend* OR "Nicotine Use Disorder***" OR Nicotinis* OR Opiate Abuse* OR Opiate Alkaloid Depend* OR Opiate Crisis OR Opiate Depend* OR Opiate Epidemic* OR Opiate Overdose* OR Opioid Abuse* OR Opioid Crisis OR Opioid Depend* OR Opioid Epidemic* OR Opioid Misuse* OR Opioid Overdose* OR Opioid Related Disorder* OR "Opioid Use Disorder***" OR Opioids Crisis OR Opioids Depend* OR Opioids Epidemic* OR Opium Abuse* OR Opium Depend* OR Opium Epidemic* OR Opium Smoking OR "Opium Use***" OR PCP Abuse* OR PCP Depend* OR Phencyclidine Abuse* OR Phencyclidine Depend* OR Phencyclidine Related Disorder* OR Physical Depend* OR "Polydrug Use***" OR Substance Abuse* OR Substance Craving OR Substance Depend* OR Substance Induced Psychoses OR Substance Related Disorder* OR "Substance Use***" OR Tobacco Abuse* OR Tobacco Depend* OR "Tobacco Use Disorder***" OR Tobaccoism OR Toxic Psychoses OR Toxicomani* OR Paranoi* OR Delus* OR Psychogenic Parasitos* OR Capgras Syndrome* OR Hebephreni* OR Hallucinosis OR Hallucinat* OR Anankastic Personalit* OR Antisocial Behavior* OR Antisocial Behaviour* OR Antisocial Personalit* OR Anti-Social Personalit* OR "As If Personality" OR "As If Personalities" OR Asthenic Personalit* OR Avoidant Personalit* OR Borderline OR Character Deviation* OR Character Disorder* OR Character Disturbance* OR Character Problem* OR Dependent Personalit* OR Diogenes Syndrome OR Dissociative Identity Disorder* OR Dual Personalit* OR Dysocial Behavior* OR Dysocial Behaviour* OR Histronic Personalit* OR Impulse-Ridden Personalit* OR Inadequate Personalit* OR Masochis* OR Multiple Identity Disorder* OR Multiple Personalit* OR Narcism OR Narcissism OR Narcissistic OR Neuropsychopath* OR Passive-
Aggressive Personality OR Personality Change OR Personality Disorder OR Personality Disturbance OR Psychological Dependence OR Psychopath OR Sadist OR Sadomasochist OR "Self Love" OR Senile Squalor Syndrome OR Social Behavior Disorder OR Social Breakdown Syndrome OR Social Disease OR Social Pathology OR Sociopath).ti,ab.

3 exp Magnetic Resonance Imaging/ OR exp Neuroimaging/ OR exp Brain Mapping/ OR Neuroradiography/ OR Diffusion Magnetic Resonance Imaging/ OR Diffusion Tensor Imaging/ OR Brain Cortical Thickness/ OR Cerebral Cortical Thinning/ OR White Matter/ OR Gray Matter/ OR Anisotropy/ OR Magnetic Resonance OR MRI OR MRIs OR MR Imag* OR NMR OR MR Tomogra* OR Zeugmatogra* OR Chemical Shift Imag* OR Magnetization Transfer OR Proton Spin Tomogra* OR fMRI OR "Spin Echo" OR Diffusion Imag* OR "Diffusion Tensor" OR DTI OR Tractogra* OR "Diffusion Weighted" OR "Echo Planar" OR Echoplanar OR Neuroimag* OR (Neural adj Imag*) OR NeuroImag* OR (Brain adj Imag*) OR Brain Mapping OR Stereotaxic Atlas OR Functional Cerebral Localization OR Connectivity Map OR Connectivity Matrix OR Cortical Thickness OR Cortex Thickness OR Grey Matter Thickness OR Neuroradio* OR DWI OR Fluid-Attenuated Inversion Recovery OR FLAIR OR GRE OR Gradient Recalled Echo* OR Gradient Echo* OR Cortical Thinning OR Subcortical Thickness OR Anisotrop* OR Anisotroph* OR Diffusivity OR Diffusion Rate OR Gray Matter OR Grey Matter OR Voxel Based Morphometry OR VBM).ti,ab.

4 and/1-3

5 exp Animals/ not Humans.sh.

6 4 not 5

7 limit 6 to undetermined

8 limit 6 to english language

9 7 OR 8

C. PsycINFO

Database: APA PsycInfo <1806 to October Week 1 2022>

1 Brain Damage/ OR exp Brain Injuries/ OR exp Traumatic Brain Injury/ OR Brain Concussion/ OR "Brain Lesions (Disorders)"/ OR exp Head Injuries/ OR Cerebral Hemorrhage/ OR Subarachnoid Hemorrhage/ OR (Traumatic OR Posttrauma* OR Brain Arachnoid Haemorrhage* OR Brain Arachnoid Hemorrhage* OR Brain Bleeding* OR Brain Bruise* OR Brain Contus* OR Brain Damage* OR Brain Haemorrhage* OR Brain Hemorrhage* OR Brain Injur* OR Brain Lesion* OR Brain System Trauma* OR Brain Trauma* OR Brain Vascular Injur* OR Brain Vascular Trauma* OR Broken Skull* OR Cerebral Bleeding OR Cerebral Concuss* OR Cerebral Contus* OR Cerebral Damage* OR Cerebral Hematoma* OR Cerebral Haemorrhage* OR Cerebral Hemorrhage* OR Cerebral Injur* OR Cerebral Lesion* OR Cerebral Trauma* OR Cerebrocranial Injur* OR Cerebrocranial Trauma* OR Cerebrovascular Trauma* OR Cerebrum Haemorrhage* OR Cerebrum Hemorrhage* OR Cerebrum Lesion* OR Commotio* OR Concuss* OR DAI OR DAI*s OR Damaged Brain* OR Depressed Cranium* OR Depressed Skull* OR Diffuse Axonal Injur* OR
Forebrain Lesion* OR Fracture Skull* OR Fractured Cranial Bone* OR Fractured Cranium* OR Fractured Skull* OR Frontal Region Trauma* OR Haemisphere Injur* OR Haemisphere Lesion* OR Head Bruis* OR Head Contus* OR Head Injur* OR Head Trauma* OR Head Wound* OR Hemisphere Injur* OR Hemisphere Lesion* OR Interhemispheric Haematoma* OR Interhemispheric Hematoma* OR Intracerebral Bleeding* OR Intracerebral Haematoma* OR Intracerebral Haemorrhage* OR Intracerebral Hemorrhage* OR Intracortical Haemorrhage* OR Intracortical Hemorrhage* OR Intracranial Bleeding* OR Intracranial Epidural Haematoma* OR Intracranial Epidural Hematoma* OR Intracranial Epidemic Haematoma* OR Intracranial Epidemic Hemorrhage* OR Intracranial Epidermal Haematoma* OR Intracranial Hemorrhage* OR Intracranial Lesion* OR Intraventricular Haemorrhage* OR Intraventricular Hemorrhage* OR Midbrain Haemorrhage* OR Midbrain Hemorrhage* OR mTBI OR mTBIs OR Nervous System Injur* OR Nervous System Trauma* OR Neuroinjur* OR Neuro-Injur* OR Neurologic Damage* OR Neurotrauma* OR Occipital Region Trauma* OR Occipital Trauma* OR Parietal Region Trauma* OR Skull Depressed Fracture* OR Skull Fracture* OR Skull Frontobasal Fracture* Skullbase Fracture* OR Subarachnoid Bleeding* OR Subarachnoid Haematoma* OR Subarachnoid Haemorrhage* OR Subarachnoid Haemorrhagia* OR Subarachnoid Hematoma* OR Subarachnoid Hemorrhage* OR Subarachnoidal Bleeding* OR Subarachnoidal Haemorrhage* OR Subarachnoidal Hemorrhage* OR Subdural Bleeding* OR Subdural Haemorrhage* OR Subdural Haemorrhage* OR Subdural Hemorrhage* OR Subependymal Haematoma* OR Subependymal Hematoma* OR Subtemporal Region Trauma* OR TBI OR TBIs)*

2 exp Psychopathology/ OR Affective Disorders/ OR Disruptive Mood Dysregulation Disorder/ OR exp Major Depression/ OR Seasonal Affective Disorder/ OR Anaclitic Depression/ OR Dysthymic Disorder/ OR Endogenous Depression/ OR Late Life Depression/ OR Reactive Depression/ OR Recurrent Depression/ OR Treatment Resistant Depression/ OR Anxiety Disorders/ OR Castration Anxiety/ OR exp Obsessive Compulsive Disorder/ OR Koro/ OR exp Hoarding Disorder/ OR exp Phobias/ OR Generalized Anxiety Disorder/ OR Panic Attack/ OR Panic Disorder/ OR Separation Anxiety Disorder/ OR Trichotillomania/ OR exp Posttraumatic Stress Disorder/ OR exp "Stress and Trauma Related Disorders" OR Acute Stress Disorder/ OR Adjustment Disorders/ OR Somatoform Disorders/ OR Body Dysmorphic Disorder/ OR exp Conversion Disorder/ OR Hysterical Paralysis/ OR Hysterical Vision Disturbances/ OR Pseudocyesis/ OR exp Factitious Disorders/ OR Munchausen Syndrome/ OR "Munchausen Syndrome by Proxy"/ OR Hypochondriasis/ OR Hysteria/ OR Mass Hysteria/ OR Neurasthenia/ OR Neurodermatitis/ OR Somatization Disorder/ OR Somatoform Pain Disorder/ OR exp Eating Disorders/ OR Anorexia Nervosa/ OR Binge Eating Disorder/ OR Bulimia/ OR Feeding Disorders/ OR Hyperphagia/ OR Pica/ OR "Purging (Eating Disorders)"/ OR "Rumination (Eating)"/ OR Acute Alcoholic Intoxication/ OR exp Addiction/ OR exp Alcohol Abuse/ OR exp Alcohol Intoxication/ OR exp "Alcohol Use Disorder"/ OR exp Alcoholism/ OR Binge Drinking/ OR "Cannabis Use Disorder"/ OR Chronic Alcoholic Intoxication/ OR exp Drug Abuse/ OR exp Drug Addiction/ OR Drug Dependency/ OR Heroin Addiction/ OR exp Inhalant Abuse/ OR Korsakoffs
Psychosis/ OR Morphine Dependence/ OR exp "Opioid Use Disorder"/ OR Polydrug Abuse/ OR "Tobacco Use Disorder"/ OR exp Psychosis/ OR exp Schizophrenia/ OR exp Acute Psychosis/ OR Acute Schizophrenia/ OR Affective Psychosis/ OR exp Alcoholic Psychosis/ OR Capgras Syndrome/ OR Catatonic Schizophrenia/ OR Chronic Psychosis/ OR exp Hallucinosis/ OR "Paranoia (Psychosis)"/ OR Paranoid Schizophrenia/ OR Process Schizophrenia/ OR Reactive Psychosis/ OR Schizoaffective Disorder/ OR "Schizophrenia (Disorganized Type)"/ OR exp Schizophrenia/ OR Schizophreniform Disorder/ OR Senile Psychosis/ OR Toxic Psychoses/ OR Undifferentiated Schizophrenia/ OR Antisocial Personality Disorder/ OR Avoidant Personality Disorder/ OR Borderline Personality Disorder/ OR Dependent Personality Disorder/ OR Histrionic Personality Disorder/ OR Narcissistic Personality Disorder/ OR Obsessive Compulsive Personality Disorder/ OR Paranoid Personality Disorder/ OR Passive Aggressive Personality Disorder/ OR exp Sadomasochistic Personality/ OR Schizoid Personality Disorder/ OR Schizotypal Personality Disorder/ OR Masochistic Personality/ OR (Abnormal Mental State* OR Behavior Disorder* OR Disease Mental State* OR Disordered Mental State* OR Disturbed Mental State* OR Insanity OR Mental Abnormality* OR Mental Change* OR Mental Confusion* OR Mental Defect* OR Mental Disorder* OR Mental Disturbance* OR Mental Illness* OR Mental Insufficiency OR Mental Symptom* OR Mentally Ill OR Neuropsychiatric Disease* OR Neuropsychiatric Disorder* OR Psychiatric Diagnosis OR Psychiatric Diseases* OR Psychiatric Disorder* OR Psychiatric Illness* OR Psychiatric Symptom* OR Psychotic* OR Schizophrenia* OR Schizophreiniform Disorder/ OR Schizophrenia/ OR Schizophreniform Disorder/ OR Schizophreniform Disorder*/ OR Schizophreniform Disorder/ OR Senile Psychosis/ OR Toxic Psychoses/ OR Undifferentiated Schizophrenia/ OR Antisocial Personality Disorder/ OR Avoidant Personality Disorder/ OR Borderline Personality Disorder/ OR Dependent Personality Disorder/ OR Histrionic Personality Disorder/ OR Narcissistic Personality Disorder/ OR Obsessive Compulsive Personality Disorder/ OR Paranoid Personality Disorder/ OR Passive Aggressive Personality Disorder/ OR exp Sadomasochistic Personality/ OR Schizoid Personality Disorder/ OR Schizotypal Personality Disorder/ OR Masochistic Personality/ OR (Abnormal Mental State* OR Behavior Disorder* OR Disease Mental State* OR Disordered Mental State* OR Disturbed Mental State* OR Insanity OR Mental Abnormality* OR Mental Change* OR Mental Confusion* OR Mental Defect* OR Mental Disorder* OR Mental Disturbance* OR Mental Illness* OR Mental Insufficiency OR Mental Symptom* OR Mentally Ill OR Neuropsychiatric Disease* OR Neuropsychiatric Disorder* OR Psychiatric Diagnosis OR Psychiatric Diseases* OR Psychiatric Disorder* OR Psychiatric Illness* OR Psychiatric Symptom* OR Psychotic* OR Schizophrenia* OR Schizophreiniform Disorder/ OR Schizophrenia/ OR Schizophreniform Disorder/ OR Schizophreniform Disorder*/ OR Schizophrenia/ OR Schizophreniform Disorder/ OR Senile Psychosis/ OR Toxic Psychoses/ OR Undifferentiated Schizophrenia/ OR Antisocial Personality Disorder/ OR Avoidant Personality Disorder/ OR Borderline Personality Disorder/ OR Dependent Personality Disorder/ OR Histrionic Personality Disorder/ OR Narcissistic Personality Disorder/ OR Obsessive Compulsive Personality Disorder/ OR Paranoid Personality Disorder/ OR Passive Aggressive Personality Disorder/ OR exp Sadomasochistic Personality/ OR Schizoid Personality Disorder/ OR Schizotypal Personality Disorder/ OR Masochistic Personality/ OR (Abnormal Mental State* OR Behavior Disorder* OR Disease Mental State* OR Disordered Mental State* OR Disturbed Mental State* OR Insanity OR Mental Abnormality* OR Mental Change* OR Mental Confusion* OR Mental Defect* OR Mental Disorder* OR Mental Disturbance* OR Mental Illness* OR Mental Insufficiency OR Mental Symptom* OR Mentally Ill OR Neuropsychiatric Disease* OR Neuropsychiatric Disorder* OR Psychiatric Diagnosis OR Psychiatric Diseases* OR Psychiatric Disorder* OR Psychiatric Illness* OR Psychiatric Symptom* OR Psychotic* OR Schizophrenia* OR Schizophreiniform Disorder/ OR Schizophrenia/ OR Schizophreniform Disorder/ OR Schizophreniform Disorder*/ OR Schizophrenia/ OR Schizophreniform Disorder/ OR Senile Psychosis/ OR Toxic Psychoses/ OR Undifferentiated Schizophrenia/ OR Antisocial Personality Disorder/ OR Avoidant Personality Disorder/ OR Borderline Personality Disorder/ OR Dependent Personality Disorder/ OR Histrionic Personality Disorder/ OR Narcissistic Personality Disorder/ OR Obsessive Compulsive Personality Disorder/ OR Paranoid Personality Disorder/ OR Passive Aggressive Personality Disorder/ OR exp Sadomasochistic Personality/ OR Schizoid Personality Disorder/ OR Schizotypal Personality Disorder/ OR Masochistic Personality/ OR (Abnormal Mental State* OR Behavior Disorder* OR Disease Mental State* OR 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Dependen* OR "Nicotine Use Disorder** OR Nicotinism OR Opiate Abuse* OR Opiate Alkaloid Dependen* OR Opiate Crisis OR Opiate Dependen* OR Opiate Epidemic* OR Opiate Overdose* OR Opioid Abuse* OR Opioid Crisis OR Opioid Dependen* OR Opioid Epidemic* OR Opioid Misuse* OR Opioid Overdose* OR Opioid Related Disorder* OR "Opioid Use Disorder**" OR Opioids Crisis OR Opioids Dependen* OR Opioids Epidemic* OR Opium Abuse* OR Opium Dependen* OR Opium Epidemic* OR Opium Smoking OR "Opium Use**" OR PCP Abuse* OR PCP Dependen* OR Phencyclidine Abuse* OR Phencyclidine Dependen* OR Phencyclidine Related Disorder* OR Physical Dependen* OR "Polydrug Use**" OR Substance Abuse* OR Substance Craving OR Substance Dependen* OR Substance Induced Psychoses OR Substance Related Disorder* OR "Substance Use**" OR Tobacco Abuse* OR Tobacco Dependen* OR "Tobacco Use Disorder**" OR Tobaccoism OR Toxic Psychoses OR Toxicomani* OR Paranoi* OR Delusi* OR Psychogenic Parasitos* OR Capgras Syndrome* OR Hebephreni* OR Hallucinosis OR Hallucinat* OR Anankastic Personalit* OR Antisocial Behavior* OR Antisocial Behaviour* OR Antisocial Personalit* OR Anti-Social Personalit* OR "As If Personality" OR "As If Personalities" OR Astenic Personalit* OR Avoidant Personalit* OR Borderline OR Character Deviation* OR Character Disorder* OR Character Disturbance* OR Character Problem* OR Dependent Personalit* OR Diogenes Syndrome OR Dissociative Identity Disorder* OR Dual Personalit* OR Dysocial Behavior* OR Dyssocial Behaviour* OR Histrionic Personalit* OR Impulse-Ridden Personalit* OR Inadequate Personalit* OR Masochis* OR Multiple Identity Disorder* OR Multiple Personalit* OR Narcism OR Narcissim OR Narcissistic Neuropsychopath* OR Passive-Aggressive Personalit* OR Personality Change OR Personality Disorder* OR Personality Disturbance* OR Psychological Dependen* OR Psychopath* OR Sadis* OR Sadomasochis* OR "Self Love" OR Senile Squalor Syndrome OR Social Behavior Disorder* OR Social Breakdown Syndrome OR Social Disease* OR Social Patholog* OR Sociopath*).ti,ab.
3 exp Magnetic Resonance Imaging/ OR exp Neuroimaging/ OR Stereotaxic Atlas/ OR Diffusion Tensor Imaging/ OR Gray Matter/ OR exp White Matter/ OR (Magnetic Resonance OR MRI OR MRIs OR MR Tomogra* OR Zeugmatogra* OR Chemical Shift Imag* OR Magneti?ation Transfer OR Proton Spin Tomogra* OR fMRI OR "Spin Echo" OR Diffusion Imag* OR "Diffusion Tensor" OR DTI OR Tractogra* OR "Diffusion Weighted" OR "Echo Planar" OR Echoplanar OR Neuroimag* OR (Neural adj Imag*) OR Neuro-Imag* OR (Brain adj Imag*) OR Brain Mapping OR Stereotaxic Atlas OR Functional Cerebral Locali?ation? OR Connectom* OR Connectivity Map OR Connectivity Matrix OR Cortical Thickness OR Cortex Thickness OR Grey Matter Thickness OR Neuroradio* OR DWI OR Fluid-Attenuated Inversion Recovery OR FLAIR OR GRE OR Gradient Recalled Echo* OR Gradient Echo* OR Cortical Thinning OR Subcortical Thickness OR Anisotrop* OR Anisotroph* OR Diffusivit* OR Diffusion Rate* OR Gray Matter* OR Grey Matter* OR Voxel Based Morphometr* OR VBM).ti,ab.
4 and/1-3
5 limit 4 to (human and English language)
Online Supplementary Materials II

Quality Assessment Tool

Title
Transdiagnostic MRI Markers of Psychopathology following Traumatic Brain Injury: A Systematic Review and Meta-Analysis Protocol

Registration ID: CRD42022358358 (PROSPERO)
### Customised Quality Assessment Tool

#### Category 1: sample characteristics

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Not applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>2. Were cases and controls matched appropriately?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>3. Were the same criteria used for identification of cases and controls?</td>
<td>□</td>
<td>□</td>
<td>□</td>
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</tr>
<tr>
<td>4. Was exposure measured in a standard, valid and reliable way?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>5. Important demographic data (age and gender) were reported with mean (or median) and standard deviations (or range)?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>6. Were confounding factors identified?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>7. Were strategies to deal with confounding factors stated?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>9. Important clinical variables (eg, depressive episodes, depression-related scale score) were reported with mean (or median) and standard deviations (or range)?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>10. Sample size per group &gt;10?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

#### Category 2: methodology and reporting characteristics

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Unclear</th>
<th>Not applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Magnet strength at least 1.5T?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>2. At least 5 min of resting state acquisition?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>3. Whole brain coverage of resting scans?</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>4. The acquisition and preprocessing techniques were clearly described so that they could be reproduced?</td>
<td>□</td>
<td>□</td>
<td>□</td>
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<tr>
<td>5.</td>
<td>Coordinates reported in a standard space?</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>6.</td>
<td>Significant results are reported after correction for multiple comparisons using a standard statistical procedure (e.g., FDR (False Discovery Rate), FWE (Family Wise Error) or permutation-based methods)?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Conclusions were consistent with the results obtained and the limitations were discussed?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>