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# Neuroimaging and Neurophysiologic Biomarkers for Mental Health: An Evidence Map

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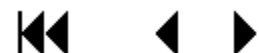
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The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.



## PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted health care topics of importance to clinicians, managers, and policymakers as they work to improve the health and health care of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program comprises 4 ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, interface with stakeholders, and address urgent evidence needs. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee composed of health system leadership and researchers. The program solicits nominations for review topics several times a year via the [program website](#).

The present report was developed in response to a request from the Office of Research and Development working group for the Commander John Scott Hannon Veterans Mental Health Care Improvement Act, Public Law 116-171, section 305 (SHA305). The scope was further developed with input from Operational Partners (below), the ESP Coordinating Center, and the review team. The ESP consulted several technical and content experts in designing the research questions and review methodology. In seeking broad expertise and perspectives, divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Ultimately, however, research questions, design, methodologic approaches, and/or conclusions of the review may not necessarily represent the views of individual technical and content experts.

## ACKNOWLEDGMENTS

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### Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

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The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence (see Appendix C for disposition of comments). Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center works to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

## TABLE OF CONTENTS

Authors.....	ii
Preface.....	iv
Acknowledgments.....	iv
Abbreviations Table.....	viii
Executive Summary.....	1
Introduction.....	12
Methods.....	14
Topic Development.....	14
Key Question (KQ).....	14
Search Strategy.....	14
Study Selection.....	14
Data Abstraction.....	15
Quality Assessment and Summary of Results.....	15
Peer Review.....	16
Results.....	17
Overview.....	17
Depression.....	20
Bipolar Disorders.....	28
Posttraumatic Stress Disorder.....	28
Traumatic Brain Injury.....	32
Substance Use Disorders.....	35
Obsessive Compulsive Disorder (OCD) and Anxiety Disorders.....	37
Systematic Reviews.....	40
Discussion.....	41
Summary of Key Findings.....	41
Implications for VA Policy.....	42
Gaps in Evidence and Future Research.....	42
Limitations.....	43
Conclusions.....	43
References.....	44
Appendix A. Search Strategy.....	67
Appendix B. Inclusion and Exclusion Criteria.....	69
Appendix C. Peer Review Disposition.....	71

Appendix D. Eligible Primary Studies.....	74
Appendix E. Eligible Systematic Reviews .....	84

## FIGURES AND TABLES

Figure 1. Identification and Selection of Eligible Studies .....	17
Figure 2. Number of Primary Studies Using Neuroimaging or Neurophysiologic Data to Evaluate Diagnosis or Prognosis for Various Mental Health Conditions .....	18
Table 1. Summary of Characteristics of Included Primary Studies.....	19
Figure 3. Median Sample Size of Included Studies Evaluating Diagnosis or Prognosis for Depression .....	21
Table 2. Summary of Characteristics of Included Studies Evaluating MRI-based Imaging Techniques for Diagnosis of Depression.....	22
Table 3. Summary of Characteristics of Included Studies Evaluating MRI-based Techniques for Treatment Response in Depression.....	24
Table 4. Characteristics of Included Studies Evaluating Electroencephalogram and Evoked Potentials for Depression.....	26
Table 5. Summary of Characteristics of Included Studies Addressing Diagnosis of Posttraumatic Stress Disorder.....	29
Table 6. Summary of Characteristics of Studies Evaluating MRI to Predict Response to Psychotherapy for Posttraumatic Stress Disorder.....	30
Table 7. Summary of Characteristics of Included Studies Addressing Traumatic Brain Injury.....	33
Table 8. Summary of Characteristics of Included Studies Addressing Substance Use Disorder.....	35
Table 9. Characteristics of Included Studies Addressing Obsessive Compulsive Disorder.....	37
Table 10. Characteristics of Included Studies Addressing Anxiety Disorders.....	39
Table 11. Summary of Eligible Systematic Reviews.....	40

## ABBREVIATIONS TABLE

AHRQ EPC	Agency for Healthcare Research and Quality Evidence-based Practice Center
ASL	Arterial spin labeling
BDI	Beck Depression Inventory
CAPS	Clinician Administered PTSD Scale
DAISY	DistillerSR's Artificial Intelligence System
DTI	Diffusion tensor imaging
ECT	Electroconvulsive therapy
EEG	Evoked potentials and electroencephalogram
ESP	Evidence Synthesis Program
fMRI	Functional magnetic resonance imaging
GOSE	Glasgow Outcome Scale-Extended
HAM-A	Hamilton Anxiety Rating Scale
HAM-D	Hamilton Depression Rating Scale
KQ	Key Question
MADRS	Montgomery-Asberg Depression Rating Scale
MEG	Magnetoencephalography
MeSH	Medical Subject Headings
MINI	Mini-International Neuropsychiatric Interview
MRI	Magnetic resonance imaging
OCD	Obsessive compulsive disorder
PCL	PTSD Checklist
PET	Positron emission tomography
PHQ	Patient Health Questionnaire
PTSD	Posttraumatic stress disorder
RCT	Randomized controlled trial
rTMS	Repetitive transcranial magnetic stimulation
SCID	Structured Clinical Interview for DSM
SHA305	Commander John Scott Hannon Veterans Mental Health Care Improvement Act, Public Law 116-171, section 305
SPECT	Single photon emission computed tomography
SUD	Substance use disorder
TBI	Traumatic brain injury
TBS	Theta burst stimulation
tDCS	Transcranial direct current stimulation
US	United States
VA	Department of Veterans Affairs
Y-BOCS	Yale Brown Obsessive Compulsive Scale
YMRS	Young Mania Rating Scale



# EVIDENCE REPORT

## INTRODUCTION

Improving diagnosis and treatment outcomes for Veterans with mental health conditions and traumatic brain injury (TBI) continues to be an important priority for the Department of Veterans Affairs (VA). Veterans enrolled in VA healthcare have a high prevalence of these conditions, estimated at 9% for posttraumatic stress disorder (PTSD), 14% for depression, 8% for substance use disorder (SUD), and 5% for anxiety disorders.<sup>1</sup> Compared with previous service eras, Veterans who served in Iraq and/or Afghanistan have higher rates of PTSD, depression, and/or TBI, due in part to increased diagnosis and the changing nature of military service and combat-related injuries.<sup>2</sup> These conditions often have substantial impacts on long-term health and functioning for individuals, as well as broader effects on their families and communities.<sup>3-6</sup> In terms of VA healthcare costs, treatment for mental health conditions accounted for \$11 billion or 13% of overall costs in fiscal year 2021 (FY 2021), with estimated annual increases in FY 2022–2024.<sup>7</sup>

In the past several decades, there have been substantial advancements in precision medicine, specifically the use of biomarkers and/or genetics in diagnosis, prognosis, and tailoring treatments for medical conditions. There are currently several ongoing large-scale population-based studies to advance precision medicine, including the VA’s Million Veterans Program.<sup>8,9</sup> In certain fields, such as oncology, the use of biomarkers and genetics to inform diagnosis and treatment decisions are now the standard of care.<sup>10,11</sup> However, despite substantial interest in the use of precision medicine techniques in mental health, there has been much more limited progress.<sup>12,13</sup> In the context of mental health, precision medicine has involved assessment of brain structure and functioning, as well as genetics and serum biomarkers. There are multiple challenges that impact advances in precision medicine for mental health conditions. These include complex and heterogeneous clinical phenotypes, high cost and technical difficulty of obtaining neuroimaging and neurophysiologic data, and differing assessments of symptoms and treatment response.<sup>14-17</sup> These challenges have contributed to substantial concerns about the reproducibility and validity of findings that rest largely on cross-sectional studies of small samples that insufficiently represent the demographic and clinical variability of affected populations.<sup>15</sup> Nevertheless, recent efforts to more systematically collect and examine large neuroimaging datasets, including across the lifespan, have yielded more promising results.<sup>15,18</sup> Thus, future work in this area may yet produce insights that improve diagnosis and treatment outcomes in mental health.

This evidence review was requested by the VA Working Group to implement the Commander John Scott Hannon Veterans Mental Health Care Improvement Act, (P.L. 116-171), Section 305: “Precision Medicine for Veterans Initiative” (SHA305). SHA305 tasks the VA with developing and implementing a precision medicine initiative focused on brain and mental health biomarkers.<sup>19</sup> SHA305 specifies that this initiative “shall include brain structure and function measurements, such as functional magnetic resonance imaging and electroencephalogram” and further coordinate with current data collection by the Million Veterans Program. To support the VA SHA305 Working Group, we conducted an evidence map to better understand characteristics of existing evidence on relationships between brain structure and functioning, and mental health conditions and TBI. An evidence map is well suited to address a broad scope covering multiple

conditions and numerous neuroimaging and neurophysiological techniques, particularly when some of the evidence base may consist of more exploratory studies. An evidence map is also appropriate for meeting the overall goals of informing research policy and potential clinical demonstrations.<sup>20,21</sup>

Therefore, in this report, we provide descriptive information about the number and types of studies that address a wide range of neuroimaging and neurophysiologic assessments for diverse mental health conditions and TBI. We also highlight weaknesses and gaps in the evidence, as determined by the volume and characteristics of studies.

## METHODS

### TOPIC DEVELOPMENT

We worked with our Operational Partners, the VA SHA305 Working Group, to refine the scope and develop the key questions for this evidence report. To meet the broad scope and main objectives of this workgroup, we conducted an evidence map to identify and describe the current state of research (including evidence gaps) involving the use of a wide variety of neuroimaging and neurophysiologic tests in the context of clinical diagnosis and/or prognosis for a number of important mental health conditions and TBI. An evidence map is also well suited for determining the current state of research areas that have mainly more exploratory or early phase studies. The protocol was developed *a priori* and registered with Open Science Framework (registration DOI: <https://doi.org/10.17605/OSF.IO/5PHG2>).

### KEY QUESTION (KQ)

*KQ*: What are the quantity, distribution, and characteristics of evidence assessing the accuracy and utility of neuroimaging and neurophysiologic biomarkers in the diagnosis and clinical management of the following conditions:

- a) Depression
- b) Anxiety
- c) Posttraumatic stress disorder (PTSD)
- d) Substance use disorder (SUD)
- e) Bipolar disorder
- f) Traumatic brain injury

### SEARCH STRATEGY

We searched for peer-reviewed English language articles from January 2010 to April 2022 in the MEDLINE and Embase databases. We used Medical Subject Headings (MeSH) and title/abstract terms for the neuroimaging and neurophysiological tests, and conditions of interest (Appendix A). We also searched websites for the VA ESP and AHRQ EPC programs for relevant reviews.

### STUDY SELECTION

After duplicates were removed, citations were uploaded into DistillerSR (Evidence Partners, Ottawa, Canada). Abstracts were screened with the assistance of DistillerSR's Artificial Intelligence System (DAISY) in 2 separate phases. In the first phase, 2 reviewers were required to exclude an abstract at screening (while only 1 reviewer was needed to include for full-text review) until the DAISY-predicted score for likelihood of inclusion was less than 0.4 and the inclusion rate had fallen to less than 5%. Approximately 12,000 abstracts were reviewed in phase 1. In the second phase, for abstracts with DAISY-predicted scores for likelihood of inclusion of 0.2–0.3 ( $k \approx 7,000$  abstracts), 1 reviewer decided on inclusion for full-text review. The remaining abstracts with DAISY-predicted likelihood scores less than 0.2 were not further reviewed for

eligibility ( $k = 25,912$ ). Based on an inclusion rate of 0.00066 for the last batch of abstracts evaluated during phase 2 ( $k = 1,526$ ), we conservatively estimate that an additional 17 abstracts may have been potentially included for full-text review, if we had continued with 1-reviewer evaluation of those abstracts with likelihood scores of less than 0.2.

For full-text review, we undertook 2 initial pilot rounds where all reviewers separately determined eligibility for 10–15 articles in each round. We discussed articles to reach consensus on eligibility, with further clarification on operationalization of inclusion and exclusion criteria. Eligibility of remaining articles was determined by 1 reviewer, with ~50% of these also undergoing evaluation by a second reviewer.

Detailed eligibility criteria are provided in Appendix B.

Briefly, eligible populations included adults ( $\geq 18$  years of age) with at least 1 of the conditions of interest, as noted in KQ above. Eligible articles also evaluated at least 1 neuroimaging or neurophysiological test of interest (*eg*, magnetic resonance imaging [MRI], including functional MRI [fMRI], diffusion tensor imaging [DTI], positron emission tomography [PET], single photon emission computed tomography [SPECT], and evoked potentials and electroencephalogram [EEG]) for diagnostic accuracy, clinical prognosis, and/or treatment response. Exclusion criteria included pediatric populations, evaluation of mental health symptoms or cognitive functioning only in the context of neurodegenerative conditions (*eg*, Alzheimer's dementia or Parkinson's disease) or intracranial injury (*eg*, due to ischemic or hemorrhagic stroke). We also excluded studies attempting to evaluate prognostic patterns using exclusively cross-sectional data (*eg*, comparing current differences in neuroimaging or neurophysiological patterns between patients with depression in remission vs those with treatment-resistant depression). There are very substantial validity concerns with use of cross-sectional data to evaluate predictors of treatment response or general prognosis, which has been noted previously.<sup>22</sup>

## DATA ABSTRACTION

We abstracted the following data from all eligible studies: population characteristics (*eg*, condition and method of diagnosis, sample size, demographic data (*eg*, mean or median age, proportion of women, focus on Veterans or combat exposure), neuroimaging test and/or EEG being evaluated (and genetic data if used), outcomes addressed (clinical diagnosis and/or prognosis), and study design (*eg*, cross-sectional or cohort, analytic methods used to assess diagnostic accuracy). To verify accuracy of abstracted results, data from ~50% of articles were over-read by a second reviewer.

## QUALITY ASSESSMENT AND SUMMARY OF RESULTS

We did not conduct formal quality assessment of eligible studies included in this report. We also did not undertake a formal synthesis of study results. Our results summaries are organized by the conditions of interest and focus on describing the characteristics of study populations, outcomes (clinical diagnosis, prognosis, and/or treatment response), and study designs (including analytic methods) of eligible studies.

## **PEER REVIEW**

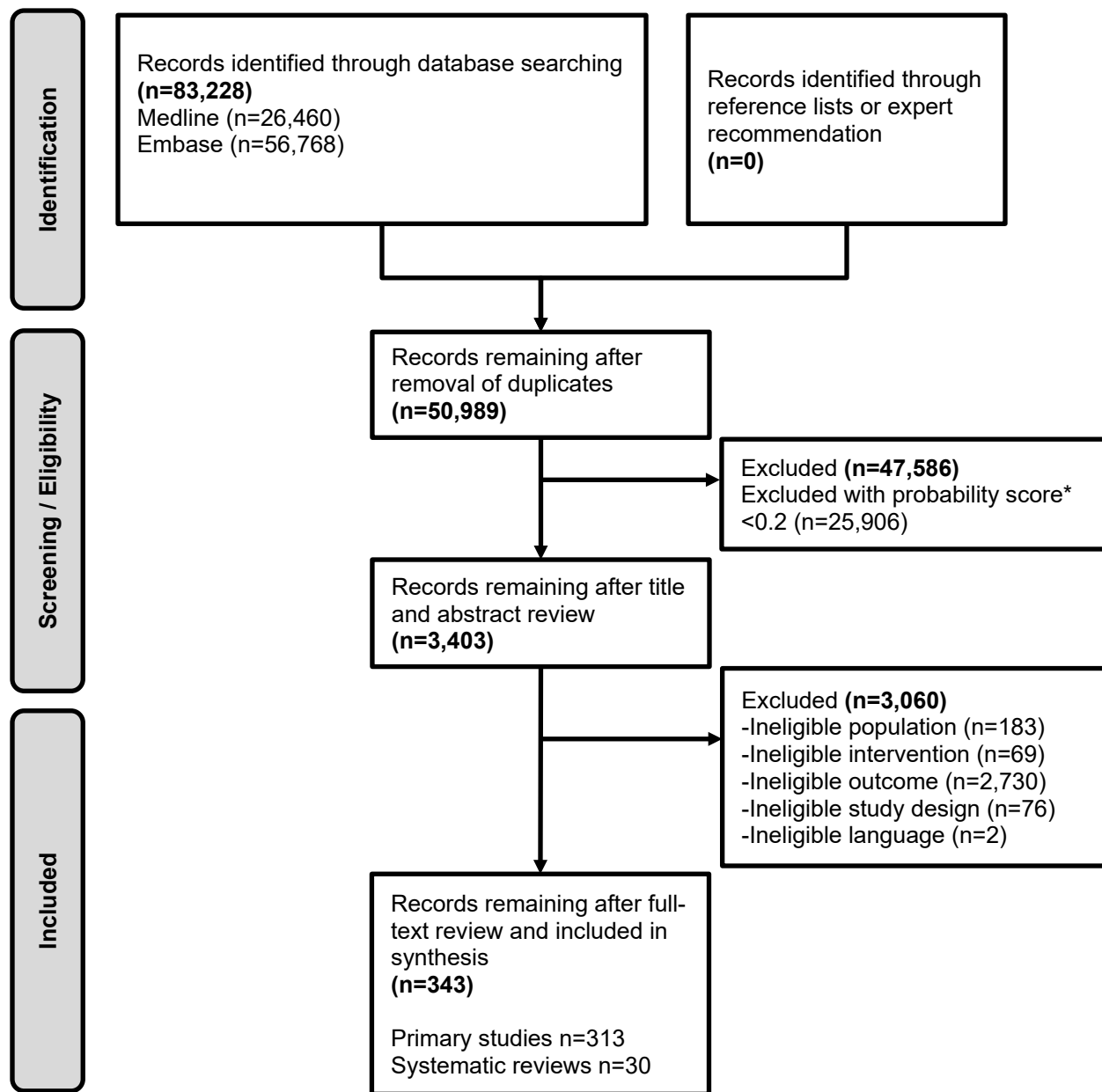
A draft version of this report was reviewed by technical experts as well as clinical leadership. Their comments and our responses are presented in Appendix C.

# RESULTS

## OVERVIEW

From 50,989 unique search results, we identified 343 eligible articles (Figure 1), consisting of 313 primary studies (Appendix D) and 30 systematic reviews (Appendix E). At abstract screening, 47,586 results were excluded, with 54% of these based on low scores from a machine-learning algorithm (see Methods and Figure 1). A list of references excluded during full-text review ( $k = 3,060$ ) and reasons for exclusion is available upon request.

**Figure 1. Identification and Selection of Eligible Studies**

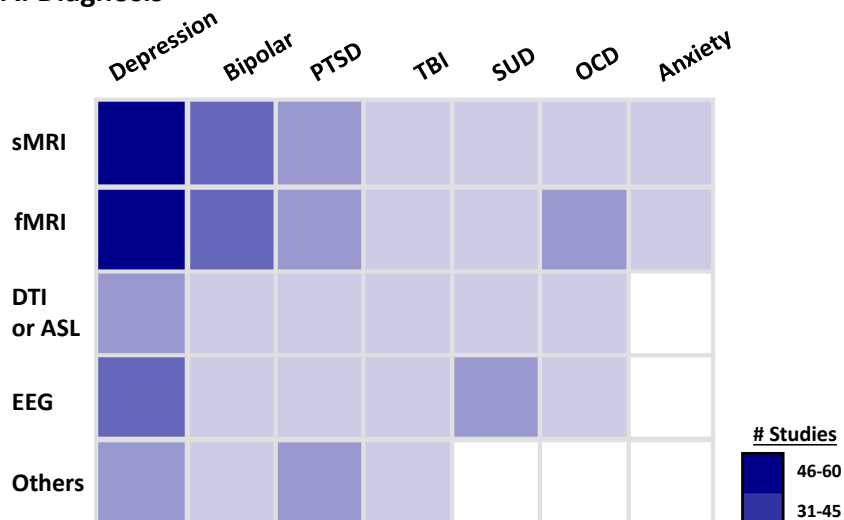


Notes. \* Machine-learning algorithm DAISY on the DistillerSR platform (Evidence Partners).

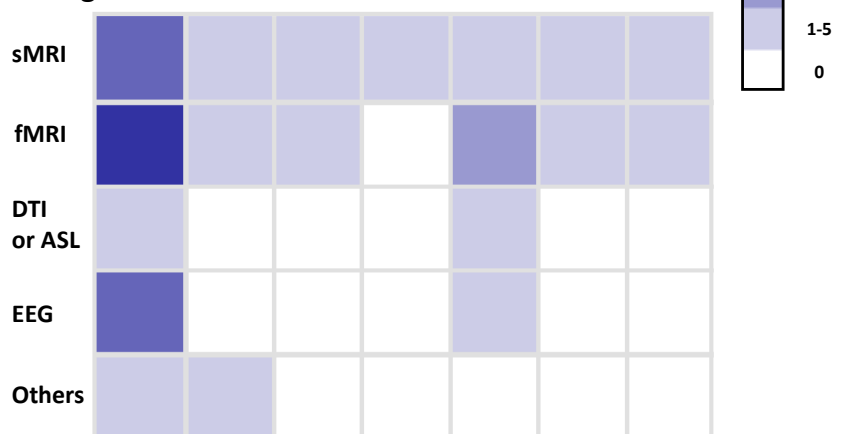
Most of the eligible primary studies and systematic reviews addressed depression ( $k = 236$ , 69%), while fewer studies and reviews evaluated other conditions. Only 2 primary studies evaluated genetic data in addition to neuroimaging or neurophysiologic data. Figure 2 summarizes the distribution of primary studies using various neuroimaging or neurophysiologic data for evaluation of diagnosis or prognosis of each condition of interest. Three-quarters of primary studies used MRI-based imaging techniques ( $k = 236$ , 75%), while a fifth used EEG data ( $k = 68$ , 22%). For multiple conditions, there were none or few studies ( $k \leq 5$ ) examining either diagnosis or prognosis.

**Figure 2. Number of Primary Studies Using Neuroimaging or Neurophysiologic Data to Evaluate Diagnosis (A) or Prognosis (B) for Various Mental Health Conditions**

**A. Diagnosis**



**B. Prognosis**



*Notes.* Others category includes positron emission tomography (PET), single-photon emission computerized tomography (SPECT), and magnetoencephalography (MEG).

*Abbreviations.* ASL=arterial spin labeling; DTI=diffusion tensor imaging; EEG=electroencephalogram; MRI=magnetic resonance imaging (structural or functional); OCD=obsessive compulsive disorder; PTSD=posttraumatic stress disorder; SUD=substance use disorder; TBI=traumatic brain injury.

Table 1 provides more information about study populations and methods for primary studies across the different conditions. Most primary studies had small sample sizes, with only 9 having more than 500 participants (range 555–4541). Two-thirds of primary studies examined diagnosis ( $k = 200$ ), 110 evaluated prognosis, and 3 addressed both diagnosis and prognosis. Most primary studies included young and middle-aged participants; only 5 studies had participants with mean ages of 65 or older, and all of these addressed depression (with 1 also including participants with bipolar disorder).<sup>23-27</sup> Following Table 1, we present results for primary studies by condition of interest and then describe results for eligible systematic reviews.

**Table 1. Summary of Characteristics of Included Primary Studies**

	Depression ( $k = 218$ )	Bipolar Disorders ( $k = 47$ )	PTSD ( $k = 30$ )	TBI ( $k = 12$ )	SUD ( $k = 20$ )	OCD ( $k = 19$ )	Anxiety Disorders <sup>a</sup> ( $k = 10$ )
<i>Neuroimaging/Neurophysiologic technique</i>							
MRI-based techniques:							
Structural MRI (sMRI)	73	24	8	5	5	5	3
Functional MRI (fMRI)	80	19	13	2	8	12	7
DTI or ASL	12	5	1	2	2	1	—
EEG	54	1	5	2	8	1	—
Others <sup>b</sup>	15	3	5	1	—	—	—
<i>Outcomes</i>							
Diagnosis	130	41	24	10	9	17	4
Prognosis:							
Treatment response <sup>c</sup>	89	6	6		11	2	6
Change in symptoms or functioning	2	—	—	2	—	—	—
<i>Study design &amp; methods</i>							
Cross-sectional	117	38	22	10	9	15	3
Cohort/longitudinal observational	88	9	6	2	10	4	7
Randomized controlled trial	13	—	2	—	1	—	—
Used machine learning	123	28	10	1	11	9	4
Models validated	145	30	12	3	8	7	4
<i>Country</i>							
US/Canada	55	12	18	10	10	1	6
China	84	9	7	—	3	14	2
UK/Europe	33	8	2	—	2	1	1
Others <sup>d</sup>	44	17	3	2	5	3	1
NR	2	1	—	—	—	—	—
<i>Sample sizes (total N)<sup>e</sup></i>							
30–99	130	23	17	7	13	9	9
100–200	63	19	8	2	6	9	1
201–500	18	5	4	1	—	1	—



	Depression ( <i>k</i> = 218)	Bipolar Disorders ( <i>k</i> = 47)	PTSD ( <i>k</i> = 30)	TBI ( <i>k</i> = 12)	SUD ( <i>k</i> = 20)	OCD ( <i>k</i> = 19)	Anxiety Disorders <sup>a</sup> ( <i>k</i> = 10)
501–1000	2	—	—	—	—	—	—
>1,000	5	—	1	—	1	—	—
<i>Age (mean or median, years)</i>							
18–25	9	7	2	—	—	4	4
26–44	160	34	22	10	13	14	5
45–64	31	4	3	1	5	—	—
>65	5	1	—	—	—	—	—
NR	13	1	3	1	2	1	1
<i>Type of Veterans included</i>							
US Veterans or active military	—	—	10	7	3	—	—
Non-US Veterans or active military	—	—	3	—	—	—	—

Notes. <sup>a</sup> Includes general anxiety disorder, panic disorder, and social anxiety disorder.

<sup>b</sup> Includes positron emission tomography (PET), single-photon emission computerized tomography (SPECT), and magnetoencephalography (MEG).

<sup>c</sup> For SUD, this was abstinence vs relapse after or during treatment.

<sup>d</sup> Includes other countries not included in categories above, as well as studies done in multiple countries.

<sup>e</sup> Also includes healthy controls if among participants.

**Abbreviations.** ASL=arterial spin labeling; DTI=diffusion tensor imaging; EEG=electroencephalogram; MRI=magnetic resonance imaging; NR=not reported; OCD=obsessive compulsive disorder; PTSD=posttraumatic stress disorder; SUD=substance use disorder; TBI=traumatic brain injury; UK=United Kingdom; US=United States.

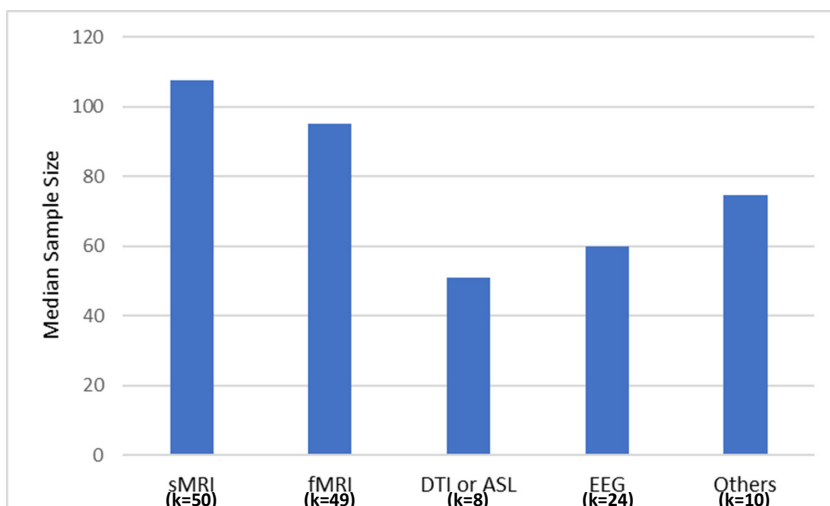
## DEPRESSION

### Overview

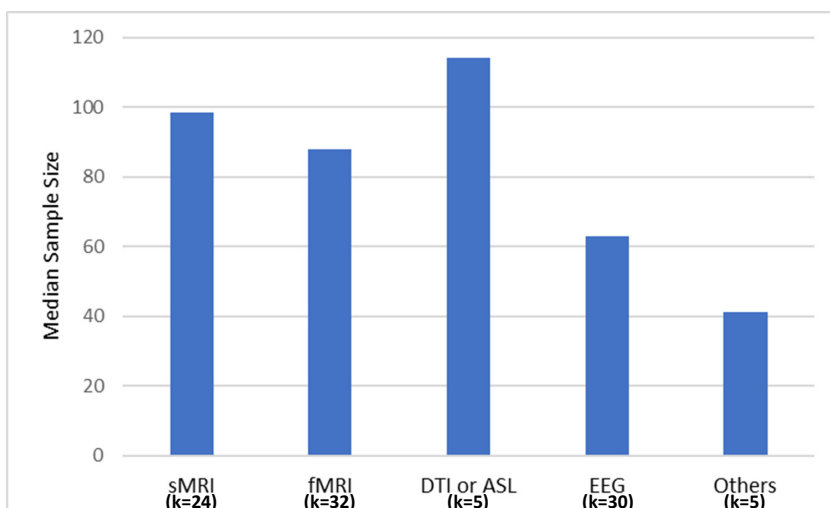
The majority of eligible primary studies evaluated depression (*k* = 218, 70%), and the vast majority of these used structural and/or functional MRI (*k* = 153) (Table 1). Fewer studies employed other MRI-based techniques like DTI (*k* = 10) and arterial spin labeling (ASL, *k* = 2). A quarter of studies addressing depression used EEG or evoked potentials (*k* = 54); others used magnetoencephalography (MEG, *k* = 8), PET (*k* = 4), or SPECT (*k* = 3). Most studies focused on whether neuroimaging tests contributed to diagnosis (*k* = 127). Less than half (*k* = 88) evaluated prognosis, and very few (*k* = 3) addressed both diagnosis and prognosis. About half of studies (*k* = 123) used machine learning methods to develop diagnostic or predictive models, including the selection of imaging features and patterns. Two-thirds of studies undertook model validation (*k* = 144). Most studies were very small with total sample sizes less than 100 (*k* = 130); only 2 studies had 500–1000 participants, and 5 studies had 1000 or more participants. Median sample size for studies using various neuroimaging or neurophysiologic data is shown in Figure 3. Studies were conducted in different regions of the world, with most common locations being the US or Canada (*k* = 55) and China (*k* = 84).

**Figure 3. Median Sample Size of Included Studies Evaluating Diagnosis (A) or Prognosis (B) for Depression**

**A. Diagnosis**



**B. Prognosis**



*Notes.* Others category includes positron emission tomography (PET), single-photon emission computerized tomography (SPECT), and magnetoencephalography (MEG). Number of included studies is indicated for each type of imaging or neurophysiologic data.

*Abbreviations.* ASL=arterial spin labeling; DTI=diffusion tensor imaging; EEG=electroencephalogram; MRI=magnetic resonance imaging (structural or functional).

**MRI-based Imaging Techniques (Structural and Functional MRI, DTI, and ASL)**

*Diagnosis*

Of 104 studies using MRI-based techniques to address diagnosis of depression, the largest proportion used structural MRI ( $k = 49$ ), fMRI ( $k = 48$ ; 39 using resting fMRI and 10 task-specific), or both ( $k = 1$ ) (Table 2). A few used other MRI-based techniques like DTI ( $k = 6$ )<sup>28-32</sup> and ASL ( $k = 2$ ).<sup>33,34</sup> Most were cross-sectional ( $k = 91$ ), while those remaining were cohort/longitudinal ( $k = 13$ ). Three-quarters used machine learning methods to develop models ( $k = 75$ ). Nearly all studies assessed diagnostic model accuracy ( $k = 100$ ) and

sensitivity/specificity ( $k = 93$ ). Three-quarters of the studies also undertook model validation ( $k = 77$ ).

Total sample sizes ranged 30–4541; half of the studies had  $N < 100$  ( $k = 57$ ) and only 4 had  $N > 1000$ . Most included healthy controls ( $k = 99$ ), while a quarter had participants with bipolar disorder ( $k = 26$ ). A third focused particularly on participants not on medications ( $k = 34$ ), with this including those who had not been on any medications and others who were not on medications at the time of the study. A fifth of studies included participants with their first episode of depression ( $k = 19$ ). Nearly every study had substantial proportions of women ( $k = 92$  with women  $>40\%$ ). Most participants were young and middle-aged; only 5 studies reported race. The most common locations were China ( $k = 57$ ) and the US ( $k = 17$ ).

The most frequently used standard for determining diagnostic accuracy was standardized clinician assessments (eg,  $k = 89$  studies used Hamilton Depression Rating Scale [HAM-D]). Clinician interviews were also commonly used, including the Structured Clinical Interview for DSM (SCID;  $k = 74$ ) and Mini-International Neuropsychiatric Interview (MINI;  $k = 18$ ). Fewer studies used patient-reported measures such as the Beck Depression Inventory (BDI;  $k = 21$ ).

**Table 2. Summary of Characteristics of Included Studies Evaluating MRI-based Imaging Techniques for Diagnosis of Depression**

	sMRI ( $k = 50$ )	fMRI ( $k = 49$ )	Other Techniques <sup>a</sup> ( $k = 8$ )
<i>Depression subgroups</i>			
Medication free	14	19	2
First episode	7	12	—
Treatment resistant	1	2	—
<i>Other groups included</i>			
Healthy controls	46	47	6
Bipolar disorder patients	12	12	3
<i>Country</i>			
US	13	6	4
China	26	32	4
UK/Europe	9	8	—
Other <sup>b</sup>	5	3	—
NR	1	—	—
<i>Sample sizes (total N)</i>			
30–99	23	27	7
100–249	21	16	1
250–499	4	3	—
500–999	—	1	—
>1,000	2	2	—

	sMRI ( <i>k</i> = 50)	fMRI ( <i>k</i> = 49)	Other Techniques <sup>a</sup> ( <i>k</i> = 8)
<i>Age (mean or median, years)</i>			
18–25	—	7	1
26–44	45	38	4
45–64	2	3	—
≥65	2	1	1
NR	1	—	2
<i>% Women</i>			
0–15	1	—	—
16–40	3	2	—
41–70	40	41	7
>70	5	6	1
NR	1	—	—
<i>Race reported?</i>			
	4	—	1
<i>Diagnostic accuracy standard</i>			
Clinician interviews	37	34	5
Clinician assessments	40	35	5
Patient-reported outcomes	8	9	1
<i>Study design</i>			
Cross-sectional	43	43	7
Cohort/longitudinal	6	6	1
<i>Analytic methods</i>			
Sensitivity/specificity	44	45	7
Machine learning	32	40	5
Models validated	47	48	7

Notes. <sup>a</sup> Includes arterial spin labeling (ASL) and diffusion tensor imaging (DTI).

<sup>b</sup> Includes other countries not included in categories above, as well as studies done in multiple countries.

Abbreviations. MRI=magnetic resonance imaging (structural or functional); NR=not reported.

## Prognosis & Treatment Response

Among 59 studies evaluating prognosis, most also used structural MRI (*k* = 22), fMRI (*k* = 31; 15 resting fMRI, 14 task-specific, and 2 both resting and task), or both (*k* = 2); 5 studies used DTI. Nearly all studies examined treatment response (*k* = 55), most commonly to antidepressant therapy (*k* = 36). Fewer evaluated response to psychotherapy (*k* = 6), electroconvulsive therapy (ECT, *k* = 9), repetitive transcranial magnetic stimulation (rTMS, *k* = 5), transcranial direct current stimulation (tDCS, *k* = 1), theta burst stimulation (TBS, *k* = 1), or inpatient multi-modal treatment (*k* = 1) (Table 3). Additionally, 2 studies evaluated general trajectories over 2 years for middle-aged<sup>35</sup> and older adults<sup>26</sup> with depression. Twenty-two studies applied machine learning approaches and 34 validated predictive models.

Most studies were cohorts/longitudinal observational (*k* = 49), and 10 were reports of RCTs. Four of these articles<sup>36-39</sup> used data from a single RCT, the international Study to Predict Optimized Treatment in Depression (iSPOT-D).<sup>40</sup> A single study included *N* > 1000,<sup>41</sup> while half had *N* < 100 participants (*k* = 31). Some studies on treatment response only included medication-

free participants, indicating those who had not received treatment for the current depressive episode or had undergone a washout period ( $k = 24$ ). Others focused on treatment-resistant depression ( $k = 11$ ). Only 2 studies distinguished participants in their first episode of depression.<sup>42,43</sup> Additionally, a third included healthy controls ( $k = 21$ ), while a few had participants with bipolar disorder ( $k = 4$ ). Studies had relatively young participants, and women were well represented. Demographic information relating to race/ethnicity was reported in 9 studies. The most common locations were the US or Canada ( $k = 21$ ) and China ( $k = 12$ ).

**Table 3. Summary of Characteristics of Included Studies Evaluating MRI-based Techniques for Treatment Response in Depression**

	Response to Treatments				
	Antidepressants ( $k = 36$ )	Psychotherapies ( $k = 6$ )	ECT ( $k = 9$ )	rTMS ( $k = 6$ )	Other <sup>a</sup> ( $k = 3$ )
<i>Imaging technique</i>					
sMRI	13	—	7	2	1
fMRI	20	6	3	5	1
DTI	4	—	—	—	1
<i>Depression subgroups</i>					
Medication free	20	3	—	—	2
Treatment resistant	1	—	6	4	—
<i>Other groups included</i>					
Healthy controls	16	3	1	3	—
Bipolar disorder	—	—	4	—	—
<i>Country</i>					
US/Canada	9	5	5	2	1
China	11	—	—	1	—
UK/Europe	5	—	—	—	1
Other <sup>b</sup>	11	1	1	2	1
<i>Sample sizes (total N)</i>					
30–99	18	3	7	4	1
100–249	15	3	2	1	2
250–499	3	—	—	—	—
500–999	—	—	—	—	—
>1,000	—	—	—	1	—
<i>Age (mean or median, years)</i>					
26–44	27	5	4	5	2
45–64	5	—	5	1	1
≥65	2	—	—	—	—
NR	2	1	—	—	—

	Response to Treatments				
	Antidepressants ( <i>k</i> = 36)	Psychotherapies ( <i>k</i> = 6)	ECT ( <i>k</i> = 9)	rTMS ( <i>k</i> = 6)	Other <sup>a</sup> ( <i>k</i> = 3)
<i>% Women</i>					
0–15	—	0	—	—	—
16–40	3	1	—	1	—
41–70	27	2	6	5	3
>70	4	0	—	—	—
NR	2	3	3	1	—
<i>Race reported?</i>	4	2	2	—	—
<i>Study design</i>					
Cohort/longitudinal	29	5	9	6	2
RCT	7	1	—	—	—
<i>Analytic methods</i>					
ROC (or sensitivity/ specificity)	17	3	2	4	1
Machine learning	12	1	7	3	—
Models validated	22	1	8	4	1

Notes. <sup>a</sup> Includes 1 study on transcranial direct current stimulation (tDCS), 1 study on theta burst stimulation (TBS) vs rTMS, and 1 using multi-modal inpatient treatment.

<sup>b</sup> Includes other countries not included in categories above, as well as studies done in multiple countries.

Abbreviations. DTI=diffusion tensor imaging; ECT=electroconvulsive therapy; MRI=magnetic resonance imaging (structural or functional); NR=not reported; ROC=receiver operating curve; rTMS=replicative transcranial magnetic stimulation.

## EEG and Evoked Potentials

### Diagnosis

Of 54 studies evaluating EEG or evoked potentials for depression, 24 examined diagnosis (*k* = 24) (Table 4). Most studies addressing diagnosis included healthy controls (*k* = 23), and most were very small with total sample sizes less than 100 (*k* = 21). Only 2 studies focused on participants in their first episode of depression,<sup>44,45</sup> and only 3 studies had more than 100 participants (range 157–400).<sup>46–48</sup> Study participants were young and middle-aged adults (mean age range 20–55), and more than half of studies had more than 40% women (*k* = 17). Studies were conducted in different regions of the world, with the most common location being China (*k* = 7); 1 study was multi-site, occurring in Japan, the US, and Taiwan.<sup>46</sup>

All diagnostic studies were cross-sectional in design and most used machine learning methods (*k* = 17). Standardized clinician assessments (HAM-D and Montgomery-Asberg Depression Rating Scale [MADRS]) were the most frequently used diagnostic standard (*k* = 14). Most studies undertook model validation (*k* = 20).

### Prognosis & Treatment Response

Thirty studies examined EEG or evoked potentials for prognosis in depression. These all examined response to specific treatments; most addressed outcomes after antidepressant therapy (*k* = 19), while fewer evaluated rTMS (*k* = 9) and 1 study each examined acupuncture<sup>49</sup> or

ketamine.<sup>50</sup> A third of prognostic studies included participants who were not on medications ( $k = 11$ ), and 8 focused on treatment-resistant participants (variably defined as not responding to sufficient course of antidepressants). No study included only participants with their first episode of depression. Six studies included participants who were healthy controls. The majority of studies were small with less than 100 participants ( $k = 22$ ), while 8 studies included somewhat more participants (range 103–220). Studies most commonly were conducted in the US or Canada ( $k = 13$ ).

Prognostic studies were most often longitudinal observational ( $k = 25$ ) but a few used data from RCTs ( $k = 4$ ).<sup>51-54</sup> A third of prognostic studies used machine learning ( $k = 9$ ). Studies most commonly used standardized clinician assessments (HAM-D and MADRS) to define treatment response ( $k = 25$ ). Just under half of studies undertook model validation ( $k = 12$ ).

**Table 4. Characteristics of Included Studies Evaluating Electroencephalogram and Evoked Potentials for Depression**

	Diagnosis (Total = 24)	Response to Treatments		
		Antidepressants (Total = 19)	rTMS (Total = 9)	Other <sup>a</sup> (Total = 2)
<i>Depression subgroups</i>				
Medication free	3	8	—	—
Treatment resistant	—	3	1	1
<i>Other groups included</i>				
Healthy controls	23	3	2	1
Bipolar disorder	2	—	—	—
<i>Country</i>				
US/Canada	3	10	3	—
China	7	4	—	1
UK/Europe	5	4	1	—
Other <sup>b</sup>	9	5	3	1
NR	—	—	1	—
<i>Sample sizes (total N)</i>				
30–99	21	13	7	2
100–249	1	6	2	—
250–500	2	—	—	—
<i>Age (mean or median, years)</i>				
18–35	5	3	—	—
36–50	16	14	6	2
51–64	1	—	—	—
NR	2	2	3	—

	Diagnosis (Total = 24)	Response to Treatments		
		Antidepressants (Total = 19)	rTMS (Total = 9)	Other <sup>a</sup> (Total = 2)
<i>% Women</i>				
16–40	1	1	—	—
41–70	14	15	6	1
>70	3	2	—	1
NR	6	1	3	—
<i>Race reported?</i>				
	—	2	—	—
<i>Diagnosis/prognosis standards</i>				
Clinician interviews	9	—	—	—
Clinician assessments	14	17	7	2
Patient-reported outcomes	7	2	3	—
<i>Study design</i>				
Cross-sectional	24	—	—	—
Cohort/longitudinal observational	—	16	8	2
Randomized controlled trial	—	3	1	—
<i>Analytic methods</i>				
Sensitivity/specificity	23	—	2	—
Machine learning	17	5	3	2
Models validated	20	6	4	2

Notes. <sup>a</sup> Includes 1 study on outcomes after acupuncture and 1 on ketamine.

<sup>b</sup> Includes other countries not included in categories above, as well as studies done in multiple countries.

Abbreviations. NR=not reported; rTMS=repulsive transcranial magnetic stimulation.

## Other Neuroimaging Techniques (MEG, PET, and SPECT)

Eight eligible studies evaluated MEG for depression; 7 of these examined diagnosis and 1 addressed treatment response to antidepressants.<sup>55</sup> Five of these studies also used MRI-based imaging techniques. All diagnostic studies had healthy controls as comparators, and 1 also included individuals with bipolar disorder.<sup>56</sup> All studies were conducted in China or Taiwan and were very small (total  $N = 41$ – $108$ ). Participants were young (mean age range 30–37) and women were well represented (37–61% across studies). Six diagnostic studies were cross-sectional, and 1 was a longitudinal cohort.<sup>57</sup> All used structured interviews as the gold standard, and 6 also used HAM-D as the standardized clinician assessment. The prognostic study on outcomes with antidepressants also used HAM-D to define response.<sup>55</sup> Three studies used machine learning methods, and 6 validated models.

We also identified 4 studies that evaluated PET for diagnosis ( $k = 2$ ) or prognosis ( $k = 2$ ) in depression. Three of these also used structural MRI to improve localization of PET data.<sup>53,58,59</sup> Both diagnostic studies were cross-sectional and were conducted in the US.<sup>58,59</sup> Both prognostic studies evaluated response to antidepressants and occurred in Taiwan; 1 was an RCT<sup>53</sup> and the other an observational cohort.<sup>60</sup> All studies were similarly very small (total  $N = 36$ – $107$ ) and included mostly young adults (mean age range 32–43). None of the studies used machine learning methods and none conducted model validation.



Lastly, 3 eligible studies used SPECT for diagnosis ( $k = 1$ ) or prognosis ( $k = 2$ ). The diagnostic study was very large ( $N = 4,541$ ), conducted in the US, used a structured clinical interview (MINI) as the gold standard, and undertook model validation.<sup>61</sup> Both prognostic studies were conducted by one research group in France, evaluated response to rTMS, and also included participants with bipolar disorder.<sup>62,63</sup> They had small samples (total  $N = 33$ – $58$ ), and used patient-reported outcome (BDI) to determine response. None of the SPECT studies used a machine learning approach.

## BIPOLAR DISORDERS

Forty-seven eligible studies evaluated diagnosis ( $k = 41$ ) or prognosis ( $k = 6$ ) for bipolar disorders. More than half of studies also included participants with depression ( $k = 27$  for diagnostic studies, and all prognostic studies). Nearly all diagnostic studies used MRI-based techniques ( $k = 24$  for structural MRI,  $k = 19$  fMRI [13 resting and 6 task-specific],  $k = 3$  DTI, and  $k = 2$  ASL), with 1 of these also using MEG.<sup>56</sup> One study examined EEG for diagnosis.<sup>64</sup> Half included healthy controls ( $k = 23$ ), and half were very small with total  $N < 100$  ( $k = 23$ ). Only 3 studies had  $N > 250$  (range 251–441).<sup>65-67</sup> Most participants were young adults, with only 2 studies having mean ages of 45 or older.<sup>27,62,68</sup> Most studies had at least 40% women ( $k = 44$ ). The most common locations were China ( $k = 15$ ) and the US ( $k = 12$ ).

Most diagnostic studies were cross-sectional ( $k = 31$ ), while 3 were longitudinal (to confirm symptoms and diagnosis over 1–2 years).<sup>69-71</sup> About half of diagnostic studies used machine learning methods ( $k = 25$ ), and undertook model validation ( $k = 24$ ). Less than half used both structured clinical interviews (MINI and/or SCID) and standardized clinician assessments (Young Mania Rating Scale [YMRS]) as the diagnostic standard for bipolar disorder ( $k = 16$ ). Another 18 studies used only structured interviews, and 3 used only YMRS. One study did not specifically identify structured interviews or a standardized assessment, indicating only that diagnosis was completed by a psychiatrist.<sup>27</sup>

All prognostic studies were included above in results for depression. Briefly, 4 used MRI-based techniques to evaluate outcomes after ECT<sup>72-75</sup> and 2 used SPECT to examine response to rTMS.<sup>62,63</sup> These were all small studies (total  $N = 33$ – $122$ ) of middle-aged adults (mean age range 39–56). Three studies used machine learning and validated models.<sup>73-75</sup>

## POSTTRAUMATIC STRESS DISORDER

### Overview

Thirty eligible articles evaluated PTSD, with most focusing on diagnosis ( $k = 24$ ) (Table 5). The majority used MRI-based techniques, including fMRI ( $k = 11$ ), structural MRI ( $k = 7$ ), both structural MRI and fMRI ( $k = 1$ ), or fMRI and DTI ( $k = 1$ ). Remaining studies used PET ( $k = 1$ ), SPECT ( $k = 2$ ), MEG ( $k = 1$ ), or EEG ( $k = 5$ ). The majority were cross-sectional ( $k = 22$ ), with fewer being longitudinal cohorts ( $k = 6$ ) or RCT ( $k = 2$ ). Most were small, with the majority having  $N < 100$  ( $k = 17$ ). The remaining sample sizes were 116–432 ( $k = 12$ ) and 2,137 for 1 large database study.<sup>76</sup> Studies were conducted mostly in the US or Canada ( $k = 18$ ) and China ( $k = 7$ ); a few were conducted in the Netherlands ( $k = 2$ ), South Korea ( $k = 2$ ), and Iran ( $k = 1$ ). One third of the studies included US Veterans or active military ( $k = 10$ ), with half of these including combat-exposed Veterans or active military ( $k = 5$ ).

**Table 5. Summary of Characteristics of Included Studies Addressing Diagnosis of Posttraumatic Stress Disorder**

	sMRI (k = 6)	fMRI <sup>a</sup> (k = 9)	DTI (k = 1)	EEG (Total=5)	Others <sup>b</sup> (Total=6)
<i>Population characteristics</i>					
Veteran or active military	2	3	1	2	4
Combat exposed	2	2	1	2	2
Included TBI	1	2	1	1	2
Trauma-exposed controls	5	1	—	—	2
<i>Country</i>					
US/Canada	2	4	1	3	6
China	3	5	—	—	—
Other <sup>c</sup>	1	—	—	2	—
<i>Sample sizes (total N)</i>					
30–99	4	4	1	4	2
100–249	2	4	—	1	3
250–499	—	—	—	—	3
500–999	—	—	—	—	—
>1,000	—	1	—	—	—
<i>Age (mean or median, years)</i>					
26–44	4	7	—	4	5
45–64	2	—	—	1	—
NR	—	1	1	—	—
<i>% Women</i>					
0–15	2	2	—	3	—
16–40	1	1	—	—	3
41–70	3	3	—	1	2
>70	—	2	—	1	—
NR	—	1	1	—	—
<i>Race reported?</i>					
	1	1	—	—	3
<i>Diagnostic accuracy standard</i>					
Clinician interviews	4	3	—	3	4
Clinician assessments	5	7	1	2	3
Patient-reported outcomes	2	4	1	4	—
<i>Study design</i>					
Cross-sectional	5	8	1	5	6
Cohort/longitudinal	1	1	—	—	—
<i>Analytic methods</i>					
Sensitivity/specificity	3	5	—	5	3
Machine learning	3	4	—	2	2
Models validated	2	4	—	1	2

Notes. <sup>a</sup> All resting fMRI studies.

<sup>b</sup> Includes positron emission tomography (PET), single-photon emission computerized tomography (SPECT), and magnetoencephalography (MEG).

<sup>c</sup> Includes other countries not included in categories above.

*Abbreviations.* DTI=diffusion tensor imaging; EEG=electroencephalogram; MRI=magnetic resonance imaging (structural or functional); NR=not reported; TBI=traumatic brain injury; US=United States.

## MRI-based Techniques (Structural and Functional MRI, and DTI)

### Diagnosis

The majority of studies evaluating diagnosis for PTSD used MRI-based techniques ( $k = 14$ , Table 5). One of these used both MRI and MEG.<sup>77</sup> Most of these were cross-sectional ( $k = 12$ ), with only 2 being cohort studies.<sup>78,79</sup> The majority of these studies were small in size, with half having  $N < 100$  ( $k = 7$ ), half with  $N = 116-217$  ( $k = 6$ ), and 1 large database study with  $N = 2,137$  (this also included multiple mental health disorders).<sup>76</sup> Participants were mostly young adults (mean age range 32–45), and women were variably represented (eg, 6 studies with no women). Half were conducted in China ( $k = 7$ ), with the remaining from the US or Canada ( $k = 6$ ) and South Korea ( $k = 1$ ). The most commonly used diagnostic standards included structured interviews (SCID,  $k = 6$ ) and clinician assessments (Clinician Administered PTSD Scale [CAPS],  $k = 8$ ). Some also used patient-reported outcome measures such as the PTSD Checklist (PCL,  $k = 6$ ). Six studies used machine learning to develop their models. All 14 studies addressed the accuracy of their predictive models, and 6 undertook model validation (Table 5). Five studies included US Veterans or active military populations, with 3 of these including combat-exposed persons; more information about these studies is provided in the section below.

### Prognosis and Treatment Response

Six studies evaluated predictive models using structural MRI ( $k = 2$ )<sup>80,81</sup> or fMRI ( $k = 4$ ; 2 resting fMRI and 2 task-specific).<sup>82-85</sup> All studies reported on predictive models for response to psychotherapy as treatment for PTSD, using CAPS to assess PTSD severity (Table 6). One study included both psychotherapy and TMS.<sup>85</sup> Two studies were RCTs<sup>82,85</sup> and the remaining were cohorts. Sample sizes ranged from 53–135, with most having  $N < 100$  ( $k = 5$ ). All studies included relatively young adults, with mean ages below 40 years of age. One study used machine learning methods,<sup>84</sup> and 3 assessed model accuracy and validation.<sup>80,84,85</sup> Two studies included combat-exposed Veterans, both conducted in the Netherlands.<sup>80,81</sup>

**Table 6. Summary of Characteristics of Studies Evaluating MRI to Predict Response to Psychotherapy for Posttraumatic Stress Disorder**

	Response to Psychotherapy ( $k = 6$ )
<i>Population characteristics</i>	
Veteran or active military	3 <sup>a</sup>
Combat exposed	2 <sup>a</sup>
TBI	—
Comorbid alcohol use disorder	1
<i>Country</i>	
US	4
Netherlands	2

	Response to Psychotherapy ( <i>k</i> = 6)
<i>Sample sizes (total N)</i>	
30–99	5
100–140	1
<i>Age (mean or median, years)</i>	
18–25	1
26–44	4
45–64	—
>65	—
NR	1
<i>% Women</i>	
0–15	3
16–60	—
61–70	2
NR	1
<i>Race reported?</i>	
	1
<i>Study design</i>	
Cohort/longitudinal	4
RCT	2
<i>Measures of response or change</i>	
Clinician assessments	6
Patient-reported outcomes	1
<i>Analytic methods</i>	
Machine learning	1
Model accuracy assessed	3
Models validated	2

Notes. <sup>a</sup> Includes 1 non-US Veteran study.

Abbreviations. MRI=magnetic resonance imaging; NR=not reported; RCT=randomized controlled trial; TBI=traumatic brain injury.

## EEG and Evoked Potentials

Five studies evaluated EEG for PTSD and all focused on diagnosis (Table 5).<sup>47,86-89</sup> All were cross-sectional and only 1 had  $N > 100$  ( $N = 157$ ).<sup>47</sup> Most were conducted in the US ( $k = 3$ ), 1 in South Korea, and 1 in Iran. Most used clinical interviews (SCID [ $k = 3$ ] and/or CAPS [ $k = 2$ ]) as the diagnostic standard ( $k = 4$ ),<sup>47,86,87,89</sup> and 1 used only patient-reported measures.<sup>88</sup> All assessed sensitivity and specificity, but only 1 undertook model validation.<sup>86</sup>

## Other Neuroimaging Techniques (MEG, SPECT, PET)

Six studies evaluated other imaging techniques, including MEG ( $k = 3$ ),<sup>77,90,91</sup> SPECT ( $k = 2$ ),<sup>92,93</sup> and PET ( $k = 1$ )<sup>94</sup>; all of these focused on diagnosis of PTSD and were cross-sectional (Table 5). Most were conducted in the US ( $k = 5$ ), with  $N = 44-397$ . Three included US Veterans,<sup>90,91,93</sup> and 2 also had participants with TBI.<sup>92,93</sup> All used the SCID and/or CAPS as the diagnostic standard and assessed the accuracy of their models; 2 undertook model validation.<sup>90,91</sup>

## Studies in Veteran Populations

Thirteen studies were conducted in Veteran populations, most with US Veterans ( $k = 10$ )<sup>76,82,86,89-91,93,95-97</sup>, 2 with combat-exposed Veterans from the Netherlands,<sup>80,81</sup> and 1 included combat-exposed members of the Canadian Armed Forces.<sup>77</sup> We focus here on the 10 studies of US Veterans.

### *Diagnosis*

Of the 10 studies in US Veteran populations, most evaluated diagnosis ( $k = 9$ )<sup>76,86,89-91,93,95-97</sup>. About half used MRI-based techniques (structural MRI  $k = 1$ , fMRI  $k = 4$ , DTI  $k = 1$ ), while fewer used other methods (SPECT  $k = 1$ , MEG  $k = 2$ , EEG  $k = 2$ ). Half of studies were conducted in populations who were also diagnosed with TBI ( $k = 5$ ), all of which also included combat-exposed persons.<sup>76,86,89-91,93,95-97</sup> These were relatively small studies with  $N = 32-196$  and 4 studies with  $N < 100$ . The diagnostic standards included the SCID, CAPS, and patient-reported measures such as BDI, PCL, or PHQ. About half undertook model validation ( $k = 6$ ).

### *Prognosis and Treatment Response*

One small RCT ( $N = 53$ ), conducted in a comorbid population with PTSD and alcohol use disorder, used fMRI data to predict response to an integrated psychotherapy for both conditions.<sup>82</sup>

## TRAUMATIC BRAIN INJURY

### Overview

Of 12 articles that addressed TBI, most evaluated diagnosis ( $k = 10$ ) and the remaining 2 reported on prognosis of disability (Table 7). The majority used MRI-based techniques ( $k = 8$ ) and fewer used EEG ( $k = 2$ ), SPECT ( $k = 2$ ), and MEG ( $k = 1$ ). Most were cross-sectional ( $k = 10$ ), small in size (eg, 9 studies with  $N < 100$ ), and included younger populations (mean age  $< 45$ ). Half of the studies included PTSD populations; all of these focused on diagnosis and were cross-sectional, and 5 evaluated combat-exposed US Veterans.

**Table 7. Summary of Characteristics of Included Studies Addressing Traumatic Brain Injury**

	Diagnosis (k = 10)	Prediction of Disability (k = 2)
<i>Neuroimaging/neurophysiologic technique</i>		
Structural MRI	3	2
Functional MRI	2	—
DTI	2	—
SPECT	2	—
MEG	1	—
EEG	2	—
<i>Population characteristics</i>		
Veterans and/or active military	7	—
Combat exposed	7	—
PTSD	6	—
<i>Country</i>		
US	10	—
Other <sup>a</sup>	—	2
<i>Sample sizes (total N)</i>		
30–99	5	2
100–199	2	—
>200	1	—
<i>Age (mean or median, years)</i>		
18–25	—	—
26–44	8	2
45–64	1	—
>65	—	—
NR	1	—
<i>% Women</i>		
0–15	6	—
16–40	3	1
NR	1	1
<i>Race reported?</i>	6	—
<i>Diagnosis/prognosis standard</i>		
Clinician interviews	4	—
Clinician assessments	6	2
Patient-reported outcomes	5	—
Hospital records	1	—
<i>Study design</i>		
Cross-sectional	10	—
Cohort/longitudinal	—	2

	Diagnosis ( <i>k</i> = 10)	Prediction of Disability ( <i>k</i> = 2)
<i>Analytic methods</i>		
Sensitivity/specificity (or PPV/NPV)	7	—
Machine learning	—	1
Models validated	3	—

Notes. <sup>a</sup> Includes Taiwan and Norway.

Abbreviations. DTI=diffusor tensor imaging; EEG=electroencephalogram; fMRI=functional magnetic resonance imaging; MEG=magnetoencephalography; MRI=magnetic resonance imaging; NPV=negative predictive value; PPV=positive predictive value; PTSD=posttraumatic stress disorder; RCT=randomized controlled trial; SPECT=single-photon emission computerized tomography.

## MRI-based Techniques (Structural and Functional MRI, DTI, and ASL)

### Diagnosis

The majority of identified studies evaluating diagnosis for TBI used MRI-based techniques (*k* = 6), including structural MRI (*k* = 3),<sup>95,98,99</sup> fMRI (*k* = 2, both resting fMRI),<sup>96,97</sup> and DTI (*k* = 2).<sup>96,100</sup> One study also included MEG.<sup>99</sup> All were cross-sectional studies conducted in the US. Diagnostic standards included patient-reported measures (*k* = 5), clinician assessments (*k* = 5), and structured clinical interviews (*k* = 1). Half assessed sensitivity and specificity (*k* = 3), and 2 undertook model validation. Most were small, with *N* < 100 (*k* = 5). Most included populations of US combat-exposed Veterans (*k* = 5).

### Prognosis and Treatment Response

Both studies evaluating prognosis for TBI used MRI-based techniques. One was conducted in Taiwan<sup>101</sup> and the other in Norway.<sup>102</sup> Both were small cohort studies (*N* = 47–70) and investigated predictive models for global disability at least 1 year after injury, measured using the Glasgow Outcome Scale-Extended (GOSE). None included Veteran or active military populations.

## EEG and Other Neuroimaging Techniques

Two cross-sectional US-based studies evaluated EEG and both focused on diagnosis of TBI.<sup>89,103</sup> One used hospital records as the indicator for TBI,<sup>103</sup> and the other used the SCID.<sup>89</sup> Both assessed sensitivity and specificity, but only 1 undertook model validation. Both were very small (*N* = 30–32). Two studies used SPECT to address diagnosis for TBI.<sup>92,93</sup> Both included participants with PTSD, and are described in the PTSD section above.

## Studies in Veteran Populations

Seven studies included combat-exposed US Veteran populations.<sup>89,93,95-97,99,100</sup> All focused on diagnosis and were cross-sectional, with most using MRI-based techniques (*k* = 5). One each used EEG, SPECT, or MEG (this study also used MRI). Most of these included participants with co-occurring PTSD and are described above (*k* = 5).<sup>89,93,95-97</sup> The other 2 studies also had small samples (*N* = 84–109) of young and middle-aged adults (mean age 28–48).<sup>99,100</sup>

## SUBSTANCE USE DISORDERS

### Overview

Twenty studies addressed SUD, with the majority evaluating alcohol use disorder ( $k = 12$ ) (Table 8).<sup>82,104-114</sup> Remaining studies focused on cocaine use disorder ( $k = 3$ ),<sup>115-117</sup> opioid use disorder ( $k = 2$ ),<sup>118,119</sup> and methamphetamine use disorder ( $k = 3$ ).<sup>120-122</sup> More than half used structural and/or functional MRI ( $k = 12$ ) or other MRI-based techniques (ASL,  $k = 2$ ).<sup>117,121</sup> Eight evaluated EEG or evoked potentials<sup>98-100,102,104,105,110,111</sup>; none used any other imaging techniques. About half focused on diagnosis ( $k = 9$ ),<sup>105,106,108,110,112,114,118,119,121</sup> while the rest evaluated prediction of relapse ( $k = 6$ ) or treatment response ( $k = 5$ ).<sup>82,104,107,109,111,113,115-117,120,122</sup> Most evaluated the accuracy of their diagnostic or prognostic models ( $k = 16$ ), and nearly half undertook model validation ( $k = 8$ ). Most studies were very small with  $N < 100$  ( $k = 14$ ); 1 study had a total sample greater than 1000 ( $N = 1,376$ ).<sup>107</sup> About half used machine learning methods to develop models ( $k = 11$ ). Studies were most commonly conducted in the US ( $k = 10$ ) and China ( $k = 3$ ).

**Table 8. Summary of Characteristics of Included Studies Addressing Substance Use Disorder**

	Diagnosis ( $k = 9$ )	Prognosis	
		Prediction of Relapse ( $k = 6$ )	Response to Treatment ( $k = 5$ )
<i>Neuroimaging/Neurophysiologic technique</i>			
Structural MRI	2	1	2
Functional MRI	1	3	4
ASL	1	—	1
EEG	6	2	—
<i>Substance</i>			
Alcohol	6	4	2
Opioid	2	—	—
Methamphetamine	1	1	1
Cocaine	—	1	2
<i>Population characteristics</i>			
Veterans and/or active military	—	1	2
Inpatient or residential treatment	4	2	3
<i>Country</i>			
US	2	4	4
China	2	—	1
Europe	—	2	—
Other <sup>a</sup>	5	—	—
<i>Sample sizes (total N)</i>			
30–99	6	4	4
100–200	3	1	1
>1,000	—	1	—



	Diagnosis ( <i>k</i> = 9)	Prognosis	
		Prediction of Relapse ( <i>k</i> = 6)	Response to Treatment ( <i>k</i> = 5)
<i>Age (mean or median, years)</i>			
18–25	—	—	—
26–44	5	5	4
45–64	3	—	1
NR	1	1	—
<i>% Women</i>			
0–15	4	1	2
16–40	1	5	3
41–70	2	—	—
NR	2	—	—
<i>Race reported?</i>	1	—	1
<i>Included information on genetics?</i>	—	1	—
<i>Study design</i>			
Cohort/longitudinal	—	2	1
Cross-sectional	9	—	—
RCT	—	—	1
<i>Analytic methods</i>			
Machine learning	6	4	1
Model accuracy assessed	9	4	3
Models validated	5	2	1

Notes. <sup>a</sup>Includes Turkey, Malaysia and India.

Abbreviations. ASL=arterial spin labeling; EEG= electroencephalogram; MRI=magnetic resonance imaging (structural or functional); NR=not reported; RCT=randomized controlled trial.

## MRI-based Techniques (Structural and Functional MRI, and ASL)

Twelve studies used MRI-based techniques for diagnosis of SUD (*k* = 3), or prognosis (*k* = 9) (Table 8). Four used structural MRI,<sup>105,111,115,121</sup> 7 used fMRI (5 resting and 2 task-specific),<sup>82,104,109,114,116,120,122</sup> and 1 used MRI, resting fMRI, and ASL.<sup>117</sup> Six evaluated alcohol use disorder,<sup>82,104,105,109,111,114</sup> 3 addressed methamphetamine use,<sup>120-122</sup> and 3 examined cocaine use.<sup>115-117</sup> Three-quarters evaluated participants in residential or inpatient treatment (*k* = 8). The most common locations were the US (*k* = 8) and China (*k* = 3). All studies were small, with *N* = 45–188. Seven used machine learning and 5 undertook model validation.

## EEG and Evoked Potentials

Eight studies used EEG data: 6 for diagnosis of SUD<sup>106,108,110,112,118,119</sup> and 2 for predicting abstinence over a year or more.<sup>107,113</sup> Most studies addressed alcohol use disorder (*k* = 6),<sup>106-108,110,112,113</sup> while the remaining 2 examined opioid use disorder.<sup>118,119</sup> Four studies used machine learning and 3 undertook model validation.

## Studies in Veteran Populations

Three studies included US Veteran populations and all focused on prognosis and treatment response. One was an RCT including participants with comorbid PTSD and alcohol use disorder,<sup>82</sup> while the other 2 were cohort studies including both Veteran and civilian populations.<sup>111,122</sup> One of these also addressed alcohol use disorder<sup>111</sup> and the other examined methamphetamine use disorder.<sup>122</sup> All three used structural MRI or fMRI. Two evaluated prediction of relapse<sup>111,122</sup> and 1 focused on response to psychotherapy.<sup>82</sup> None validated their predictive models.

## OBSESSIVE COMPULSIVE DISORDER (OCD) AND ANXIETY DISORDERS

### Obsessive Compulsive Disorder

#### Diagnosis

Seventeen studies focused on diagnosis of OCD, with 4 using structural MRI data,<sup>123-126</sup> 11 using resting fMRI,<sup>127-137</sup> and 1 each with DTI<sup>138</sup> and EEG<sup>139</sup> (Table 9). Eleven used SCID as the diagnostic standard,<sup>123-127,131,134-138</sup> while 14 studies used the Yale Brown Obsessive Compulsive Scale (Y-BOCS).<sup>123-132,134,135,137,138</sup> Nearly all studies assessed sensitivity and specificity ( $k = 14$ ) and evaluated model accuracy ( $k = 14$ ). Seven studies undertook model validation and 5 used machine learning. All studies had  $N < 200$  and included young adults. Half had 16–40% women participants ( $k = 9$ ), and 6 included 41–70% women. Most included healthy controls as the comparator ( $k = 14$ ) and were conducted in China ( $k = 14$ ).

#### Prognosis & Treatment Response

Only 2 studies evaluated prognosis of OCD; 1 Korean study employed structural MRI to predict response to psychotherapy,<sup>140</sup> and 1 US study used fMRI to examine response to antidepressants (Table 9).<sup>141</sup> Both studies used machine learning analyses and validated models. Total study sample sizes were 42 and 131, and both included young adults and substantial proportions of women (38–52%).

**Table 9. Characteristics of Included Studies Addressing Obsessive Compulsive Disorder**

	Diagnosis ( $k = 17$ )	Treatment Response ( $k = 2$ )
<i>Neuroimaging/Neurophysiologic technique</i>		
Structural MRI	5	1
Functional MRI (fMRI)	12	1
DTI	1	—
EEG	1	—
<i>Other groups included</i>		
Healthy controls	14	1
Unmedicated controls	1	—

	Diagnosis ( <i>k</i> = 17)	Treatment Response ( <i>k</i> = 2)
<i>Country</i>		
US	—	1
China	14	—
UK/Europe	—	—
Other <sup>a</sup>	3	1
<i>Sample sizes (total N)</i>		
30–99	7	1
100–249	9	1
<i>Age (mean or median, years)</i>		
18–25	3	1
26–44	13	1
NR	1	—
<i>% Women</i>		
16–40	9	1
41–70	7	2
NR	1	—
<i>Race reported?</i>		
	1	—
<i>Diagnosis/prognosis standards</i>		
Clinician interviews	12	—
Clinician assessments	8	1
Patient-reported outcomes	16	1
<i>Study design</i>		
Cross-sectional	16	—
Cohort/longitudinal observational	1	2
<i>Analytic approach</i>		
Sensitivity/specificity	15	—
Machine learning	7	2
Models validated	8	—

Notes. <sup>a</sup>Includes Turkey, Korea, Japan.

Abbreviations. DTI=diffusion tensor imaging; EEG=electroencephalogram; MRI=magnetic resonance imaging; NR=not reported.

## Anxiety Disorders

### Diagnosis

Four studies addressed diagnosis of anxiety disorders, all using either structural MRI (*k* = 1)<sup>142</sup> or fMRI (*k* = 3; 1 resting and 2 task-specific) (Table 10).<sup>143-145</sup> All studies used the SCID and/or the Hamilton Anxiety Rating Scale (HAM-A) as the diagnostic standards. Three studies were cross-sectional<sup>142-144</sup> and 1 was a cohort.<sup>145</sup> All evaluated the sensitivity, specificity, and accuracy of models, and 3 undertook model validation. Two studies used machine learning. Sample sizes were small (*N* = 40–93) and included young adults with substantial representation of women.

### Prognosis and Treatment Response

Six studies evaluated prognosis in anxiety disorders, with 2 using structural MRI<sup>146,147</sup> and 4 fMRI (all task-specific)<sup>83,148-150</sup> (Table 10). Specific disorders examined were general anxiety disorder ( $k = 4$ ),<sup>83,146-148</sup> social anxiety disorder ( $k = 1$ ),<sup>149</sup> and panic disorder ( $k = 2$ ).<sup>83,150</sup> Four studies addressed response to psychotherapy,<sup>83,147,149,150</sup> 1 evaluated outcomes after antidepressant therapy,<sup>146</sup> and 1 examined response to a computer-based behavioral intervention.<sup>148</sup> Sample sizes ranged from 34–135, most participants were young adults, and most studies had more than 50% women ( $k = 5$ ).<sup>83,146,148-150</sup> Four studies were conducted in the US,<sup>83,147-149</sup> while the other 2 occurred in Europe.<sup>146,150</sup> Most studies assessed model accuracy and undertook model validation ( $k = 5$ ).<sup>146-150</sup> Two studies used machine learning.<sup>146,150</sup>

**Table 10. Characteristics of Included Studies Addressing Anxiety Disorders**

	Diagnosis ( $k = 4$ )	Treatment Response ( $k = 6$ )
<i>Anxiety disorder</i>		
Generalized anxiety disorder	3	4
Social anxiety disorder	1	1
Panic disorder	1	2
<i>Neuroimaging/neurophysiologic technique</i>		
Structural MRI	1	2
Functional MRI	3	4
<i>Other groups included</i>		
Healthy controls	4	1
Unmedicated controls	—	1
<i>Country</i>		
US	2	4
China	2	—
UK/Europe	—	2
<i>Sample sizes (total N)</i>		
30–99	4	5
100–249	—	1
<i>Age (mean or median, years)</i>		
18–25	2	2
26–44	1	4
NR	1	—
<i>% Women</i>		
16–40	1	1
41–70	2	3
>70	1	1
<i>Race reported?</i>	1	2

	Diagnosis ( <i>k</i> = 4)	Treatment Response ( <i>k</i> = 6)
<i>Diagnosis/prognosis standards</i>		
Clinician interviews	3	—
Clinician assessments	3	3
Patient-reported outcomes	3	2
<i>Study design</i>		
Cross-sectional	3	—
Cohort/longitudinal observational	1	6
<i>Analytic approach</i>		
Sensitivity/specificity	4	—
Machine learning	2	2
Models validated	2	5

*Abbreviations.* MRI=magnetic resonance imaging; NR=not reported.

## SYSTEMATIC REVIEWS

We identified 30 eligible systematic reviews. Consistent with our findings for primary studies, the majority of reviews addressed depression (*k* = 17) with fewer evaluating the other conditions: anxiety disorders (*k* = 3), bipolar disorders (*k* = 4), PTSD (*k* = 2), TBI (*k* = 3), or OCD (*k* = 1). No eligible review addressed SUD, and none reported on more than 1 condition (Table 11). Most systematic reviews included MRI-based techniques (*k* = 16) or a number of neuroimaging or neurophysiologic data (*k* = 7). Fewer focused on EEG (*k* = 5), PET (*k* = 1), or SPECT (*k* = 1).

About half of reviews examined diagnosis (*k* = 16), 15 addressed response to treatment, and 3 evaluated change in symptoms or functioning. Four reviews reported on both diagnosis and prognosis (Table 11).<sup>151-154</sup>

The number of studies included by reviews varied widely, ranging from 11–352. Eight reviews included less than 20 primary studies, 10 reviews included 20-49, 10 reviews had 50-99, and 2 reviews included ≥100 primary studies. One was an umbrella review that included 24 other systematic reviews, comprising 352 individual primary studies.<sup>155</sup>

Appendix E provides detailed characteristics of eligible systematic review, including condition studied, outcomes reported, and number of studies included.

**Table 11. Summary of Eligible Systematic Reviews**

	Depression ( <i>k</i> = 17)	Bipolar Disorders ( <i>k</i> = 4)	PTSD ( <i>k</i> = 2)	TBI ( <i>k</i> = 3)	OCD ( <i>k</i> = 1)	Anxiety Disorders ( <i>k</i> = 3)
Diagnosis	9	3	1	2	1	2
<i>Prognosis</i>						
Response to treatment	11	2	—	—	—	1
Change in symptoms or functioning	1	—	1	1	—	—

*Abbreviations.* OCD=obsessive compulsive disorder; PTSD=posttraumatic stress disorder; TBI=traumatic brain injury.

## DISCUSSION

### SUMMARY OF KEY FINDINGS

To assist the VA with determining next steps in the application of precision medicine to Veterans' healthcare and research, we conducted an evidence map of neuroimaging and neurophysiologic biomarkers in mental health and TBI. We identified 313 eligible primary studies and 30 eligible systematic reviews. The majority of primary studies (70%) and reviews (57%) addressed depression, while fewer studies and reviews examined other conditions of interest. Most primary studies used MRI-based neuroimaging techniques (75%) and a fifth employed EEG (22%). Two-thirds of primary studies (64%) focused on diagnosis for conditions of interest, and nearly all of these (91%) were cross-sectional. Half of primary studies (52%) employed machine learning to analyze neuroimaging or neurophysiologic data and develop diagnostic or prognostic models. Primary studies generally included young and middle-aged adults, with only 5 studies having participants with mean ages of 65 or older. Studies were conducted in diverse locations around the world, with the most common being China (35%) and the US or Canada (30%); very few studies (5%) were conducted in more than 1 country. Overall, most of the evidence came from very small studies. For example, among 98 studies using structural and/or functional MRI to address diagnosis for depression, 51% had less than 100 participants, while only 5% had 500 or more participants. Only 14 primary studies included US Veterans or active military service members; 12 addressed PTSD and/or TBI, and 2 evaluated SUD.

Key findings for primary studies include:

- Many studies evaluated the use of structural or functional MRI in diagnosis and prognosis of depression, but there were important methodological concerns:
  - Nearly all diagnostic studies were cross-sectional, small in size, and included participants with variable past histories of symptoms and treatments.
  - Prognostic studies mostly focused on response to antidepressants, and were also generally small.
- A substantial number of studies used EEG for diagnosis and prognosis of depression, but these had similar methodological issues as noted above.
- Most studies on bipolar disorder were small and cross-sectional, included participants with depression, and focused on diagnosis.
- Studies evaluating PTSD were small and cross-sectional, and mainly used structural or functional MRI to address diagnosis.
- Studies examining TBI were small and cross-sectional, often included participants with co-occurring PTSD, and mainly used structural or functional MRI to address diagnosis.
- Studies on SUD used structural or functional MRI and EEG, most addressed alcohol use disorder, and half evaluated prediction of relapse or response to treatment.
- Studies on OCD and anxiety disorders were small and cross-sectional, mainly used structural or functional MRI, and focused on diagnosis.

- Fourteen studies included US Veterans, addressing PTSD and/or TBI, or SUD:
  - All 11 diagnostic studies were cross-sectional, 2 prognostic studies were cohorts, and 1 was an RCT.
- None evaluated prediction of adverse or side effects from treatments.

## IMPLICATIONS FOR VA POLICY

We found a large number of studies mainly using MRI-based techniques to evaluate diagnosis and prognosis for depression, but there were substantial methodological limitations for the majority of this evidence. Additionally, none of the depression studies were conducted with US Veterans or military service members. Given that neuroimaging tests are costly and time-consuming to conduct (and analyze), it is not clear that using such tests adds value in the clinical setting or that they could replace current standards for diagnosis of depression, which involve structured interviews and clinician assessments. Regarding prognosis, neuroimaging techniques may potentially aid in predicting early response and/or selection of appropriate therapies, but most studies included participants with variable histories of symptoms and past treatments. Only 2 studies focused on participants with their first episode of depression. Furthermore, no study evaluated prediction of adverse or side effects of treatments, whereas this is often an important factor in patient and clinician decisions to stop or switch antidepressants. There were fewer studies using EEG to examine depression, and this evidence base has similar limitations as that evaluating MRI-based techniques. Thus, it is unclear how these data could be incorporated into current clinical practice to improve diagnosis or treatment selection and/or monitoring for depression. Future systematic reviews focused on these techniques for diagnosis and/or prognosis in depression may also be needed to better characterize their potential utility for clinical care.

We found considerably less evidence addressing other mental health conditions and TBI, and fewer studies using other neuroimaging and neurophysiologic techniques. Although there were some studies on PTSD, TBI, and SUD that included US Veterans or military service members; overall, these shared the same methodological limitations as noted above. Therefore, it also appears premature to implement MRI (and other neuroimaging and neurophysiologic techniques) in the clinical diagnosis and treatment of these other conditions.

## GAPS IN EVIDENCE AND FUTURE RESEARCH

As noted above, there are important methodological concerns regarding the evidence on neuroimaging and neurophysiological techniques for evaluating diagnosis and prognosis of mental health conditions and TBI. While there are a large number of studies examining depression (using MRI or EEG), these are largely small in sample size and the majority used cross-sectional data to evaluate diagnosis. Additionally, participants often had variable trajectories of symptoms and treatments preceding data collection. These study design issues have been previously noted as contributing to problems with replicability and validity of neuroimaging and neurophysiologic studies in mental health.<sup>15,18,156</sup> Whereas most of the identified primary studies had less than 100 participants, current estimates are that thousands of individuals are needed to provide stable and valid results regarding important associations between neuroimaging findings and clinical phenotypes.<sup>15</sup> Furthermore, to account for changes in brain structure and functioning over time, current recommendations are to use comparisons

with age-standardized findings (developed from large populations),<sup>18</sup> instead of using data from small samples of age-matched controls. To better understand clinical phenotypes, it is also important to have longitudinal data on symptoms and exposures, in addition to considering transdiagnostic dimensional approaches.<sup>157-159</sup> Having data before certain exposures may be particularly important for studies evaluating PTSD and TBI.

The acquisition and analysis of (longitudinal) data from a large number of individuals will likely require large ongoing investments in this research, as well as fundamental changes in research organization and incentives that currently promote competition and inhibit data sharing.<sup>16,17,160</sup> Current projects that exemplify the level of resources, organization, and cooperation needed for such efforts include the Adolescent Brain Cognitive Development (ABCD) study in the US<sup>161</sup> and the UK Biobank.<sup>162</sup>

Therefore, we recommend the following for future research:

- Consider investment in larger studies (thousands of participants) to identify reproducible and precise associations between neuroimaging and neurophysiologic findings and mental health phenotypes.
- Conduct longitudinal studies with data on exposures, symptoms, and neuroimaging and neurophysiologic data over the life course.
- Consider transdiagnostic approaches for describing mental health phenotypes.
- Particularly for addressing Veterans' health and outcomes, develop longitudinal studies with initial data that precede combat and other service-related exposures.

## LIMITATIONS

We sought to identify and describe the evidence for a broad range of neuroimaging and neurophysiologic tests used to evaluate the diagnosis and prognosis of a large number of mental health conditions and TBI. Therefore, we conducted an evidence map that provides descriptive information about research studies examining these questions and highlights gaps in the existing evidence. Thus, we did not abstract detailed results on the factors included, nor performance metrics of, diagnostic or prognostic models using neuroimaging and/or neurophysiologic data. We also did not formally evaluate the quality of included primary studies or systematic reviews. Additionally, we employed machine learning techniques to assist with the selection of relevant studies and reviews; it is possible that we may have missed some eligible studies. We also limited our search of the evidence to English language studies and reviews.

## CONCLUSIONS

Most existing evidence on neuroimaging and neurophysiologic data for mental health conditions evaluated use of MRI for diagnosis and prognosis in depression. In addition to the lack of evidence on other conditions or using other types of neuroimaging and neurophysiologic data, existing studies were limited by small sample sizes and cross-sectional designs. These methodological concerns need to be addressed by future research using larger samples with longitudinal data. Existing evidence gaps and limitations indicate that it may be premature to apply neuroimaging and neurophysiologic tests to evaluate and treat mental health conditions and TBI in clinical settings.



## REFERENCES

1. Trivedi RB, Post EP, Sun H, et al. Prevalence, Comorbidity, and Prognosis of Mental Health Among US Veterans. *Am J Public Health*. 2015;105(12):2564-2569.
2. Seal KH, Metzler TJ, Gima KS, Bertenthal D, Maguen S, Marmar CR. Trends and risk factors for mental health diagnoses among Iraq and Afghanistan veterans using Department of Veterans Affairs health care, 2002-2008. *Am J Public Health*. 2009;99(9):1651-1658.
3. In: *Treatment for Posttraumatic Stress Disorder in Military and Veteran Populations: Final Assessment*. Washington (DC)2014.
4. Kessler RC, Bromet EJ. The epidemiology of depression across cultures. *Annu Rev Public Health*. 2013;34:119-138.
5. World Health Organization. Depression and other common mental disorders. <https://www.who.int/publications/i/item/depression-global-health-estimates>. Published 2017. Accessed September 12, 2022.
6. Zhdanova M, Pilon D, Ghelerter I, et al. The Prevalence and National Burden of Treatment-Resistant Depression and Major Depressive Disorder in the United States. *J Clin Psychiatry*. 2021;82(2).
7. Department of Veterans Affairs. FY 2023 Budget Submission for Medical Programs and Information Technology Programs. <https://www.va.gov/budget/docs/summary/fy2023-va-budget-volume-ii-medical-programs-and-information-technology.pdf>. Published 2022. Accessed September 12, 2022.
8. Stein MB, Levey DF, Cheng Z, et al. Genome-wide association analyses of post-traumatic stress disorder and its symptom subdomains in the Million Veteran Program. *Nat Genet*. 2021;53(2):174-184.
9. Department of Veterans Affairs. Million Veteran Program. <https://www.mvp.va.gov/pwa/>. Accessed September 12, 2022.
10. Bode AM, Dong Z. Recent advances in precision oncology research. *NPJ Precis Oncol*. 2018;2:11.
11. Nadauld LD, Ford JM, Pritchard D, Brown T. Strategies For Clinical Implementation: Precision Oncology At Three Distinct Institutions. *Health Aff (Millwood)*. 2018;37(5):751-756.
12. Fernandes BS, Williams LM, Steiner J, Leboyer M, Carvalho AF, Berk M. The new field of 'precision psychiatry'. *BMC Med*. 2017;15(1):80.
13. Williams LM. Precision psychiatry: a neural circuit taxonomy for depression and anxiety. *Lancet Psychiatry*. 2016;3(5):472-480.
14. Benkarim O, Paquola C, Park BY, et al. Population heterogeneity in clinical cohorts affects the predictive accuracy of brain imaging. *PLoS Biol*. 2022;20(4):e3001627.
15. Marek S, Tervo-Clemmens B, Calabro FJ, et al. Reproducible brain-wide association studies require thousands of individuals. *Nature*. 2022;603(7902):654-660.
16. Specht K. Current Challenges in Translational and Clinical fMRI and Future Directions. *Front Psychiatry*. 2019;10:924.
17. White T, Blok E, Calhoun VD. Data sharing and privacy issues in neuroimaging research: Opportunities, obstacles, challenges, and monsters under the bed. *Hum Brain Mapp*. 2022;43(1):278-291.
18. Bethlehem RAI, Seidlitz J, White SR, et al. Brain charts for the human lifespan. *Nature*. 2022;604(7906):525-533.

19. Commander John Scott Hannon Veterans Mental Health Care Improvement Act of 2019. <https://www.govinfo.gov/content/pkg/PLAW-116publ171/pdf/PLAW-116publ171.pdf>. Accessed September 12, 2022.
20. Bragge P, Clavisi O, Turner T, Tavender E, Collie A, Gruen RL. The Global Evidence Mapping Initiative: scoping research in broad topic areas. *BMC Med Res Methodol*. 2011;11:92.
21. Miake-Lye IM, Hempel S, Shanman R, Shekelle PG. What is an evidence map? A systematic review of published evidence maps and their definitions, methods, and products. *Syst Rev*. 2016;5:28.
22. Runia N, Yucel DE, Lok A, et al. The neurobiology of treatment-resistant depression: A systematic review of neuroimaging studies. *Neurosci Biobehav Rev*. 2022;132:433-448.
23. Karim HT, Wang M, Andreescu C, et al. Acute trajectories of neural activation predict remission to pharmacotherapy in late-life depression. *Neuroimage Clin*. 2018;19:831-839.
24. Lebedeva AK, Westman E, Borza T, et al. MRI-Based Classification Models in Prediction of Mild Cognitive Impairment and Dementia in Late-Life Depression. *Front Aging Neurosci*. 2017;9:13.
25. Patel MJ, Andreescu C, Price JC, Edelman KL, Reynolds CF, 3rd, Aizenstein HJ. Machine learning approaches for integrating clinical and imaging features in late-life depression classification and response prediction. *Int J Geriatr Psychiatry*. 2015;30(10):1056-1067.
26. Taylor WD, McQuoid DR, Payne ME, Zannas AS, MacFall JR, Steffens DC. Hippocampus atrophy and the longitudinal course of late-life depression. *Am J Geriatr Psychiatry*. 2014;22(12):1504-1512.
27. Niida A, Niida R, Matsuda H, Inada T, Motomura M, Uechi A. Identification of atrophy of the subgenual anterior cingulate cortex, in particular the subcallosal area, as an effective auxiliary means of diagnosis for major depressive disorder. *Int J Gen Med*. 2012;5:667-674.
28. Bi K, Luo G, Tian S, et al. An enriched granger causal model allowing variable static anatomical constraints. *Neuroimage Clin*. 2019;21:101592.
29. Deng F, Wang Y, Huang H, et al. Abnormal segments of right uncinate fasciculus and left anterior thalamic radiation in major and bipolar depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2018;81:340-349.
30. Schnyer DM, Clasen PC, Gonzalez C, Beevers CG. Evaluating the diagnostic utility of applying a machine learning algorithm to diffusion tensor MRI measures in individuals with major depressive disorder. *Psychiatry Res Neuroimaging*. 2017;264:1-9.
31. Bi K, Hua L, Wei M, Qin J, Lu Q, Yao Z. Dynamic functional-structural coupling within acute functional state change phases: Evidence from a depression recognition study. *J Affect Disord*. 2016;191:145-155.
32. Korgaonkar MS, Cooper NJ, Williams LM, Grieve SM. Mapping inter-regional connectivity of the entire cortex to characterize major depressive disorder: a whole-brain diffusion tensor imaging tractography study. *Neuroreport*. 2012;23(9):566-571.
33. He Z, Sheng W, Lu F, et al. Altered resting-state cerebral blood flow and functional connectivity of striatum in bipolar disorder and major depressive disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2019;90:177-185.
34. Almeida JR, Mourao-Miranda J, Aizenstein HJ, et al. Pattern recognition analysis of anterior cingulate cortex blood flow to classify depression polarity. *Br J Psychiatry*. 2013;203(3):310-311.

35. Schmaal L, Marquand AF, Rhebergen D, et al. Predicting the Naturalistic Course of Major Depressive Disorder Using Clinical and Multimodal Neuroimaging Information: A Multivariate Pattern Recognition Study. *Biol Psychiatry*. 2015;78(4):278-286.
36. Braund TA, Breukelaar IA, Griffiths K, et al. Intrinsic Functional Connectomes Characterize Neuroticism in Major Depressive Disorder and Predict Antidepressant Treatment Outcomes. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2022;7(3):276-284.
37. Korgaonkar MS, Goldstein-Piekarski AN, Fornito A, Williams LM. Intrinsic connectomes are a predictive biomarker of remission in major depressive disorder. *Mol Psychiatry*. 2020;25(7):1537-1549.
38. Gyurak A, Patenaude B, Korgaonkar MS, Grieve SM, Williams LM, Etkin A. Frontoparietal Activation During Response Inhibition Predicts Remission to Antidepressants in Patients With Major Depression. *Biol Psychiatry*. 2016;79(4):274-281.
39. Williams LM, Korgaonkar MS, Song YC, et al. Amygdala Reactivity to Emotional Faces in the Prediction of General and Medication-Specific Responses to Antidepressant Treatment in the Randomized iSPOT-D Trial. *Neuropsychopharmacology*. 2015;40(10):2398-2408.
40. Grieve SM, Korgaonkar MS, Etkin A, et al. Brain imaging predictors and the international study to predict optimized treatment for depression: study protocol for a randomized controlled trial. *Trials*. 2013;14:224.
41. Drysdale AT, Grosenick L, Downar J, et al. Resting-state connectivity biomarkers define neurophysiological subtypes of depression. *Nat Med*. 2017;23(1):28-38.
42. Zhang Y, Kong Y, Liu X, et al. Desynchronized Functional Activities Between Brain White and Gray Matter in Major Depression Disorder. *J Magn Reson Imaging*. 2021;53(5):1375-1386.
43. Tian S, Sun Y, Shao J, et al. Predicting escitalopram monotherapy response in depression: The role of anterior cingulate cortex. *Hum Brain Mapp*. 2020;41(5):1249-1260.
44. Liu S, Liu X, Yan D, et al. Alterations in Patients With First-Episode Depression in the Eyes-Open and Eyes-Closed Conditions: A Resting-State EEG Study. *IEEE Trans Neural Syst Rehabil Eng*. 2022;30:1019-1029.
45. Li X, La R, Wang Y, et al. EEG-based mild depression recognition using convolutional neural network. *Med Biol Eng Comput*. 2019;57(6):1341-1352.
46. Wu CT, Huang HC, Huang S, et al. Resting-State EEG Signal for Major Depressive Disorder Detection: A Systematic Validation on a Large and Diverse Dataset. *Biosensors (Basel)*. 2021;11(12).
47. Shim M, Jin MJ, Im CH, Lee SH. Machine-learning-based classification between post-traumatic stress disorder and major depressive disorder using P300 features. *Neuroimage Clin*. 2019;24:102001.
48. Ding X, Yue X, Zheng R, Bi C, Li D, Yao G. Classifying major depression patients and healthy controls using EEG, eye tracking and galvanic skin response data. *J Affect Disord*. 2019;251:156-161.
49. Fan X, Huang X, Zhao Y, Wang L, Yu H, Zhao G. Predicting Prognostic Effects of Acupuncture for Depression Using the Electroencephalogram. *Evid Based Complement Alternat Med*. 2022;2022:1381683.
50. Zehong C, Chin-Teng L, Weiping D, Mu-Hong C, Cheng-Ta L, Tung-Ping S. Identifying Ketamine Responses in Treatment-Resistant Depression Using a Wearable Forehead EEG. *IEEE Trans Biomed Eng*. 2019;66(6):1668-1679.

51. Isserles M, Daskalakis ZJ, George MS, Blumberger DM, Sackeim HA, Shahaf G. Simple Electroencephalographic Treatment-Emergent Marker Can Predict Repetitive Transcranial Magnetic Stimulation Antidepressant Response-A Feasibility Study. *J ECT*. 2018;34(4):274-282.
52. Jaworska N, de la Salle S, Ibrahim MH, Blier P, Knott V. Leveraging Machine Learning Approaches for Predicting Antidepressant Treatment Response Using Electroencephalography (EEG) and Clinical Data. *Front Psychiatry*. 2018;9:768.
53. Li CT, Hsieh JC, Huang HH, et al. Cognition-Modulated Frontal Activity in Prediction and Augmentation of Antidepressant Efficacy: A Randomized Controlled Pilot Study. *Cereb Cortex*. 2016;26(1):202-210.
54. Cook IA, Hunter AM, Gilmer WS, et al. Quantitative electroencephalogram biomarkers for predicting likelihood and speed of achieving sustained remission in major depression: a report from the biomarkers for rapid identification of treatment effectiveness in major depression (BRITE-MD) trial. *J Clin Psychiatry*. 2013;74(1):51-56.
55. Wang Q, Tian S, Zhao P, Cao Q, Lu Q, Yao Z. Association Between Antidepressant Efficacy and Interactions of Three Core Depression-Related Brain Networks in Major Depressive Disorder. *Front Psychiatry*. 2022;13:862507.
56. Liu TY, Chen YS, Su TP, Hsieh JC, Chen LF. Abnormal early gamma responses to emotional faces differentiate unipolar from bipolar disorder patients. *Biomed Res Int*. 2014;2014:906104.
57. Wang Q, Tian S, Tang H, et al. Identification of major depressive disorder and prediction of treatment response using functional connectivity between the prefrontal cortices and subgenual anterior cingulate: A real-world study. *J Affect Disord*. 2019;252:365-372.
58. Pillai RL, Zhang M, Yang J, et al. Molecular connectivity disruptions in males with major depressive disorder. *J Cereb Blood Flow Metab*. 2019;39(8):1623-1634.
59. Kaufman J, Sullivan GM, Yang J, et al. Quantification of the Serotonin 1A Receptor Using PET: Identification of a Potential Biomarker of Major Depression in Males. *Neuropsychopharmacology*. 2015;40(7):1692-1699.
60. Yeh YW, Ho PS, Kuo SC, et al. Disproportionate Reduction of Serotonin Transporter May Predict the Response and Adherence to Antidepressants in Patients with Major Depressive Disorder: A Positron Emission Tomography Study with 4-[18F]-ADAM. *Int J Neuropsychopharmacol*. 2015;18(7):pyu120.
61. Amen DG, Krishnamani P, Meysami S, Newberg A, Raji CA. Classification of Depression, Cognitive Disorders, and Co-Morbid Depression and Cognitive Disorders with Perfusion SPECT Neuroimaging. *J Alzheimers Dis*. 2017;57(1):253-266.
62. Richieri R, Verger A, Boyer L, et al. Predictive value of dorso-lateral prefrontal connectivity for rTMS response in treatment-resistant depression: A brain perfusion SPECT study. *Brain Stimul*. 2018;11(5):1093-1097.
63. Richieri R, Boyer L, Fariisse J, et al. Predictive value of brain perfusion SPECT for rTMS response in pharmaco-resistant depression. *Eur J Nucl Med Mol Imaging*. 2011;38(9):1715-1722.
64. Tekin Erguzel T, Tas C, Cebi M. A wrapper-based approach for feature selection and classification of major depressive disorder-bipolar disorders. *Comput Biol Med*. 2015;64:127-137.
65. Schnack HG, Nieuwenhuis M, van Haren NE, et al. Can structural MRI aid in clinical classification? A machine learning study in two independent samples of patients with schizophrenia, bipolar disorder and healthy subjects. *Neuroimage*. 2014;84:299-306.

66. Mwangi B, Wu MJ, Cao B, et al. Individualized Prediction and Clinical Staging of Bipolar Disorders using Neuroanatomical Biomarkers. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2016;1(2):186-194.
67. Yang T, Frangou S, Lam RW, et al. Probing the clinical and brain structural boundaries of bipolar and major depressive disorder. *Transl Psychiatry*. 2021;11(1):48.
68. Niida R, Yamagata B, Niida A, Uechi A, Matsuda H, Mimura M. Aberrant Anterior Thalamic Radiation Structure in Bipolar Disorder: A Diffusion Tensor Tractography Study. *Front Psychiatry*. 2018;9:522.
69. Frangou S, Dima D, Jogia J. Towards person-centered neuroimaging markers for resilience and vulnerability in Bipolar Disorder. *Neuroimage*. 2017;145(Pt B):230-237.
70. Shi J, Geng J, Yan R, et al. Differentiation of Transformed Bipolar Disorder From Unipolar Depression by Resting-State Functional Connectivity Within Reward Circuit. *Front Psychol*. 2018;9:2586.
71. Serpa MH, Ou Y, Schaufelberger MS, et al. Neuroanatomical classification in a population-based sample of psychotic major depression and bipolar I disorder with 1 year of diagnostic stability. *Biomed Res Int*. 2014;2014:706157.
72. Tsolaki E, Narr KL, Espinoza R, et al. Subcallosal Cingulate Structural Connectivity Differs in Responders and Nonresponders to Electroconvulsive Therapy. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2021;6(1):10-19.
73. Sun H, Jiang R, Qi S, et al. Preliminary prediction of individual response to electroconvulsive therapy using whole-brain functional magnetic resonance imaging data. *Neuroimage Clin*. 2020;26:102080.
74. Wade BS, Joshi SH, Njau S, et al. Effect of Electroconvulsive Therapy on Striatal Morphometry in Major Depressive Disorder. *Neuropsychopharmacology*. 2016;41(10):2481-2491.
75. Bruin WB, Oltedal L, Bartsch H, et al. Development and validation of a multimodal neuroimaging biomarker for electroconvulsive therapy outcome in depression: a multicenter machine learning analysis. *medRxiv*. 2022.
76. Lanka P, Rangaprakash D, Dretsch MN, Katz JS, Denney TS, Jr., Deshpande G. Supervised machine learning for diagnostic classification from large-scale neuroimaging datasets. *Brain Imaging Behav*. 2020;14(6):2378-2416.
77. Zhang J, Richardson JD, Dunkley BT. Classifying post-traumatic stress disorder using the magnetoencephalographic connectome and machine learning. *Sci Rep*. 2020;10(1):5937.
78. Suo X, Lei D, Li W, et al. Individualized Prediction of PTSD Symptom Severity in Trauma Survivors From Whole-Brain Resting-State Functional Connectivity. *Front Behav Neurosci*. 2020;14:563152.
79. Im JJ, Kim B, Hwang J, et al. Diagnostic potential of multimodal neuroimaging in posttraumatic stress disorder. *PLoS One*. 2017;12(5):e0177847.
80. Zhutovsky P, Thomas RM, Olf M, et al. Individual prediction of psychotherapy outcome in posttraumatic stress disorder using neuroimaging data. *Transl Psychiatry*. 2019;9(1):326.
81. van Rooij SJ, Kennis M, Vink M, Geuze E. Predicting Treatment Outcome in PTSD: A Longitudinal Functional MRI Study on Trauma-Unrelated Emotional Processing. *Neuropsychopharmacology*. 2016;41(4):1156-1165.
82. Stout DM, Harle KM, Norman SB, Simmons AN, Spadoni AD. Resting-state connectivity subtype of comorbid PTSD and alcohol use disorder moderates

- improvement from integrated prolonged exposure therapy in Veterans. *Psychol Med.* 2021;1-10.
83. Klumpp H, Jimmy J, Burkhouse KL, et al. Brain response to emotional faces in anxiety and depression: neural predictors of cognitive behavioral therapy outcome and predictor-based subgroups following therapy. *Psychol Med.* 2020;1-11.
  84. Etkin A, Maron-Katz A, Wu W, et al. Using fMRI connectivity to define a treatment-resistant form of post-traumatic stress disorder. *Sci Transl Med.* 2019;11(486).
  85. Fonzo GA, Goodkind MS, Oathes DJ, et al. PTSD Psychotherapy Outcome Predicted by Brain Activation During Emotional Reactivity and Regulation. *Am J Psychiatry.* 2017;174(12):1163-1174.
  86. Laxminarayan S, Wang C, Oyama T, Cashmere JD, Germain A, Reifman J. Identification of Veterans With PTSD Based on EEG Features Collected During Sleep. *Front Psychiatry.* 2020;11:532623.
  87. Kim YW, Kim S, Shim M, et al. Riemannian classifier enhances the accuracy of machine-learning-based diagnosis of PTSD using resting EEG. *Prog Neuropsychopharmacol Biol Psychiatry.* 2020;102:109960.
  88. Tahmasian M, Jamalabadi H, Abedini M, et al. Differentiation chronic post traumatic stress disorder patients from healthy subjects using objective and subjective sleep-related parameters. *Neurosci Lett.* 2017;650:174-179.
  89. Shu IW, Onton JA, O'Connell RM, Simmons AN, Matthews SC. Combat veterans with comorbid PTSD and mild TBI exhibit a greater inhibitory processing ERP from the dorsal anterior cingulate cortex. *Psychiatry Res.* 2014;224(1):58-66.
  90. James LM, Leuthold AF, Georgopoulos AP. Classification of posttraumatic stress disorder and related outcomes in women veterans using magnetoencephalography. *Exp Brain Res.* 2022;240(4):1117-1125.
  91. Georgopoulos AP, Tan HR, Lewis SM, et al. The synchronous neural interactions test as a functional neuromarker for post-traumatic stress disorder (PTSD): a robust classification method based on the bootstrap. *J Neural Eng.* 2010;7(1):16011.
  92. Amen DG, Raji CA, Willeumier K, et al. Functional Neuroimaging Distinguishes Posttraumatic Stress Disorder from Traumatic Brain Injury in Focused and Large Community Datasets. *PLoS One.* 2015;10(7):e0129659.
  93. Raji CA, Willeumier K, Taylor D, et al. Functional neuroimaging with default mode network regions distinguishes PTSD from TBI in a military veteran population. *Brain Imaging Behav.* 2015;9(3):527-534.
  94. Neumeister A, Normandin MD, Pietrzak RH, et al. Elevated brain cannabinoid CB1 receptor availability in post-traumatic stress disorder: a positron emission tomography study. *Mol Psychiatry.* 2013;18(9):1034-1040.
  95. Rangaprakash D, Dretsch MN, Venkataraman A, Katz JS, Denney TS, Jr., Deshpande G. Identifying disease foci from static and dynamic effective connectivity networks: Illustration in soldiers with trauma. *Hum Brain Mapp.* 2018;39(1):264-287.
  96. Rangaprakash D, Deshpande G, Daniel TA, et al. Compromised hippocampus-striatum pathway as a potential imaging biomarker of mild-traumatic brain injury and posttraumatic stress disorder. *Hum Brain Mapp.* 2017;38(6):2843-2864.
  97. Rangaprakash D, Dretsch MN, Katz JS, Denney TS, Jr., Deshpande G. Dynamics of Segregation and Integration in Directional Brain Networks: Illustration in Soldiers With PTSD and Neurotrauma. *Front Neurosci.* 2019;13:803.

98. Hanks R, Millis S, Scott S, et al. The relation between cognitive dysfunction and diffusion tensor imaging parameters in traumatic brain injury. *Brain Inj.* 2019;33(3):355-363.
99. Huang M, Lee RR. Magnetoencephalography (MEG) Slow-Wave Imaging for Diagnosing Non-acute Mild Traumatic Brain Injury. *Current Radiology Reports.* 2015;3(10):41.
100. Main KL, Soman S, Pestilli F, et al. DTI measures identify mild and moderate TBI cases among patients with complex health problems: A receiver operating characteristic analysis of U.S. veterans. *Neuroimage Clin.* 2017;16:1-16.
101. Chen YC, Chen YL, Kuo DP, et al. Personalized Prediction of Postconcussive Working Memory Decline: A Feasibility Study. *J Pers Med.* 2022;12(2).
102. Brezova V, Moen KG, Skandsen T, et al. Prospective longitudinal MRI study of brain volumes and diffusion changes during the first year after moderate to severe traumatic brain injury. *Neuroimage Clin.* 2014;5:128-140.
103. McBride J, Zhao X, Nichols T, et al. Scalp EEG-based discrimination of cognitive deficits after traumatic brain injury using event-related Tsallis entropy analysis. *IEEE Trans Biomed Eng.* 2013;60(1):90-96.
104. Camchong J, Haynos AF, Hendrickson T, et al. Resting Hypoconnectivity of Theoretically Defined Addiction Networks during Early Abstinence Predicts Subsequent Relapse in Alcohol Use Disorder. *Cereb Cortex.* 2022;32(12):2688-2702.
105. Dai X, Gao L, Zhang H, Wei X, Liu Z. A combination of support vector machine and voxel-based morphometry in adult male alcohol use disorder patients with cognitive deficits. *Brain Res.* 2021;1771:147644.
106. Kamarajan C, Ardekani BA, Pandey AK, et al. Random Forest Classification of Alcohol Use Disorder Using EEG Source Functional Connectivity, Neuropsychological Functioning, and Impulsivity Measures. *Behav Sci (Basel).* 2020;10(3).
107. Kinreich S, McCutcheon VV, Aliev F, et al. Predicting alcohol use disorder remission: a longitudinal multimodal multi-featured machine learning approach. *Transl Psychiatry.* 2021;11(1):166.
108. Mishra P, Nizamie SH, Jahan M, et al. Predictors of chronicity in alcohol use disorder: an evoked response potential study. *J Addict Dis.* 2020;38(4):411-419.
109. Sekutowicz M, Guggenmos M, Kuitunen-Paul S, et al. Neural Response Patterns During Pavlovian-to-Instrumental Transfer Predict Alcohol Relapse and Young Adult Drinking. *Biol Psychiatry.* 2019;86(11):857-863.
110. Mumtaz W, Saad M, Kamel N, Ali SSA, Malik AS. An EEG-based functional connectivity measure for automatic detection of alcohol use disorder. *Artif Intell Med.* 2018;84:79-89.
111. Durazzo TC, Meyerhoff DJ. Psychiatric, Demographic, and Brain Morphological Predictors of Relapse After Treatment for an Alcohol Use Disorder. *Alcohol Clin Exp Res.* 2017;41(1):107-116.
112. Mumtaz W, Vuong PL, Xia L, Malik AS, Rashid RBA. An EEG-based machine learning method to screen alcohol use disorder. *Cogn Neurodyn.* 2017;11(2):161-171.
113. Januszko P, Gmaj B, Piotrowski T, et al. Delta resting-state functional connectivity in the cognitive control network as a prognostic factor for maintaining abstinence: An eLORETA preliminary study. *Drug Alcohol Depend.* 2021;218:108393.
114. Zhu X, Du X, Kerich M, Lohoff FW, Momenan R. Random forest based classification of alcohol dependence patients and healthy controls using resting state MRI. *Neurosci Lett.* 2018;676:27-33.

115. Zhai T, Gu H, Yang Y. Cox Regression Based Modeling of Functional Connectivity and Treatment Outcome for Relapse Prediction and Disease Subtyping in Substance Use Disorder. *Front Neurosci.* 2021;15:768602.
116. McHugh MJ, Demers CH, Salmeron BJ, Devous MD, Sr., Stein EA, Adinoff B. Cortico-amygdala coupling as a marker of early relapse risk in cocaine-addicted individuals. *Front Psychiatry.* 2014;5:16.
117. Adinoff B, Gu H, Merrick C, et al. Basal Hippocampal Activity and Its Functional Connectivity Predicts Cocaine Relapse. *Biol Psychiatry.* 2015;78(7):496-504.
118. Erguzel TT, Uyulan C, Unsalver B, et al. Entropy: A Promising EEG Biomarker Dichotomizing Subjects With Opioid Use Disorder and Healthy Controls. *Clin EEG Neurosci.* 2020;51(6):373-381.
119. Erguzel TT, Noyan CO, Eryilmaz G, et al. Binomial Logistic Regression and Artificial Neural Network Methods to Classify Opioid-Dependent Subjects and Control Group Using Quantitative EEG Power Measures. *Clin EEG Neurosci.* 2019;50(5):303-310.
120. Yan C, Yang X, Yang R, et al. Treatment Response Prediction and Individualized Identification of Short-Term Abstinence Methamphetamine Dependence Using Brain Graph Metrics. *Front Psychiatry.* 2021;12:583950.
121. Li Y, Cui Z, Liao Q, et al. Support vector machine-based multivariate pattern classification of methamphetamine dependence using arterial spin labeling. *Addict Biol.* 2019;24(6):1254-1262.
122. Gowin JL, Ball TM, Wittmann M, Tapert SF, Paulus MP. Individualized relapse prediction: Personality measures and striatal and insular activity during reward-processing robustly predict relapse. *Drug Alcohol Depend.* 2015;152:93-101.
123. Chen Y, Ou Y, Lv D, et al. Decreased Nucleus Accumbens Connectivity at Rest in Medication-Free Patients with Obsessive-Compulsive Disorder. *Neural Plast.* 2021;2021:9966378.
124. Liu W, Qin J, Tang Q, et al. Disrupted pathways from the frontal-parietal cortices to basal nuclei and the cerebellum are a feature of the obsessive-compulsive disorder spectrum and can be used to aid in early differential diagnosis. *Psychiatry Res.* 2020;293:113436.
125. Zhou C, Cheng Y, Ping L, et al. Support Vector Machine Classification of Obsessive-Compulsive Disorder Based on Whole-Brain Volumetry and Diffusion Tensor Imaging. *Front Psychiatry.* 2018;9:524.
126. Hu X, Liu Q, Li B, et al. Multivariate pattern analysis of obsessive-compulsive disorder using structural neuroanatomy. *Eur Neuropsychopharmacol.* 2016;26(2):246-254.
127. Liu J, Bu X, Hu X, et al. Temporal variability of regional intrinsic neural activity in drug-naive patients with obsessive-compulsive disorder. *Hum Brain Mapp.* 2021;42(12):3792-3803.
128. Lv D, Ou Y, Wang Y, et al. Altered Functional Connectivity Strength at Rest in Medication-Free Obsessive-Compulsive Disorder. *Neural Plast.* 2021;2021:3741104.
129. Yang P, Zhao C, Yang Q, et al. Diagnosis of obsessive-compulsive disorder via spatial similarity-aware learning and fused deep polynomial network. *Med Image Anal.* 2022;75:102244.
130. Luo Q, Liu W, Jin L, Chang C, Peng Z. Classification of Obsessive-Compulsive Disorder Using Distance Correlation on Resting-State Functional MRI Images. *Front Neuroinform.* 2021;15:676491.
131. Liu W, Hua M, Qin J, et al. Disrupted pathways from frontal-parietal cortex to basal ganglia and cerebellum in patients with unmedicated obsessive compulsive disorder as



- observed by whole-brain resting-state effective connectivity analysis - a small sample pilot study. *Brain Imaging Behav.* 2021;15(3):1344-1354.
132. Kwak S, Kim M, Kim T, et al. Defining data-driven subgroups of obsessive-compulsive disorder with different treatment responses based on resting-state functional connectivity. *Transl Psychiatry.* 2020;10(1):359.
  133. Wang YM, Cai XL, Zhang RT, et al. Searchlight classification based on Amplitude of Low Frequency Fluctuation and functional connectivity in individuals with obsessive-compulsive symptoms. *Cogn Neuropsychiatry.* 2019;24(5):322-334.
  134. Yang X, Hu X, Tang W, et al. Multivariate classification of drug-naive obsessive-compulsive disorder patients and healthy controls by applying an SVM to resting-state functional MRI data. *BMC Psychiatry.* 2019;19(1):210.
  135. Takagi Y, Sakai Y, Lisi G, et al. A Neural Marker of Obsessive-Compulsive Disorder from Whole-Brain Functional Connectivity. *Sci Rep.* 2017;7(1):7538.
  136. Hu X, Zhang L, Bu X, et al. Localized Connectivity in Obsessive-Compulsive Disorder: An Investigation Combining Univariate and Multivariate Pattern Analyses. *Front Behav Neurosci.* 2019;13:122.
  137. Cui G, Ou Y, Chen Y, et al. Altered Global Brain Functional Connectivity in Drug-Naive Patients With Obsessive-Compulsive Disorder. *Front Psychiatry.* 2020;11:98.
  138. Li F, Huang X, Tang W, et al. Multivariate pattern analysis of DTI reveals differential white matter in individuals with obsessive-compulsive disorder. *Hum Brain Mapp.* 2014;35(6):2643-2651.
  139. Altuglu TB, Metin B, Tulay EE, et al. Prediction of treatment resistance in obsessive compulsive disorder patients based on EEG complexity as a biomarker. *Clin Neurophysiol.* 2020;131(3):716-724.
  140. Yun JY, Jang JH, Kim SN, Jung WH, Kwon JS. Neural Correlates of Response to Pharmacotherapy in Obsessive-Compulsive Disorder: Individualized Cortical Morphology-Based Structural Covariance. *Prog Neuropsychopharmacol Biol Psychiatry.* 2015;63:126-133.
  141. Reggente N, Moody TD, Morfini F, et al. Multivariate resting-state functional connectivity predicts response to cognitive behavioral therapy in obsessive-compulsive disorder. *Proc Natl Acad Sci U S A.* 2018;115(9):2222-2227.
  142. Liu F, Guo W, Fouche JP, et al. Multivariate classification of social anxiety disorder using whole brain functional connectivity. *Brain Struct Funct.* 2015;220(1):101-115.
  143. Xing M, Fitzgerald JM, Klumpp H. Classification of Social Anxiety Disorder With Support Vector Machine Analysis Using Neural Correlates of Social Signals of Threat. *Front Psychiatry.* 2020;11:144.
  144. Qiao J, Li A, Cao C, Wang Z, Sun J, Xu G. Aberrant Functional Network Connectivity as a Biomarker of Generalized Anxiety Disorder. *Front Hum Neurosci.* 2017;11:626.
  145. Pantazatos SP, Talati A, Schneier FR, Hirsch J. Reduced anterior temporal and hippocampal functional connectivity during face processing discriminates individuals with social anxiety disorder from healthy controls and panic disorder, and increases following treatment. *Neuropsychopharmacology.* 2014;39(2):425-434.
  146. Frick A, Engman J, Alaie I, et al. Neuroimaging, genetic, clinical, and demographic predictors of treatment response in patients with social anxiety disorder. *J Affect Disord.* 2020;261:230-237.
  147. Whitfield-Gabrieli S, Ghosh SS, Nieto-Castanon A, et al. Brain connectomics predict response to treatment in social anxiety disorder. *Mol Psychiatry.* 2016;21(5):680-685.

148. Price RB, Cummings L, Gilchrist D, et al. Towards personalized, brain-based behavioral intervention for transdiagnostic anxiety: Transient neural responses to negative images predict outcomes following a targeted computer-based intervention. *J Consult Clin Psychol*. 2018;86(12):1031-1045.
149. Klumpp H, Roberts J, Kennedy AE, et al. Emotion regulation related neural predictors of cognitive behavioral therapy response in social anxiety disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2017;75:106-112.
150. Hahn T, Kircher T, Straube B, et al. Predicting treatment response to cognitive behavioral therapy in panic disorder with agoraphobia by integrating local neural information. *JAMA Psychiatry*. 2015;72(1):68-74.
151. Hozer F, Houenou J. Can neuroimaging disentangle bipolar disorder? *J Affect Disord*. 2016;195:199-214.
152. Khosla A, Khandnor P, Chand T. Automated diagnosis of depression from EEG signals using traditional and deep learning approaches: A comparative analysis. *Biocybernetics and Biomedical Engineering*. 2022;42(1):108-142.
153. Scheepens DS, van Waarde JA, Lok A, de Vries G, Denys D, van Wingen GA. The Link Between Structural and Functional Brain Abnormalities in Depression: A Systematic Review of Multimodal Neuroimaging Studies. *Front Psychiatry*. 2020;11:485.
154. Sinha P, Joshi H, Ithal D. Resting State Functional Connectivity of Brain With Electroconvulsive Therapy in Depression: Meta-Analysis to Understand Its Mechanisms. *Front Hum Neurosci*. 2020;14:616054.
155. Fullana MA, Abramovitch A, Via E, et al. Diagnostic biomarkers for obsessive-compulsive disorder: A reasonable quest or ignis fatuus? *Neurosci Biobehav Rev*. 2020;118:504-513.
156. Esterman M, Stumps A, Jagger-Rickels A, et al. Evaluating the evidence for a neuroimaging subtype of posttraumatic stress disorder. *Sci Transl Med*. 2020;12(568).
157. Dalgleish T, Black M, Johnston D, Bevan A. Transdiagnostic approaches to mental health problems: Current status and future directions. *J Consult Clin Psychol*. 2020;88(3):179-195.
158. Gillan CM, Seow TXF. Carving Out New Transdiagnostic Dimensions for Research in Mental Health. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2020;5(10):932-934.
159. Yucel M, Oldenhof E, Ahmed SH, et al. A transdiagnostic dimensional approach towards a neuropsychological assessment for addiction: an international Delphi consensus study. *Addiction*. 2019;114(6):1095-1109.
160. Kozlov M. Your brain expands and shrinks over time - these charts show how. *Nature*. 2022;604(7905):230-231.
161. ABCD Research Consortium. Adolescent Brain Cognitive Development (ABCD) Study. <https://abcdstudy.org/about/>. Accessed September 13, 2022.
162. Biobank UK. <https://www.ukbiobank.ac.uk/>. Accessed September 13, 2022.
163. Achalia R, Sinha A, Jacob A, et al. A proof of concept machine learning analysis using multimodal neuroimaging and neurocognitive measures as predictive biomarker in bipolar disorder. *Asian J Psychiatr*. 2020;50:101984.
164. Ambrosi E, Arciniegas DB, Madan A, et al. Insula and amygdala resting-state functional connectivity differentiate bipolar from unipolar depression. *Acta Psychiatr Scand*. 2017;136(1):129-139.
165. Arns M, Cerquera A, Gutierrez RM, Hasselman F, Freund JA. Non-linear EEG analyses predict non-response to rTMS treatment in major depressive disorder. *Clin Neurophysiol*. 2014;125(7):1392-1399.

166. Arns M, Drinkenburg WH, Fitzgerald PB, Kenemans JL. Neurophysiological predictors of non-response to rTMS in depression. *Brain Stimul.* 2012;5(4):569-576.
167. Arribas JJ, Calhoun VD, Adali T. Automatic Bayesian classification of healthy controls, bipolar disorder, and schizophrenia using intrinsic connectivity maps from fMRI data. *IEEE Trans Biomed Eng.* 2010;57(12):2850-2860.
168. Bachmann M, Lass J, Hinrikus H. Single channel EEG analysis for detection of depression. *Biomedical Signal Processing and Control.* 2017;31:391-397.
169. Bailey NW, Hoy KE, Rogasch NC, et al. Responders to rTMS for depression show increased fronto-midline theta and theta connectivity compared to non-responders. *Brain Stimul.* 2018;11(1):190-203.
170. Baranger D, Halchenko Y, Satz S, et al. Aberrant Levels of Cortical Myelin Distinguish Individuals With Unipolar Depression From Healthy Controls. *Biological Psychiatry.* 2021;89(9):S364.
171. Bares M, Novak T, Vlcek P, Hejzlar M, Brunovsky M. Early change of prefrontal theta cordance and occipital alpha asymmetry in the prediction of responses to antidepressants. *Int J Psychophysiol.* 2019;143:1-8.
172. Bares M, Novak T, Brunovsky M, Kopecek M, Hoschl C. The Comparison of Effectiveness of Various Potential Predictors of Response to Treatment With SSRIs in Patients With Depressive Disorder. *J Nerv Ment Dis.* 2017;205(8):618-626.
173. Bares M, Novak T, Kopecek M, Brunovsky M, Stopkova P, Hoschl C. The effectiveness of prefrontal theta cordance and early reduction of depressive symptoms in the prediction of antidepressant treatment outcome in patients with resistant depression: analysis of naturalistic data. *Eur Arch Psychiatry Clin Neurosci.* 2015;265(1):73-82.
174. Bartlett EA, DeLorenzo C, Sharma P, et al. Pretreatment and early-treatment cortical thickness is associated with SSRI treatment response in major depressive disorder. *Neuropsychopharmacology.* 2018;43(11):2221-2230.
175. Baskaran A, Farzan F, Milev R, et al. The comparative effectiveness of electroencephalographic indices in predicting response to escitalopram therapy in depression: A pilot study. *J Affect Disord.* 2018;227:542-549.
176. Bi K, Chattun MR, Liu X, et al. Abnormal early dynamic individual patterns of functional networks in low gamma band for depression recognition. *J Affect Disord.* 2018;238:366-374.
177. Brandt IM, Kohler-Forsberg K, Ganz M, et al. Reward processing in major depressive disorder and prediction of treatment response - Neuropharm study. *Eur Neuropsychopharmacol.* 2021;44:23-33.
178. Burger C, Redlich R, Grotegerd D, et al. Differential Abnormal Pattern of Anterior Cingulate Gyrus Activation in Unipolar and Bipolar Depression: an fMRI and Pattern Classification Approach. *Neuropsychopharmacology.* 2017;42(7):1399-1408.
179. Cash RFH, Cocchi L, Anderson R, et al. A multivariate neuroimaging biomarker of individual outcome to transcranial magnetic stimulation in depression. *Hum Brain Mapp.* 2019;40(16):4618-4629.
180. Chen Q, Bi Y, Zhao X, et al. Regional amplitude abnormalities in the major depressive disorder: A resting-state fMRI study and support vector machine analysis. *J Affect Disord.* 2022;308:1-9.
181. Chen ST, Ku LC, Chen SJ, Shen TW. The Changes of qEEG Approximate Entropy during Test of Variables of Attention as a Predictor of Major Depressive Disorder. *Brain Sci.* 2020;10(11).

182. Chen VC, Wong FT, Tsai YH, et al. Convolutional Neural Network-Based Deep Learning Model for Predicting Differential Suicidality in Depressive Patients Using Brain Generalized q-Sampling Imaging. *J Clin Psychiatry*. 2021;82(2).
183. Cheng Y, Xu J, Arnone D, et al. Resting-state brain alteration after a single dose of SSRI administration predicts 8-week remission of patients with major depressive disorder. *Psychol Med*. 2017;47(3):438-450.
184. Chin Fatt CR, Jha MK, Cooper CM, et al. Effect of Intrinsic Patterns of Functional Brain Connectivity in Moderating Antidepressant Treatment Response in Major Depression. *Am J Psychiatry*. 2020;177(2):143-154.
185. Colle R, Chupin M, Cury C, et al. Depressed suicide attempters have smaller hippocampus than depressed patients without suicide attempts. *J Psychiatr Res*. 2015;61:13-18.
186. Cook IA, Hunter AM, Caudill MM, Abrams MJ, Leuchter AF. Prospective testing of a neurophysiologic biomarker for treatment decisions in major depressive disorder: The PRISE-MD trial. *J Psychiatr Res*. 2020;124:159-165.
187. Costafreda SG, Fu CH, Picchioni M, et al. Pattern of neural responses to verbal fluency shows diagnostic specificity for schizophrenia and bipolar disorder. *BMC Psychiatry*. 2011;11:18.
188. Crane NA, Jenkins LM, Bhaumik R, et al. Multidimensional prediction of treatment response to antidepressants with cognitive control and functional MRI. *Brain*. 2017;140(2):472-486.
189. Crowther A, Smoski MJ, Minkel J, et al. Resting-state connectivity predictors of response to psychotherapy in major depressive disorder. *Neuropsychopharmacology*. 2015;40(7):1659-1673.
190. de la Salle S, Jaworska N, Blier P, Smith D, Knott V. Using prefrontal and midline right frontal EEG-derived theta cordance and depressive symptoms to predict the differential response or remission to antidepressant treatment in major depressive disorder. *Psychiatry Res Neuroimaging*. 2020;302:111109.
191. Duan L, Duan H, Qiao Y, et al. Machine Learning Approaches for MDD Detection and Emotion Decoding Using EEG Signals. *Front Hum Neurosci*. 2020;14:284.
192. Dunlop BW, Rajendra JK, Craighead WE, et al. Functional Connectivity of the Subcallosal Cingulate Cortex And Differential Outcomes to Treatment With Cognitive-Behavioral Therapy or Antidepressant Medication for Major Depressive Disorder. *Am J Psychiatry*. 2017;174(6):533-545.
193. Ellard KK, Zimmerman JP, Kaur N, et al. Functional Connectivity Between Anterior Insula and Key Nodes of Frontoparietal Executive Control and Salience Networks Distinguish Bipolar Depression From Unipolar Depression and Healthy Control Subjects. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2018;3(5):473-484.
194. Erguzel TT, Ozekes S, Gultekin S, Tarhan N, Hizli Sayar G, Bayram A. Neural Network Based Response Prediction of rTMS in Major Depressive Disorder Using QEEG Cordance. *Psychiatry Investig*. 2015;12(1):61-65.
195. Erguzel TT, Ozekes S, Gultekin S, Tarhan N. Ant Colony Optimization Based Feature Selection Method for QEEG Data Classification. *Psychiatry Investig*. 2014;11(3):243-250.
196. Fang P, Zeng LL, Shen H, et al. Increased cortical-limbic anatomical network connectivity in major depression revealed by diffusion tensor imaging. *PLoS One*. 2012;7(9):e45972.

197. Farb NAS, Desormeau P, Anderson AK, Segal ZV. Static and treatment-responsive brain biomarkers of depression relapse vulnerability following prophylactic psychotherapy: Evidence from a randomized control trial. *Neuroimage Clin.* 2022;34:102969.
198. Feder S, Sundermann B, Wersching H, et al. Sample heterogeneity in unipolar depression as assessed by functional connectivity analyses is dominated by general disease effects. *J Affect Disord.* 2017;222:79-87.
199. Gao Y, Wang X, Xiong Z, et al. Abnormal Fractional Amplitude of Low-Frequency Fluctuation as a Potential Imaging Biomarker for First-Episode Major Depressive Disorder: A Resting-State fMRI Study and Support Vector Machine Analysis. *Front Neurol.* 2021;12:751400.
200. Gao C, Xu Z, Tan T, et al. Combination of spontaneous regional brain activity and HTR1A/1B DNA methylation to predict early responses to antidepressant treatments in MDD. *J Affect Disord.* 2022;302:249-257.
201. Gartner M, Ghisu ME, Scheidegger M, et al. Aberrant working memory processing in major depression: evidence from multivoxel pattern classification. *Neuropsychopharmacology.* 2018;43(9):1972-1979.
202. Ge R, Downar J, Blumberger DM, Daskalakis ZJ, Vila-Rodriguez F. Functional connectivity of the anterior cingulate cortex predicts treatment outcome for rTMS in treatment-resistant depression at 3-month follow-up. *Brain Stimul.* 2020;13(1):206-214.
203. Ge R, Downar J, Blumberger DM, Daskalakis ZJ, Lam RW, Vila-Rodriguez F. Structural network integrity of the central executive network is associated with the therapeutic effect of rTMS in treatment resistant depression. *Prog Neuropsychopharmacol Biol Psychiatry.* 2019;92:217-225.
204. Godlewska BR, Browning M, Norbury R, Igoumenou A, Cowen PJ, Harmer CJ. Predicting Treatment Response in Depression: The Role of Anterior Cingulate Cortex. *Int J Neuropsychopharmacol.* 2018;21(11):988-996.
205. Godlewska BR, Browning M, Norbury R, Cowen PJ, Harmer CJ. Early changes in emotional processing as a marker of clinical response to SSRI treatment in depression. *Transl Psychiatry.* 2016;6(11):e957.
206. Goldstein-Piekarski AN, Staveland BR, Ball TM, Yesavage J, Korgaonkar MS, Williams LM. Intrinsic functional connectivity predicts remission on antidepressants: a randomized controlled trial to identify clinically applicable imaging biomarkers. *Transl Psychiatry.* 2018;8(1):57.
207. Gong Q, Li L, Du M, et al. Quantitative prediction of individual psychopathology in trauma survivors using resting-state FMRI. *Neuropsychopharmacology.* 2014;39(3):681-687.
208. Gong Q, Li L, Tognin S, et al. Using structural neuroanatomy to identify trauma survivors with and without post-traumatic stress disorder at the individual level. *Psychol Med.* 2014;44(1):195-203.
209. Gong Q, Wu Q, Scarpazza C, et al. Prognostic prediction of therapeutic response in depression using high-field MR imaging. *Neuroimage.* 2011;55(4):1497-1503.
210. Gosnell SN, Curtis KN, Velasquez K, et al. Habenular connectivity may predict treatment response in depressed psychiatric inpatients. *J Affect Disord.* 2019;242:211-219.
211. Grieve SM, Korgaonkar MS, Gordon E, Williams LM, Rush AJ. Prediction of nonremission to antidepressant therapy using diffusion tensor imaging. *J Clin Psychiatry.* 2016;77(4):e436-443.

212. Grotegerd D, Stuhrmann A, Kugel H, et al. Amygdala excitability to subliminally presented emotional faces distinguishes unipolar and bipolar depression: an fMRI and pattern classification study. *Hum Brain Mapp.* 2014;35(7):2995-3007.
213. Guo M, Wang T, Zhang Z, et al. Diagnosis of major depressive disorder using whole-brain effective connectivity networks derived from resting-state functional MRI. *J Neural Eng.* 2020;17(5):056038.
214. Guo W, Cui X, Liu F, et al. Decreased interhemispheric coordination in the posterior default-mode network and visual regions as trait alterations in first-episode, drug-naive major depressive disorder. *Brain Imaging Behav.* 2018;12(5):1251-1258.
215. Guo H, Cao X, Liu Z, Li H, Chen J, Zhang K. Machine learning classifier using abnormal brain network topological metrics in major depressive disorder. *Neuroreport.* 2012;23(17):1006-1011.
216. Guo WB, Liu F, Chen JD, et al. Abnormal neural activity of brain regions in treatment-resistant and treatment-sensitive major depressive disorder: a resting-state fMRI study. *J Psychiatr Res.* 2012;46(10):1366-1373.
217. Hahn T, Marquand AF, Ehlis AC, et al. Integrating neurobiological markers of depression. *Arch Gen Psychiatry.* 2011;68(4):361-368.
218. Hasanzadeh F, Mohebbi M, Rostami R. Graph theory analysis of directed functional brain networks in major depressive disorder based on EEG signal. *J Neural Eng.* 2020;17(2):026010.
219. Hasanzadeh F, Mohebbi M, Rostami R. Prediction of rTMS treatment response in major depressive disorder using machine learning techniques and nonlinear features of EEG signal. *J Affect Disord.* 2019;256:132-142.
220. Hellewell SC, Welton T, Maller JJ, et al. Profound and reproducible patterns of reduced regional gray matter characterize major depressive disorder. *Transl Psychiatry.* 2019;9(1):176.
221. Hopman HJ, Chan SMS, Chu WCW, et al. Personalized prediction of transcranial magnetic stimulation clinical response in patients with treatment-refractory depression using neuroimaging biomarkers and machine learning. *J Affect Disord.* 2021;290:261-271.
222. Hou Z, Kong Y, Yin Y, Zhang Y, Yuan Y. Identification of first-episode unmedicated major depressive disorder using pretreatment features of dominant coactivation patterns. *Prog Neuropsychopharmacol Biol Psychiatry.* 2021;104:110038.
223. Hou Z, Kong Y, He X, Yin Y, Zhang Y, Yuan Y. Increased temporal variability of striatum region facilitating the early antidepressant response in patients with major depressive disorder. *Prog Neuropsychopharmacol Biol Psychiatry.* 2018;85:39-45.
224. Hou Z, Gong L, Zhi M, et al. Distinctive pretreatment features of bilateral nucleus accumbens networks predict early response to antidepressants in major depressive disorder. *Brain Imaging Behav.* 2018;12(4):1042-1052.
225. Hou Z, Song X, Jiang W, et al. Prognostic value of imbalanced interhemispheric functional coordination in early therapeutic efficacy in major depressive disorder. *Psychiatry Res Neuroimaging.* 2016;255:1-8.
226. Hu X, Zhang L, Hu X, et al. Abnormal Hippocampal Subfields May Be Potential Predictors of Worse Early Response to Antidepressant Treatment in Drug-Naive Patients With Major Depressive Disorder. *J Magn Reson Imaging.* 2019;49(6):1760-1768.
227. Ichikawa N, Lisi G, Yahata N, et al. Primary functional brain connections associated with melancholic major depressive disorder and modulation by antidepressants. *Sci Rep.* 2020;10(1):3542.

228. Jaworska N, Blondeau C, Tessier P, et al. Examining relations between alpha power as well as anterior cingulate cortex-localized theta activity and response to single or dual antidepressant pharmacotherapies. *J Psychopharmacol*. 2014;28(6):587-595.
229. Jaworska N, Blondeau C, Tessier P, et al. Response prediction to antidepressants using scalp and source-localized loudness dependence of auditory evoked potential (LDAEP) slopes. *Prog Neuropsychopharmacol Biol Psychiatry*. 2013;44:100-107.
230. Jiang C, Li Y, Tang Y, Guan C. Enhancing EEG-Based Classification of Depression Patients Using Spatial Information. *IEEE Trans Neural Syst Rehabil Eng*. 2021;29:566-575.
231. Jiang H, Dai Z, Lu Q, Yao Z. Magnetoencephalography resting-state spectral fingerprints distinguish bipolar depression and unipolar depression. *Bipolar Disord*. 2020;22(6):612-620.
232. Jiang R, Abbott CC, Jiang T, et al. SMRI Biomarkers Predict Electroconvulsive Treatment Outcomes: Accuracy with Independent Data Sets. *Neuropsychopharmacology*. 2018;43(5):1078-1087.
233. Kipli K, Kouzani AZ. Degree of contribution (DoC) feature selection algorithm for structural brain MRI volumetric features in depression detection. *Int J Comput Assist Radiol Surg*. 2015;10(7):1003-1016.
234. Koller-Schlaud K, Strohle A, Barwolf E, Behr J, Rentzsch J. EEG Frontal Asymmetry and Theta Power in Unipolar and Bipolar Depression. *J Affect Disord*. 2020;276:501-510.
235. Koo PC, Berger C, Kronenberg G, et al. Combined cognitive, psychomotor and electrophysiological biomarkers in major depressive disorder. *Eur Arch Psychiatry Clin Neurosci*. 2019;269(7):823-832.
236. Korgaonkar MS, Rekshan W, Gordon E, et al. Magnetic Resonance Imaging Measures of Brain Structure to Predict Antidepressant Treatment Outcome in Major Depressive Disorder. *EBioMedicine*. 2015;2(1):37-45.
237. Korgaonkar MS, Williams LM, Song YJ, Usherwood T, Grieve SM. Diffusion tensor imaging predictors of treatment outcomes in major depressive disorder. *Br J Psychiatry*. 2014;205(4):321-328.
238. Kraus C, Klobl M, Tik M, et al. The pulvinar nucleus and antidepressant treatment: dynamic modeling of antidepressant response and remission with ultra-high field functional MRI. *Mol Psychiatry*. 2019;24(5):746-756.
239. Leaver AM, Wade B, Vasavada M, et al. Fronto-Temporal Connectivity Predicts ECT Outcome in Major Depression. *Front Psychiatry*. 2018;9:92.
240. Lee TW, Wu YT, Yu YW, Chen MC, Chen TJ. The implication of functional connectivity strength in predicting treatment response of major depressive disorder: a resting EEG study. *Psychiatry Res*. 2011;194(3):372-377.
241. Li R, Yang J, Li L, et al. Integrating Multilevel Functional Characteristics Reveals Aberrant Neural Patterns during Audiovisual Emotional Processing in Depression. *Cereb Cortex*. 2021;32(1):1-14.
242. Li CT, Cheng CM, Juan CH, et al. Task-Modulated Brain Activity Predicts Antidepressant Responses of Prefrontal Repetitive Transcranial Magnetic Stimulation: A Randomized Sham-Control Study. *Chronic Stress (Thousand Oaks)*. 2021;5:24705470211006855.
243. Li H, Song S, Wang D, et al. Individualized diagnosis of major depressive disorder via multivariate pattern analysis of thalamic sMRI features. *BMC Psychiatry*. 2021;21(1):415.

244. Li J, Chen H, Fan F, et al. White-matter functional topology: a neuromarker for classification and prediction in unmedicated depression. *Transl Psychiatry*. 2020;10(1):365.
245. Li H, Cui L, Cao L, et al. Identification of bipolar disorder using a combination of multimodality magnetic resonance imaging and machine learning techniques. *BMC Psychiatry*. 2020;20(1):488.
246. Li CT, Cheng CM, Chen MH, et al. Antidepressant Efficacy of Prolonged Intermittent Theta Burst Stimulation Monotherapy for Recurrent Depression and Comparison of Methods for Coil Positioning: A Randomized, Double-Blind, Sham-Controlled Study. *Biol Psychiatry*. 2020;87(5):443-450.
247. Li M, Das T, Deng W, et al. Clinical utility of a short resting-state MRI scan in differentiating bipolar from unipolar depression. *Acta Psychiatr Scand*. 2017;136(3):288-299.
248. Li Y, Dai X, Wu H, Wang L. Establishment of Effective Biomarkers for Depression Diagnosis With Fusion of Multiple Resting-State Connectivity Measures. *Front Neurosci*. 2021;15:729958.
249. Liao W, Li J, Duan X, Cui Q, Chen H, Chen H. Static and dynamic connectomics differentiate between depressed patients with and without suicidal ideation. *Hum Brain Mapp*. 2018;39(10):4105-4118.
250. Liu W, Zhang C, Wang X, et al. Functional connectivity of major depression disorder using ongoing EEG during music perception. *Clin Neurophysiol*. 2020;131(10):2413-2422.
251. Liu Y, Admon R, Mellem MS, et al. Machine Learning Identifies Large-Scale Reward-Related Activity Modulated by Dopaminergic Enhancement in Major Depression. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2020;5(2):163-172.
252. Liu F, Xie B, Wang Y, et al. Characterization of post-traumatic stress disorder using resting-state fMRI with a multi-level parametric classification approach. *Brain Topogr*. 2015;28(2):221-237.
253. Liu F, Guo W, Yu D, et al. Classification of different therapeutic responses of major depressive disorder with multivariate pattern analysis method based on structural MR scans. *PLoS One*. 2012;7(7):e40968.
254. Lord A, Horn D, Breakspear M, Walter M. Changes in community structure of resting state functional connectivity in unipolar depression. *PLoS One*. 2012;7(8):e41282.
255. Lu F, Cui Q, He Z, et al. Prefrontal-limbic-striatum dysconnectivity associated with negative emotional endophenotypes in bipolar disorder during depressive episodes. *J Affect Disord*. 2021;295:422-430.
256. Lu Q, Jiang H, Luo G, Han Y, Yao Z. Multichannel matching pursuit of MEG signals for discriminative oscillation pattern detection in depression. *Int J Psychophysiol*. 2013;88(2):206-212.
257. Manelis A, Iyengar S, Swartz HA, Phillips ML. Prefrontal cortical activation during working memory task anticipation contributes to discrimination between bipolar and unipolar depression. *Neuropsychopharmacology*. 2020;45(6):956-963.
258. Matsuo K, Harada K, Fujita Y, et al. Distinctive Neuroanatomical Substrates for Depression in Bipolar Disorder versus Major Depressive Disorder. *Cereb Cortex*. 2019;29(1):202-214.
259. Matsuoka K, Yasuno F, Kishimoto T, et al. Microstructural Differences in the Corpus Callosum in Patients With Bipolar Disorder and Major Depressive Disorder. *J Clin Psychiatry*. 2017;78(1):99-104.



260. Meng Q, Zhang A, Cao X, et al. Brain Imaging Study on the Pathogenesis of Depression & Therapeutic Effect of Selective Serotonin Reuptake Inhibitors. *Psychiatry Investig.* 2020;17(7):688-694.
261. Meyer BM, Rabl U, Huemer J, et al. Prefrontal networks dynamically related to recovery from major depressive disorder: a longitudinal pharmacological fMRI study. *Transl Psychiatry.* 2019;9(1):64.
262. Modinos G, Mechelli A, Pettersson-Yeo W, Allen P, McGuire P, Aleman A. Pattern classification of brain activation during emotional processing in subclinical depression: psychosis proneness as potential confounding factor. *PeerJ.* 2013;1:e42.
263. Mohammadi M, Al-Azab F, Raahemi B, et al. Data mining EEG signals in depression for their diagnostic value. *BMC Med Inform Decis Mak.* 2015;15:108.
264. Mourao-Miranda J, Almeida JR, Hassel S, et al. Pattern recognition analyses of brain activation elicited by happy and neutral faces in unipolar and bipolar depression. *Bipolar Disord.* 2012;14(4):451-460.
265. Mulders PCR, Llera A, Beckmann CF, et al. Structural changes induced by electroconvulsive therapy are associated with clinical outcome. *Brain Stimul.* 2020;13(3):696-704.
266. Mumtaz W, Qayyum A. A deep learning framework for automatic diagnosis of unipolar depression. *Int J Med Inform.* 2019;132:103983.
267. Mumtaz W, Malik AS. A Comparative Study of Different EEG Reference Choices for Diagnosing Unipolar Depression. *Brain Topogr.* 2018;31(5):875-885.
268. Mumtaz W, Ali SSA, Yasin MAM, Malik AS. A machine learning framework involving EEG-based functional connectivity to diagnose major depressive disorder (MDD). *Med Biol Eng Comput.* 2018;56(2):233-246.
269. Mumtaz W, Xia L, Mohd Yasin MA, Azhar Ali SS, Malik AS. A wavelet-based technique to predict treatment outcome for Major Depressive Disorder. *PLoS One.* 2017;12(2):e0171409.
270. Mumtaz W, Xia L, Ali SSA, Yasin MAM, Hussain M, Malik AS. Electroencephalogram (EEG)-based computer-aided technique to diagnose major depressive disorder (MDD). *Biomedical Signal Processing and Control.* 2017;31:108-115.
271. Nguyen KP, Fatt CC, Treacher A, Mellema C, Trivedi MH, Montillo A. Predicting Response to the Antidepressant Bupropion using Pretreatment fMRI. *Predict Intell Med.* 2019;11843:53-62.
272. Nicholson AA, Densmore M, McKinnon MC, et al. Machine learning multivariate pattern analysis predicts classification of posttraumatic stress disorder and its dissociative subtype: a multimodal neuroimaging approach. *Psychol Med.* 2019;49(12):2049-2059.
273. Nogovitsyn N, Muller M, Souza R, et al. Hippocampal tail volume as a predictive biomarker of antidepressant treatment outcomes in patients with major depressive disorder: a CAN-BIND report. *Neuropsychopharmacology.* 2020;45(2):283-291.
274. Nord CL, Halahakoon DC, Limbachya T, et al. Neural predictors of treatment response to brain stimulation and psychological therapy in depression: a double-blind randomized controlled trial. *Neuropsychopharmacology.* 2019;44(9):1613-1622.
275. Olbrich S, Sander C, Minkwitz J, et al. EEG vigilance regulation patterns and their discriminative power to separate patients with major depression from healthy controls. *Neuropsychobiology.* 2012;65(4):188-194.
276. Oliveira-Maia AJ, Press D, Pascual-Leone A. Modulation of motor cortex excitability predicts antidepressant response to prefrontal cortex repetitive transcranial magnetic stimulation. *Brain Stimul.* 2017;10(4):787-794.

277. Yang J, Palaniyappan L, Xi C, et al. Aberrant integrity of the cortico-limbic-striatal circuit in major depressive disorder with suicidal ideation. *J Psychiatr Res*. 2022;148:277-285.
278. Pang Y, Zhang H, Cui Q, et al. Combined static and dynamic functional connectivity signatures differentiating bipolar depression from major depressive disorder. *Aust N Z J Psychiatry*. 2020;54(8):832-842.
279. Qin K, Lei D, Pinaya WHL, et al. Using graph convolutional network to characterize individuals with major depressive disorder across multiple imaging sites. *EBioMedicine*. 2022;78:103977.
280. Qin J, Shen H, Zeng LL, Jiang W, Liu L, Hu D. Predicting clinical responses in major depression using intrinsic functional connectivity. *Neuroreport*. 2015;26(12):675-680.
281. Qin J, Wei M, Liu H, et al. Abnormal hubs of white matter networks in the frontal-parieto circuit contribute to depression discrimination via pattern classification. *Magn Reson Imaging*. 2014;32(10):1314-1320.
282. Qiu L, Huang X, Zhang J, et al. Characterization of major depressive disorder using a multiparametric classification approach based on high resolution structural images. *Journal of psychiatry & neuroscience : JPN*. 2014;39(2):78-86.
283. Rabinoff M, Kitchen CM, Cook IA, Leuchter AF. Evaluation of quantitative EEG by classification and regression trees to characterize responders to antidepressant and placebo treatment. *Open Med Inform J*. 2011;5:1-8.
284. Redlich R, Almeida JJ, Grotegerd D, et al. Brain morphometric biomarkers distinguishing unipolar and bipolar depression. A voxel-based morphometry-pattern classification approach. *JAMA Psychiatry*. 2014;71(11):1222-1230.
285. Rentzsch J, Adli M, Wiethoff K, Gomez-Carrillo de Castro A, Gallinat J. Pretreatment anterior cingulate activity predicts antidepressant treatment response in major depressive episodes. *Eur Arch Psychiatry Clin Neurosci*. 2014;264(3):213-223.
286. Rive MM, Redlich R, Schmaal L, et al. Distinguishing medication-free subjects with unipolar disorder from subjects with bipolar disorder: state matters. *Bipolar Disord*. 2016;18(7):612-623.
287. Rocha-Rego V, Jogia J, Marquand AF, Mourao-Miranda J, Simmons A, Frangou S. Examination of the predictive value of structural magnetic resonance scans in bipolar disorder: a pattern classification approach. *Psychol Med*. 2014;44(3):519-532.
288. Rottstaedt F, Weidner K, Strauss T, et al. Size matters - The olfactory bulb as a marker for depression. *J Affect Disord*. 2018;229:193-198.
289. Rubin-Falcone H, Zanderigo F, Thapa-Chhetry B, et al. Pattern recognition of magnetic resonance imaging-based gray matter volume measurements classifies bipolar disorder and major depressive disorder. *J Affect Disord*. 2018;227:498-505.
290. Sacchet MD, Livermore EE, Iglesias JE, Glover GH, Gotlib IH. Subcortical volumes differentiate Major Depressive Disorder, Bipolar Disorder, and remitted Major Depressive Disorder. *J Psychiatr Res*. 2015;68:91-98.
291. Sadat Shahabi M, Shalhaf A, Maghsoudi A. Prediction of drug response in major depressive disorder using ensemble of transfer learning with convolutional neural network based on EEG. *Biocybernetics and Biomedical Engineering*. 2021;41(3):946-959.
292. Sankar A, Zhang T, Gaonkar B, et al. Diagnostic potential of structural neuroimaging for depression from a multi-ethnic community sample. *BJPsych Open*. 2016;2(4):247-254.

293. Schultz J, Becker B, Preckel K, et al. Improving therapy outcome prediction in major depression using multimodal functional neuroimaging: A pilot study. *Personalized Medicine in Psychiatry*. 2018;11-12:7-15.
294. Shalhaf R, Brenner C, Pang C, et al. Non-linear Entropy Analysis in EEG to Predict Treatment Response to Repetitive Transcranial Magnetic Stimulation in Depression. *Front Pharmacol*. 2018;9:1188.
295. Shan X, Qiu Y, Pan P, et al. Disrupted Regional Homogeneity in Drug-Naive Patients With Bipolar Disorder. *Front Psychiatry*. 2020;11:825.
296. Shan X, Cui X, Liu F, et al. Shared and distinct homotopic connectivity changes in melancholic and non-melancholic depression. *J Affect Disord*. 2021;287:268-275.
297. Shao J, Dai Z, Zhu R, et al. Early identification of bipolar from unipolar depression before manic episode: Evidence from dynamic rfMRI. *Bipolar Disord*. 2019;21(8):774-784.
298. Shi Y, Zhang L, He C, et al. Sleep disturbance-related neuroimaging features as potential biomarkers for the diagnosis of major depressive disorder: A multicenter study based on machine learning. *J Affect Disord*. 2021;295:148-155.
299. Shimizu Y, Yoshimoto J, Toki S, et al. Toward Probabilistic Diagnosis and Understanding of Depression Based on Functional MRI Data Analysis with Logistic Group LASSO. *PLoS One*. 2015;10(5):e0123524.
300. Siegle GJ, Thompson WK, Collier A, et al. Toward clinically useful neuroimaging in depression treatment: prognostic utility of subgenual cingulate activity for determining depression outcome in cognitive therapy across studies, scanners, and patient characteristics. *Arch Gen Psychiatry*. 2012;69(9):913-924.
301. Squarcina L, Dagneu TM, Rivolta MW, Bellani M, Sassi R, Brambilla P. Automated cortical thickness and skewness feature selection in bipolar disorder using a semi-supervised learning method. *J Affect Disord*. 2019;256:416-423.
302. Stange JP, Jenkins LM, Pocius S, et al. Using resting-state intrinsic network connectivity to identify suicide risk in mood disorders. *Psychol Med*. 2020;50(14):2324-2334.
303. Stoyanov D, Kandilarova S, Paunova R, Barranco Garcia J, Latypova A, Kherif F. Cross-Validation of Functional MRI and Paranoid-Depressive Scale: Results From Multivariate Analysis. *Front Psychiatry*. 2019;10:869.
304. Sun F, Liu Z, Yang J, Fan Z, Yang J. Differential Dynamical Pattern of Regional Homogeneity in Bipolar and Unipolar Depression: A Preliminary Resting-State fMRI Study. *Front Psychiatry*. 2021;12:764932.
305. Sun K, Liu Z, Chen G, et al. A two-center radiomic analysis for differentiating major depressive disorder using multi-modality MRI data under different parcellation methods. *J Affect Disord*. 2022;300:1-9.
306. Sun F, Liu Z, Fan Z, Zuo J, Xi C, Yang J. Dynamical regional activity in putamen distinguishes bipolar type I depression and unipolar depression. *J Affect Disord*. 2022;297:94-101.
307. Sverdlov O, Curcic J, Hannesdottir K, et al. A Study of Novel Exploratory Tools, Digital Technologies, and Central Nervous System Biomarkers to Characterize Unipolar Depression. *Front Psychiatry*. 2021;12:640741.
308. Tang Q, Cui Q, Chen Y, et al. Shared and distinct changes in local dynamic functional connectivity patterns in major depressive and bipolar depressive disorders. *J Affect Disord*. 2022;298(Pt A):43-50.

309. Tenke CE, Kayser J, Manna CG, et al. Current source density measures of electroencephalographic alpha predict antidepressant treatment response. *Biol Psychiatry*. 2011;70(4):388-394.
310. Uyulan C, de la Salle S, Erguzel TT, et al. Depression Diagnosis Modeling With Advanced Computational Methods: Frequency-Domain eMVAR and Deep Learning. *Clin EEG Neurosci*. 2022;53(1):24-36.
311. van Waarde JA, Scholte HS, van Oudheusden LJ, Verwey B, Denys D, van Wingen GA. A functional MRI marker may predict the outcome of electroconvulsive therapy in severe and treatment-resistant depression. *Mol Psychiatry*. 2015;20(5):609-614.
312. Voineskos D, Blumberger DM, Zomorodi R, et al. Altered Transcranial Magnetic Stimulation-Electroencephalographic Markers of Inhibition and Excitation in the Dorsolateral Prefrontal Cortex in Major Depressive Disorder. *Biol Psychiatry*. 2019;85(6):477-486.
313. Wade BSC, Sui J, Njau S, et al. Data-Driven Cluster Selection for Subcortical Shape and Cortical Thickness Predicts Recovery from Depressive Symptoms. *Proc IEEE Int Symp Biomed Imaging*. 2017;2017:502-506.
314. Wade BSC, Sui J, Hellemann G, et al. Inter and intra-hemispheric structural imaging markers predict depression relapse after electroconvulsive therapy: a multisite study. *Transl Psychiatry*. 2017;7(12):1270.
315. Wang Y, Gong N, Fu C. Major depression disorder diagnosis and analysis based on structural magnetic resonance imaging and deep learning. *J Integr Neurosci*. 2021;20(4):977-984.
316. Wang Y, Sun K, Liu Z, et al. Classification of Unmedicated Bipolar Disorder Using Whole-Brain Functional Activity and Connectivity: A Radiomics Analysis. *Cereb Cortex*. 2020;30(3):1117-1128.
317. Wang Y, Wang J, Jia Y, et al. Topologically convergent and divergent functional connectivity patterns in unmedicated unipolar depression and bipolar disorder. *Transl Psychiatry*. 2017;7(7):e1165.
318. Wang X, Ren Y, Zhang W. Depression Disorder Classification of fMRI Data Using Sparse Low-Rank Functional Brain Network and Graph-Based Features. *Comput Math Methods Med*. 2017;2017:3609821.
319. Wu Z, Wang C, Ma Z, et al. Abnormal functional connectivity of habenula in untreated patients with first-episode major depressive disorder. *Psychiatry Res*. 2020;285:112837.
320. Wu P, Zhang A, Sun N, et al. Cortical Thickness Predicts Response Following 2 Weeks of SSRI Regimen in First-Episode, Drug-Naive Major Depressive Disorder: An MRI Study. *Front Psychiatry*. 2021;12:751756.
321. Wu MJ, Mwangi B, Bauer IE, et al. Identification and individualized prediction of clinical phenotypes in bipolar disorders using neurocognitive data, neuroimaging scans and machine learning. *Neuroimage*. 2017;145(Pt B):254-264.
322. Xi C, Liu Z, Zeng C, et al. The centrality of working memory networks in differentiating bipolar type I depression from unipolar depression: A task-fMRI study. *Can J Psychiatry*. 2022;7067437221078646.
323. Xiao H, Yuan M, Li H, et al. Functional connectivity of the hippocampus in predicting early antidepressant efficacy in patients with major depressive disorder. *J Affect Disord*. 2021;291:315-321.
324. Xue L, Pei C, Wang X, et al. Predicting Neuroimaging Biomarkers for Antidepressant Selection in Early Treatment of Depression. *J Magn Reson Imaging*. 2021;54(2):551-559.

325. Yan B, Xu X, Liu M, et al. Quantitative Identification of Major Depression Based on Resting-State Dynamic Functional Connectivity: A Machine Learning Approach. *Front Neurosci.* 2020;14:191.
326. Yan DD, Zhao LL, Song XW, Zang XH, Yang LC. Automated detection of clinical depression based on convolution neural network model. *Biomed Tech (Berl).* 2022;67(2):131-142.
327. Yan M, Cui X, Liu F, et al. Abnormal Default-Mode Network Homogeneity in Melancholic and Nonmelancholic Major Depressive Disorder at Rest. *Neural Plast.* 2021;2021:6653309.
328. Yan M, He Y, Cui X, et al. Disrupted Regional Homogeneity in Melancholic and Non-melancholic Major Depressive Disorder at Rest. *Front Psychiatry.* 2021;12:618805.
329. Yang J, Zhang M, Ahn H, et al. Development and evaluation of a multimodal marker of major depressive disorder. *Hum Brain Mapp.* 2018;39(11):4420-4439.
330. Yang J, Yin Y, Zhang Z, et al. Predictive brain networks for major depression in a semi-multimodal fusion hierarchical feature reduction framework. *Neurosci Lett.* 2018;665:163-169.
331. Yang J, Pu W, Ouyang X, et al. Abnormal Connectivity Within Anterior Cortical Midline Structures in Bipolar Disorder: Evidence From Integrated MRI and Functional MRI. *Front Psychiatry.* 2019;10:788.
332. Yang H, Li L, Peng H, et al. Alterations in regional homogeneity of resting-state brain activity in patients with major depressive disorder screening positive on the 32-item hypomania checklist (HCL-32). *J Affect Disord.* 2016;203:69-76.
333. Yoshida K, Shimizu Y, Yoshimoto J, et al. Prediction of clinical depression scores and detection of changes in whole-brain using resting-state functional MRI data with partial least squares regression. *PLoS One.* 2017;12(7):e0179638.
334. Yu H, Li F, Wu T, et al. Functional brain abnormalities in major depressive disorder using the Hilbert-Huang transform. *Brain Imaging Behav.* 2018;12(6):1556-1568.
335. Zeng LL, Shen H, Liu L, et al. Identifying major depression using whole-brain functional connectivity: a multivariate pattern analysis. *Brain.* 2012;135(Pt 5):1498-1507.
336. Zhang A, Wang X, Li J, et al. Resting-State fMRI in Predicting Response to Treatment With SSRIs in First-Episode, Drug-Naive Patients With Major Depressive Disorder. *Front Neurosci.* 2022;16:831278.
337. Zhang B, Liu S, Liu X, et al. Discriminating subclinical depression from major depression using multi-scale brain functional features: A radiomics analysis. *J Affect Disord.* 2022;297:542-552.
338. Zhang Q, Wu Q, Zhu H, et al. Multimodal MRI-Based Classification of Trauma Survivors with and without Post-Traumatic Stress Disorder. *Front Neurosci.* 2016;10:292.
339. Zhao J, Huang J, Zhi D, et al. Functional network connectivity (FNC)-based generative adversarial network (GAN) and its applications in classification of mental disorders. *J Neurosci Methods.* 2020;341:108756.
340. Zhao L, Wang Y, Jia Y, et al. Microstructural Abnormalities of Basal Ganglia and Thalamus in Bipolar and Unipolar Disorders: A Diffusion Kurtosis and Perfusion Imaging Study. *Psychiatry Investig.* 2017;14(4):471-482.
341. Zhdanov A, Atluri S, Wong W, et al. Use of Machine Learning for Predicting Escitalopram Treatment Outcome From Electroencephalography Recordings in Adult Patients With Depression. *JAMA Netw Open.* 2020;3(1):e1918377.

342. Zheng Y, Chen X, Li D, et al. Treatment-naïve first episode depression classification based on high-order brain functional network. *J Affect Disord.* 2019;256:33-41.
343. Zhong X, Shi H, Ming Q, et al. Whole-brain resting-state functional connectivity identified major depressive disorder: A multivariate pattern analysis in two independent samples. *J Affect Disord.* 2017;218:346-352.
344. Zhu Z, Lei D, Qin K, et al. Combining Deep Learning and Graph-Theoretic Brain Features to Detect Posttraumatic Stress Disorder at the Individual Level. *Diagnostics (Basel).* 2021;11(8).
345. Zhu X, Yuan F, Zhou G, et al. Cross-network interaction for diagnosis of major depressive disorder based on resting state functional connectivity. *Brain Imaging Behav.* 2021;15(3):1279-1289.
346. Zhu H, Yuan M, Qiu C, et al. Multivariate classification of earthquake survivors with post-traumatic stress disorder based on large-scale brain networks. *Acta Psychiatr Scand.* 2020;141(3):285-298.
347. Zhu J, Cai H, Yuan Y, et al. Variance of the global signal as a pretreatment predictor of antidepressant treatment response in drug-naïve major depressive disorder. *Brain Imaging Behav.* 2018;12(6):1768-1774.
348. Zhu Y, Qi S, Zhang B, et al. Connectome-Based Biomarkers Predict Subclinical Depression and Identify Abnormal Brain Connections With the Lateral Habenula and Thalamus. *Front Psychiatry.* 2019;10:371.
349. Bruun CF, Arnbjerg CJ, Kessing LV. Electroencephalographic Parameters Differentiating Melancholic Depression, Non-melancholic Depression, and Healthy Controls. A Systematic Review. *Front Psychiatry.* 2021;12:648713.
350. Cohen SE, Zantvoord JB, Wezenberg BN, Bockting CLH, van Wingen GA. Magnetic resonance imaging for individual prediction of treatment response in major depressive disorder: a systematic review and meta-analysis. *Transl Psychiatry.* 2021;11(1):168.
351. De Crescenzo F, Ciliberto M, Menghini D, Treglia G, Ebmeier KP, Janiri L. Is (18)F-FDG-PET suitable to predict clinical response to the treatment of geriatric depression? A systematic review of PET studies. *Aging Ment Health.* 2017;21(9):889-894.
352. Dichter GS, Gibbs D, Smoski MJ. A systematic review of relations between resting-state functional-MRI and treatment response in major depressive disorder. *J Affect Disord.* 2015;172:8-17.
353. Enneking V, Leehr EJ, Dannlowski U, Redlich R. Brain structural effects of treatments for depression and biomarkers of response: a systematic review of neuroimaging studies. *Psychol Med.* 2020;50(2):187-209.
354. Fu CH, Steiner H, Costafreda SG. Predictive neural biomarkers of clinical response in depression: a meta-analysis of functional and structural neuroimaging studies of pharmacological and psychological therapies. *Neurobiol Dis.* 2013;52:75-83.
355. Gillett G, Tomlinson A, Efthimiou O, Cipriani A. Predicting treatment effects in unipolar depression: A meta-review. *Pharmacol Ther.* 2020;212:107557.
356. Levy A, Taib S, Arbus C, et al. Neuroimaging Biomarkers at Baseline Predict Electroconvulsive Therapy Overall Clinical Response in Depression: A Systematic Review. *J ECT.* 2019;35(2):77-83.
357. Long Z, Du L, Zhao J, Wu S, Zheng Q, Lei X. Prediction on treatment improvement in depression with resting state connectivity: A coordinate-based meta-analysis. *J Affect Disord.* 2020;276:62-68.

358. Masse-Sibille C, Djamila B, Julie G, Emmanuel H, Pierre V, Gilles C. Predictors of Response and Remission to Antidepressants in Geriatric Depression: A Systematic Review. *J Geriatr Psychiatry Neurol*. 2018;31(6):283-302.
359. Siegel-Ramsay JE, Bertocci MA, Wu B, Phillips ML, Strakowski SM, Almeida JRC. Distinguishing between depression in bipolar disorder and unipolar depression using magnetic resonance imaging: a systematic review. *Bipolar Disord*. 2022.
360. Simon L, Blay M, Galvao F, Brunelin J. Using EEG to Predict Clinical Response to Electroconvulsive Therapy in Patients With Major Depression: A Comprehensive Review. *Front Psychiatry*. 2021;12:643710.
361. van der Vinne N, Vollebregt MA, van Putten M, Arns M. Frontal alpha asymmetry as a diagnostic marker in depression: Fact or fiction? A meta-analysis. *Neuroimage Clin*. 2017;16:79-87.
362. Widge AS, Bilge MT, Montana R, et al. Electroencephalographic Biomarkers for Treatment Response Prediction in Major Depressive Illness: A Meta-Analysis. *Am J Psychiatry*. 2019;176(1):44-56.
363. Librenza-Garcia D, Kotzian BJ, Yang J, et al. The impact of machine learning techniques in the study of bipolar disorder: A systematic review. *Neurosci Biobehav Rev*. 2017;80:538-554.
364. Seeberg I, Kjaerstad HL, Miskowiak KW. Neural and Behavioral Predictors of Treatment Efficacy on Mood Symptoms and Cognition in Mood Disorders: A Systematic Review. *Front Psychiatry*. 2018;9(JUL):337.
365. Whalley HC, Pappmeyer M, Sprooten E, Lawrie SM, Sussmann JE, McIntosh AM. Review of functional magnetic resonance imaging studies comparing bipolar disorder and schizophrenia. *Bipolar Disord*. 2012;14(4):411-431.
366. Colvonen PJ, Glassman LH, Crocker LD, et al. Pretreatment biomarkers predicting PTSD psychotherapy outcomes: A systematic review. *Neurosci Biobehav Rev*. 2017;75:140-156.
367. Nelson MD, Tumpap AM. Posttraumatic stress disorder symptom severity is associated with left hippocampal volume reduction: a meta-analytic study. *CNS Spectr*. 2017;22(4):363-372.
368. Haghbayan H, Boutin A, Laflamme M, et al. The Prognostic Value of MRI in Moderate and Severe Traumatic Brain Injury: A Systematic Review and Meta-Analysis. *Crit Care Med*. 2017;45(12):e1280-e1288.
369. Hulkower MB, Poliak DB, Rosenbaum SB, Zimmerman ME, Lipton ML. A decade of DTI in traumatic brain injury: 10 years and 100 articles later. *AJNR Am J Neuroradiol*. 2013;34(11):2064-2074.
370. Raji CA, Tarzwell R, Pavel D, et al. Clinical utility of SPECT neuroimaging in the diagnosis and treatment of traumatic brain injury: a systematic review. *PLoS One*. 2014;9(3):e91088.
371. Qing X, Gu L, Li D. Abnormalities of Localized Connectivity in Obsessive-Compulsive Disorder: A Voxel-Wise Meta-Analysis. *Front Hum Neurosci*. 2021;15:739175.
372. Santos VA, Carvalho DD, Van Ameringen M, Nardi AE, Freire RC. Neuroimaging findings as predictors of treatment outcome of psychotherapy in anxiety disorders. *Prog Neuropsychopharmacol Biol Psychiatry*. 2019;91:60-71.
373. Xu J, Van Dam NT, Feng C, et al. Anxious brain networks: A coordinate-based activation likelihood estimation meta-analysis of resting-state functional connectivity studies in anxiety. *Neurosci Biobehav Rev*. 2019;96:21-30.