Physiological monitoring of stress and major depression: A review of the current monitoring techniques and considerations for the future

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A B S T R A C T

Mental illnesses such as clinical and major depression have taken its toll on the global burden of disease, leading to unprecedented cases worldwide. Commonly, the diagnostic and prognostic procedures for such mental illnesses comprise of qualitative and subjective measures of stress, which can often lead to misdiagnosis and improper treatment courses. In recent years, the quantification and objectification of stress has given rise to an alternative approach to dated practices in the psychophysiological evaluation of stressed and depressed individuals. This has been made possible in recent years through the advancements in heart rate variability (HRV), electrodermal activity (EDA) and electroencephalography (EEG). This review comprehensively evaluates the current state-of-the-art technology in these fields and their applications within mental health monitoring and diagnosis. We have seen an escalation in the application of multimodal approaches towards stress monitoring for major depression, further emphasizing the need for technological advancements in this space, for the betterment of the global burden of disease.

1. Introduction

Confronting the global crises surrounding mental health management is an immense challenge. With over 264 million cases worldwide, depression has become a major contributor to the global burden of disease. The debilitating mental illness can severely damage cognitive ability, diminish quality of life and inevitably, in some cases lead to suicide. There are several barriers that impede the correct management of depression, which include lack of resources and trained professionals, as well as inaccuracies in the assessment, diagnosis and monitoring of the mental illness. Currently, the procedure for diagnosing depression involves self-reported questionnaires, interviews by trained professionals i.e., psychologists and psychiatrists; and the use of standardised qualitative surveys and scoring systems, such as the Hamilton Depression Rating Scale (HAM-D) or the Beck Depression Inventory (BDI-II) for evaluation of depression severity [1–3]. The absence of physical tests is cause for alarming concern, as the common mental illness takes its toll on global productivity, economy and social health [4]. The concept of monitoring the physiological signals associated with stress has been established for many years, primarily focusing on the effects that different stresses can have on the sympathetic and parasympathetic nervous systems[5]. Physiological monitoring has provided essential information regarding mental illness sufferers that cannot be obtained through the existing diagnostic means. Monitoring techniques such as electrocardiography, electroencephalography and electrodermal responses are pioneering the realisation of the quantified form of stress and major depression. Such technologies have proven to be significantly effective in the classification of mental illnesses, despite its lack of presence in clinical psychology diagnostic applications[6].

The primary aims of this review are to comprehensively and rigorously review the common physiological monitoring techniques and their applications within stress and depression monitoring. Previous reviews within this field of physiological monitoring have referred to the use of one primary method of monitoring whereby the recent advancements in monitoring technologies has given rise to the use of highly complex computations and multi-modal monitoring systems which will be reviewed extensively. Furthermore, the fundamental principles of such technologies will be highlighted, as well as results from notable physiological measurement studies. This will lead to a discussion focusing on the significance of standardised stress testing, the strengths and shortcomings of physiological monitoring techniques and, the technical aspects that should be considered as psychological diagnosis approaches the concept of physical testing.

2. Methods

The purpose of this review is to encapsulate studies of certain physiological measurement techniques and its utilisation in the monitoring of psychological stress, as it leads to the manifestation of mental illnesses, particularly clinical depression. English-written articles were obtained from SCOPUS and PubMed databases and selected based on the search criteria of inclusion of specific words in their title, abstract or keywords. The search criteria comprised of two stationary terms: ((‘Psychological Stress’) AND (‘Depression’)). Also, 3 independent terms were used to obtain articles relating to each of the physiological monitoring techniques of interest: (‘HRV’ OR ‘Heart Rate Variability’); (‘GSR’ OR ‘EDA’ OR ‘Galvanic Skin Response’ OR ‘Electrodermal Activity’); (‘EEG’ or ‘Electroencephalography’). Additionally, related articles were selected through reference lists and the ‘related articles’ feature on SCOPUS and PUBMED. After removal of duplicates, a total of 725 papers were obtained. Following the reading of the abstracts, 237 papers were selected for further evaluation and classified according to the monitoring/diagnostic focus, i.e., psychological stress, physical stress, major depressive disorder, schizophrenia, bipolar disorder, co-morbid depression, and post-traumatic stress disorder. The review focuses primarily on the physiological monitoring of psychological stress and the development of major depression therefore, the most relevant papers that matched these criteria were selected. Eventually, 42 papers were chosen for complete evaluation and inclusion in this review. Fig. 1 depicts a flow chart of the database search procedure and selection process for the review. The exclusion criteria for this review were non-human studies, papers which did not aim to evaluate stress through the chosen monitoring techniques i.e. HRV, EDA and EEG measurements were not taken, and papers which involved participants with multiple mental disorders or co-morbid depression. Non-human studies were excluded as the human stress response is different to other animals, which often involve a variety of stress hormones, not commonly found in humans. Furthermore, studies which did not involve HRV, EDA or EEG methods were not included as the aim of this review was to evaluate the state-of-the-art technologies within these fields. Finally, studies involving participants suffering from multiple mental disorders and co-morbid depression were not included as the stress response in these individuals is more complex due to the presence of other mental disorders e.g. anxiety and bipolar disorder which are governed by different hormones and neurotransmitters.

3. The relationship between stress and depression

Stress is the biological or physiological response to a stressor, which may exist in the form of environmental conditions, external stimuli or biological agents that interrupt homeostasis within a living organism [7]. Essentially, stress exists when the human body is subjected to a condition that requires an immediate change in its system to restore homeostasis. The physiological changes that occur in the body during a response to stress is described by the general adaptation syndrome. The general adaptation syndrome depicts stress in three stages: the alarm reaction, resistance and the exhaustion stage. Upon perception of a stressor the alarm reaction or the ‘fight or flight’ response is triggered. Once triggered, several biochemical chain reactions lead to the mobilisation of energy required for the responses[8]. Subsequently, several physiological changes occur as a result of the biochemical reactions, such as those in the sympathetic and parasympathetic nervous systems,

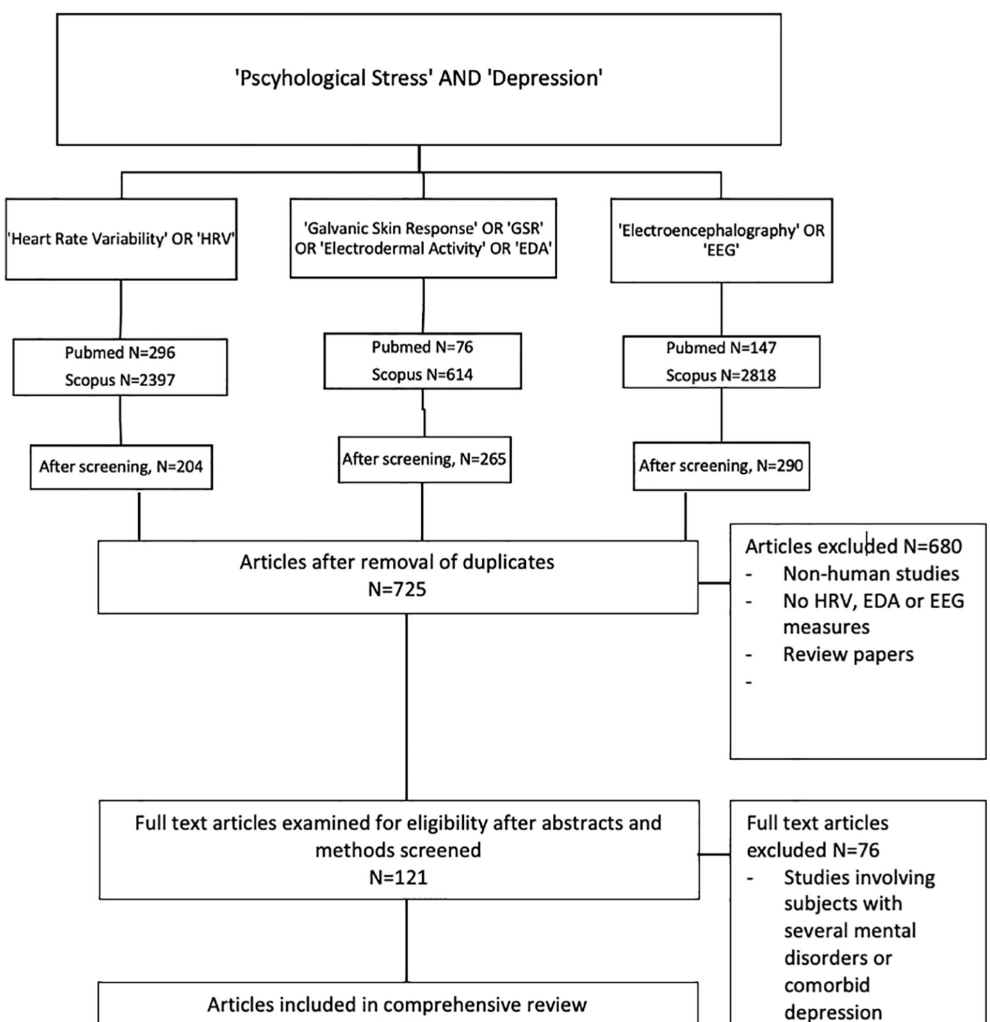

Fig. 1. Flow chart of article selection for comprehensive review of physiological monitoring of stress and depression.

affecting heart rate, muscular tension and blood glucose levels[7,9]. During the resistance stage, the body continues to activate pathways in a series of allostatic mechanisms for further physiological changes to restore balance and reach homeostasis. The 'exhaustion' stage occurs in certain scenarios that involve persistent stressors, wherein the resources for prolonged adaptive responses are exhausted. This is identified as allostatic overload, or chronic stress, which inevitably leads to the deterioration of the body and the possible manifestation of metabolic diseases and mental illnesses, like diabetes or clinical depression respectively[8,10,11].

Prolonged or chronic stress commonly leads to the imbalance of stress mediators and hormones within the body. Such imbalances are often referred to as 'allostatic states', such as blunted cortisol responses to a stressor or chronic insomnia[11–13]. Several articles have highlighted the significance of chronic stress and the manifestation of depressive symptoms from the allostatic overloads, caused by psychological stressors and extreme environmental conditions. The relationship that exists between recurrent stress and depression is reflected within the human body in several forms; whether it is through biochemical reactivity and allostatic states, or the physiological changes that they pose on the body[14–17]. These physiological changes have been a primary focus for several studies, as they can contribute greatly to the quantification of stress and depression. These are pioneering techniques that are shifting efforts from the subjective manner of psychological diagnoses, towards objective classifications of depression.

4. Physiological monitoring techniques for stress and depression

As previously mentioned, the comprehension of stress and its effects on the body is significant for the quantitative evaluation of depression, and major depressive disorder. Agelink et al. presented a study concerning the relationship between heart rate variability and major depression in 2002[18]. Through comparing time and frequency domain HRV indices between 32 patients suffering from Major Depressive Disorder (MDD), classified through the Hamilton Depression Scale (HAM-D), Agelink concluded that a negative correlative relationship existed between the HAM-D scores and the vagal HRV indices. Altered vagal tone suggests changes within the parasympathetic nervous system, which is illustrated in the low-frequency to high-frequency ratio (LF/HF) HRV index. Reduced vagal modulation translates to a higher LF/HF ratio, and reduced activation of the parasympathetic nervous system [19,20]. This could indicate that MDD patients take a longer period of time to reach a resting state in post-stress situations, when compared to healthy controls.

Additionally, Branković reported on the skin conductance responses of 57 depressed individuals, compared to 52 healthy controls in a 2008 stress study[21]. Branković developed a mathematical model to showcase the regulation of Skin Conductance Responses (SCRs) in the body during emotional arousal, resulting in the realisation of positive and negative feedback loops. The interlinked positive and negative feedback loops shape the SCR feedback structure. This was modelled as a fast-positive loop which occurs early in the feedback response[22]. This is followed by a negative feedback stage followed by a slow-positive feedback loop which originates from the regulatory chain of the SCR process. The fast-positive feedback loop reflects the initiation of the regulation of emotional arousal whereas the negative feedback look is proportional to the rate of change of emotional arousal and reflects feedback inhibition. Finally, the slow-positive feedback loop represents the actual level of emotional arousal and the actual value of the SCR signal[21].

These feedback loops exhibited significantly stronger signals from depressed individuals when compared to healthy subjects. Thus, facilitating the comprehension of the neurochemical characteristics of depression and its expression in SCR. Furthermore, several studies have involved the development of an electroencephalography-based diagnostic tool for major depression. Notably, Cai's study with a 3-electrode EEG system for depression diagnosis compared the successes and shortcomings of four feature selection algorithms for the selection of the optimum feature selection technique for the best classification performance[23]. This study revealed that in the case of distinguishing between 152 depressed patients and 113 healthy subjects, the decision tree classifier exhibited the highest accuracy of 76.4%. Several studies carried out a multimodal approach to stress monitoring which included heart rate variability, electroencephalography, galvanic skin response, etc. These are highlighted in Table 5. Such studies present the robust power in the utilisation of physiological signals as alternative, or complimentary tools to the current diagnostic and monitoring practices for clinical depression, its progression and treatment efficacy in modern societies.

a. Fundamental principles and applications of heart rate variability

The significance of heart rate variability (HRV) in the field of psychophysiology was introduced by Wolf in 1967, which described HRV as an indicator of brain and vagal-heart communication[24]. HRV is variation in the time intervals that exist between successive heartbeats. This interval is referred to as 'inter-beat intervals' or IBIs[5]. Heart rate variability is known to be influenced by heart-brain interactions and the non-linear dynamics of the autonomic nervous system (ANS)[25]. The ANS can be separated into the sympathetic (SNS) and parasympathetic nervous system (PNS) branches. The balancing mechanisms between the two branches influence heart rate and are moderated by specific mediators. The parasympathetic branch is mediated by acetylcholine, released from the vagal nerve. Whereas the sympathetic branch is facilitated by the release of epinephrine (E) and norepinephrine (NE) from the adrenal medulla[9,26]. Interactions between acetylcholine and, epinephrine and norepinephrine and their corresponding receptors leads to modulations in parasympathetic and sympathetic activity, respectively. Balance changes between the SNS and PNS lead to cardiovascular variations[25]. Wherein, a ratio of increased SNS activity to decreased PNS activity leads to cardio acceleration, whereas the opposite ratio (High PNS and low SNS) leads to cardio deceleration. The constant interactions and balancing mechanisms between the vagal and sympathetic activity encapsulates heart rate variability. Through electrocardiography (ECG), the rhythmic contributions of sympathetic and parasympathetic activity on the variations between heartbeats can be observed[5,25]. Due to the natural irregularity of successive heartbeats, variations in IBIs are expected in healthy humans, whereas regularity and decreased variation can be indicative of homeostatic changes within the body, changes in the environment, or physical and mental disorders [27].

For the comprehension of psychophysiological stress, there are several HRV indices of interest within the time and frequency domains. Time domain analysis of HRV involves the calculations of mean normal-to-normal (NN) intervals and the variance between these intervals[27]. NN intervals are defined as the distance, in milliseconds (ms) that exist between successive normal heartbeats i.e., between the R peak of the QRS complex in the ECG[5]. Comparatively, frequency domain HRV indices are obtained through utilisation of Fast Fourier Transformation (FFT) or Auto-Regressive modelling (AR). HRV measures within the time and frequency domain are summarised in Table 1

Abbreviation	Definition
HRV	Heart Rate Variability
EEG	Electroencephalography
EDA	Electrodermal Activity
GSR	Galvanic Skin Response or Galvanic Skin Resistance
SCL	Skin Conductance Levels
SCR	Skin Conductance Responses
SC	Skin Conductance
MDD	Major Depressive Disorder
HAM-D	Hamilton Depression Rating Scale

Table 1
Heart Rate Variability (HRV) measures within the time and frequency domains.

Variable	Units	Description	Domain	Frequency Range
SDNN	ms	Standard deviation of all NN intervals	Time	
SDANN	ms	Standard deviation of average NN intervals for each 5 min segment in 24-hour recording	Time	
SDNN Index	ms	Mean of standard deviation of all NN intervals for each 5 min segments in 24-hour recording	Time	
RMSSD	ms	Square root of the mean of the sum of squares of differences between successive NN intervals	Time	
SDSD	ms	Standard deviation of differences between successive NN intervals	Time	
NN50		Number of pairs of adjacent NN intervals differing by more than 50 ms in the complete recording	Time	
pNN50	%	NN50 divided by total number of all NN intervals	Time	
VLF	ms^2	Power in the very low frequency range	Frequency	<0.04 Hz
LF	ms^2	Power in the low frequency range	Frequency	0.04–0.15 Hz
LF_{norm}	ν (nu)	Ratio between absolute value of the Low Frequency and difference between Total Power and Very Low Frequency i.e. (LF/ (Total Power-VLF) x100). This measure minimises effect of changes in VLF and emphasizes changes in sympathetic regulation. Calculated in percentile units	Frequency	
HF	ms^2	Power in the high frequency range	Frequency	0.15–0.4 Hz
HF_{norm}	ν (nu)	Ratio between absolute value of the High Frequency and difference between Total Power and Very Low Frequency i.e. (HF/ (Total Power-VLF) x100). This measure minimises effect of changes in VLF and emphasizes changes in parasympathetic regulation. Calculated in percentile units	Frequency	
Total power	ms^2	Variance of all NN intervals	Frequency	<0.4 Hz

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Abbreviation	Definition
BDI	Beck Depression Inventory
ICD-10	International Classification of Diseases -10th Revision
STAI	State-Trait Anxiety Inventory
DSM-IV/DSM-III-R	Diagnostic and Statistical Manual on Mental Disorders
SDS	Self-rating Depression Scale
SRI	Stress Response Inventory
TSST	Trier Social Stress Test
ICG	Inventory of Complicated Grief
SNS	Sympathetic Nervous System
PNS	Parasympathetic Nervous System
ANS	Autonomic Nervous System
ECG	Electrocardiography
RSA	Respiratory Sinus Arrhythmia
HR	Heart Rate
BVP	Blood Volume Pulse
LF	Low Frequency
VLF	Very Low Frequency
LF_{norm}	Normalised Low Frequency
LF ν	LF/ (LF+HF)
HF	High Frequency
HF_{norm}	Normalised High Frequency
HF ν	HF/ (LF+HF)
LF/HF ratio	Low frequency power to high frequency power ratio
NN	Normal-to-normal heartbeat intervals
SDNN	Standard deviation of NN intervals
SDANN	Standard deviation of average NN intervals in 5-minute segments over 24-hour recording
RMSSD	Root mean square of successive differences between normal heartbeats
NN50	Number of pairs of adjacent NN intervals differing by more than 50ms in the complete recording
pNN50	Proportion of NN50 divided by total number of NN intervals
NN20	Number of pairs of adjacent NN intervals differing by more than 20ms in the complete recording.
pNN20	Proportion of NN20 divided by total number of NN intervals
SD	Standard Deviation
RR	Time between two successive R-waves of the QRS complex on an ECG
SDRR	Standard deviation of RR intervals
SDSD	Standard deviation of successive RR interval differences
SDHR	Standard deviation of Heart Rate
BP	Blood Pressure
PEP	Pre-ejection Period
ACTH	Adrenocorticotropic hormone
FFT	Fast Fourier Transformation
AR Modelling	Auto-Regressive Modelling
CV	Coefficient of Variation
E	Epinephrine
NE	Norepinephrine

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Notably, the low-frequency/high-frequency (LF/HF) ratio has great emphasis in several HRV stress studies[28]. Delaney et.al. conducted an HRV stress study in 2000, which involved the HRV measurement of 30 healthy volunteers within a competitive setting whereby the Stroop Colour Word Conflict Test was conducted[28,29]. Heart rate variability monitoring revealed that during stages of psychological stress, there was a significant reduction in the high frequency component, and a significant increase in the low frequency component. Therefore, it was evident that psychological stress from the stress test led to a significant increase in the LF/HF ratio. Similarly, in 2007 Udupa et.al. led a study amongst 40 patients suffering from major depression disorder and age- and gender-matched controls using heart rate variability measures. The LF/HF ratio in MDD patients were significantly higher than those in healthy controls. This would suggest that both psychological stress and the presence of depressive symptoms have a similar effect on the sympathovagal balance within the body. The sympathovagal balance, reflected by the LF/HF ratio was increased in both cases, signifying increased sympathetic activity, which is modulated by stress hormones, epinephrine and norepinephrine[9,26]. Although, it should be noted that the former study involved healthy volunteers undergoing a standardised stress test whereas, the latter comprised of MDD patients that had undergone a deep breathing test, Valsalva manoeuvre and an orthostatic test. Therefore, direct comparisons cannot be made between the two studies as one focuses primarily on the effects of the stress inflicted on HRV measures whilst the other focuses on the HRV indices in MDD patients, without the presence of a stress test. However, Agelink et. al. 2002 study of the relationship between major depression and HRV examines the sympathovagal balance in MDD patients with a similar set of tests to Udupa's study and has shown findings which resonate with that of Udupa[18]. Psychological stress-based studies that have demonstrated the effects on HRV measures are summarised in Table 2.

b. Fundamental principles and applications of Galvanic skin resistance

Electrodermal activity (EDA) describes the active and passive

Table 2
Studies of heart rate variability (HRV) monitoring for psychological stress evaluation in depressed and non-depressed groups.

Authors	Year	N (Number of participants)	Age in years (mean ± Standard Deviation)	Aim and Stress Evaluation	Test	HR measures	Major Findings
Agelink, M. W.[18]	2002	32 MDD patients (16 mildly depressed i.e. M−HAMD; 16 severely depressed i.e. S-HAMD) and 64 non-depressed controls.	44.3 ± 12.6 (M−HAMD); 53.5 ± 15.8 (S-HAMD) 46.6 ± 11.9 (controls)	Authors compared time and frequency domain HRV indices between 32 medicated MDD patients via HRV, Blood pressure, DSM-III-R and Hamilton Depression Scale (HAM-D)	Standardised 5 min resting study, deep breathing test, Valsalva manoeuvre	HR, log CV (coefficient of variation), log RMSSD, LF power, log HF power, HF power, LF/HF ratio, Valsalva ratio	S-HAMD patients had lowest HRV indices. Mean CV and RMSSD (during deep respiration test) for S-HAMD group was significantly lower in comparison to healthy controls, as well as M−HAMD group. Higher LF/HF ratio and resting HR in S-HAMD group compared to healthy controls. Negative correlation between depression severity and vagal HRV indices.
Bosch, J.A. [30]	2009	61 healthy participants	20.3 ± 1.09	Authors aimed to determine stress through HRV via ECG, salivary cortisol, ICG and Test Anxiety Scale for affective responses during social evaluative threat	2 back-to-back speeches, with 2 mins preparation and 4 mins of speech delivery in front of an audience.	HR, RMSSD	Affective response, salivary cortisol, HR, HRV and pre-ejection period all differentiated in different task conditions. Physiological reactivity increased with increasing audience size. Cortisol increase predicted by sympathetic activation (pre-ejection) but not by affective responses. RMSSD responses were larger in 1 and 4 audience member settings than control, difference did not reach statistical significance.
Brugnera, A. [31]	2019	65 healthy participants	24.7 ± 3.9	Authors evaluated resting state HRV for psychosocial stress evaluation using Beck Depression Inventory III (BD), State and Trait Anxiety Inventory, Cook-Medley Hostility Scale, Stress Rating Questionnaire (SRQ), Type D Scale-14 and HRV via ECG	Montreal Imaging Stress Task (MIST) – involves mental arithmetic task	HR, SDNN, RMSSD, total power, HF power, LF power, HFν, LFν, LF/HF	Significant changes in HF power and RMSSD, with the lowest value reached during stress task. Only depressive symptoms positively correlated to higher resting HRV and to blunted reactivity in stress task. LF/HF variations were insignificant.
Castaldo, R. [32]	2016	42 healthy participants	18.7 ± 28.7	Authors aimed to detect mental stress during oral academic examinations using HRV via ECG	Oral academic examination	RR, SDNN, RMSSD, pNN50, LF, HF, LF/HF	Higher values of all-time domain features were observed during stress phase except RMSSD. During stress phase, LF and HF also increased. Nonlinear HRV features were also assessed and showcased better discrimination ability.
Chang, H.-A. [33]	2012	498 unmedicated MDD participants; 662 healthy participants	39.13 ± 14.12 (MDD); 40.66 ± 14.89 (controls)	Authors aimed to understand the relationship between major depression and cardiac autonomic dysregulation via DSM-IV, HAM-D, BDI, HRV via ECG and blood pressure		RMSSD, variance, LF, HF, LF/HF	MD patients exhibit reduced cardiac vagal control compared to healthy subjects. Reduced RR, variance, LF, HF in MDD patients compared with controls.
Delaney, J. P.A.[28]	2000	30 healthy participants	30.9 ± 3.9 (Women); 34.4 ± 8.7(Men)	Authors' aims were to understand the effects of short-term psychological stress through use of Visual Analog Scales and HRV via ECG	Stroop Word Colour Conflict Test	HR, SD, RMSSD, pNN50, total power, VLF, LF, LF $_{norm}$, HF $_{norm}$, LF/HF	Stress task caused significant increase in HR and overall reduction in autonomic system activity (decrease in SD of normal interbeat intervals). RMSSD was also significantly reduced. In frequency domain, there was significant decrease in total power. High frequency component also showed decrease and LF component showed significant increase.
	2000		18.7 ± 1.53				

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Table 2 (*continued*)

Authors	Year	N (Number of participants)	Age in years (mean ± Standard Deviation)	Aim and Stress Evaluation	Test	HR measures	Major Findings
Hughes, J. W. W[34]		53 healthy participants		Authors aimed to evaluate HRV via ECG, BDI, STAI, blood pressure, respiratory rate and respiration amplitude during emotional speech task which invoked depressed mood	Videotaped speech task, 3-minute forehead cold pressor task	HR via R peak detection, IBIs, HF via Fast Fourier Transform (FFT)	Significant main effects of depressed mood on BP. High depressed mood participants had significantly higher BP than low depressed mood patients. No other significant main changes on interaction terms involving depressed mood. Participants with higher BDI had significantly different patterns of HF response to stressors than those with low BDI i.e. greater decreases in HF to speech task and smaller increases to cold pressor task.
Light, K.C. [35]	1998	60 healthy women; 15 with highest BDI score formed depressed group vs 15 with lowest BDI score formed healthy control group	32.5 ± 9.9 (Depressed); 30.1 ± 9.0 (Controls)	Authors aimed to determine cardiovascular and catecholamine responses in women with depressive symptoms. This was done through BDI, HAM-D, Interpersonal Support Evaluation List (ISEL), blood pressure, PEP, HRV via ECG, and plasma epinephrine and norepinephrine	Postural challenge, speech task	HR, RMSSD	Depressive group had higher BP at rest and during stressors compared to healthy controls. Both groups showed equivalent increase in BP to stressors. Depressed group had shorter PEP and reduced HRV. Baseline levels of E and NE didn't differ between the two groups. Depressed group showed greater increase in plasma NE to speech task and posture challenge. Plasma E increased from baseline in depressed group and decreased from baseline in healthy group for the speech task.
Moser, M. [36]	1998	26 unmedicated MDD patients and 26 healthy controls	33.7 (MDD);32.1 (Controls)	Authors evaluated difference between resting HRV measures in depressed patients and healthy subjects through use of BDI, STAI, HRV via ECG and blood pressure		HR, HF	Heart rate was significantly higher in patients and diastolic BP was significantly higher in controls. Depressed patients showed slightly lower vagal tone but not significantly different from healthy control group.
Pereira, T. [19]	2017	14 healthy participants		Authors evaluated the use of HRV metrics for stress level assessment by utilising STAI and HRV via ECG	Trier Social Stress Test (TSST)	AVNN (average value of NN intervals), SDNN, RMSSD, pNN20, pNN50, LF, HF, LF/HF and nonlinear measures	STAI scores validated that subjects had higher stress levels during tasks compared to baseline. All HRV metrics negatively correlated with STAI scores except LF/HF, LF (ν) and (alpha1) which showed positive correlation. AVNN, RMSSD, SDNN and pNN20 showed consistent differences between stress and non-stress phases of the TSST. AVNN, SDNN and pNN50 significantly reduced during stressor activation periods.
Pulopulos, M.M.[37]	2020	52 female participants	21.06 ± 2.58	Authors assessed the role of expectancy and anticipation during stressful tasks via BDI-II, Ruminative Responses Scale, Rosenberg Self-Esteem Scale, Perceived Stress Scale, Generalized Self-Efficacy Scale, Visual Analog Scales, salivary cortisol and HRV via telemetric HR monitor	modified TSST	RMSSD, pNN50	RMSSD (HRV) showed significant decrease from habituation phase to anticipation of stress phase. RMSSD was also lower during stress phase. There were no significant differences between groups in anticipatory HRV responses, HRV responses to stress and cortisol indexes. More negative anticipatory cognitive stress appraisal

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Table 2 (*continued*)

Authors	Year	N (Number of participants)	Age in years (mean ± Standard Deviation)	Aim and Stress Evaluation	Test	HR measures	Major Findings
							was associated with larger decreases in HRV during stress anticipation and higher cortisol reactivity.
Schulz, S. [20]	2010	57 unmedicated MDD patients; 57 healthy controls	30 ± 9 (MDD);29 ± 8 (Controls)	Authors compared the complexity of cardiovascular regulation in depressed patients matched with healthy controls through DSM-IV, HAM-D, BDI, HRV via ECG and, blood pressure		AVNN, SDNN, RMSSD, pNN50, LF_{norm}, HF_{norm}, LF/HF and nonlinear measures	All parameters from time and frequency domain of HRV showed no significant differences between MDD patients and controls. Time domain parameters tended to be reduced in MDD compared to controls, frequency domain parameters were unaffected. Time domain parameters of BVP (Blood Volume Pulse) tended to be higher in MDD compared to controls.
Ahrens, T. [38]	2008	22 female MDD patients; 20 healthy female controls	51.0 ± 1.7 (MDD);54.2 ± 1.6 (Controls)	Authors evaluated the SNS responses in women with remitted recurrent MDD versus healthy matched controls through DSM-IV, HAM-D, HRV via ECG, salivary cortisol, blood pressure, Visual Analog Scales, serum cortisol, ACTH, epinephrine and norepinephrine and urinary cortisol measurements for stress evaluation	Speech task, mental arithmetic, cognitive challenge	RR variance, LF, HF, LF/HF ratio, total power	Morning saliva cortisol lower in MDD than healthy. No differences in afternoon or night-time cortisol. Baseline after resting showed lower serum cortisol and NE in MDD than healthy, serum ACTH didn't differ. E levels below range of detection. No group differences in HRV. Blunted cortisol levels in MDD patients.
Udupa, K. [29]	2007	40 MDD patients (26 males, 14 females); 40 age- and gender-matched controls	30.58 ± 7.4 (MDD);30.73 ± 7.1 (Controls)	Authors compared alterations in cardiovascular function between MDD patients and healthy participants using DSM-IV-TR, HAM-D, resting HRV, deep breathing test, Valsalva manoeuvre and orthostatic test (BP)		HR, RR, SDNN, RMSSD, LF_{norm}, HF_{norm}, LF/HF	MDD patients showed significantly lower Valsalva ratio, and greater LF/HF ratio compared to healthy controls. This suggested depression is associated with decreased parasympathetic activity and increased sympathetic activity.
Vaccarino, V.[39]	2008	288 male twins of varying depression severity		Authors aimed to determine HRV differences between co-twins using DSM-IV, BDI, HRV via 24-hour ambulatory ECG, blood pressure to determine depressive symptoms.		RR interval, ultra-low frequency (ULF), very low frequency (VLF), LF, HF, total power, LF/HF	Current depressive symptoms were associated with lower HRV. Increasingly higher BDI scores were associated with progressively lower HRV indices. Power in each HRV frequency band was 19–36% lower in the highest compared with the lowest BDI scoring categories. HRV was 12–21% lower in twins with MDD history than those without. None of the HRV spectra remained significantly associated with a lifetime history of MDD in multivariate analysis.

electrical properties of the skin and is known to be modulated exclusively by the sympathetic nervous system[40]. Variations in sweat gland activity give rise to the tonic and phasic dynamics of EDA[41,42]. Sympathetic innervations of sweat glands contribute to EDA dynamics, which are known to be affected by arousal of emotional and cognitive states[42]. Thus, clinical research within psychophysiology often highlights the significance of EDA monitoring. The inclusion of EDA monitoring in stress studies is further reinforced by the characteristic increase in EDA responses. The signals mirror other well-known physiological changes that occur in response to stress i.e., 'the fight or flight response', such as increases in heart rate and blood pressure[43]. Several studies have noted the significance of EDA as an objective measure for emotional behaviour and arousal[41,44,45]. There are distinct regions of the brain that are involved with the homeostatic control of sympathetic arousal which leads to the manifestation of EDA responses[42]. EDA responses can be classified based on the characteristics of the signal. Slow changes in the basal components are referred to as skin conductance levels (SCLs), whereas rapid transient peaks are known as skin conductance responses or galvanic skin responses (SCRs or GSRs, respectively)[41,42].

A prominent study in the field of psychophysiological monitoring via EDA was the development of a system for continuous EDA measurement for the detection of MDD in 2018 by Kim et.al.[44]. The study involved a machine learning approach to the classification of major depressive disorder in 30 MDD patients and 37 healthy controls. Continuous EDA measurements were recorded during 5 experimental phases including baseline, stress and recovery stages to evaluate the alterations in autonomic activity for feature selection via support vector machines (SVMs). Selected features were used in a decision tree classifier, generating an accuracy of 74%. Kim et.al demonstrated the robust power of EDA responses in preliminary studies through the decomposition of the tonic and phasic components of obtained EDA signals, to facilitate feature extraction for time and frequency analysis[44]. Through feature extraction in preliminary studies, it was evident that all SCRs features were significantly lower in MDD patients than healthy controls, between the experimental phases, suggesting its efficacy in distinguishing between depressed and non-depressed subjects[46]. There are several studies which highlight the use of electrodermal activity measurements for the comprehension of psychophysiological stress, these are summarised in Table 3.

c. Fundamental principles and applications of electroencephalography

Electroencephalography (EEG) is the measurement of electrical impulses from the surface of the scalp to record spontaneous rhythmic brain activity[47]. The relationship between EEG signals and emotional states has been studied for several decades. Numerous studies have shown how certain components of EEG signals can be reflective of specific behavioural and emotional tendencies in humans[48,49]. The EEG signal can be classified into 5 frequency-based bands, each wave contributing to specific functionality in the brain. The delta wave (<4Hz) characterises adult slow-wave sleep, whilst the theta wave (4–8 Hz) is prevalent in adults reaching the stage of sleep[47,50]. Additionally, the alpha band (8–14 Hz) illustrates resting, relaxed states, whereas the beta band (14–30 Hz) signifies active thinking phases[47,50]. The gamma band (14–30 Hz) indicates working memory and attention, often amplified by neurostimulation or meditation[51].

EEG monitoring for depression has been highlighted in numerous studies[52–54]. Predominantly, the findings of these studies presented the increase in absolute power in the theta and beta bands during eyes open and eyes closed conditions, in depressed individuals[52,55]. Furthermore, Kan et.al. showcased the significance of alpha band frequencies in the discrimination between depressed and normal groups in a 2015 electroencephalogram study[56]. Kan highlighted the low alpha frequency signals originating from the parietal, occipital and temporal lobes, suggesting the lack of attentiveness in depressed individuals, when compared to healthy controls[56]. Depending on the frequency bands that are analysed, there are different characteristics that may be indicative of depressive symptoms within individuals under examination. For example, in a study by Debener et.al. on physiological markers of depression, the EEG frequency that was analysed was alpha wave asymmetry[54]. The findings from this study illustrated the increase in anterior alpha wave asymmetry in the depressed patients when compared to the healthy controls[53]. These studies have emphasised the differences in brain activity amongst depressed individuals, in comparison to healthy controls, as well as noting the influences of antidepressant treatments on the electroencephalographic signals of depressed patients[53]. A comprehensive summary of these studies can be found in Table 4.

5. Discussion

HRV reactivity is profoundly dependent on variations in ANS activity, which may be caused by stress induction or emotional arousal[5]. Several studies have presented the relationship that exists between psychological stress and the manifestation of changes in physiological signals within the body[18,28,19]. Evidently, the monitoring of heart rate variability in response to elicitation of psychological stress has revealed the significance of the balance between sympathetic and parasympathetic activity i.e., the sympathovagal balance. The LF/HF ratio in HRV indices reflects the sympathovagal balance and indicates vagal activity dominance in scenarios where the ratio is low, and sympathetic activity dominance when the ratio is high[5]. As it is known that the 'fight or flight' or stress response is activated by high sympathetic activity, a high LF/HF ratio can suggest increased stress in individuals[9]. Furthermore, in cases of persistent stress or mental illnesses, such as major depressive disorder, the LF/HF ratio is expected to increase. This is potentially due to the exhaustive stage of the Generalised Adaptation Syndrome which depicts the depletion of efforts to challenge persistent stressors[8,13]. Exhaustion of the ANS can be signified by decreased vagal tone, increased LF values and decreased HF values i.e., overall increase in LF/HF ratio. This concept is in line with the findings from Delaney et.al's study of HRV monitoring in participants undergoing the Stroop Word Colour Conflict Test, Agelink et.al.'s study in the examination of HRV reactivity in MDD patients, and partially with Hughes' study of HRV during a stress task, which reported HF power decline in the presence of stressors[18,28,34].

However, several studies have suggested that the LF/HF ratio may

Table 3
Studies of electrodermal activity (EDA) monitoring for psychological stress evaluation in depressed and non-depressed groups.

Authors	Year	N (Number of participants)	Age in years (mean ± Standard Deviation)	Aim and Stress Evaluation	Test	Major Findings
Branković, S.B.[21]	2008	57 MDD patients; 52 healthy controls	43.1 ± 10.9 (MDD); 39.8 ± 8.1(Control)	Authors aimed to determine differences between skin conductance responses in depressed and healthy subjects through use of DSM-IV, HAM-D and Skin conductance (SC). Authors also monitored HR and respiration for stress evaluation.	11 short stories to elicit arousal	Stronger SCR signals in depression compared to healthy controls
Kim, A.Y. [44]	2018	30 MDD patients; 37 healthy controls	42.5 ± 16.96 (MDD); 41.3 ± 15.97 (Control)	Authors aimed to automatically detect MDD using electrodermal activity-based algorithms by using HAM-D, Hamilton Anxiety Rating Score (HAM-A), Stress Response Inventory (SRI), Skin conductance levels (SCL), skin conductance response (SCR) for stress evaluation	Mental arithmetic task	MSCL (mean amplitude of SCL), SDSCL (standard deviation of SCL), NSSCR (non-specific SCR) were significantly affected by group and task. SKSCL (skewness of SCL) was significantly affected by arithmetic task.
Kim, A.Y. [46]	2019	30 MDD patients; 31 healthy controls	42.5 ± 19.70 (MDD); 43.7 ± 20.77 (Control)	Authors compared SCRs between MDD patients and healthy controls under mental arithmetic stress via SRI, PSS (Perceived Stress Scale), HAM-D and SC	Mental arithmetic task	All 6 SC features were lower in MDD patients compared to control groups during all phases of study.

Table 4
Studies of electroencephalography (EEG) monitoring for psychological stress evaluation in depressed and non-depressed groups.

Authors	Year	N (Number of participants)	Age in years (mean ± Standard Deviation)	Aim and Stress Evaluation	Test	EEG measures	Major Findings
Billones, R. K.C.[57]	2019	8 healthy participants		Authors analysed cardiac and brain activity correlation during a psychological stress task using EEG and HR via ECG	2-minute jog, watching thriller clip with jump-scare sequence	alpha, beta, delta, theta band measurements from 3 electrode EEG	Increase in HR and alpha, beta, delta and theta waves upon stimulus activation. Dominance of delta activity after jog and theta waves after watching video.
Al-Shargie, F.[58]	2018	18 healthy male participants		Authors aimed to create multi-level mental stress assessment process using EEG and self-reporting about task load (NASA-TLX rating scale)	Mental arithmetic task of 3 levels of difficulty	alpha rhythm power, EEG from prefrontal cortex (PFC) with 7 active electrodes	no significant differences in EEG when compared to self-reporting questionnaire. Mean EEG alpha rhythm power significantly reduced with increasing difficulty.
Bachmann, M.[59]	2015	17 female MDD patients; 17 healthy female controls	39 ± 12	Authors determined EEG complexity between healthy and depressed female students using ICD-10, HAM-D and resting EEG		Lempel-Zig complexity (LZC) from 18 channel EEG in 10–20-electrode position classification system	Increased complexity in depressive subjects compared to normal controls, even in single channel EEG.
Baehr, E. [60]	1998	13 MDD patients; 11 healthy controls	43.5 ± 6.99 (MDD);44.2 ± 13.3 (Control)	Authors compared EEG asymmetry indices between depressed patients and healthy controls via DSM-IV, BDI and EEG		alpha asymmetry from 3 electrode commercial EEG system	Percent index (percentage of time in which asymmetry was greater than 0) was better discriminator between depressed and control groups compared to asymmetry score.
Cai, H. [47]	2018	152 MDD patients; 113 healthy controls	18–55	Authors investigated 3-channel EEG for depression diagnosis tool using DSM, EEG		EEG linear and non-linear features from delta, theta, alpha, beta and gamma bands.	Four feature selection algorithms were used, of which WrapperSubsetEval gave the highest performance classification accuracy (76.4%). WrapperSubsetEval produces five feature subsets for five different classifiers.
Debener, S. [54]	2000	15 MDD patients; 22 healthy controls	48.5 (range:23–64 MDD);45.9 (range:26–64 Control);	Authors aimed to investigate anterior EEG alpha power asymmetry differences between depressed patients and healthy adults using BDI, Edinburgh Handedness Inventory, Positive and Negative Affect Scales and EEG		Anterior EEG alpha wave asymmetry	Increased anterior alpha wave asymmetry in depressed patients compared to healthy controls. Increased variability of anterior EEG asymmetry may be characteristic feature of depression.
Hinrikus, H [61]	2010	18 female MDD patients; 18 healthy female controls	36 ± 10 (MDD);35 ± 10.5 (Control)	Authors investigated differences in EEG spectral features between unmedicated MDD patients and healthy controls using ICD-10, HAM-D and EEG		Spectral asymmetry (SA) in alpha band from 19 electrode commercial EEG system	SA values were positive for depressive subjects, negative for healthy subjects. SA differences between 2 groups were significant in all EEG channels.
Kan, D.P.X. [56]	2015	4 MDD patients;4 healthy controls	23.38	Authors detected EEG alpha wave differences between depressed and healthy participants via DSM-IV, Patient Health Questionnaire (PHQ-9), Depression, Anxiety and Stress Scale (DASS-21), EEG		delta, theta, beta and alpha band analysis from 32 channel commercial EEG system	Alpha waves in depressed subjects were decreased compared to normal subjects significantly. Low alpha frequency in parietal lobe, occipital lobe and temporal lobe.

not accurately reflect ANS activity, especially during stress tasks. Brugnera et.al's protocol involved HRV monitoring of 65 healthy volunteers during the Montreal Imaging Stress Task (MIST)[31]. Findings from this study revealed that although statistically significant decreases in HF power were presented during the stress task; the LF/HF ratio variations were insignificant. Similarly, Castaldo's 2016 study comprised of HRV monitoring of 42 healthy volunteers during oral academic examinations, which disclosed increases in both LF power, as well as HF power during the stress phase[32]. Discrepancies in LF/HF ratio in some HRV stress studies suggests that the complexity of psychophysiological stress cannot be illustrated through one HRV index, implying the necessity for the inclusion of other physiological signal monitoring methods.

Numerous articles have presented the utilisation of electrodermal activity responses to stressors for the monitoring of psychophysiological stress, such as those by Branković et. al[21]. Similarly, Kim et.al. led two studies in the application of electrodermal responses for the discrimination between MDD patients and healthy volunteers undergoing stress tasks[44,46]. Kim et. al. studies involved mental arithmetic tasks as the stressor and the measurement of skin conductance levels (SCLs) and skin conductance responses (SCRs) for stress evaluation. Feature extraction from the acquired physiological signals demonstrated the reduction in skin conductance as a response to stress in MDD patients, compared to their healthy control counterparts[67].

Comparatively, electroencephalographic studies in the field of psychological stress analysis have proven to be successful in the discrimination between depressed and non-depressed individuals. Notable EEG studies include Al-Shargie et.al's 2018 EEG study involving electroencephalographic monitoring from the prefrontal cortex (PFC) on 18 healthy male participants undergoing a mental arithmetic task of 3 levels of difficulty[68]. The EEG frequency band of interest in this protocol was the alpha wave (8–14 Hz), which demonstrated reduced power with increasing arithmetic difficulty levels[50,68]. Furthermore, this phenomenon was also reported by Kan et.al. in 2015 whereby, it was found that alpha waves in depressed and stressed subjects were significantly reduced, when compared to their healthy control counterparts [56]. In Kan's study, low alpha frequency was found in EEG measurements from the parietal, occipital and temporal lobes.

Evidently, the mentioned studies have primarily focused on the alpha EEG band which is one of the most common EEG signals of interest, in its relation to stress. Chandra's study on the neurophysiology of mental stress reported similar decreases in alpha band power with accumulating mental stress, as well as reductions in frontal brain asymmetry as stress tolerance increased[69]. This feature has given rise to the utilisation of power ratios in EEG stress studies to reflect the brain activity during stress assessment. Wen et.al. describes the use of alpha/beta ratio and theta/beta ratio in a protocol of 40 subject undergoing a virtual reality (VR) session for stress elicitation[70]. EEG monitoring and signal processing of the subjects' physiological signals led to the acquisition of the alpha, beta and theta frequency bands. Subsequent

Table 5
Studies of multimodal monitoring for psychological stress evaluation in depressed and non-depressed groups.

Authors	Year	N (Number of participants)	Age in years (mean ± Standard Deviation)	Aim and Stress Evaluation	Test	Measurements	Major Findings
Avdeeva,D. K. [71]	2017	14 healthy volunteers	23–27	Authors evaluated stress through series of emotional and neutral questions via 3-lead ECG, bipolar lead GSR and 7-electrode EEG with aim to develop nanosensor-based apparatus to assess psycho-emotional states	Non-standardised test	ECG, GSR, EEG	An ECG, EEG and GSR-based psycho-emotional state assessment device was developed. Ultra-slow changes in EEG cannot be measured through standard EEG setups so delta rhythm variation was not available for analysis.
Cipresso, P. [62]	2019	60 healthy participants	21.2 ± 2.25	Authors applied computational psychometrics for acute mental stress assessment using psychophysiological measures including respiration, BVP, GSR and HRV via BVP	Stroop Colour Word Task, mental arithmetic task	moment-to-moment HRV i.e. PRV (pulse rate variability), SDRR, SDHR, VLF, LF, HF, LF/HF, respiration rate, SC	Increase in sympathetic activity with significantly higher LF during acute mental stress. However, HF also increased suggesting increased parasympathetic activity. RSA shows HRV in synchrony with respiration, reduced vagal tone during acute mental stress.
Guinjoan, S.M.[63]	1995	18 MDD patients; 18 healthy controls	44 ± 12 (MDD); 40 ± 13 (Control)	Authors assessed cardiovascular and sympathetic skin responses in MDD patients and healthy controls through use of the Minnesota multiphasic personality inventory (MMPI), DSM-III-R, blood pressure, HR and HRV, GSR	Lying to standing manoeuvre, hand grip manoeuvre, mental arithmetic task, explosive sound, cold pressor task, hyperventilation	Systolic and diastolic BP, HR, GSR	Depressed patients had significantly lower indices than control subjects for parasympathetic activity as seen by HRV. Sympathetic skin responses were significantly larger in depressed individuals.
Papousek, I.[64]	2002	111 healthy participants	21	Authors investigated autonomic regulation of stress through FBL-R (Freiburg Complaint Checklist), 17-point bipolar rating scale (KUSTA), Eysenck Personality Questionnaire (EPQ), EDA and HRV via ECG	Public speech task	EDA, LF, HF	All participants showed increase in EDA and decreases in HRV-HF from rest to stress condition. Changes were larger in subjects that reported greater stress.
Reinhardt, T.[65]	2012	Study 1: 80 female participants. Study 2: 30 healthy participants	25.4 ± 4.5 (Study 1); 24.7 ± 4.6 (Study 2)	Authors investigated stress responses using DSM-IV, SCID II Personality Questionnaire, International Personality Disorder Examination (IPDE), salivary cortisol (study 2), SCL (study 1) and HR during a stress test	Mannheim Multicomponent Stress Test (MMST)	HR via HR sensors in study 1 along with GSR. HR via ECG in study 2 along with salivary cortisol.	Significant increase in subjective stress ratings in response to MMST. HR significantly increased in response to MMST. Significant increases of SCL found in response to stress induction. In second study subjective stress ratings were significantly increased along with HR and salivary free cortisol. Mean peak of cortisol level observed 20 mins after stress cessation.
Ding, X. [66]	2019	144 MDD patients; 204 healthy controls	27.65 ± 9.50 (MDD); 27.46 ± 9.61 (Control)	Authors classified between MDD patients and healthy controls using ICD-10, SDS, eye tracking, EEG and GSR	Open Affective Standardised Image Set (OASIS) for eye tracking task. Watching 8 short videos	Eye tracking data, EEG, GSR	MDD patients had higher SDS scores than control. MDD showed significantly lower absolute EEG power in theta, alpha, beta and gamma bands than HC. MDD also showed attentional bias towards negative images during eye tracking.

computation of power spectral density (PSD) of each frequency facilitated the calculation of absolute power ratios. The alpha/beta ratio was used to determine the differences in absolute power between the baseline session and the stress task, whereas the beta/theta ratio signified the differences between the relaxed state and stress state[70]. These correspond with the known associations between the brain activity and frequency bands in the existing literature[47,50].

Although, it should be noted that respective studies have narrated increases in all EEG frequency band powers upon stress activation[57]. However, it should also be noted that such studies often involved non-standardised stress tests and lacked affective stress evaluations, which may have led to discrepancies in stress elicitation and subsequent inconsistencies in the results.

a. Stress studies and considerations

The significance of standardised stress tests is mentioned throughout this comprehensive review. Various studies have shown promising findings and results in accordance with the existing literature, as well as some studies which have given contradictory results[38,57,71]. However, in both cases, the legitimacy of the findings of numerous studies is diminished by the lack of standardised stress testing. Standardised stress tests such as the Trier Social Stress Test (TSST) or the Mannheim Multicomponent Stress Test (MMST) are vastly known to reliably elicit stress responses. Therefore, the utilisation of such tests certifies that the subjects of the protocol experienced stress, which can be monitored through physiological signals. In the case of non-standardised stress testing, such as those by Avdeeva et.al., Billones et.al, Castaldo et.al and Ahrens et.al, the major findings of the protocols found inconsistencies with the existing literature[32,57,71]. This could have been caused by the elicitation of other responses through the supposed stress tasks, due to lack of standardisation and previous utilisation.

b. Multimodal approaches to stress monitoring

A multimodal approach to physiological monitoring of stress and depressive symptoms may be the future of psychophysiological stress evaluation. Numerous preliminary studies have shown promising results in the use of multiple monitoring techniques for the evaluation of stress, or discrimination between depressed and non-depressed individuals as showcased in Table 5 [62,64–66,63]. Notably, Reinhardt et al.'s 2012 study on the effects of the Mannheim Multicomponent Stress Test (MMST) on salivary cortisol, electrodermal activity and heart rate demonstrated the synchrony in these physiological signals in the event of stress elicitation[65]. However, the article clarifies that two separate studies were conducted in conjunction to evaluate the stress response in the physiological signals of interest. Therefore, future elaborations within this field may involve the development of a multimodal structure to fuse the significant features of interest from the physiological signals for a complete system, which evaluates psychological stress responses in the human body.

6. Conclusion

In conclusion, the prominence of physiological monitoring for the evaluation of psychological stress and major depressive disorder is inevitable. Further elaborations within multimodal systems could direct efforts away from the existing diagnostic and monitoring practices, towards a rejuvenated complete stress evaluation process which considers both the physiological elements of the stress response, as well as the psychological considerations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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