REVIEW ARTICLE OPEN

Check for updates

Heart rate variability in mental disorders: an umbrella review of meta-analyses

Zuxing Wang[1,2], Yazhu Zou[1,2], Jingwen Liu[1], Wei Peng[1], Mingmei Li[1] and Zhili Zou[1]✉

Heart rate variability (HRV) monitoring is increasingly applied in the realm of mental disorders; however, it remains a subject of controversy. This umbrella review summarizes HRV differences between individuals with mental disorders and healthy controls (HCs), as well as changes in HRV before and after treatment in patients with mental disorders. A literature search was conducted using Medline, PubMed, Embase, and the Cochrane Database. Meta-analyses on HRV changes in patients with mental disorders, as well as meta-analyses comparing HCs and patients with mental disorders were included. We computed the summary effect size using random effects models, along with 95% confidence and prediction intervals. We assessed heterogeneity, *p* value of the largest study, excess significance bias, and small-study effects. Evidence levels were classified as convincing, highly suggestive, suggestive, weak, or not significant. Twenty-one systematic reviews on HRV, covering 19 mental disorders (53 meta-analyses) and 8 treatment modalities (18 meta-analyses), included 442 primary studies and 34,625. For differences between mental disorders and HCs, evidence was suggestive for 7 (13.2%) pooled analyses, indicating decreased HRV in dementia, PTSD, somatic symptom disorders, functional somatic syndromes, and schizophrenia. For other disorders, including autism spectrum disorder, alcohol use disorder, bipolar disorder, generalized anxiety disorder, insomnia, and major depressive disorder, the evidence was weaker and below the suggestive level. For treatment effects, 5 pooled analyses (27.8%) had weak evidence, indicating altered HRV before and after antipsychotic treatment, repetitive transcranial magnetic stimulation treatment, physiotherapy, and psychotherapy. The credibility of HRV evidence in mental disorders varied across HRV variables and diseases. No two diseases exhibited identical altered HRV patterns, highlighting the potential significance of overall HRV profiles in delineating distinct disorders.

Translational Psychiatry (2025)15:104 ; https://doi.org/10.1038/s41398-025-03339-x

INTRODUCTION

Mental disorders, including conditions like depression, anxiety disorders, schizophrenia, and bipolar disorder among others, impose a substantial burden on global health [1]. These conditions impact individuals across various aspects of their lives, posing challenges for both patients and healthcare systems worldwide [1, 2]. Individuals with mental disorders often exhibit dysregulation in autonomic nervous system activity, with changes in the balance between sympathetic and parasympathetic nervous system functions [3–6]. For instance, in patients with anxiety disorders, common emotional and physiological responses may lead to overactivation of the sympathetic nervous system, which is manifested by changes in physiological indicators such as increased heart rate and elevated blood pressure [3, 6]. On the other hand, in certain mental illnesses like depression, activity of the parasympathetic nervous system may be diminished, resulting in symptoms such as sleep disturbances and digestive issues [4].

Heart Rate Variability (HRV) refers to the changes in the time intervals between heartbeats. Under normal circumstances, the heart rate does not remain completely steady; rather, it fluctuates to a certain extent, and this variability is what HRV represents. HRV reflects the regulatory capacity of the autonomic nervous system (ANS) over the heart rhythm, including the interaction between the sympathetic nervous system and the parasympathetic nervous system [7]. Higher levels of HRV, particularly those associated with parasympathetic-dominated indices, are typically regarded as a sign of good health, as they reflect the flexibility and adaptability of the autonomic nervous system [8]. Conversely, decreased HRV may be linked to cardiovascular diseases, psychological stress, anxiety, depression, and other issues [8, 9]. Psychological stress and emotional states can directly impact the activity of the autonomic nervous system, thus influencing HRV levels [10]. Additionally, certain medications can affect the activity of the autonomic nervous system, and the HRV levels of individuals with mental illnesses may change after receiving treatment [11, 12]. Therefore, studying the changes of HRV in mental disorders may reveal the neurobiological mechanisms of specific conditions, revealing neural commonalities and differences. This could potentially enhance diagnostic classifications and may offer insights for improving clinical management.

Numerous case-control and longitudinal studies have documented varied changes in HRV across various mental disorder [13, 14], with some disorders having undergone meta-analytic scrutiny [15]. However, meta-analyses can be limited by methodological rigor and are vulnerable to reporting bias, publication bias, residual confounding, and other issues [16–19], which may

[1]Sichuan Provincial Center for Mental Health, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu, China. [2]These authors contributed equally: Zuxing Wang, Yazhu Zou. ✉email: zou_zhili@163.com

Received: 11 October 2024 Revised: 21 February 2025 Accepted: 19 March 2025
Published online: 28 March 2025

obscure the true relationship between HRV and mental disorders. This underscores the need for more robust evidence synthesis to accurately assess the neurobiological mechanisms underlying HRV alterations in mental health [20]. Umbrella reviews offer a more comprehensive and systematic approach to evaluating evidence by consolidating findings from multiple meta-analyses [21, 22]. Unlike traditional meta-analyses, which focus on singular topics, umbrella reviews offer the advantage of examining evidence across a broad, high-quality database, providing a comprehensive overview [23]. Given the growing complexity of psychiatric research, umbrella reviews provide an essential tool for navigating large volumes of evidence on HRV alterations in mental disorders, ensuring a more accurate and nuanced understanding of the findings [24].

To our knowledge, no umbrella review has explored HRV changes in mental disorders. Given the involvement of the ANS in these diseases, such a review could offer unique insights. Thus, we conducted the first umbrella review of relevant meta-analyses of longitudinal and case-control studies, aiming to offer a thorough evaluation of evidence strength, estimate precision, presence of bias, and HRV alterations in patients with mental disorders compared to healthy controls (HCs), as well as patients before and after treatment for psychiatric conditions.

METHODS

The systematic umbrella review protocol has been prospectively registered on PROSPERO and the outcomes are presented in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [25] (PROSPERO ID: CRD42023430149).

Literature search

We searched MEDLINE, PubMed, Embase, and the Cochrane Database from inception through May 2023 to identify meta-analyses of both observational and interventional studies exploring HRV in patients with mental disorders compared with HCs or HRV changes after treatment modalities for mental disorders. Designated search terms were searched in title and abstract: (heart rate variability OR HRV) AND (meta-analysis or metaanaly* or meta-analy* or meta analy*). Supplementary Table S1 contains the specific search strategies employed for each literature database. Two authors (ZXW and YZZ) separately conducted electronic searches to screen the titles and abstracts retrieved from the databases and selected potential eligible meta-analyses. Eligible articles were identified through manual screening of the references in relevant studies. Any discrepancies in the literature screening between the two reviewers were resolved by a third author (ZLZ). Furthermore, we conducted an updated literature search utilizing the same search strategies on April 1, 2024, to identify any newly published meta-analyses.

Eligibility criteria

We included systematic reviews and meta-analyses following these eligibility criteria: (1) meta- analyses exploring differences in HRV parameters (i.e., HRV in hierarchical order, high-frequency (HF), low-frequency (LF), root mean square of the successive differences between normal heartbeats (RMSSD), standard deviation of NN intervals (SDNN), LF/HF) between patients with mental disorders and healthy controls as well as before and after receiving common treatments for mental illnesses; (2) patients were diagnosed with mental disorders based on criteria from any edition of the Diagnostic and Statistical Manual (DSM), or the International Classification of Diseases (ICD), or through structured psychiatric diagnostic interviews; (3) Eligible meta-analyses were published in English peer-reviewed journals. In cases where multiple meta-analyses on the same topic were encountered, we included the most recent one containing the largest number of studies. Exclusions comprised articles that did not examine HRV in mental disorders, those lacking a meta-analysis, and those lacking sufficient data for re-analysis (such as individual study estimates or necessary data for calculations). Additionally, we excluded non-human studies, genetic studies, primary studies, and conference abstracts. It should be noted that many meta-analyses combine various individual HRV indices into a single composite HRV measure following a hierarchical order, including: respiratory sinus arrhythmia, HF (absolute, logarithmically transformed, and normalized values), RMSSD, total power (absolute and logarithmically transformed values), and SDNN [26–28]. In this paper, all HRV indices mentioned refer to the composite HRV measure constructed using this method.

Data extraction and quality assessment

Two reviewers (ZXW and YZZ) independently extracted the following information from each eligible study: the first author's name, publication year, number of included studies, population demographics (children, adolescents, adults, or elderly individuals), and primary outcome. Additionally, we extracted the number of cases and HCs, the study-specific estimated effect sizes of HRV parameters, and their corresponding 95% confidence intervals (CIs) in each study. In cases where the eligible article only provided pooled effect sizes without reporting the study-specific effect size, we extracted this information from the individual component studies within each eligible article and recalculated the effect sizes. Any discrepancies in the extracted data between the two researchers were resolved by a third author (ZLZ).

The methodological quality of the included meta-analyses underwent critical appraisal using AMSTAR 2 (A Measurement Tool to Assess Systematic Reviews), a 16-item rating scale known for its strong interrater reliability and usability [29]. Unlike traditional scoring systems, AMSTAR 2 does not produce an overall score; rather, it categorizes the confidence in systematic reviews into four broad classifications (high, moderate, low, and critically low) based on various criteria,

including review design, literature screening, data extraction, and assessment of individual study quality. All detailed quality assessments of the included meta-analyses, as well as the evaluation criteria of AMSTAR 2, are presented in Supplementary Table S2.

Data analysis

All meta-analyses included in our study reported effect sizes as standardized mean differences (SMDs), consistent with the standard practice in HRV studies. We re-estimated these SMDs with 95% CI using common metric random effects methods. Heterogeneity between studies was assessed through Cochran's Q test and the $I2$ statistic ($I2 > 50\%$ suggests high heterogeneity). Furthermore, we calculated the 95% prediction interval to anticipate HRV differences between groups in future studies. We identified instances where prediction intervals, excluding the null value (0 for SMDs), suggest persistent statistically significant HRV changes in patients with mental disorders across future studies. We examined evidence for small-study effects using Egger's regression asymmetry test. A p-value below 0.1, along with more conservative effect sizes in larger researches relative to those in random effects meta-analysis, indicated small-study effects.

Excess significance was assessed to determine if the observed number of studies (O) with nominally statistically significant results ($p < 0.05$) exceeded the expected number (E) [27]. The expected number of significant studies for each meta-analysis was estimated based on the sum of statistical power estimates for individual studies, utilizing an algorithm from a noncentral t distribution. The effect size of the largest study in each meta-analysis served as the plausible power for the tested association. The significance threshold for excess significance bias was set at $p < 0.10$. Excess significance for a single meta-analysis was

Table 1. Level of evidence for grading levels.

	Convincing (class I)	Highly suggestive (class II)	Suggestive (class III)	Weak (class IV)	Not significant (NS)
Random effects *p* value	<0.000001	<0.000001	<0.001	<0.05	>0.05
Number of patients with mental disorder	>1000	>1000	>1000	—	_
p value of the largest study	<0.05	<0.05	—	—	—
Heterogeneity (I^2)	<50%	—	—	—	—
Small study effects	Not detected	—	—	—	—
Excess significance bias	Not detected	—	—	—	—
95% prediction interval	Excludes the null	—	—	—	—

confirmed at $p < 0.10$ (1-sided $p < 0.05$ with O > E, as previously proposed) [30]. All statistical analyses were conducted using R version 4.3.0 and the *p* values were all 2-tailed.

Credibility of evidence

Consistent with prior umbrella reviews [24], we categorized the eligible meta-analyses based on the strength of evidence regarding the HRV difference between mental illness patients and HCs as well as the HRV difference before and after psychiatric treatment modalities into five classes: convincing (class I), highly suggestive (class II), suggestive (class III), weak (class IV), and not significant (NS). Criteria for each level of evidence included *p* values under a random effects model, the number of patients with mental disorder, the statistical significance of the largest study, small study effects, the I^2 statistic, random effects summary estimate under a 10% credibility ceiling, the 95% prediction interval, and the excess significance bias. The detailed information and rating criteria are shown in Table 1.

RESULTS

Our systematic database search identified 757 records. After removing duplicates and the inspection of titles and abstracts, 92 full-text articles were assessed for eligibility. Twenty-one systematic reviews investigating HRV, involving 19 mental disorders (53 meta-analyses) and 8 treatment modalities (18 meta-analyses) related to mental disorders, comprising 71 meta-analyses, met the inclusion criteria for the umbrella review and were included for reanalysis (Fig. 1).

Details of the excluded reviews with the reasons for exclusion were provided in Supplementary Table S3. Overall, 21 systematic reviews were included, comprising 442 primary studies and 34,625 participants [11, 12, 14, 15, 26–28, 31–44]. From the included systematic reviews, we extracted information regarding the role of assessed HRV in mental disorders of interest (Tables 2 and 3). Among these 71 pooled analyses of different indicators of HRV, there were 1 on attention-deficit/hyperactivity disorder (ADHD), 4 on autism spectrum disorders (ASD), 3 on alcohol use disorders (AUD), 1 on bulimia nervosa (BN), 4 on bipolar disorder (BP), 1 on borderline personality disorder (BPD), 6 on dementia or neurocognitive disorders, 4 on generalized anxiety disorder (GAD), 1 on insomnia disorders, 5 on major depressive disorder (MDD), 1 on children and adolescents MDD, 1 on late-life MDD, 1 on obsessive compulsive disorder (OCD), 4 on panic disorder (PD), 1 on problematic internet use, 4 on post-traumatic stress disorder (PTSD), 4 on social anxiety disorder (SAD), 5 on somatic symptom disorders and functional somatic syndromes, 2 on schizophrenia, 1 on the impact of antidepressants, 1 on the impact of antipsychotics, 1 on the impact of mindfulness, 4 on the impact of repetitive transcranial magnetic stimulation (rTMS), 1 on the impact of virtual reality biofeedback, 3 on the impact of physiotherapy, 4 on the impact of psychotherapy, and 3 on the impact of pharmacotherapy.

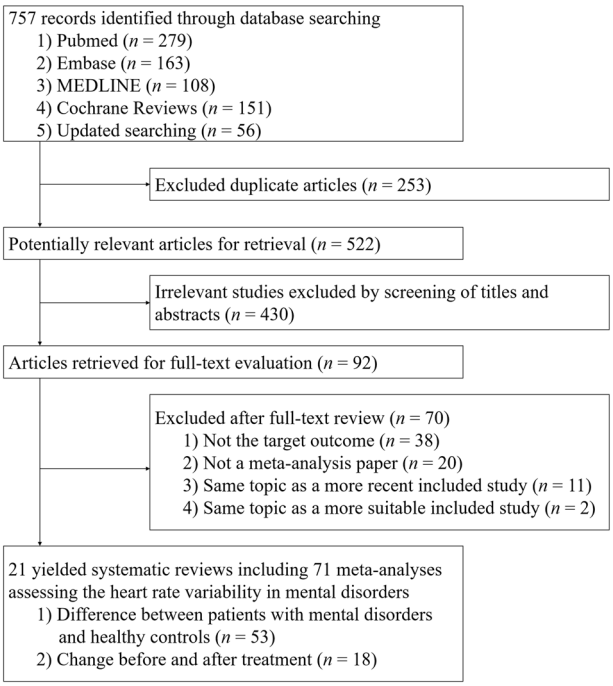

Fig. 1 Flow chart of literature search.

Difference in HRV between patients with mental disorders and HCs

In the meta-analyses comparing HRV between patients with mental disorders and HCs, 25 out of 53 pooled analyses (47.17%) yielded statistically significant results with *p*-values < 0.05, 12 (22.6%) with $p < 0.001$, and 3 (5.7%) with $p < 10\text{-}6$. Among the 12 pooled analyses involving cases of mental disorders with case sample sizes exceeding 1000, one (8.3%) were non-significant, four (33.3%) had *p*-values less than 0.05, five (41.7%) had *p*-values less than 0.001, and two (16.7%) had *p*-values less than 10-6. In 24 out of the 53 (45.3%) comparisons, the effect sizes of the largest study were nominally statistically significant at $p < 0.05$. Furthermore, 42 out of 53 pooled analyses (79.2%) exhibited substantial heterogeneity ($I2 > 50\%$). The 95% prediction interval excluded the null in only 9 out of 53 (17.0%) included comparisons. Small-study effects were observed in 28 pooled analyses (52.8%), and we did not detect excess significance bias in all 53 meta-analyses (Table 2).

As shown in Fig. 2, none of the 53 pooled analyses demonstrated convincing or highly suggestive efficacy according to the quantitative umbrella review criteria. Additionally, the credibility of the evidence was suggestive for seven (13.2%) pooled analyses, indicating decreased HRV in dementia or neurocognitive disorders and PTSD, as well as decreased HRV,

Table 2. Characteristics, quantitative synthesis, and evidence grading of the included HRV meta-analyses comparing healthy controls and individuals with mental disorders.

Outcomes	Number of comparisons	Number of cases/ controls or pre/ post cases	Random-effects summary estimate (95% CI)	Random effects *p* value	Largest study Estimate (95% CI)	I^2 (%)	95% prediction interval	Egger *p* value	Small-study effects	Significant studies observed/ expected/ *p* value	Grading
Robe et al. [33], Attention-Deficit/Hyperactivity Disorder								Quality assessments: High			
Tr-HRV	19	869/909	0.24 (0.01, 0.46)	0.04	0.10 (−0.08, 0.29)	93.74%	(−0.63, 1.11)	0.05	Yes	5/7/0.79	IV
Cheng et al. [26], Autism Spectrum Disorders								Quality assessments: Low			
Rs-HRV	31	962/977	−0.52 (−0.77, −0.28)	3.38×10^{-5}	−0.11 (−0.59, 0.36)	84.86%	(−1.80, 0.75)	0.73	No	14/15/0.64	IV
Ss-HRV	12	361/460	−0.46 (−0.75, −0.17)	1.66×10^{-3}	−0.76 (−1.47, −0.05)	69.02%	(−1.34, 0.41)	0.57	No	6/7/0.71	IV
Sd-HRV	5	92/249	−0.50 (−0.79, −0.21)	6.75×10^{-4}	−0.36 (−1.07, 0.35)	0.00%	(−0.79, −0.21)	0.76	No	1/0/0.50	IV
Ct-HRV	11	331/337	−0.25 (−0.68, 0.17)	0.24	−0.24 (−0.62, 0.15)	85.81%	(−1.62, 1.11)	0.43	No	3/4/0.77	NS
Cheng et al. [28], Alcohol Use Disorders								Quality assessments: High			
HRV	15	511/873	−0.43 (−0.76, −0.10)	0.01	0.26 (0.10, 0.43)	84.12%	(−1.61, 0.75)	0.01	Yes	8/8/0.60	IV
HF	10	237/305	−0.21 (−0.52, 0.09)	0.17	−0.20 (−0.60, 0.20)	66.33%	(−1.05, 0.63)	0.55	No	3/3/0.66	NS
RMSSD	4	92/140	−0.78 (−1.18, −0.37)	1.63×10^{-4}	−0.39 (−0.79, 0.01)	47.36%	(−1.47, −0.09)	0.04	Yes	3/2/0.50	IV
Peschel et al. [31], Bulimia Nervosa								Quality assessments: Low			
HF	8	137/190	0.51 (0.04, 0.99)	0.03	0.59 (0.08, 1.09	74.60%	(−0.72, 1.75)	0.60	No	0/3/1.00	IV
Faurholt-Jepsen et al. [43], Bipolar Disorder								Quality assessments: High			
HRV	10	495/1086	−2.08 (−3.60, −0.56)	0.01	−0.22 (−0.43, −0.02)	99.24%	(−7.07, 2.91)	5.44×10^{-19}	Yes	9/10/0.68	IV
HF	11	490/911	−0.32 (−3.05, 2.41)	0.82	−0.35 (−0.56, −0.15)	99.75%	(−9.72, 9.09)	0.42	No	6/6/0.61	NS
LF	10	469/883	−1.17 (−3.15, 0.82)	0.25	−0.16 (−0.37, 0.04)	99.51%	(−7.71, 5.38)	0.08	Yes	5/5/0.62	NS
LF/HF	9	454/837	−0.26 (−2.91, 2.40)	0.85	0.35 (0.15, 0.56)	99.72%	(−8.61, 8.09)	0.02	Yes	1/1/0.75	NS
Koenig et al. [14], Borderline Personality Disorder								Quality assessments: Low			
HRV	5	96/105	−0.58 (−1.11, −0.06)	0.03	−0.57 (−1.10, −0.04)	67.60%	(−1.68, 0.51)	0.90	No	3/2/0.50	IV
Cheng et al. [27], Dementia or Neurocognitive Disorders								Quality assessments: Low			
HRV	24	1107/1017	−0.37 (−0.58, −0.16)	6.58×10^{-4}	0.09 (−0.21, 0.39)	78.62%	(−1.30, 0.55)	4.04×10^{-3}	Yes	9/12/0.81	III
HF	18	644/825	−0.37 (−0.63, −0.11)	0.01	0.09 (−0.21, 0.39)	77.90%	(−1.34, 0.60)	2.9×10^{-3}	Yes	5/7/0.81	IV
LF	15	687/755	−0.55 (−1.02, −0.09)	0.02	−0.43 (−0.85, −0.00)	92.71%	(−2.33, 1.23)	0.47	No	7/7/0.60	IV
LF/HF	14	525/474	0.08 (−0.27, 0.43)	0.65	0.07 (−0.31, 0.46)	88.99%	(−1.13, 1.29)	0.05	Yes	2/4/0.69	NS
RMSSD	11	529/564	−0.31 (−0.64, 0.01)	0.06	0.04 (−0.26, 0.34)	81.05%	(−1.31, 0.69)	8.00×10^{-4}	Yes	3/3/0.66	NS
SDNN	10	497/548	−0.26 (−0.40, −0.12)	2.15×10^{-4}	−0.16 (−0.46, 0.14)	0.01%	(−0.40, −0.12)	0.09	Yes	1/3/0.88	IV
Cheng et al. [27], Generalized Anxiety Disorder								Quality assessments: High			
HRV	17	1080/1736	−0.66 (−1.09, −0.22)	3.06×10^{-3}	−0.43 (−0.52, −0.33)	94.08%	(−2.41, 1.10)	0.07	Yes	7/15/0.70	IV
HF	8	909/1612	−0.29 (−0.80, 0.22)	0.27	−0.43 (−0.52, −0.33)	93.86%	(−1.76, 1.18)	0.52	No	3/3/0.66	NS
RMSSD	6	206/243	−0.12 (−0.31, 0.07)	0.20	−0.15 (−0.51, 0.21)	0.00%	(−0.31, 0.07)	0.14	No	0/1/1	NS
LF/HF	4	745/1274	1.46 (−1.64, 4.57)	0.36	6.16 (5.94, 6.38)	99.48%	(−5.46, 8.39)	4.41×10^{-7}	Yes	0/1/1	NS
Zhao and Jiang, [41], Insomnia Disorders								Quality assessments: Critically Low			
HRV	15	437/418	−0.41 (−0.68, −0.13)	4.24×10^{-3}	0.13 (−0.21, 0.47)	70.78%	(−1.32, 0.50)	0.40	No	6/6/0.61	IV
Wang et al. [15], Major Depressive Disorder								Quality assessments: Low			
HF	17	1009/1055	−0.38 (−0.61, −0.15)	1.17×10^{-3}	−0.32 (−0.45, −0.19)	78.88%	(−1.21, 0.44)	0.98	No	6/8/0.79	IV
LF	17	1009/1044	−0.07 (−0.42, 0.27)	0.68	−0.28 (−0.41, −0.15)	90.96%	(−1.42, 1.28)	0.07	Yes	4/4/0.64	NS
LF/HF	18	1072/1174	0.14 (0.05, 0.22)	1.48×10^{-3}	0.13 (−0.00, 0.25)	0.00%	(0.05, 0.22)	0.65	No	2/7/0.94	IV

Table 2. continued

Outcomes	Number of comparisons	Number of cases/ controls or pre/ post cases	Random-effects summary estimate (95% CI)	Random effects *p* value	Largest study Estimate (95% CI)	I^2 (%)	95% prediction interval	Egger *p* value	Small-study effects	Significant studies observed/ expected/ *p* value	Grading
RMSSD	14	503/585	−0.66 (−1.12, −0.19)	5.92×10^{-3}	−0.62 (−0.92, −0.33)	92.30%	(−2.38, 1.07)	0.12	No	7/7/0.60	IV
SDNN	9	385/412	−0.40 (−0.56, −0.25)	5.44×10^{-7}	−0.54 (−0.83, −0.24)	16.30%	(−0.65, −0.16)	0.15	No	5/5/0.62	IV
Baumeister-Lingens et al. [37], Children and Adolescents Major Depressive Disorder								Quality assessments: Low			
HRV	9	356/337	−0.59 (−1.17, −0.01)	0.05	−0.52 (−1.18, 0.14)	90.87%	(−2.33, 1.15)	3.50×10^{-3}	Yes	3/3/0.66	IV
Brown et al. [35], Late Life Major Depressive Disorder								Quality assessments: Critically Low			
HRV	5	555/348	−0.34 (−0.60, −0.07)	0.01	−0.25 (−0.76, 0.25)	66.01%	(−0.87, 0.19)	0.43	No	2/2/0.69	IV
Chalmers et al. [32], Obsessive Compulsive Disorder								Quality assessments: Critically Low			
HF	2	65/41	−0.41 (−1.22, 0.40)	0.32	−0.83 (−1.42, −0.24)	75.09%	Na	Na	Na	1/0/0.50	NS
Cheng et al. [27], Panic Disorder								Quality assessments: High			
HRV	34	926/1113	−0.26 (−0.48, −0.05)	0.02	−0.27 (−0.54, 0.01)	80.08%	(−1.39, 0.86)	0.96	No	8/8/0.76	IV
HF	25	811/926	−0.22 (−0.44, −0.00)	0.05	−0.81 (−1.13, −0.48)	76.70%	(−1.18, 0.73)	0.07	Yes	5/7/0.81	IV
RMSSD	5	144/109	−0.25 (−0.51, −0.00)	0.05	−0.27 (−0.73, 0.20)	0.00%	(−0.51, −0.00)	0.52	No	1/0/0.5	IV
LF/HF	17	546/601	−0.06 (−0.43, 0.31)	0.76	0.17 (−0.15, 0.48)	87.43%	(−1.51, 1.40)	0.42	No	3/3/0.66	NS
Cheng et al. [34], Problematic Internet Use								Quality assessments: Low			
HRV	11	340/605	−0.38 (−0.69, −0.06)	0.02	−0.62 (−0.93, −0.31)	78.16%	(−1.34, 0.59)	0.67	No	6/6/0.6	IV
Cheng et al. [27], Post-traumatic Stress Disorder								Quality assessments: High			
HRV	38	1207/1417	−0.70 (−1.11, −0.30)	8.39×10^{-4}	−0.00 (−0.26, 0.26)	95.73%	(−3.17, 1.77)	8.94×10^{-8}	Yes	12/18/0.90	III
HF	18	543/600	−1.38 (−2.32, −0.44)	3.98×10^{-3}	−0.00 (−0.26, 0.26)	97.99%	(−5.38, 2.63)	4.74×10^{-9}	Yes	10/11/0.67	IV
RMSSD	12	464/466	−1.17 (−1.86, −0.48)	9.34×10^{-4}	−0.05 (−0.31, 0.21)	95.40%	(−3.57, 1.24)	0.04	Yes	7/7/0.60	IV
LF/HF	10	242/375	0.94 (0.48, 1.39)	6.22×10^{-5}	0.14 (−0.24, 0.51)	81.43%	(−0.41, 2.28)	0.03	Yes	6/7/0.64	IV
Cheng et al. [27], Social Anxiety disorder								Quality assessments: High			
HRV	8	224/339	−0.58 (−1.14, −0.03)	0.04	−0.28 (−0.69, 0.13)	89.10%	(−2.16, 0.99)	0.01	Yes	3/3/0.66	IV
HF	4	123/224	−0.35 (−0.59, −0.12)	2.58×10^{-3}	−0.28 (−0.69, 0.13)	0.00%	(−0.59, −0.12)	0.49	No	1/0/0.5	IV
RMSSD	4	125/168	−0.38 (−0.63, −0.13)	2.43×10^{-3}	−0.40 (−0.79, −0.02)	0.00%	(−0.63, −0.13)	0.60	No	1/0/0.5	IV
LF/HF	3	92/142	0.47 (0.19, 0.74)	7.85×10^{-4}	0.71 (0.09, 1.34)	0.00%	(0.19, 0.74)	0.29	No	2/2/0.67	IV
Cheng et al. [26], Somatic Symptom Disorders and Functional Somatic Syndromes								Quality assessments: Critically Low			
HRV	85	3242/2321	−0.46 (−0.61, −0.31)	4.00×10^{-9}	−0.14 (−0.36, 0.08)	85.52%	(−1.74, 0.82)	3.28×10^{-14}	Yes	26/32/0.82	III
HF	72	2761/2132	−0.38 (−0.59, −0.18)	2.94×10^{-4}	−0.72 (−1.29, −0.16)	91.24%	(−2.03, 1.27)	0.41	No	15/21/0.79	III
RMSSD	33	1160/991	−0.37 (−0.47, −0.23)	6.68×10^{-9}	−0.18 (−0.53, 0.17)	39.24%	(−0.78, 0.08)	2.30×10^{-3}	Yes	9/15/0.92	III
SDNN	25	872/657	−0.58 (−0.87, −0.28)	1.43×10^{-3}	−0.20 (−0.45, 0.04)	85.57%	(−1.95, 0.79)	0.08	Yes	9/12/0.81	IV
LF/HF	45	1672/1294	0.41 (0.11, 0.71)	0.01	−0.33 (−0.57, −0.08)	93.19%	(0.11, 0.71)	1.51×10^{-5}	Yes	14/16/0.87	IV
Clamor et al. [38], Schizophrenia								Quality assessments: Critically Low			
HF	29	1353/1702	−0.97 (−1.37, −0.57)	2.33×10^{-6}	2.23 (2.07, 2.40)	95.13%	(−3.08, 1.15)	3.23×10^{-6}	Yes	20/23/0.73	III
RMSSD	24	1016/1469	−0.93 (−1.13, −0.54)	3.12×10^{-6}	−0.91 (−1.15, −0.77)	94.07%	(−2.80, 0.94)	1.40×10^{-3}	Yes	17/19/0.69	III

HRV heart rate variability, *HF* high-frequency, *LF* low-frequency, *RMSSD* root mean square of the successive differences between normal heartbeats, *SDNN* standard deviation of NN intervals, *HCs* healthy controls, *CI* confidence interval, *Tr-HRV* task-related HRV, *Rs-HRV* resting state HRV, *Ss-HRV* social stress HRV, *Sb-HRV* social debriefing HRV, *Ct-HRV* cognitive tasks HRV, *NS* not significant.

Table 3. Characteristics, quantitative synthesis, and evidence grading of the included HRV meta-analyses comparing patients with mental disorders before and after treatment.

Outcomes	Number of comparisons	Number of cases/ controls or pre/ post cases	Random-effects summary estimate (95% CI)	Random effects *p* value	Largest study Estimate (95% CI)	I^2 (%)	95% prediction interval	Egger *p* value	Small-study effects	Significant studies observed/ expected/ *p* value	Grading
Alvares et al. [44], The Impact of Antidepressants								Quality assessments: Critically Low			
HRV	30	562/562	−0.19 (−0.40, 0.03)	0.09	−0.28 (−0.54, −0.01)	86.61%	(−1.29, 0.92)	0.17	No	14/14/0.57	NS
Alvares et al. [44], The Impact of Antipsychotic								Quality assessments: Critically Low			
HRV	9	209/209	−0.28 (−0.50, −0.06)	0.01	−0.35 (−0.53, −0.16)	69.17%	(−0.85, 0.29)	0.78	No	5/5/0.62	IV
Brown et al. [11], The Impact of Mindfulness								Quality assessments: Low			
HRV	16	1720/1720	0.38 (−0.01, 0.77)	0.06	1.09 (0.72, 1.47)	89.13%	(−1.12, 1.88)	0.26	No	2/4/0.68	NS
Lee et al. [39], The Impact of Repetitive Transcranial Magnetic Stimulation								Quality assessments: High			
HF	7	134/134	0.29 (−0.33, 0.91)	0.36	−0.46 (−0.90, −0.03)	84.31%	(−1.31, 1.89)	0.49	No	1/1/0.75	NS
LF	4	90/90	1.05 (−0.59, 2.69)	0.21	0.50 (0.06, 0.94)	96.55%	(−2.52, 4.62)	3.01×10^{-4}	Yes	2/1/0.50	NS
RMSSD	4	77/77	0.42 (0.11, 0.73)	8.70×10^{-3}	0.25 (−0.33, 0.82)	31.49%	(−0.05, 0.89)	0.59	No	2/1/0.50	IV
LF/HF	5	102/102	−0.23 (−0.55, −0.03)	0.03	−0.46 (−0.89, −0.02)	0.00%	(−0.55, −0.03)	0.87	No	1/0/0.50	IV
Kothgassner et al. [36], The Impact of Virtual Reality Biofeedback								Quality assessments: Critically Low			
HRV	3	63/63	0.14 (−0.21, 0.48)	0.44	0.10 (−0.39, 0.59)	0.00%	(−0.21, 0.48)	0.81	No	0/1/1	NS
Chen et al. [12], The Impact of physiotherapy on Major Depressive Disorder								Quality assessments: Low			
HF	7	107/107	0.22 (−0.19, 0.63)	0.29	0.62 (0.07, 1.16)	53.16%	(−0.66, 1.11)	0.59	No	2/2/0.65	NS
LF	7	107/107	−0.39 (−0.74, −0.05)	0.03	−0.66 (−1.21, −0.11)	34.22%	(−1.03, 0.24)	0.41	No	2/2/0.69	IV
LF/HF	5	73/73	−0.24 (−0.82, 0.34)	0.42	−0.70 (−1.25, −0.15)	65.02%	(−1.43, 0.95)	0.77	No	2/2/0.69	NS
Chen et al. [12], The Impact of psychotherapy on Major Depressive Disorder								Quality assessments: Low			
HF	7	178/178	0.24 (0.03, 0.44)	0.03	0.04 (−0.42, 0.50)	0.00%	(0.03, 0.44)	0.45	No	1/1/0.75	IV
LF	5	105/105	0.27 (−0.00, 0.54)	0.05	0.12 (−0.30, 0.55)	0.00%	(−0.00, 0.54)	0.74	No	0/1/1	NS
SDNN	5	105/105	0.26 (−0.05, 0.57)	0.10	0.09 (−0.34, 0.51)	17.06%	(−0.16, 0.69)	0.78	No	1/1/0.75	NS
LF/HF	5	105/105	0.09 (−0.18, 1.63)	0.61	−0.22 (−0.65, 0.20)	32.15%	(−0.47, 0.65)	0.19	No	0/1/1	NS
Chen et al. [12], The Impact of pharmacotherapy on Major Depressive Disorder								Quality assessments: Low			
HF	6	195/195	0.67 (−0.09, 1.42)	0.08	1.12 (0.73, 1.53)	91.61%	(−1.25, 2.58)	0.35	No	2/2/0.69	NS
LF	5	183/183	0.46 (−0.07, 1.00)	0.09	1.32 (0.90, 1.74)	83.92%	(−0.76, 1.68)	1.70×10^{-3}	Yes	2/2/0.69	NS
LF/HF	7	231/231	−0.64 (−1.44, 0.17)	0.12	−1.96 (−2.42, −1.49)	93.85%	(−2.86, 1.58)	0.07	Yes	2/2/0.69	NS

HRV heart rate variability, *HF* high-frequency, *LF* low-frequency, *RMSSD* root mean square of the successive differences between normal heartbeats, *SDNN* standard deviation of NN intervals, *HCs* healthy controls, *CI* confidence interval, *NS* not significant.

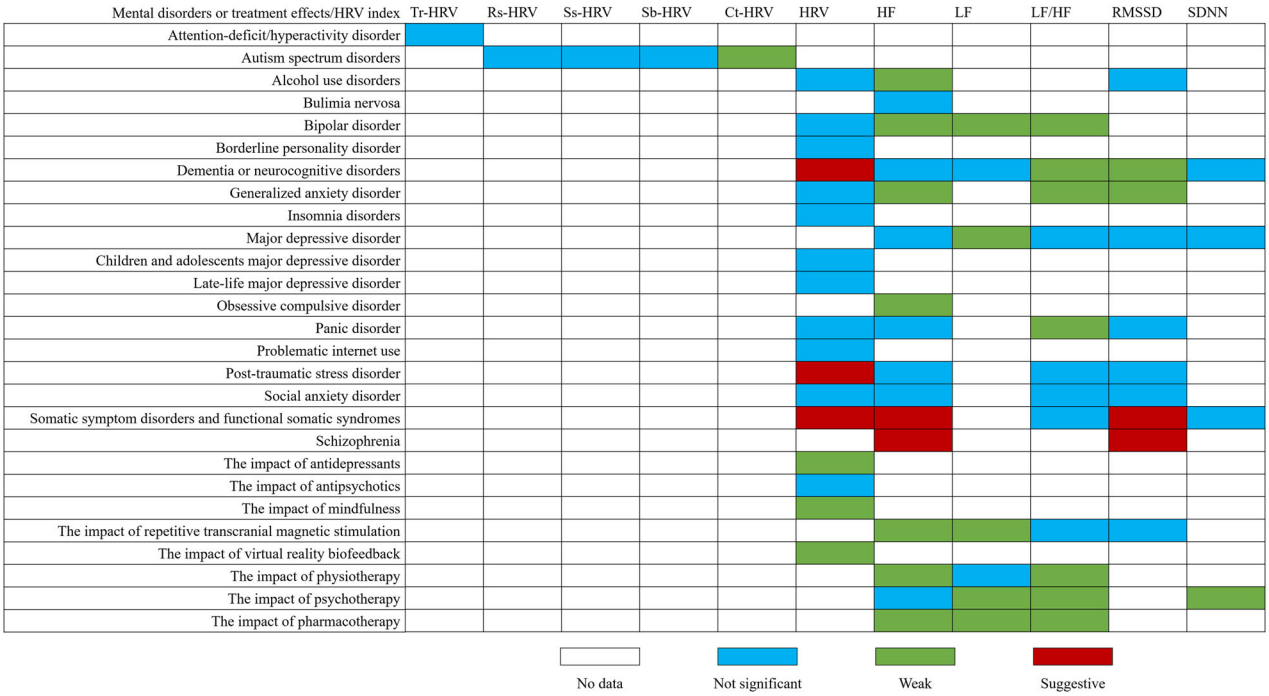

Fig. 2 Credibility of heart rate variability alterations in mental disorders. HRV heart rate variability, HF high-frequency, LF low-frequency, RMSSD, root mean square of the successive differences between normal heartbeats, SDNN standard deviation of NN intervals, Tr-HRV task-related HRV, Rs-HRV resting state HRV, Ss-HRV social stress HRV, Sb-HRV social debriefing HRV, Ct-HRV cognitive tasks HRV.

RMSSD, and HF in somatic symptom disorders and functional somatic syndromes, along with decreased RMSSD and HF in schizophrenia. Thirty-three (62.3%) were supported by weak evidence, showing decreased task-related HRV in ADHD, resting state HRV, social stress HRV, and social debriefing HRV in ASD, decreased HRV and RMSSD in AUD, decreased HF in BN, decreased HRV in BP, decreased HRV in BPD, decreased HF, LF, and SDNN in dementia or neurocognitive disorders, decreased HRV in GAD, decreased HRV in insomnia, decreased HF, RMSSD, and SDNN, and increased LF/HF in adult MDD, decreased HRV in children and adolescents and late-life MDD, decreased HRV, HF, and RMSSD in PD, decreased HRV in problematic internet use, decreased HF, RMSSD, and increased LF/HF in PTSD, decreased HRV, HF, RMSSD, and increased LF/HF in SAD, and decreased SDNN and increased LF/HF in somatic symptom disorders and functional somatic syndromes. Additionally, fifteen (26.4%) meta-analyses showed no significant differences in HRV parameters in mental disorders compared with HCs.

Alterations in HRV following treatment modalities for mental disorders

For the pooled analyses of HRV-associated indicators following treatment modalities for mental disorders, 5 out of 18 pooled analyses (16.7%) yielded statistically significant results with p-values < 0.05; the remaining analyses were not significant. Additionally, only one meta-analysis included a sample size exceeding 1000, and the statistical results were not significant. In 12 out of the 18 (66.7%) comparisons, the effect sizes of the largest study were nominally statistically significant at $p < 0.05$. Furthermore, 8 out of 18 pooled analyses (44.4%) exhibited substantial heterogeneity ($I2 > 50\%$). The 95% prediction interval excluded the null in only 2 out of 18 (11.1%) included comparisons. Small-study effects were observed in 3 pooled analyses (16.7%), and we did not detect excess significance bias in all 18 meta-analyses (Table 3).

As presented in Fig. 2, none of the 18 pooled analyses demonstrated convincing, highly suggestive or suggestive evidence according to the quantitative umbrella review criteria. There were 5 pooled analyses (27.8%) supported by week evidence, suggesting decreased HRV after antipsychotic treatment, decreased LF/HF and increased RMSSD after rTMS treatment, decreased LF after physiotherapy for MDD, and increased HF after psychotherapy for MDD. Furthermore, 13 (72.2%) pooled analyses showed no significant changes in HRV parameters before and after treatment.

DISCUSSION

To the best of our knowledge, this represents the first umbrella review of alterations in HRV parameters within mental disorders. A notable strength of our umbrella review lies in its comprehensive hierarchical classification of published evidence. We examined 21 systematic reviews comprising 71 pooled analyses of HRV alterations across various mental disorders. Overall, the existing experimental evidence suggests that individuals with mental disorders demonstrate altered HRV patterns compared to those without such conditions. Additionally, many patients undergoing various treatments for mental disorders, such as medication, physical therapy, and psychological interventions, also exhibit significant alterations in HRV and its related parameters. Moreover, the robustness of these significant findings varied considerably. Among the 44 statistically significant meta-analyses, only 7 were supported by suggestive evidence, lacking highly suggestive or convincing evidence.

The mechanisms underlying HRV alterations in mental disorders are complex and multifactorial. Reduced HRV is often associated with an imbalance between the sympathetic and parasympathetic branches of the autonomic nervous system, reflecting a dysregulated stress response [45]. Chronic stress, a common feature in many mental disorders, can lead to prolonged activation of the sympathetic nervous system, suppressing parasympathetic activity and resulting in lower HRV [46]. Furthermore, neuroinflammation and changes in brain structure, particularly in regions like the prefrontal cortex and amygdala, have been implicated in HRV

dysfunction [45, 47, 48]. These brain areas are critical in regulating emotional responses and autonomic functions, and their dysfunction may contribute to both the development and progression of mental disorders [49]. Additionally, treatments such as psychotropic medications, psychotherapy, and physical therapies may influence HRV through their effects on autonomic regulation and stress pathways [11, 12, 36, 39, 44]. However, the exact mechanisms by which these treatments alter HRV remain underexplored, warranting further investigation to elucidate potential therapeutic targets.

Aligned with umbrella review criteria, several factors commonly downgraded the overall confidence of published meta-analyses, including non-significant *p*-values of the largest study, random effects *p* value > 10-6, small sample sizes (<1000 cases), high between-study heterogeneity, prediction intervals encompassing the null value, and biases due to small-study effects [24, 50, 51]. Our umbrella review indicates that random effects *p* value > 10-6, and small sample sizes in meta-analyses constitute the primary factors attenuating HRV findings in mental disorders. This phenomenon may stem from the relatively low incidence rates of certain diseases (e.g., bulimia nervosa, borderline personality disorder, and social anxiety disorder) in the general population. Additionally, the limited clinical application of HRV assessment in mental disorders, possibly owing to limited awareness or perceived insignificance of HRV disturbances compared to recognized differential diagnostic examination such as endocrine dysregulation [52], metabolic disorders [53], or structural brain abnormalities [54], may further contribute to the underutilization of HRV examinations among patients with mental disorders. For prevalent instances of random effects with *p*-values > 10-6, the primary culprit often lies in small sample sizes. Moreover, variations in HRV measurement methods (e.g., 5 min-HRV and 24h-HRV) and calculation techniques (e.g., absolute, logarithmic transformation, and normalized values) [55], as well as uncontrolled confounding variables or covariates in HRV studies of mental disorders (e.g., age, gender, severity of symptoms) [56], may introduce additional noise, potentially affecting detection of effects and significance outcomes.

Nevertheless, from a clinical standpoint, exploring HRV characteristics in mental disorders can offer valuable insights. HRV serves as a reliable indicator of autonomic nervous system balance, offering insights into the status and interaction of the sympathetic and parasympathetic nervous systems [57]. Our umbrella review identified decreased HRV in dementia or neurocognitive disorders and PTSD, as well as decreased HRV, RMSSD, and HF in somatic symptom disorders and functional somatic syndromes, as suggestive evidence. These findings were also observed in other mental disorders (e.g., MDD, GAD, and schizophrenia), albeit with lower levels of evidence credibility. It is important to note that the ability of individual HRV indices to distinguish between mental disorders is limited, as these indices often overlap across conditions [42]. For example, indices like RMSSD and HF, typically linked to parasympathetic activity [57], are reduced in various mental disorders [15, 42]. This reduction in parasympathetic activity, reflected by lower HRV values, seems to be a common feature across psychiatric conditions, suggesting that specific single HRV alteration may indicate a general autonomic dysfunction rather than a disorder-specific signature. Therefore, individual HRV indices should be viewed more as markers of autonomic dysregulation than as diagnostic tools for specific mental disorders. However, different HRV-related indices demonstrate significant differences when comparing disease and health statuses, as well as pre- and post-treatment evaluations, suggesting their potential utility as objective biomarkers for distinguishing disease and health statuses and assessing treatment efficacy. Crucially, by comparison, examining various HRV variables highlights the uniqueness of HRV profiles across different mental disorders (Fig. 2). This suggests that a combination of specific HRV indices may provide more accurate differentiation between distinct mental disorders than relying on a single HRV measure. Given the multifaceted nature of autonomic regulation, integrating various HRV parameters could capture a broader, more nuanced picture of autonomic dysfunction, allowing for more precise identification of psychiatric conditions and their responses to treatment. Thus, using a multi-index approach could enhance diagnostic accuracy and treatment monitoring, ultimately supporting the clinical utility of HRV as a diagnostic tool.

Extensive research has explored genes, proteins, and brain imaging in the quest for biomarkers capable of identifying or predicting mental disorders [58]. Nevertheless, as of now, no singular marker has been discovered that confidently discriminates between different mental disorders. Particularly concerning cognition, mood, behavior, and psychotic symptoms—elements traditionally regarded as fundamental dimensions of mental disorders—psychiatrists can only glean insights from clinical interviews and observations [59]. Our findings indicate that the overall patterns of change in parameters related to HRV should be comprehensively evaluated as significant fundamental dimensions and potential disease-specific biomarkers for mental disorders. However, the umbrella review method we employed precluded statistical analysis aimed at assessing the efficacy of overall HRV profiles in identifying or distinguishing different mental disorders. This hypothesis could potentially be investigated further through machine learning methodologies in large-scale research encompassing diverse mental disorders.

Our research indicates that following various treatments for mental disorders, some meta-analyses exhibit significant changes in HRV-related metrics, although the evidence is somewhat limited due to constraints posed by sample size [39]. Nevertheless, integrating findings from other disciplines yields practical insights. Numerous studies suggest that reduced HRV serves as an adverse prognostic factor for cardiovascular diseases such as myocardial infarction, chronic heart failure, unstable angina, hypertension, and diabetes [8, 60, 61]. Moreover, individuals with mental disorders who chronically use antipsychotic medications are at a heightened risk for cardiovascular and metabolic diseases [62]. Our findings reveal a significant decrease in HF associated with antipsychotic medication use, underscoring the importance of HRV in monitoring medication side effects and preventing cardiovascular events in patients using antipsychotic medications. Additionally, after receiving rTMS treatment, patients show significant improvements in RMSSD and LF/HF indices alongside symptom amelioration, potentially providing objective biomarkers for treatment efficacy prediction. In the treatment of MDD patients, both psychological and physical therapies significantly enhance HRV. From the perspective of improving HRV metrics, traditional pharmacological and psychosocial interventions exhibit characteristics of transdiagnostic treatments, capable of improving HRV disturbances across patients with various mental diagnoses. Transdiagnostic therapy approaches could alleviate the burden on clinicians, who required to learn numerous specific therapy approaches sharing common theoretical underpinnings and components [63]. However, given the diverse HRV patterns across different mental disorders identified in our review, a 'one size fits all' method to therapy approaches may be inadequate for improving HRV across all conditions. Instead, targeted therapy protocols should focus on disease-specific modified HRV profiles when devising intervention protocols for different mental disorders. This implies that new intervention protocols should incorporate fundamental therapeutic components delivered irrespective of diagnosis, alongside optional modules addressing disorder-specific symptoms.

Our umbrella review encounters several limitations. First, we refrained from evaluating the quality of individual researches within every meta-analysis, as it fell outside the scope of our review. Second, the biases potentially stemming from individual

study characteristics, such as sex, age, race/ethnicity, socioeconomic status, and genetic factors, were not comprehensively assessed due to inadequate information provided in the majority of studies. Third, our review omitted certain mental disorders, such as intellectual developmental disorders, tic disorders, and brief psychotic disorders, as corresponding meta-analyses were absent from the literature search. Consequently, the evidence map for HRV characteristics remains partial. Fourth, during our research selection process, we came across several meta-analyses addressing the same topic, though not necessarily containing identical studies. We prioritized the most recent meta-analysis with the largest sample size in such cases. It's noteworthy that different meta-analyses on identical topics may employ distinct eligibility criteria and search terms, leading to variations in the included researches. This discrepancy implies that some pertinent data from meta-analytic studies may have been overlooked. Although this issue has been acknowledged in prior literature and may be addressed as umbrella review methodologies evolve, no definitive solution is currently available [64, 65]. Furthermore, the use of LF/HF as an HRV measure remains controversial due to its ambiguous interpretation and limited ability to reliably reflect autonomic balance, suggesting the need for further research to clarify its physiological significance. Finally, the quality assessment revealed that only five [12, 27, 33, 39, 43] of the 21 included studies met high-quality standards based on AMSTAR 2, raising concerns about the reliability of the findings. Low-quality studies may introduce biases, distort effect sizes, and weaken the overall strength of the evidence, potentially limiting the generalizability of the results [29]. Specifically, the reported effect sizes, while useful, may be influenced by the methodological limitations of the included studies. Distortions in effect sizes could occur due to factors such as study heterogeneity, varying measurement techniques, and small sample sizes, further complicating the interpretation of the results. Future meta-analyses should incorporate sensitivity analyses, such as excluding low-quality studies, to evaluate the robustness of the findings. Upholding higher methodological standards in future research is essential to ensure more reliable and generalizable evidence.

In summary, our umbrella review thoroughly examined HRV characteristics across 19 mental disorders and 8 treatment modalities. Among the 71 identified HRV comparisons, pooled analyses provided suggestive evidence for reduced HRV in dementia or neurocognitive disorders and PTSD, decreased HRV, RMSSD, and HF in somatic symptom disorders and functional somatic syndromes, as well as decreased RMSSD and HF in schizophrenia. While we cannot disregard other HRV comparisons supported by weak evidence, they do entail uncertainties requiring resolution. The credibility of HRV characteristics evidence in mental disorders varied across different HRV variables and diseases. Nonetheless, these findings serve as a foundation for advancing research on HRV in mental disorders, fostering a better understanding of these features. Importantly, no two diseases exhibited identical altered HRV patterns, underscoring the potential significance of overall HRV profiles in delineating distinct disorders. In the future, meticulously designed studies with robust sample sizes and thorough evaluations of potential biases are essential to validate and expand upon these findings.

REFERENCES

1. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry. 2022;9:137–50.
2. Dragioti E, Radua J, Solmi M, Gosling CJ, Oliver D, Lascialfari F, et al. Impact of mental disorders on clinical outcomes of physical diseases: an umbrella review assessing population attributable fraction and generalized impact fraction. World Psychiatry. 2023;22:86–104.
3. Chida Y, Hamer M. Chronic psychosocial factors and acute physiological responses to laboratory-induced stress in healthy populations: a quantitative review of 30 years of investigations. Psychol Bull. 2008;134:829–85.
4. Fisher AJ, Song J, Soyster PD. Toward a systems-based approach to understanding the role of the sympathetic nervous system in depression. World Psychiatry. 2021;20:295–6.
5. Rosenblatt S, Leighton WP, Chanley JD. Dopamine-beta-hydroxylase: evidence for increased activity in sympathetic neurons during psychotic states. Science. 1973;182:923–4.
6. Sousa VC, Mantas I, Stroth N, Hager T, Pereira M, Jiang H, et al. P11 deficiency increases stress reactivity along with HPA axis and autonomic hyperresponsiveness. Mol Psychiatry. 2021;26:3253–65.
7. Hämmerle P, Aeschbacher S, Schlageter V, Coslovsky M, Hennings E, Krisai P, et al. Heart rate variability and stroke or systemic embolism in patients with atrial fibrillation. Heart Rhythm. 2024;21:1509–16.
8. Matusik PS, Matusik PT, Stein PK. Heart rate variability and heart rate patterns measured from wearable and implanted devices in screening for atrial fibrillation: potential clinical and population-wide applications. Eur Heart J. 2023;44:1105–7.
9. Koenig J, Kemp AH, Beauchaine TP, Thayer JF, Kaess M. Depression and resting state heart rate variability in children and adolescents - a systematic review and meta-analysis. Clin Psychol Rev. 2016;46:136–50.
10. Hamilton JL, Alloy LB. Atypical reactivity of heart rate variability to stress and depression across development: systematic review of the literature and directions for future research. Clin Psychol Rev. 2016;50:67–79.
11. Brown L, Rando AA, Eichel K, Van Dam NT, Celano CM, Huffman JC, et al. The effects of mindfulness and meditation on vagally mediated heart rate variability: a meta-analysis. Psychosom Med. 2021;83:631–40.
12. Chen S, Wang H, Yue J, Guan N, Wang X. Intervention methods for improving reduced heart rate variability in patients with major depressive disorder: a systematic review and meta-analysis. Compr Psychiatry. 2022;119:152347.
13. Kircanski K, Williams LM, Gotlib IH. Heart rate variability as a biomarker of anxious depression response to antidepressant medication. Depress Anxiety. 2019;36:63–71.
14. Koenig J, Kemp AH, Feeling NR, Thayer JF, Kaess M. Resting state vagal tone in borderline personality disorder: a meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry. 2016;64:18–26.
15. Wang Z, Luo Y, Zhang Y, Chen L, Zou Y, Xiao J, et al. Heart rate variability in generalized anxiety disorder, major depressive disorder and panic disorder: a network meta-analysis and systematic review. J Affect Disord. 2023;330:259–66.
16. Solmi M, Correll CU, Carvalho AF, Ioannidis J. The role of meta-analyses and umbrella reviews in assessing the harms of psychotropic medications: beyond qualitative synthesis. Epidemiol Psychiatr Sci. 2018;27:537–42.
17. Ioannidis J. Next-generation systematic reviews: prospective meta-analysis, individual-level data, networks and umbrella reviews. Br J Sports Med. 2017;51:1456–8.
18. Ioannidis JP. Why most discovered true associations are inflated. Epidemiology. 2008;19:640–8.
19. Ioannidis JP, Munafò MR, Fusar-Poli P, Nosek BA, David SP. Publication and other reporting biases in cognitive sciences: detection, prevalence, and prevention. Trends Cogn Sci. 2014;18:235–41.
20. Ioannidis JP. The mass production of redundant, misleading, and conflicted systematic reviews and meta-analyses. Milbank Q. 2016;94:485–514.
21. Fusar-Poli P, Hijazi Z, Stahl D, Steyerberg EW. The science of prognosis in psychiatry: a review. JAMA Psychiatry. 2018;75:1289–97.
22. Bougioukas KI, Bouras E, Apostolidou-Kiouti F, Kokkali S, Arvanitidou M, Haidich AB. Reporting guidelines on how to write a complete and transparent abstract for overviews of systematic reviews of health care interventions. J Clin Epidemiol. 2019;106:70–79.
23. Ioannidis JP. Integration of evidence from multiple meta-analyses: a primer on umbrella reviews, treatment networks and multiple treatments meta-analyses. CMAJ. 2009;181:488–93.
24. Zhang Y, Ren R, Yang L, Zhang H, Shi Y, Vitiello MV, et al. Patterns of polysomnography parameters in 27 neuropsychiatric diseases: an umbrella review. Psychol Med. 2023;53:4675–95.
25. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
26. Cheng YC, Huang YC, Huang WL. Heart rate variability in individuals with autism spectrum disorders: a meta-analysis. Neurosci Biobehav Rev. 2020;118:463–71.
27. Cheng YC, Huang YC, Huang WL. Heart rate variability in patients with dementia or neurocognitive disorders: A systematic review and meta-analysis. Aust N Z J Psychiatry. 2022;56:16–27.
28. Cheng YC, Huang YC, Huang WL. Heart rate variability as a potential biomarker for alcohol use disorders: a systematic review and meta-analysis. Drug Alcohol Depend. 2019;204:107502.

29. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017;358:j4008.
30. Ioannidis JP, Trikalinos TA. An exploratory test for an excess of significant findings. Clin Trials. 2007;4:245–53.
31. Peschel SK, Feeling NR, Vögele C, Kaess M, Thayer JF, Koenig J. A meta-analysis on resting state high-frequency heart rate variability in bulimia nervosa. Eur Eat Disord Rev. 2016;24:355–65.
32. Chalmers JA, Quintana DS, Abbott MJ, Kemp AH. Anxiety disorders are associated with reduced heart rate variability: a meta-analysis. Front Psychiatry. 2014;5:80.
33. Robe A, Dobrean A, Cristea IA, Păsărelu CR, Predescu E. Attention-deficit/hyperactivity disorder and task-related heart rate variability: a systematic review and meta-analysis. Neurosci Biobehav Rev. 2019;99:11–22.
34. Cheng YC, Huang YC, Huang WL. Can Heart Rate Variability be Viewed as a Biomarker of Problematic Internet Use? A Systematic Review and Meta-Analysis. Appl Psychophysiol Biofeedback. 2023;48:1–10.
35. Brown L, Karmakar C, Gray R, Jindal R, Lim T, Bryant C. Heart rate variability alterations in late life depression: a meta-analysis. J Affect Disord. 2018;235:456–66.
36. Kothgassner OD, Goreis A, Bauda I, Ziegenaus A, Glenk LM, Felnhofer A. Virtual reality biofeedback interventions for treating anxiety: a systematic review, meta-analysis and future perspective. Wien Klin Wochenschr. 2022;134:49–59.
37. Baumeister-Lingens L, Rothe R, Wolff L, Gerlach AL, Koenig J, Sigrist C. Vagally-mediated heart rate variability and depression in children and adolescents - a meta-analytic update. J Affect Disord. 2023;339:237–55.
38. Clamor A, Lincoln TM, Thayer JF, Koenig J. Resting vagal activity in schizophrenia: meta-analysis of heart rate variability as a potential endophenotype. Br J Psychiatry. 2016;208:9–16.
39. Lee H, Lee JH, Hwang MH, Kang N. Repetitive transcranial magnetic stimulation improves cardiovascular autonomic nervous system control: a meta-analysis. J Affect Disord. 2023;339:443–53.
40. Ying-Chih C, Yu-Chen H, Wei-Lieh H. Heart rate variability in patients with somatic symptom disorders and functional somatic syndromes: a systematic review and meta-analysis. Neurosci Biobehav Rev. 2020;112:336–44.
41. Zhao W, Jiang B. Heart rate variability in patients with insomnia disorder: a systematic review and meta-analysis. Sleep Breath. 2023;27:1309–13.
42. Cheng YC, Su MI, Liu CW, Huang YC, Huang WL. Heart rate variability in patients with anxiety disorders: a systematic review and meta-analysis. Psychiatry Clin Neurosci. 2022;76:292–302.
43. Faurholt-Jepsen M, Kessing LV, Munkholm K. Heart rate variability in bipolar disorder: a systematic review and meta-analysis. Neurosci Biobehav Rev. 2017;73:68–80.
44. Alvares GA, Quintana DS, Hickie IB, Guastella AJ. Autonomic nervous system dysfunction in psychiatric disorders and the impact of psychotropic medications: a systematic review and meta-analysis. J Psychiatry Neurosci. 2016;41:89–104.
45. Olivieri F, Biscetti L, Pimpini L, Pelliccioni G, Sabbatinelli J, Giunta S. Heart rate variability and autonomic nervous system imbalance: potential biomarkers and detectable hallmarks of aging and inflammaging. Ageing Res Rev. 2024;101:102521.
46. Badovinac SD, Chow C, Di Lorenzo-Klas MG, Edgell H, Flora DB, Pillai Riddell RR. Parents' physiological reactivity to child distress and associations with parenting behaviour: a systematic review. Neurosci Biobehav Rev. 2023;151:105229.
47. Alaerts K, Daniels N, Moerkerke M, Evenepoel M, Tang T, Van der Donck S, et al. At the head and heart of oxytocin's stress-regulatory neural and cardiac effects: a chronic administration RCT in children with autism. Psychother Psychosom. 2023;92:315–28.
48. Triana AM, Salmi J, Hayward N, Saramäki J, Glerean E. Longitudinal single-subject neuroimaging study reveals effects of daily environmental, physiological, and lifestyle factors on functional brain connectivity. PLoS Biol. 2024;22:e3002797.
49. Harnett NG, Fleming LL, Clancy KJ, Ressler KJ, Rosso IM. Affective visual circuit dysfunction in trauma and stress-related disorders. Biol Psychiatry. 2025;97:405–416.
50. Gao X, Su X, Han X, Wen H, Cheng C, Zhang S, et al. Unsaturated fatty acids in mental disorders: an umbrella review of meta-analyses. Adv Nutr. 2022;13:2217–36.
51. Singh B, Olds T, Curtis R, Dumuid D, Virgara R, Watson A, et al. Effectiveness of physical activity interventions for improving depression, anxiety and distress: an overview of systematic reviews. Br J Sports Med. 2023;57:1203–9.
52. Marinovic DA, Hunter RL. Examining the interrelationships between mindfulness-based interventions, depression, inflammation, and cancer survival. CA Cancer J Clin. 2022;72:490–502.
53. Moulton CD, Pickup JC, Ismail K. The link between depression and diabetes: the search for shared mechanisms. Lancet Diabetes Endocrinol. 2015;3:461–71.
54. Banasr M, Sanacora G, Esterlis I. Macro- and microscale stress-associated alterations in brain structure: translational link with depression. Biol Psychiatry. 2021;90:118–27.
55. Wang Z, Jiang F, Xiao J, Chen L, Zhang Y, Li J, et al. Heart rate variability changes in patients with obstructive sleep apnea: a systematic review and meta-analysis. J Sleep Res. 2023;32:e13708.
56. Hamidovic A, Van Hedger K, Choi SH, Flowers S, Wardle M, Childs E. Quantitative meta-analysis of heart rate variability finds reduced parasympathetic cardiac tone in women compared to men during laboratory-based social stress. Neurosci Biobehav Rev. 2020;114:194–200.
57. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. Front Public Health. 2017;5:258.
58. Voineskos AN, Hawco C, Neufeld NH, Turner JA, Ameis SH, Anticevic A, et al. Functional magnetic resonance imaging in schizophrenia: current evidence, methodological advances, limitations and future directions. World Psychiatry. 2024;23:26–51.
59. Cuthbert BN, Kozak MJ. Constructing constructs for psychopathology: the NIMH research domain criteria. J Abnorm Psychol. 2013;122:928–37.
60. Agarwal SK, Norby FL, Whitsel EA, Soliman EZ, Chen LY, Loehr LR, et al. Cardiac autonomic dysfunction and incidence of atrial fibrillation: results from 20 years follow-up. J Am Coll Cardiol. 2017;69:291–9.
61. Barzilay JI, Tressel W, Biggs ML, Stein PK, Kizer JR, Shitole SG, et al. The association of measures of cardiovascular autonomic function, heart rate, and orthostatic hypotension with incident glucose disorders: the cardiovascular health study. Diabetes Care. 2022;45:2376–82.
62. Correll CU, Solmi M, Croatto G, Schneider LK, Rohani-Montez SC, Fairley L, et al. Mortality in people with schizophrenia: a systematic review and meta-analysis of relative risk and aggravating or attenuating factors. World Psychiatry. 2022;21:248–71.
63. Scott J, Iorfino F, Capon W, Crouse J, Nelson B, Chanen AM, et al. Staging 2·0: refining transdiagnostic clinical staging frameworks to enhance reliability and utility for youth mental health. Lancet Psychiatry. 2024;11:461–71.
64. Correll CU, Cortese S, Croatto G, Monaco F, Krinitski D, Arrondo G, et al. Efficacy and acceptability of pharmacological, psychosocial, and brain stimulation interventions in children and adolescents with mental disorders: an umbrella review. World Psychiatry. 2021;20:244–75.
65. Köhler-Forsberg O, Stiglbauer V, Brasanac J, Chae WR, Wagener F, Zimbalski K, et al. Efficacy and safety of antidepressants in patients with comorbid depression and medical diseases: an umbrella systematic review and meta-analysis. JAMA Psychiatry. 2023;80:1196–207.

AUTHOR CONTRIBUTIONS

Conceptualization, ZXW, YZZ and ZLZ; data curation, ZXW, YZZ, JWL, WP and MML; formal analysis, ZXW; funding acquisition, ZXW, ZLZ; investigation, ZXW and ZLZ; methodology, ZXW, YZZ; project administration, ZXW, YZZ and ZLZ; software, ZXW; supervision, ZLZ; visualization, ZXW and YZZ; writing—original draft, ZXW; writing—review and editing, YZZ and ZLZ. All authors have read and agreed to the published version of the manuscript.

FUNDING

This work was supported by the Sichuan Science and Technology Program (2025ZNSFSC0784), Health Commission of Sichuan Province Medical Science and Technology Program (grant number 24QNMP013), and Chengdu Science and Technology Program(2024-YF05-01704-SN). The funders of the study did not participate in the design of the study, collection of data, analysis of data, interpretation of the data, or the writing of the report. The first authors had full access to the data in the study, and all authors final responsibility for the decision to submit for publication.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41398-025-03339-x.

Correspondence and requests for materials should be addressed to Zhili Zou.

Declaration of generative AI and AI-assisted technologies in the writing process:: During the preparation of this work the authors used ChatGPT in order to language polishing. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.