RUNNING HEAD: TRANSDIAGNOSTIC COGNITIVE BIASES

Transdiagnostic cognitive biases in psychiatric disorders:

A systematic review and network meta-analysis

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Abstract

Psychiatric disorders are characterized by cognitive deficits, which have been proposed as a transdiagnostic feature of psychopathology ("C" factor). Similarly, cognitive biases (e.g., in attention, memory, and interpretation) represent common tendencies in information processing that are often associated with psychiatric symptoms. However, the question remains whether cognitive biases are also transdiagnostic or are specific to certain psychiatric disorders/symptoms. The current systematic review (osf.io/znf4q) sought to address whether the proposed "C" factor of transdiagnostic cognitive dysfunction in psychopathology can be extended to cognitive biases. Overall, 31 studies comprising 4401 participants (2536 patients, 1865 non-clinical controls) across 21 diagnostic categories met inclusion criteria, assessing 19 cognitive biases with most studies focusing on interpretation (k = 22) and attention (k = 11) biases, with only 2 assessing memory biases. Traditional meta-analyses found a moderate effect size (g = 0.32) for more severe cognitive biases in all patients relative to non-clinical controls, as well as small but significant associations between interpretation biases and transdiagnostic symptom categories (general psychopathology: r = .20, emotion dysfunction: r = 0.17, psychotic symptoms: r = 0.25). Network meta-analyses revealed significant patient versus control differences on attention and interpretation biases across diagnoses, as well as significant differences between diagnoses, with highest severity in panic disorder for attention biases and obsessive-compulsive disorder for interpretation biases. The current findings support a big "C" interpretation of transdiagnostic cognitive dysfunction in psychiatric disorders, extending the concept to cognitive biases and transdiagnostic symptom dimensions. They also suggest that while the presence of cognitive biases is transdiagnostic, bias severity differs across diagnoses, as in traditional neurocognitive deficits.

KEYWORDS: attention bias, interpretation bias, memory bias, anxiety, depression, schizophrenia

Introduction

Cognitive deficits (e.g., in memory and attention) are a core feature of many psychiatric disorders and have been proposed as a transdiagnostic dimension of psychopathology (the "C" factor; Abramovitch et al., 2021). Similarly, cognitive biases, which refer to systematic distortions in information processing, are common yet less often studied dimensions of cognition that contribute to clinical symptoms and poor outcomes across psychiatric disorders (Barry et al., 2015; Beevers et al., 2019; Sauve et al., 2020; Williamson et al., 2000). Whether the transdiagnostic “C” factor is specific to neurocognitive deficits (little “c”) or extends to cognitive biases (big “C”) is unclear.

Cognitive biases can typically be classified within one of three categories: attention biases, memory biases, and interpretation biases (Everaert and Koster, 2020). Attention biases refer to tendencies in perceptual information processing where certain stimuli (e.g., negative or threatening in mood and anxiety disorders) are preferentially salient. This can lead to interference effects, for example in an emotional Stroop task where word reading is delayed for negative versus neutral words in depression (Williams et al., 1996). However, in other cases (e.g., emotional face dot probe task), attentional biases can enhance processing, as information presented with emotional stimuli are attended to more quickly (Wirth and Wentura, 2020). Memory biases have also been noted in psychiatric disorders, with evidence of enhanced memory for negatively valenced stimuli and impaired memory for positively valenced stimuli (Duyser et al., 2020; Romano et al., 2020). Finally, interpretation biases consist of a wide range of reasoning tendencies, including attributional biases (e.g., favouring internal, stable, and global interpretations for negative events in depression), jumping to conclusions (i.e., making a decision with very little evidence, prevalent in schizophrenia), and thought-action fusion (e.g., believing that thinking about negative events makes them more probable, common in obsessive-compulsive disorder). While specific biases have commonly been associated with one or two key disorders, there is growing evidence that cognitive biases

may transcend across diagnostic boundaries, including depression, anxiety, schizophrenia-spectrum disorders, bipolar disorder, obsessive-compulsive disorder, and eating disorders (Everaert et al., 2018; Lee et al., 2020; Sanford and Woodward, 2017).

Cognitive biases are also strongly associated with psychiatric symptoms. For example, "jumping to conclusions" in schizophrenia has been associated with the formation of delusions (Broyd et al., 2017; Dudley et al., 2016). In mood disorders, negative attentional bias, the tendency to focus or attend to information with negative valence, has been associated with depression (Mennen et al., 2019). Coupled with evidence that interventions targeting cognitive biases improve not only cognitive biases, but also clinical symptoms, insight, and functioning (Jones and Sharpe, 2017; Penney et al., 2022; Sauve et al., 2020), cognitive biases appear to be strongly linked to clinical and functional outcomes.

While cognitive biases have been widely studied within specific psychiatric disorders and symptoms, it remains to be determined whether cognitive biases are transdiagnostic features of psychopathology, similar to cognitive deficits, and whether they are associated with transdiagnostic symptom dimensions of psychopathology. Duyser and colleagues (2020) examined negative memory bias across a broad range of diagnostic categories and found that negative memory biases were greater in all patient groups relative to controls, but were also associated with depressive symptom severity, even after controlling for diagnosis. Transdiagnostic symptoms of psychopathology refer to a set of common underlying factors that cut across traditional diagnostic categories and are thought to reflect underlying psychological processes that contribute to the development and maintenance of multiple mental health disorders, particularly those high with comorbidity (Dalgleish et al., 2020). For example, the Hierarchical Taxonomy of Psychopathology (HiTOP) proposes a model of transdiagnostic symptom dimensions, including a general psychopathology factor, lower-order factors of emotional dysfunction, psychosis, and externalizing symptoms that can cut across diagnostic boundaries.

A transdiagnostic approach has important implications for the understanding and treatment of mental health disorders, as it (1) focuses on common underlying mechanisms and (2) puts emphasis on a more holistic and integrated approach to psychotherapy (Fairholme et al., 2010). This approach may be more beneficial to address the full range of psychopathology (Barlow et al., 2016). For example, cognitive deficits are considered transdiagnostic because they are highly prevalent across a wide range of disorders, even if the degree of deficit may vary across disorders (Abramovitch et al., 2021; Millan et al., 2012). At the same time, disorder-specific features of psychiatric disorders may provide additional insight into the manifestation of psychopathology and improved precision in predictive psychiatry (Maj, 2011). Thus, it is important to identify and distinguish between both transdiagnostic and disorder-specific features of psychopathology.

Network meta-analysis (NMA) provides a framework within which we can synthesize the literature on cognitive biases in psychiatric disorders and gain insight into their transdiagnostic or disorder-specific nature as well as associations with transdiagnostic symptom dimensions. It also offers an opportunity to bring together disparate literatures examining cognitive biases primarily as a function of specific disorders by providing insight into both directly assessed and indirectly assessed comparisons between diagnoses. NMA is a special application of graph theory, a technique with a rich history stemming from mathematics in the 18th century (Euler (1736), as cited in Biggs et al., 1986) and has impacted various fields, including computer science (Riaz and Ali, 2011), linguistics (Mota et al., 2012), neuroscience (Sporns, 2018), and psychiatry (Galderisi et al., 2018). For example, graph theory is used extensively in neuroimaging to illustrate brain networks (Bullmore and Sporns, 2009). Generally, graphs are representations of data consisting of nodes (e.g., brain regions, symptom categories, language elements) that are connected by edges (i.e., values representing associations between nodes, such as correlations). To date, NMA has primarily been used in studies examining treatment efficacy (Cipriani et al., 2013), though there is also a

growing literature using NMA for other applications, including diagnostic accuracy (N Nyaga et al., 2018; Rübsamen et al., 2022) and transdiagnostic brain morphology (McCutcheon et al., 2023). NMA nodes consist of the variables of interest (e.g., interventions, diagnostic tests, diagnoses) and edges consist of values derived from statistical techniques relevant for meta-analysis (e.g., effect sizes for comparisons between nodes). Thus, NMA allows for indirect interpretations between nodes even when assessed in different studies. In the current meta-analysis, we extend NMA to investigate transdiagnostic features of cognitive biases in psychiatric disorders, by designating nodes as distinct diagnoses as in previous neuroimaging work (McCutcheon et al., 2023), which allows for direct and indirect effects of group differences across diagnoses.

Rationale & Objectives

The aim of this systematic review and meta-analysis was to evaluate cognitive biases as potential transdiagnostic features of psychopathology. The primary research questions were as follows: (1) which cognitive biases are prevalent in psychiatric disorders?; (2) are certain cognitive biases specific to a given psychiatric disorder?; and (3) do cognitive biases relate to transdiagnostic symptoms of psychopathology?

Methods

Registration & Protocol

The protocol was registered on the Open Science Framework on December 22nd, 2022 (https://doi.org/10.17605/OSF.IO/ZNF4Q). Amendments were made to the protocol as follows: (1) limited to papers with 2 or more psychiatric diagnoses and (2) excluded intervention studies. This study followed the PRISMA 2020 Checklist for Abstracts and the PRISMA 2020 Checklist (see Tables S1 and S2 in supplementary material).

Eligibility criteria

Study eligibility was assessed with the following criteria: (1) adults with a diagnosis of a DSM or ICD psychiatric disorder within the following classifications: Schizophrenia Spectrum and Other Psychotic Disorders, Bipolar and Related Disorders, Depressive Disorders, Anxiety Disorders, Obsessive-Compulsive and Related Disorders, Trauma- and Stressor-Related Disorders, Feeding and Eating Disorders, Substance-Related and Addictive Disorders from the various editions of the DSM or from the ICD with or without non-psychiatric comparison subjects, (2) assessed group differences and/or associations with symptoms on one or more cognitive biases , including but not limited to confirmation bias, jumping to conclusions, bias against disconfirmatory evidence, negative bias, attributional biases, attention bias, and interpretation bias. Eligible study designs included cohort studies, case-control studies, cross-sectional (prevalence) studies, longitudinal studies, reviews (systematic, scoping, narrative), and (randomized) controlled trials. Diagnoses assessed in our inclusion criteria were limited to the following editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) and International Classification of Diseases (ICD): the DSM-IV (1994), DSM-IV-TR (2000), DSM-5 (2013), DSM–5-TR (2022), ICD-10 (1993) and the ICD-11 (2018).

Information sources

The following databases were searched: MEDLINE (Ovid), EMBASE (Ovid), PsycINFO (Ovid), Web of Science, and CINAHL (EBSCO) from January 30, 2023, to February 13, 2023. The grey literature was also searched through the PROSPERO and ProQuest databases to identify in-progress reviews and dissertations.

Search strategy

The search strategy was informed by an institutional librarian. We searched the electronic databases listed above and limited the results to titles and abstracts to avoid retrieving articles that only

referred to psychiatric diagnoses without assessing them, such as articles with psychiatric diagnoses mentioned only in the future research directions section in their discussion. No restrictions were placed on date, setting (e.g., in-lab, remote, or hybrid studies), study design (cross-sectional or longitudinal studies), or language. Our search was restricted to human subjects aged 18 years or older, and only peer-reviewed articles or reviews, editorials/letters/comments, and dissertations were included. We excluded books, book chapters, book reviews, conference proceedings, abstracts, pre-prints, and newspapers.

Our search terms (Table 1) were tailored to identify articles examining a broad range of cognitive biases in samples with a diagnosed psychiatric disorder as defined by the DSM (IV-TR, 5th edition, 5-TR) or the ICD (10th, 11th revision). Detailed search terms by database are provided in Table S3.

Selection process

Search results were managed using the systematic review software Rayyan (Ouzzani et al., 2016). De-duplication of records was first performed automatically in Endnote using Title, Author, Year, and Journal as joint criteria, after which all ten other possible combinations of two or more criteria were produced and duplicates were discarded. Retained records were then uploaded to Rayyan and a final automated de-duplication was performed. The remaining records were each randomly assigned to 2 reviewers for screening. All screeners were trained in Rayyan and took part in a screening training session.

Screening of titles and abstract was performed by 2 reviewers based on the eligibility criteria. Reviewers were blind to the other reviewer's decisions. Reasons for exclusion were recorded with reference to the eligibility criteria. Inter-rater agreement was calculated using Gwet's AC1 statistic (unweighted) via the R irrCAC package (version 1.0), which showed good agreement between raters: percent agreement = 83%, percent chance agreement = 48%, AC1 = 0.671, SE = 0.013, CI = [0.645, 0.698], $p < 0.001$. After screening, conflicts were resolved via input from 1 to 3 additional reviewers and a

consensus decision was made. Full texts were acquired for conflicting articles that could not reach a consensus via title and abstract screening as well as articles that were rated as “include” by two or more reviewers. Consensus for meta-analysis inclusion decisions were reached after full texts revision followed by data extraction.

Data collection process

A standardized data extraction form was developed, piloted, and refined based on one exemplary article. A spreadsheet software (i.e., Google sheets) was used to store extracted data. It included prespecified response options and data validation checks to streamline and standardize data extraction. Data items were extracted independently and in duplicate to check for accuracy. Disagreements in data extraction were resolved through discussion between the reviewers.

Data items

The following information was extracted from each selected article: study design (cross-sectional/longitudinal), sample characteristics (diagnosis, diagnostic manual, number of participants by group, mean age by group, sex ratio by group), cognitive biases (bias assessed, measure used, scoring details, means, standard deviations, sample proportions, and/or effect sizes), and additional outcomes (symptom measures and correlations with biases). Studies with multiple outcome measures were extracted separately to include in the meta-analyses. Biases were then categorized as either attention, memory, or interpretation biases and were reverse coded when necessary (e.g., reaction times, difference scores) to ensure that higher values equated to greater bias severity. Bias task stimuli were also classified as neutral, symptom-related, or mixed to allow for assessment of the relevance of bias content. Symptoms were also categorized into transdiagnostic spectra based on the Hierarchical Taxonomy of Psychopathology (HiTOP; Kotov et al., 2021): somatoform, internalizing, thought disorder, detachment, disinhibited

externalizing, and antagonistic internalizing. Due to a lack of variability in assessed symptomatology, these were further classified into HiTOP hypothesized super-spectra (emotional dysfunction, psychosis, and externalizing) for analysis.

Study risk of bias of assessment

Risk of bias of individual studies was assessed using the JBI critical appraisal tool for case-control studies (Barker et al., 2023) as that was the most prevalent study design assessed. Studies were rated on 10 criteria (comparable groups, matched groups, same eligibility criteria, valid exposures, comparable measures, confounding factors identified, confounding factors controlled, standard outcomes, reasonable exposure length, and appropriate statistics) using the following options: yes, no, unsure, not applicable. Total risk of bias scores were calculated as the percentage of yes responses out of the ten criteria and categorized as low bias (≥80%), moderate bias (50%-79%), and high bias (≤49%). Risk of bias categories were used in subgroup meta-analyses to determine whether study quality influenced their findings.

Effect measures

Synthesis methods

Study results were synthesized via a series of traditional and network meta-analyses, all using random effects models. The R code is available via the Open Science Framework (https://osf.io/c2m8z/). Included studies were eligible for meta-analysis if they met the following criteria: (1) reported the number of participants per group, and (2a) reported means and standard deviations or sample proportions representing cognitive bias severity for each group, or (2b) provided correlations between symptoms and cognitive bias scores. To prepare the data for synthesis, supplementary materials were searched. Standardized mean differences (Hedge's g) were computed using the *pairwise* function in R's netmeta package version 2.8.2 (Balduzzi et al., 2023) to quantify group differences. For symptom outcomes, Fisher's

r-to-Z transformations were computed via the meta package version 6.5-0 (Schwarzer et al., 2015) prior to conducting meta-analyses. Results were visually displayed using forest plots for traditional analyses, and a combination of forest plots, network graphs, and heatmaps for network analyses. Traditional meta-analyses comparing patients and controls and examining associations between cognitive biases and symptoms were computed with R's *meta* package version 6.5-0. Network meta-analyses were computed with R's *netmeta* package version 2.8.2 (Balduzzi et al., 2023).

First, an overarching meta-analysis was conducted to compare the severity of all assessed cognitive biases in all patients versus non-clinical controls to examine the transdiagnostic nature of cognitive biases at a general level. In this analysis, all cognitive biases and all psychiatric diagnoses were included. To assess the robustness of results, this was followed by a series of subgroup analyses that subset studies by cognitive bias category (i.e., attention, memory, and interpretation biases) and by bias measure content (symptom-related, neutral, mixed). *Second*, network meta-analyses were conducted to compare direct and indirect effects between diagnoses at the overall level and within each cognitive bias category (i.e., attention, memory, interpretation biases). For these analyses, non-clinical controls were included as a reference group. *Finally*, to examine transdiagnostic associations between cognitive biases and psychiatric symptoms, meta-analyses were conducted on studies that reported correlations between biases and symptom measures. Following the HiTOP model, we first conducted an overall meta-analysis on all symptoms, to assess associations with a general "p" factor of psychopathology. Then subgroup analyses were computed on proposed HiTOP super-schema categorized by emotional dysfunction, psychosis, and externalizing symptoms.

Reporting of bias assessment

Heterogeneity of studies was assessed with Cochrane's Q statistic and I^2 index. We examined publication bias using the Egger asymmetry test. In addition, the impact of study quality was examined by

performing subgroup analyses with low, medium, and high risk of bias categories calculated from the JBI critical appraisal tool for case-control studies, as this was the study design primarily used.

Results

Study selection

The search and selection process are illustrated in using the PRISMA flowchart template. A total of 7194 articles were retrieved in the initial search. After removing duplicates, 3110 articles were divided at random between 5 reviewers. There were 143 reports sought for full text retrieval, of which 5 reports were not recovered. Based on reviewers' ratings, full texts of 138 articles were reviewed and 96 were excluded based on our selection criteria. Overall, 31 studies were synthesized by traditional and/or network meta-analysis, comprising 4401 participants (2536 patients, 1865 non-clinical controls).

Study characteristics

Characteristics of each study are presented in Table 2. Included studies were published between 2001 and 2022. All included studies used a cross-sectional design; thus, study design is not depicted in Table 1. Briefly, most studies (n = 23 out of 31) used the DSM-IV diagnostic criteria. A total of 21 different psychiatric diagnoses were investigated in the included studies: major depressive disorder (MDD; k = 16); panic disorder (with and without agoraphobia, PD; k = 8); schizophrenia (SZ; k = 8); social anxiety disorder/social phobia (SAD; k = 8); obsessive-compulsive disorder (OCD; k = 7); anorexia nervosa (AN; k = 3); bulimia nervosa (BN; k = 3); generalized anxiety disorder (GAD, k = 3); hypochondriasis/health anxiety (HA; k = 3); psychotic disorder not otherwise specified (PSY-NOS; k = 2); bipolar disorder (BP; k = 1); body dysmorphic disorder (BDD; k = 1); bulimia nervosa (BN; k = 3); brief psychotic disorder (BPSY; k = 1); delusional disorder (DD; k = 1); dissociative identity disorder (DID; k = 1); dysthymic disorder (DYS; k =1); post-traumatic stress disorder (PTSD; k = 1); schizoaffective disorder (SZaff; k = 1); schizophreniform

disorder (SZf; k = 1); somatoform disorder (SD; k =1). Two studies assessed psychotic disorders (Krkovic et al., 2023) and schizophrenia spectrum disorders (Zhu et al., 2020) without specifying further diagnoses. Several studies reported means for several diagnoses combined together into broader categories, for example, anxiety disorders (De Cort et al., 2008; Lichtenstein-Vidne et al., 2017; Neng and Weck, 2015), depressive disorders (Duddu et al., 2003; Wittorf et al., 2012), and schizophrenia-spectrum disorders (Krkovic et al., 2023; Samson et al., 2022; Wittorf et al., 2012; Zhu et al., 2020), thus limiting the feasible categories for network meta-analysis.

Included studies assessed 19 cognitive biases within the three broader categories: attention (body vigilance, negative, positive), memory (explicit negative, explicit positive, implicit negative, implicit positive), and interpretation (attributional bias, bias against disconfirmatory evidence, catastrophizing, confirmation bias, dichotomous thinking, emotional reasoning bias, jumping to conclusions, intolerance of uncertainty, negative bias, positive bias, thought-action fusion, unrealistic optimism bias). The most studied were related to interpretation biases (k = 22), followed by attentional biases (k = 11), and memory biases (k = 2). One study assessed both attention and interpretation biases (Deacon and Abramowitz, 2008), one study assessed both attention and memory biases (Rinck and Becker, 2005), and one study assessed all three categories (Gotlib, I. H. et al., 2004). No included studies examined cognitive biases and substance use disorders.

Nine studies assessed associations between cognitive biases and symptoms, including depression (k = 6), anxiety (k = 5), general psychopathology (k = 4), negative (k = 4), and positive (k = 4) psychotic symptoms, mania (k = 1), obsessive-compulsive symptoms (k = 1), and post-traumatic stress symptoms (k = 1). Symptom associations were further categorized into transdiagnostic dimensions following the HiTOP model: emotional dysfunction (depression, anxiety, obsessive-compulsive, post-traumatic stress, k = 8),

psychosis (positive, negative, k = 4), and externalizing symptoms (k = 0). Symptoms related to general psychopathology were only included in the overall correlation meta-analysis.

Risk of bias in studies

Assessments of the risk of bias according to the JBI appraisal tool for each study are presented in Table S4. Bias scores based on the percentage of "Yes" ratings ranged from 40% to 100% (mean = 73.75%, SD = 16.41%). Seventeen studies were classified as low risk (≥80%), 14 studies as medium risk (50%-79%), and 1 study as high risk (≤ 49%). Subsequent subgroup analyses combined medium and high risk of bias studies to create "low" and "high" risk categories.

Results of syntheses

Transdiagnostic patients versus non-clinical controls

Figure 2 presents the summarized forest plot for the first meta-analysis comparing overall cognitive bias severity in all patients versus non-clinical controls. Regardless of their psychiatric diagnosis, results indicated that patients overall had greater cognitive bias severity than non-clinical control participants, Hedges g = 0.32, 95% CI = [0.26, 0.38], z = 10.49, $p < 0.0001$. Significant heterogeneity was observed, Q_{428} = 2286.92, $p < 0.0001$, I^2 = 81.3%, 95% CI = [79.6%, 82.8%]. Egger's test also indicated significant publication bias, intercept = 2.24, 95% CI = [1.44, 3.04], $t(427)$ = 5.51, $p < 0.0001$. There was no significant difference in effects for low risk of bias (g = 0.32, 95% CI = [0.23, 0.41]) and high bias (g = 0.32, 95% CI = [0.24, 0.41]) studies, Q_1 = 0.01, p = 0.91.

Subgroup analyses on bias categories did not find significant differences between bias categories, Q_2 = 1.61, p = 0.45, though attention biases (g = 0.36, 95% CI = [0.25, 0.46]) and interpretation biases (g = 0.32, 95% CI = [0.24, 0.39]) showed moderate effect sizes, whereas a small effect size was observed for memory biases (g = 0.15, 95% CI = [-0.16, 0.46]). Subgroup analyses on symptom-relatedness of bias

content did not find significant differences between neutral (g = 0.33, 95% CI = [0.26, 0.40]), symptom-related (g = 0.28, 95% CI = [0.16, 0.41]), and mixed (g = 0.44, 95% CI = [0.31, 0.58]) task stimuli, Q_2 = 3.22, p = 0.20.

Network meta-analysis on diagnostic categories

The network meta-analyses are summarized in Figure 3, with direct and indirect evidence and detailed heatmaps presented in the supplement (Figures S1-S6). The left panels show network graphs representing study comparisons between diagnoses, with line thickness denoting the number of comparisons. The middle panels show summarized forest plots by disorder. The right panels are heatmaps representing the direct and indirect effects between diagnoses.

Attention biases (Figure 3A) were significantly greater than non-clinical controls in: panic disorder (g = 0.85, 95% CI = [0.69, 1.01], z = 10.55, p < 0.0001); mixed anxiety disorders (g = 0.55, 95% CI = [0.31, 0.80], z = 4.41, p < 0.0001); obsessive-compulsive disorder (g = 0.55, 95% CI = [0.33, 0.77], z = 4.84, p < 0.0001); health anxiety (g = 0.51, 95% CI = [0.29, 0.74], z = 4.44, p < 0.0001); social anxiety disorder (g = 0.32, 95% CI = [0.16, 0.49], z = 3.82, p < 0.001); and major depressive disorder (g = 0.27, 95% CI = [0.10, 0.44], z = 3.12, p < 0.005). No significant differences were observed for anorexia nervosa, bulimia nervosa, dissociative identity disorder, or generalized anxiety disorder (ps > .18). There was significant heterogeneity within disorders, Q_{236} = 891.08, p < 0.0001, and inconsistency between disorders, Q_{11} = 47.74, p < 0.0001. Significant differences were also noted between diagnoses, with panic disorder greater than all other groups except dissociative identity disorder, due to extensive variability in the latter group.

Memory biases (Figure 3B) in major depressive disorder (g = 0.14, 95% CI = [-0.21, -0.49], z = 0.81, p = 0.42) and social anxiety disorder (g = 0.07, 95% CI = [-0.28, 0.41], z = 0.40, p = 0.69) were not significantly different than non-clinical controls. There was significant heterogeneity within disorders, Q_{33}

= 410.18, $p < 0.0001$, but no inconsistency between disorders, $Q_1 = 0.04$, $p = 0.85$. Pairwise comparisons did not a significant difference between major depressive disorder and control (Figure 3B, right panel).

Interpretation biases (Figure 3C) were significantly greater than non-clinical controls in: obsessive-compulsive disorder ($g = 0.79$, 95% CI = [0.58, 1.00], $z = 7.35$, $p < 0.0001$); social anxiety disorder ($g = 0.56$, 95% CI = [0.41, 0.70], $z = 7.57$, $p < 0.0001$); generalized anxiety disorder ($g = 0.55$, 95% CI = [0.30, 0.80], $z = 4.27$, $p < 0.0001$); panic disorder ($g = 0.54$, 95% CI = [0.39, 0.69], $z = 6.88$, $p < 0.0001$); schizophrenia ($g = 0.46$, 95% CI = [0.37, 0.55], $z = 9.85$, $p < 0.0001$); bipolar disorder ($g = 0.45$, 95% CI = [0.13, 0.76], $z = 2.79$, $p < 0.01$); health anxiety ($g = 0.36$, 95% CI = [0.03, 0.69], $z = 2.15$, $p < 0.05$); and major depressive disorder ($g = 0.16$, 95% CI = [0.07, 0.25], $z = 3.53$, $p < 0.0005$). No significant differences emerged for mixed anxiety disorders, anorexia nervosa, bulimia nervosa, post-traumatic stress disorder, or somatization disorder (ps > .16). There was significant heterogeneity within disorders, $Q_{371} = 1651.93$, $p < 0.0001$, and inconsistency between disorders, $Q_{21} = 102.50$, $p < 0.0001$. Significant differences were observed between diagnoses, with obsessive-compulsive disorder greater than all other groups except bulimia nervosa and post-traumatic stress disorder, due to extensive variability in these latter groups.

Associations with transdiagnostic symptom dimensions

A significant overall association between cognitive biases and symptoms was found, $r = 0.19$, 95% CI = [0.16, 0.23], $z = 10.22$, $p < 0.001$ (Figure 4). Significant heterogeneity was observed, $Q_{217} = 771.34$, $p < 0.0001$, $I^2 = 71.9\%$, 95% CI = [67.8%, 75.4%]. Egger's test indicated significant publication bias, intercept = -1.91, 95% CI = [-1.87, -0.51], $t(216) = -3.44$, $p < 0.001$. There was no significant difference in effects for low risk of bias ($r = 0.18$, 95% CI = [0.08, 0.28]) and high bias ($r = 0.19$, 95% CI = [0.16, 0.23]) studies, $Q_1 = 0.04$, $p = 0.84$.

Subgroup analyses on bias categories revealed significant differences between bias categories, Q_2 = 60.63, p < 0.0001, with interpretation biases (r = 0.25, 95% CI = [0.21, 0.28]) showing greater effects than attention (r = -0.04, 95% CI = [-0.11, 0.03]) and memory (r = 0.01, 95% CI = [-0.08, 0.10]) biases. Subgroup analyses on symptom-relatedness of bias content were also significant, with the greatest effects in mixed content tasks (r = 0.37, 95% CI = [0.31, 0.42]), followed by neutral (r = 0.17, 95% CI = [0.12, 0.22]), and symptom-related (r = 0.15, 95% CI = [0.09, 0.21]) task stimuli, Q_2 = 33.94, p < 0.0001.

As not all symptom ratings, such as those for general psychopathology, could be classified into HiTOP superspectra, a separate meta-analysis was computed to enable subgroup comparisons for transdiagnostic symptom dimensions. The overall meta-analysis on this subsample of symptom associations was similar to the larger sample, in terms of effect, r = 0.19, 95% CI = [0.15, 0.23], z = 9.16, p < 0.0001. heterogeneity, Q_{194} = 713.67, p < 0.0001, I^2 = 72.8%, 95% CI = [68.7%, 76.4%], and between low risk of bias (r = 0.17, 95% CI = [0.05, 0.28]) and high bias (r = 0.19, 95% CI = [0.15, 0.23]) studies, Q_1 = 0.08, p = 0.77. Subgroup analyses on transdiagnostic symptom dimensions revealed significantly greater effects for psychotic symptoms (r = 0.25, 95% CI = [0.20, 0.29]) than emotional dysfunction (r = 0.18, 95% CI = [0.13, 0.23]), Q_1 = 4.41, p < 0.05.

Discussion

Summary

The present study provides a systematic review and meta-analysis of the transdiagnostic nature of cognitive biases in psychiatry. We first observed an overall moderate effect of cognitive biases in psychiatric disorders relative to non-clinical controls that was evident across attention, memory, and interpretation biases. Network meta-analysis demonstrated patient versus control effects in almost all diagnostic categories assessed, as well as significant differences between diagnoses, with the highest bias severity in panic disorder for attention biases, major depressive disorder for memory biases, and

obsessive-compulsive disorder for interpretation biases. Cognitive biases (especially interpretation biases) were also associated with transdiagnostic symptom dimensions put forth by the Hierarchical Taxonomy of Psychopathology (HiTOP), specifically, emotion dysfunction and psychosis. Symptom-relatedness of bias content did not contribute to patient-control differences but is likely relevant for associations with symptoms. These findings support the notion of a "big C" transdiagnostic factor of psychopathology, including cognitive biases in attention, memory, and interpretation that are affected across disorders and transdiagnostic symptom dimensions. They also suggest bias severity may fluctuate as a function of diagnosis.

Transdiagnostic cognitive biases in patients versus controls

The moderate significant effect observed when comparing cognitive biases between all patients and non-clinical controls suggests that cognitive biases are transdiagnostic features of psychopathology. This finding was driven by attention and interpretation biases due to the relative lack of studies assessing memory biases. This trend was consistent across studies with both low and high risk of bias. The transdiagnostic nature of cognitive biases was further supported by the network meta-analysis in which almost all diagnostic categories demonstrated greater cognitive bias severity relative to controls. Those categories that did not emerge as more severely affected relative to controls were generally based on fewer studies (e.g., eating disorders in attention biases, major depressive disorder in memory biases). These findings mirror transdiagnostic cognitive deficits – coined the "C" factor of psychopathology – reported by Abramovitch and colleagues (2021), and suggests cognitive biases are also transdiagnostic in nature. The link between cognitive biases and cognitive deficits is still not fully understood, yet there is evidence they represent distinct, but interrelated constructs (Andreou et al., 2015; Garcia et al., 2012; Hezel and McNally, 2016).

Disorder-related bias severity

In addition to widespread increases in cognitive biases in psychiatric disorders relative to controls, network meta-analysis allowed for both direct and indirect comparisons between disorders. These results revealed that, even within the context of increased cognitive biases in patients relative to controls, many between-diagnosis differences emerged. For example, attention biases were generally highest in anxiety disorders, yet panic disorder showed significantly higher biases than all other groups. Memory biases were strongest in patients with schizophrenia and panic disorder, who did not differ significantly from one another. Finally, interpretation biases were highest in patients with OCD, who differed significantly from other groups. These findings echo those in the cognitive deficits' literature, which reports impaired cognition across diagnoses with varying levels of impairment depending on the disorder in question (Abramovitch et al., 2021; Millan et al., 2012). Thus, like cognitive deficits, cognitive biases are transdiagnostic by nature, yet also show disorder-related variations in severity.

Associations with transdiagnostic symptom dimensions

We also found that cognitive biases were associated with transdiagnostic symptom dimensions, following the superspectra proposed in the HiTOP model (Kotov et al., 2021), which includes a general psychopathology ('p') factor and hypothesized emotional dysfunction, psychosis, and externalizing factors. Overall, cognitive biases were significantly associated with general psychopathology, emotional dysfunction, and psychosis, with psychosis showing stronger associations than emotional dysfunction. Interpretation biases were also more strongly associated with general psychopathology than memory and attention biases. Interestingly, subgroup analyses on the content of bias measures revealed that mixed content bias measures (i.e., measures that include both neutral and symptom-relevant content) outperformed either content type individually. This finding contrasts with some previous literature suggesting that symptom-related bias content (e.g., sad words for depressive symptoms) better captures cognitive biases in psychiatric disorders (Pergamin-Hight et al., 2015; Vancleef and Peters, 2008; Zinchenko et al., 2017). As this pattern was seen only in the symptom association but not in the comparison between

patients and controls meta-analysis, it further indicates that mixed content measures might be preferable when associations between cognitive biases and symptoms is the outcome of interest. This might be due to the capability of mixed content measures to capture a broader array of biased thoughts that are related to various symptoms (Pergamin-Hight et al., 2015; Vancleef and Peters, 2008; Zinchenko et al., 2017)Future studies should include a wider range of bias content and additional symptom dimensions (e.g., externalizing) to allow for further direct comparisons.

Limitations and Future Directions

This study presents some limitations. First, NMA has mainly been used in the context of comparing treatments or interventions, where there is still debate regarding the validity of indirect comparisons (Cote et al., 2021). However, NMA stems from graph theory, which has been used extensively in neuroimaging and psychiatry research in the context of brain and symptom networks. The use of NMA in the present context, thus, represents an exciting new avenue for its application across a wide range of meta-analytic perspectives. In future research, NMA would also allow for meta-analytic synthesis of single-diagnosis studies to extend the current work. Second, diagnostic criteria evolve over time and could have influenced our results that were based on studies spanning multiple diagnostic manual revisions. We used random-effects models to circumvent this limitation. Third, the effects of psychiatric comorbidity were not investigated in the context of this study. While this is in line with our approach of analyzing the transdiagnostic features of psychopathology, it could affect interpretations between diagnoses. Finally, the transdiagnostic applicability of these findings is limited to the psychiatric disorders assessed in the literature and does not cover the full spectrum of psychiatric diagnoses. Identified studies were primarily concerned with mood, anxiety, and psychotic disorders, and none were identified that addressed substance use disorders, for which cognitive biases are highly relevant (Sofuoglu et al., 2016).

Implications

This meta-analysis provides evidence for cognitive biases as transdiagnostic features of psychopathology, which has important theoretical and clinical implications. Regarding the former, it opens new avenues for research exploring or comparing cognitive biases in unconventional diagnostic categories. It also aligns with the RDoC (Dalgleish et al., 2020) and p-factor (Caspi and Moffitt, 2018) frameworks. Indeed, proponents of the p-factor give most credence to the hypothesis that the superordinate level of "p" may reflect a dimension in thought dysfunction (including cognitive biases) across transdiagnostic boundaries (Caspi and Moffitt, 2018). In line with this theory, Abramovitch et al. (2021)'s "C" factor of transdiagnostic cognitive dysfunction suggests it is closely related to the p-factor. Further, cognitive biases represent important and malleable therapeutic targets (Andersen et al., 2016; García-Escalera et al., 2016; Jones and Sharpe, 2017; Penney et al., 2022; Sauve et al., 2020). Given their clear associations with symptoms derived from transdiagnostic initiatives (e.g., HiTOP), particularly emotion dysregulation and psychosis, cognitive bias interventions could represent interesting first-line targets of psychological interventions.

Conclusion

The current study used systematic review and network meta-analysis methodologies to investigate the transdiagnostic nature of cognitive biases in psychiatry. Our results suggest that cognitive biases are transdiagnostic features of psychopathology, are associated with transdiagnostic symptom dimensions, and may fluctuate in severity across diagnostic categories. These findings bring new insights into the investigation of cognitive biases in a variety of diagnostic categories and their usefulness as therapeutic targets.

Table 1. Database search terms.

1.	"cogniti* bias*" OR "reasoning bias*" OR "jump* to conclusions" OR "bias against disconfirmatory evidence" OR "disconfirmat* bias" OR "confirmat* bias*" OR "attribution* bias*" OR "attribution* style" OR "negative* bias*" OR "attention* bias*" OR "interpretation* bias*" **[title, abstract]**
	AND
2.	"psychiatric disorder*" OR "mental illness*" OR "mental disorder*" OR "transdiagnos*" OR "schizophreni*" OR "schizoaffective" OR "psychotic disorder*" OR "psychosis" OR "bipolar disorder*" OR "major depression" OR "depressive disorder*" OR "mood disorder*" OR "affective disorder*" OR "anxiety disorder*" OR "panic disorder*" OR "obsessive-compulsive disorder*" OR "posttraumatic stress disorder*" OR "post traumatic stress disorder*" OR "substance use disorder*" OR "substance-related disorder*" OR "addictive disorder*" OR "eating disorder*" OR "anorexi*" OR "bulimi*" **[title, abstract]**

Table 2. Study characteristics and main findings for included studies.

Study	Diagnostic Manual	Bias Category	Bias(es)	Symptom(s)	Groups	Age Mean (SD)	Sex Ratio (M:F)
Abramowitz et al. (2003)	DSM-IV	INT	TAF	Anxiety Depressive	OCD	34.9 (10.4)	11:9
					GAD	37.8 (12.0)	8:11
					PD	42.7 (14.8)	10:7
					SAD	36.3 (12.5)	12:8
					MDD	37.8 (13.4)	9:10
					CON	35.5 (9.3)	13:12
Dalgleish et al. (2001)	DSM-IV	INT	AS	N/A	AN	27.6 (8.6)	0:18
					BN	29.7 (9.4)	2:13
					CON	28.3 (5.7)	1:21
De Cort et al. (2008)	DSM-IV	ATT	NEG	Anxiety Depressive	PD	42.5 (12.3)	15:17
					AD	36.0 (13.6)	6:19
					CON	43.8 (10.5)	18:12
Deacon & Abramowitz (2008)	DSM-IV	ATT INT	BV IU	Health anxiety OCD Panic	PD	37.4 (13.7)	30:64
					OCD		
					HA		
Dorahy et al. (2006)	DSM-IV	ATT	NEG	Anxiety Dissociative	DID	46.3 (8.9)	0:12
					GAD	46.3 (11.2)	0:12
					CON	39.5 (6.8)	0:12
Duddu et al. (2003)	ICD-10	INT	AS	Somatic	SD	34.4 (7.7)	9:21
					MDD	33.1 (9.4)	7:23
					CON	33.7 (6.6)	8:22
Gawęda et al. (2018)	DSM-IV	INT	AS	Disorganization Excitement Emotion (Anxiety/Depression) Positive psychotic Negative psychotic	SZ	40.5 (11.3)	62:43
					MDD	45.8 (12.9)	17:39
					CON	22.9 (3.3)	40:112

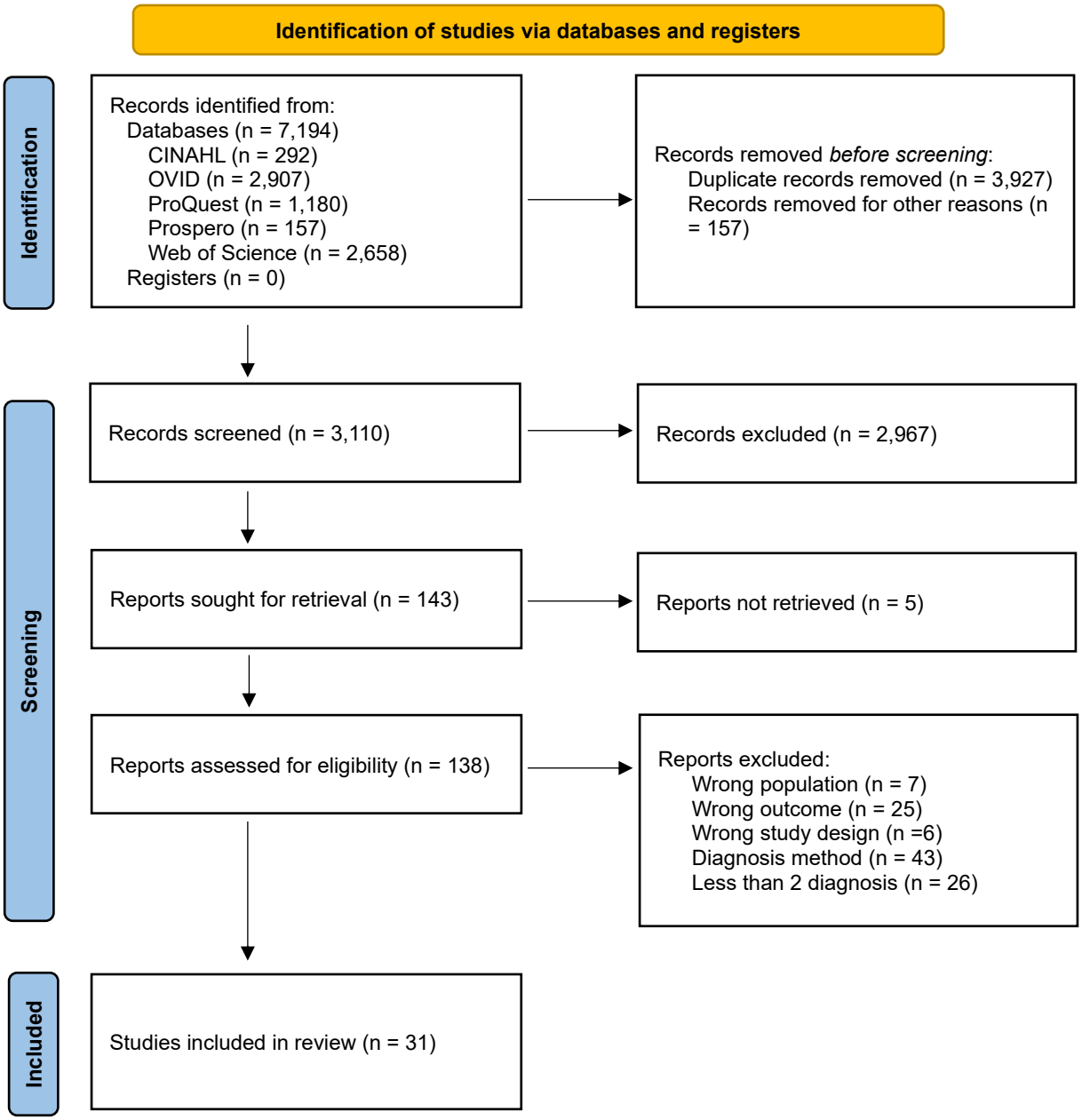
Gonzalo et al. (2012)	DSM-IV	INT	AS	Depressive PTSD	MDD	-	-
					PTSD	-	-
					CON	-	-
Gotlib, Kasch, et al. (2004)	DSM-IV	INT MEM ATT	NEG POS	Anxiety Depressive	MDD	34.5 (11.0)	26:62
					SAD	33.2 (9.2)	12:23
					CON	33.6 (11.4)	14:41
Gotlib, Krasnoperova, et al. (2004)	DSM-IV	ATT	NEG POS	Anxiety Depressive	MDD	38.6 (8.1)	0:19
					GAD	32.3 (9.0)	0:18
					CON	34.3 (11.5)	0:16
Ishikawa et al. (2016)	DSM-V	INT	JTC	Anxiety Depressive Negative psychotic Positive psychotic	SZ	41.8 (9.8)	74:37
					MDD	36.8 (8.5)	29:11
					CON	41.9 (11.1)	16:19
Kollei et al. (2017)	DSM-IV	ATT	NEG POS	Body dysmorphic Depressive Eating disorder	BDD	23.8 (4.3)	0:19
					BN	23.7 (4.3)	0:21
					CON	23.5 (2.8)	0:21
Kollei et al. (2022)	DSM-V	ATT	NEG POS	Depressive Eating disorder	AN	24.9 (5.3)	0:42
					BN	26.4 (6.3)	0:24
					CON	24.1 (3.4)	0:38
Krkovic et al. (2023)	DSM-V	INT	BADE JTC	Depressive Negative psychotic Positive psychotic	PSY	37.7 (9.6)	19:19
					OCD	35.9 (11.0)	14:25
					CON	36.3 (11.2)	20:18
Lackner et al. (2015)	DSM-IV-TR	INT	AS		MDD	22.7 (5.0)	51:120
					GAD		
Lahera et al. (2015)	DSM-IV	INT	AS	Depressive Manic Negative psychotic Positive psychotic	SZ	38.6 (10.6)	17:29
					BP	40.4 (10.5)	28:21
					CON	43.4 (13.6)	21:29
Lichtenstein-Vidne et al. (2017)	DSM-IV-TR	ATT	NEG	Anxiety	AD	46.1 (12.5)	5:12

			POS	Depressive	MDD	49.2 (12.2)	3:16
					CON	45.5 (14.2)	6:12
Neng et al. (2015)	DSM-IV	INT	AS	Anxiety Depressive	HA	38.1 (10.0)	22:28
					AD	36.0 (12.5)	23:27
					CON	32.9 (11.5)	23:27
Rinck & Becker (2005)	DSM-IV	ATT MEM	NEG POS EMB IMB	Anxiety Depressive Social anxiety	SAD	22.1 (3.1)	0:35
					MDD	23.5 (4.6)	0:27
					CON	21.4 (2.4)	0:55
Rosmarin et al. (2009)	DSM-IV	INT	AS	Anxiety sensitivity Social anxiety	PD	41.0 (10.4)	12:13
					SAD	37.6 (12.4)	11:14
					CON	37.5 (9.4)	7:17
Samson et al. (2022)	DSM-V	INT	IT CAT DiThink JTC ER		PSY	31.7 (6.3)	21:9
					MDD	43.8 (10.6)	4:27
					CON	24.6 (7.0)	158:215
Sanford et al. (2014)	DSM-IV	INT	BADE	Negative psychotic Positive psychotic	OCD	30.3 (9.6)	9:11
					SZ low delusional	33.9 (10.8)	72:49
					SZ high delusional	37.1 (11.6)	26:17
					CON	32.2 (9.6)	19:11
Serrano-Guerrero et al. (2018)	DSM-IV-TR	INT	JTC	Negative psychotic OCD Positive psychotic	OCD	43.7 (14.4)	12:7
					SZ	37.0 (14.0)	15:4
					CON	38.8 (13.8)	14:5
Strube et al. (2022)	ICD-10	INT	JTC	Depressive Negative psychotic Positive psychotic	SZ	37.3 (11.9)	26:19
					MDD	37.6 (11.3)	19:26
					CON	37.9 (11.4)	23:22
Uren et al. (2004)	DSM-IV	INT	NEG	Depressive	SAD	34.6 (10.8)	9:14

				Panic Social anxiety	PD	37.8 (11.3)	5:17
					CON	41.0 (12.2)	25:37
van den Heuvel et al. (2005)	DSM-IV	ATT	NEG	Health anxiety OCD Panic	PD	33.7 (2.5)	8:7
					OCD	33.4 (2.4)	6:12
					HA	40.6 (3.2)	12:2
					CON	30.3 (1.9)	10:9
Vrolling et al. (2016)	DSM-IV	INT	CONF	Social anxiety	SAD	31.5 (10.6)	28:17
					PD	37.5 (14.0)	13:11
					CON	31.2 (11.6)	28:17
Wenzel (2006)	DSM-IV	ATT	ATT	Anxiety Depressive Social anxiety	SAD	39.9	2:16
					PD	-	10:9
					CON	-	4:15
Wittorf et al. (2012)	DSM-IV	INT	AS JTC	Depressive Negative psychotic Positive psychotic	SZ	35.3 (9.0)	13:7
					MDD	36.3 (9.7)	8:12
					AN	23.9 (5.7)	0:15
Zetsche et al. (2015)*	DSM-IV	INT	UOP	Anxiety Depressive OCD Social anxiety	OCD	29.3 (8.8)	8:14
					SAD	30.3 (9.1)	15:15
					CON	28.9 (7.3)	14:17
Zhu et al. (2020)	DSM-IV	INT	AS BADE	Anxiety Depressive Negative psychotic Positive psychotic	SZ	41.5 (13.8)	30:26
					MDD	45.7 (13.1)	10:47
					CON	44.9 (14.0)	14:16

Note. *represents study containing only correlational data; **Disorders**: AD = Mixed Anxiety Disorder, AN = Anorexia Nervosa, BDD = Body Dysmorphic Disorder, BN = Bulimia Nervosa, BP = Bipolar Disorder, DD = Delusional Disorder, DID = Dissociative Identity Disorder, GAD = Generalized Anxiety Disorder, HA = Health Anxiety/Hypochondriasis, MDD = Major Depressive Disorder, OCD = Obsessive-Compulsive Disorder, PD = Panic Disorder, PSY = Psychotic Disorder, PTSD = Post-Traumatic Stress Disorder, SAD = Social Anxiety Disorder, SSD = Somatoform Disorder, SZ = non-affective Schizophrenia-Spectrum Disorder; **Bias**: ATT = Attentional Bias, AS = Attributional Bias, BADE = Bias Against Disconfirmatory Evidence, BV = Body Vigilance, CONF = Confirmatory Bias, DiThink = Dichotomous Thinking Bias, EMB = Explicit Memory Bias, ER = Emotional Reasoning Bias, IMB = Implicit Memory Bias, INT = Interpretation Bias, IT = Intentionalizing, IU = Intolerance of Uncertainty, JTC = Jumping to Conclusion, NEG = Negative Bias, TAF = Thought-action fusion, UOP = unrealistic optimism bias.

Figure 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases.



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Figure 2. Summarized forest plot for overall meta-analysis (patients versus control) and subgroup analyses (bias categories, risk of bias). CI = confidence interval, SMD = standardized mean difference.

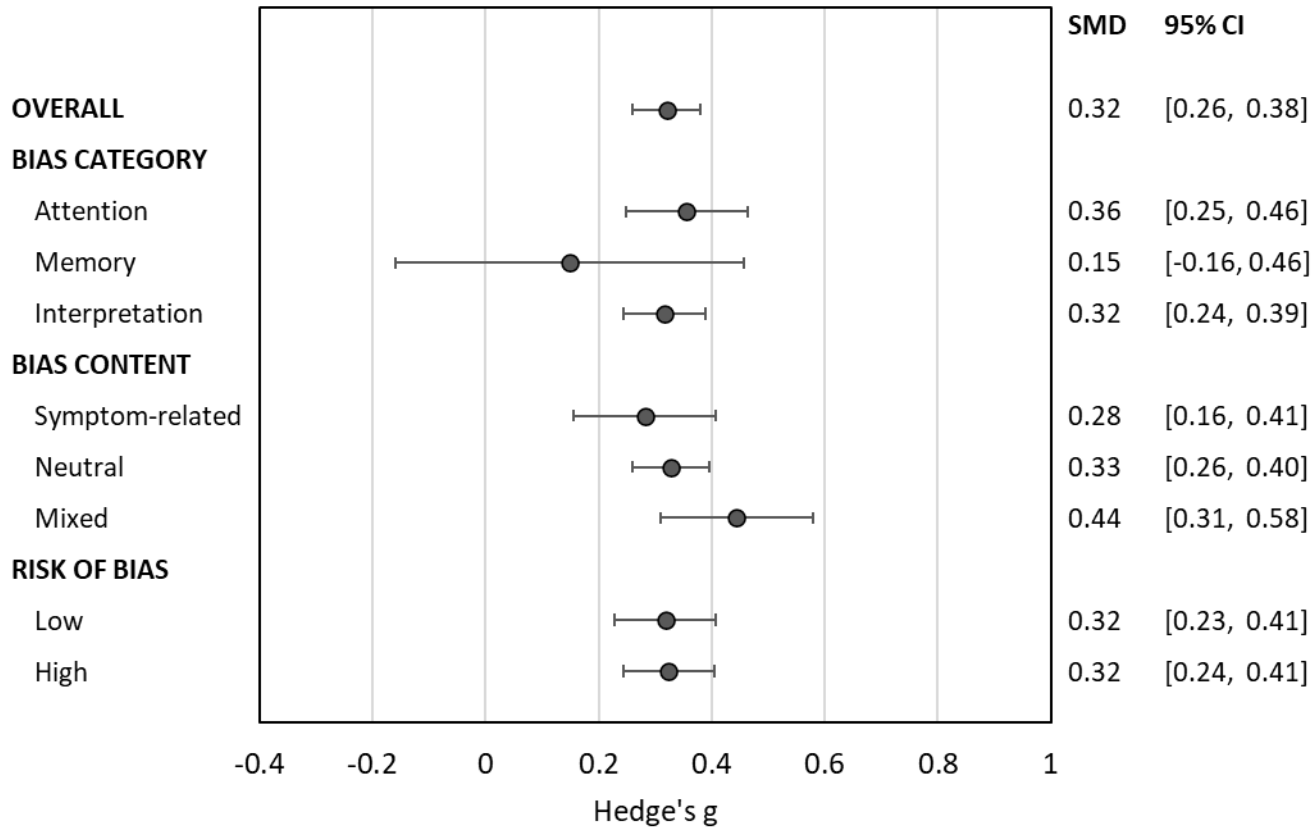


Figure 3. Network meta-analyses: A: Attention (ATT) biases, B: Memory (MEM) biases, C: Interpretation (INT) biases. Left panels show network graphs representing study comparisons between diagnoses; line thickness depicts the number of comparisons. Middle panels show summarized forest plots by disorder. Right panels are heatmaps of the direct and indirect effects between diagnoses (* = significant comparison). AD = mixed anxiety disorders, AN = anorexia nervosa, BDD = body dysmorphic disorder, BN = bulimia nervosa, BP = bipolar disorder, CI = confidence interval, DID = dissociative identity disorder, GAD = generalized anxiety disorder, HA = health anxiety, MDD = major depressive disorder, OCD = obsessive-compulsive disorder, PD = panic disorder, PTSD = post-traumatic stress disorder, SAD = social anxiety disorder, SD = somatization disorder, SMD = standardized mean difference, SZ = schizophrenia.

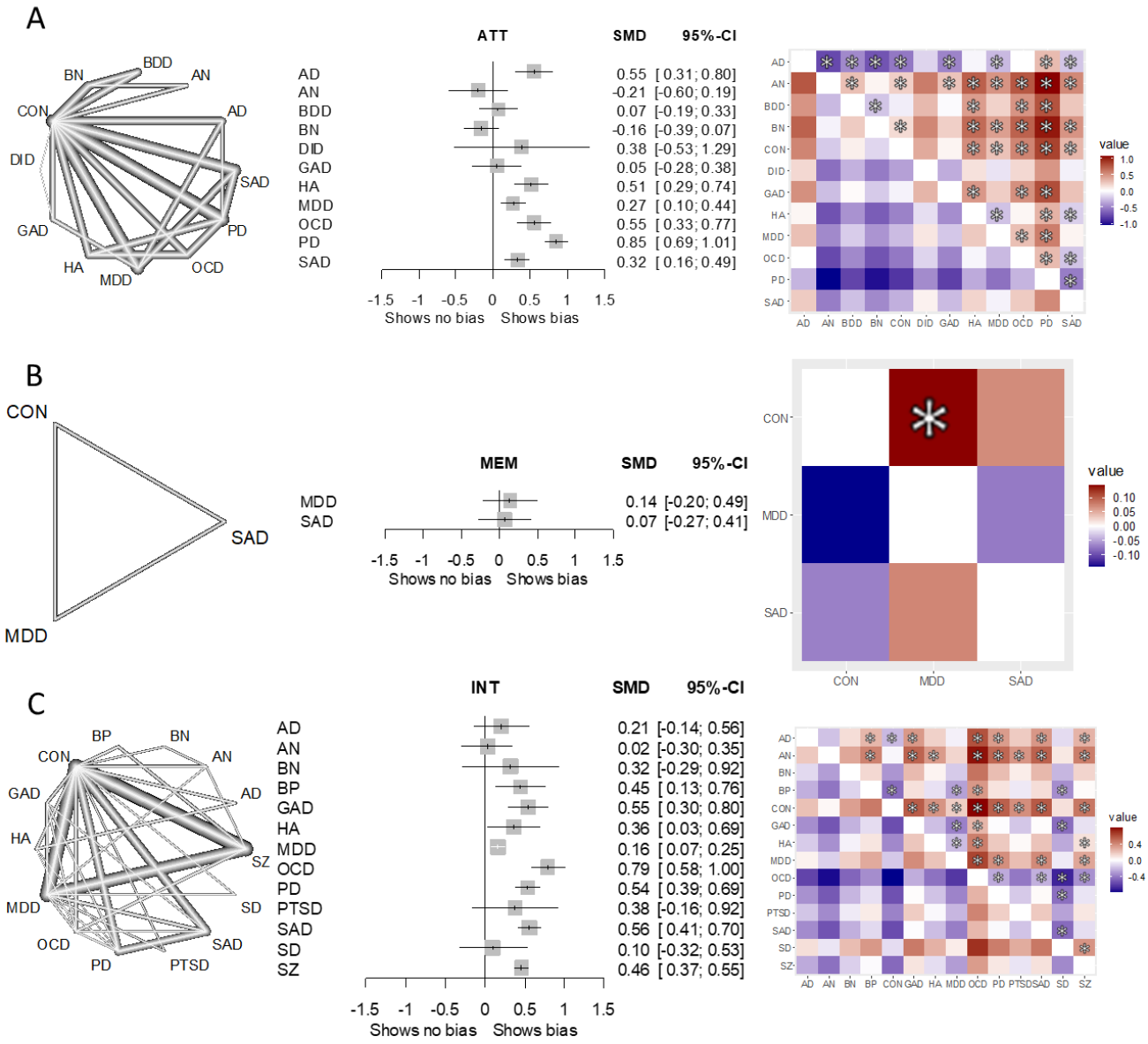
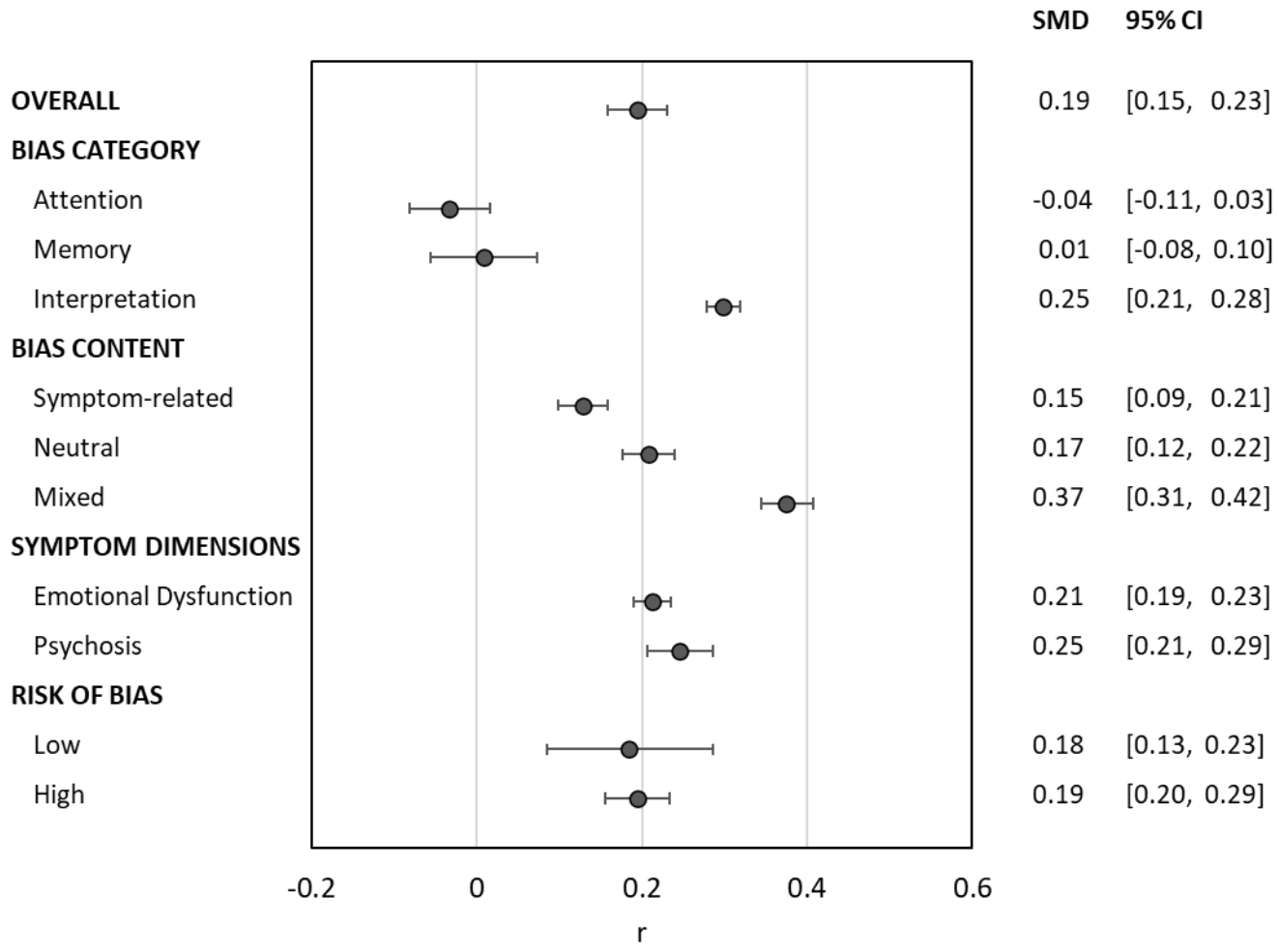


Figure 4. Summarized forest plot for overall meta-analysis (patients versus control) and subgroup analyses (symptom categories, risk of bias). CI = confidence interval, SMD = standardized mean difference.



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