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Biomarkers of Anxiety and Depression – A Novel Method of Tracking the Autonomic Nervous System with Machine Learning

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Abstract

This study presents a novel method to understand biomarkers of anxiety and depression by using a concept called Sympathetic Transition Points (STP), which is indicative of Autonomic Nervous System (ANS) dynamics. Wearables-based Electrodermal Activity (EDA) and Blood Volume Pulse (BVP) data were collected from 61 controls, 60 individuals with depressive symptoms, and 110 individuals with anxiety. By monitoring ANS activity, patterns related to anxiety and mood states and their transitions in real-time were identified, using machine learning. Analysis revealed clear distinctions between groups and enabled tracking of mental state changes. A score of .99 F1, with an ROC of 1 was achieved in automatically classifying anxiety, depression, and neutral states with this method. The method lays the groundwork for automated mental health assessments in real-world settings, introducing an efficient and objective screening protocol. By utilizing wearable technology, machine learning, and ANS monitoring, this work advocates for improved early detection and intervention strategies in mental healthcare.

1 Introduction

970 million people around the world live with a mental disorder, with anxiety and depressive disorders among the most common.[1] The prevalence of these common mental disorders is increasing, particularly in low and middle-income countries, with many people experiencing both depression and anxiety disorders simultaneously.[2 3] The consequences of these disorders in terms of lost health are huge. Depression is ranked by WHO as the single largest contributor to global disability (7.5% of all years lived with disability in 2015), while anxiety disorders are ranked 6th (3.4%). Mental disorders, especially mood and psychotic syndromes are associated with self-harm, suicidal thoughts and behaviors, increasing the risk of death by suicide.[4] Depression is also the major contributor to suicide deaths, with close to 800,000 deaths per year.[5]

The diagnosis of mental health disorders is generally based on the guidelines given in The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) and the International Classification of Diseases (ICD) 11.[6]

Diagnosis using DSM-5 or ICD 11 depends on a clinician's judgement, self-reporting by patients or the 'ambiguous or unstated perspective' of patients and caregivers.[7] Several studies have shown that the correct diagnosis of mood and anxiety disorders is lacking in the primary care setting.[8 9 10] Some of the most frequently misdiagnosed mental health disorders include depression[11], bipolar disorder[12], borderline personality disorder[13], ADHD[14], PTSD, and anxiety[15 16]. In one study, it was shown that non-detection rates of common mental health disorders by primary care physicians is about 65.9% for patients with major depressive disorder, 92.7% of patients with bipolar disorder, 85.8% of patients with panic disorder, 71.0% of patients with generalized anxiety disorder, and an outstanding 97.8% of individuals with social anxiety disorder.[17] In the case of depression alone, a meta-analysis of 50,000 patients found that general practitioners only correctly identified depression in only 47.3% of cases.[18] On the other hand, 60% of people who receive a diagnosis of major depression may not actually have it.[19]

To improve the quality of mental health services, measurement-based care has been recommended by experts, [20] along with the "adoption of digital platforms to facilitate the delivery of interventions across the continuum of care."[21]

1.1 Traditional technologies in mental health

Biofeedback and neurofeedback technologies[22] are valuable tools in psychiatric practice, offering innovative methods for assessment and intervention. They are primarily used as adjuncts to therapy rather than for diagnostic purposes. These non-invasive technologies enable clinicians to monitor and modulate physiological processes such as brain activity (EEG), heart rate variability (HRV), skin conductance, and muscle tension (EMG), showing real-time physiological responses. For example, EEG-based neurofeedback may be used to assess patterns of brain activity associated with conditions like anxiety, but it is not used as the sole diagnostic criterion. Similarly, Heart Rate Variability (HRV) biofeedback may be utilized to assess autonomic nervous system function and stress reactivity, but it is not a standalone diagnostic test for psychiatric disorders. Thus, in clinical practice, biofeedback and neurofeedback are typically integrated into comprehensive assessment protocols that include clinical interviews, symptom questionnaires, and other standardized assessments to inform diagnosis and treatment planning.

Challenges typically seen in the implementation of these technologies include the need for expertise in using the equipment, manual interpretations of results, and the potential for variability in individual responses. The access to hospital-grade equipment is also limited, and the cost of equipment and training makes it impractical for use in individual practice.

1.2 Advent of newer technologies for mood and anxiety disorders

Newer technologies, including wearables, smartphones, sensors and remote monitoring have been used by practitioners and researchers alike to understand mood and anxiety disorders.[23] These newer methodologies are accessible, cost-effective and can be deployed without extensive training. The use of such technology has increased access to care, enhanced practitioner capacity, led to positive patient and family outcomes, and have improved quality of life.[24]

Research has demonstrated the effectiveness of Internet-based programs in addressing a range of mental health concerns, including the treatment and alleviation of symptoms associated with anxiety and depression.[25] [26] The successful usage of smartphones in solving issues related to depression and anxiety has also been documented in literature.[27] [28] The use of data science to measure behavioural phenotypes across time and at the scale of millions of healthy and mentally ill individuals is likely to shed light on the phenotypic distribution of normal and abnormal behaviours that are currently difficult to diagnose.[29]

By using machine learning, it is possible to extract meaningful information from sensor data and to continuously monitor the mental state.[30] The advent of sensors and Artificial Intelligence (AI)-enabled technologies have shown great promise in bringing a paradigm shift in the management of mental disorders.[31] [32] Tremendous work have been done to understand depression and anxiety diagnosis[33] [34] and treatment with the help of AI, showing the effectiveness of using such technologies to aid diagnostics and care.[35] [36] [37] [38]

2 ANS as the gateway to understanding mental health

The study of the Autonomic Nervous System (ANS) in the assessment of psychological stress is well established.[39] Throughout history, stress has been defined as a shift from a state of calm to one of heightened alertness, all in the pursuit of safeguarding an organism's well-being. [40] This concept traces back to early 450 BC, when Empedocles conceptualized stress as a threat to the harmonious balance of an organism's vital elements. Claude Bernard further refined this notion, introducing the term "milieu intérieur" to denote the internal environment containing these vital elements. According to Bernard, a stress response is a mechanism aimed at protecting this internal milieu.[41] Walter Cannon later coined the term "homeostasis" to refer to the stable or "steady state" of the organism, with stress representing a transient "fight or flight" reaction designed to preserve this state of equilibrium.[42]

These definitions endorse the concept of stress as a transition from a state of calm to one of heightened arousal, indicating an inherent negative bias. Bernard characterized the reactions as protective, while Cannon emphasized "fight or flight" rather than "fight or joy."[43] Bernard's hypothesis was that as organisms evolve and become more independent of their outer environment, they develop more complex mechanisms to preserve the interior from the exterior. For an organism as highly developed and independent of the natural environment as socialized man, most stressors are intellectual, emotional and perceptual, and physical stressors occur far less frequently.

The ANS consists of numerous pathways of neurons that control various organ systems in the human body, using diverse chemicals and signals.[44] The ANS functions without conscious and voluntary control and innervates cardiac muscle, smooth muscle, and various endocrine and exocrine glands, [45] playing a crucial role in maintaining homeostasis.[46] The ANS is composed of two systems, namely the Sympathetic Nervous System (SNS) and the Parasympathetic Nervous System (PNS). The ANS undergoes a dynamic shift in response to acute stress, characterized by heightened sympathetic activity (arousal) alongside a simultaneous reduction in parasympathetic function (vagal withdrawal).[47] In conditions frequently linked with chronic stress, like major depressive disorder, the sympathetic nervous system may remain constantly active, lacking the typical regulatory influence of the parasympathetic nervous system.[48]

The two most common techniques used for the non-invasive assessment of the ANS are Electrodermal Activity (EDA).[49] [50] and Heart Rate Variability (HRV).[51] There is strong evidence of the usage of EDA[52] [53] and HRV[54] [55] for the identification and prediction of anxiety and mood disorders. Changes in the electrical properties of the skin have been used successfully to study several dimensions of mind for a long time.[56] The study of the ANS through electrophysiology has shown that variations of pupillary responses, cardiovascular activity and electrical properties of the skin are potential markers of affective or cognitive expressions.[57] Electrodermal and cardiovascular responses are reported to index the activation level and the valence of emotional stimuli.[58]

2.1 Electrodermal Activity and ANS

EDA refers to the variation of the electrical properties of the skin in response to sweat secretion.[59] Such secretion may happen due to sympathetic innervation in response to environmental temperature, leading to thermoregulatory sweating.[60] Activities of the central nervous system related to affective and cognitive states lead to palmar, mental or emotional sweating.[61] [62] EDA has been recognized as a reliable indicator of sympathetic arousal.[63] EDA is measured to explore multiple mind-states, namely emotions, cognition, [64] [65] [66] decision-making, reasoning bias,[67] and several behavioural adaptations.[68] Multiple studies on anxiety and depression[69] have used EDA measurements to show the effects of the ANS on mood states.

A commonly used measure of EDA is the continuous exosomatic recording of skin conductance (SC).[70] The SC level or the tonic component of EDA is the slow-moving, spontaneous electrical fluctuations of the sweat gland activity that results from an interaction between tonic discharges of sympathetic innervation and local factors like skin temperature and hydration.[71] The fast-changing element of the EDA signal is referred to as the Skin Conductance Response (SCR) and SCR is correlated with phasic sympathetic nervous discharges.[72] Another aspect of EDA is the Sudomotor Nerve Activity (SMNA), which plays a major role in thermoregulation,[73] enabling sensory discrimination by the skin[74], and providing information about emotional arousal. [75] With the EDA sensors, it is thus possible to estimate the time and amplitude of stimuli generated from control centres in the brain.[76]

2.2 Heart Rate Variability and ANS

The Blood Volume Pulse (BVP) signal reflects the flow of blood that occur during a cardiac cycle, and hence, it has been used as an alternative to ECG to assess the instantaneous heart rate and the RR[77] or inter-beat-interval (IBI), along with the Breathing Rate,[78] Pulse Transit Time (PTT) and peripheral vasodilatation.[79] Heart rate and rhythm are largely under the control of the autonomic nervous system.[80].

HRV, which is the beat-to-beat alteration of heartbeats, is widely used as a reliable indicator of ANS arousal. HRV serves to index the central-peripheral autonomic nervous system integration,[81] and thus, is considered a psychophysiological marker for adaptive environmental engagement,[82] [83] especially as a potential marker of

stress.[84] The High Frequency (HF) component of HRV is considered a reliable measure for the assessment of parasympathetic activity. [85] Alterations in HRV are reported in people with clinical anxiety disorders[86] and anxiety disorders are also related to cardiovascular disease.[87] [88] Cardiovascular diseases are commonly seen among patients with Major Depressive Disorder(MDD), [89] [90] [91] implying autonomous regulation of the heart rate as a potential pathophysiological mechanism in depression.[92] [93] [94] [95] [96] [97]

2.3 Identifying mental state transition with ANS

To track the progression of mental states temporally, we introduced a concept called Sympathetic Transition Points (STP) and tracked the activities of the sympathetic branch of the ANS with the help of EDA. The decision to track EDA to understand state transitions was made as laboratory studies,[98] [99] [100] have shown that skin conductivity varies linearly with arousal ratings,[101] and thus it was felt that EDA could provide better understanding of mental state transitions. EDA is a predominantly sympathetic measure,[102] and the eccrine sweat glands are innervated by only the sympathetic nerves. Additionally, skin conductivity has also been found to be one of the most robust non-invasive physiological measures of autonomic nervous system activity.[103]

To illustrate the concept of state transition further, according to the portal valve method of Edelberg104, assuming initially empty sweat ducts, an impulse-triggered activation of the Autonomic Nervous System (ANS) leads to secretions that fill the sweat ducts. The influx raises hydraulic pressure inside, facilitating increased diffusion into both the stratum corneum and its deeper layers. This leads to a modest elevation in the tonic or skin conduction (SC) level. If pressure surpasses a certain threshold, sweat duct pores open, resulting in a portion of sweat being directly secreted through the pores. This directly secreted sweat, along with the sweat remaining in the ducts, contributes to conductance, leading to a sharp increase in the SC level. Direct secretion refers to sweat being expelled through the pore to the skin's surface, while sweat secretion via diffusion occurs when sweat gradually traverses the sweat duct wall to hydrate the stratum corneum.

As direct secretion and diffusion decrease hydraulic pressure, dropping below a specific threshold triggers pore closure, isolating sweat in the ducts and discontinuing its contribution to conductance. Consequently, a more rapid decline in SC level is observed due to accelerated re-absorption, resulting in a quicker decay time in SC. The remaining secreted sweat in the stratum corneum undergoes slow re-absorption into the deeper dermis and is cleared from the periductal area. Additionally, a fraction of the reduction in SC is attributable to surface evaporation. These processes collectively lead to a gradual decline in SC level.

To study the phenomena, we used exponential moving averages (EMA), a concept used in finance[105], on the EDA data. Unlike simple moving averages, EMAs assign greater importance to recent data points, making them more responsive to immediate changes in the dataset.

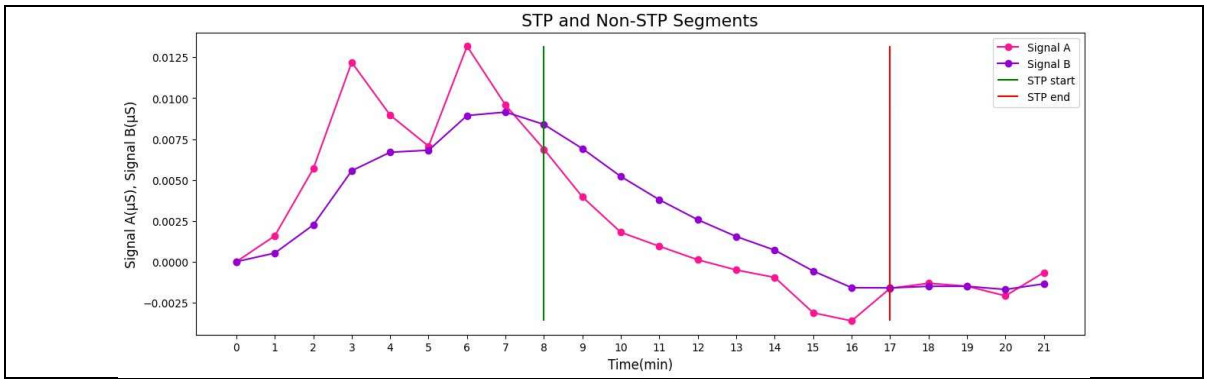
We applied this concept to the EDA signals to understand the trend of the Sympathetic Nervous System (SNS). The objective was to identify specific time intervals within a subject's data where there was a decrease in sympathetic state compared to preceding periods. It was believed this analysis could provide indications of evolving sympathetic states over time. The process involved computing the EMA of the EDA data using both a 1-minute (representing a fast-moving average) and a 10-minute (representing a slow-moving average) window. Subsequently, the slow-moving EMA was subtracted from the fast-moving EMA for each minute, resulting in the creation of a data stream labelled Signal A. Next, another EMA was calculated using a 5-minute window, generating Signal B. Signal A and Signal B were then compared to gain insights into the short-term and long-term behavior of the EDA signal. In these comparisons, instances where the value of Signal B exceeded that of Signal A were designated as H-SNS (H stands for high), indicating shifts towards heightened sympathetic activity. Conversely, points where Signal B fell below Signal A were labelled as L-SNS (L stands for low), signifying reductions in sympathetic activity.

Analyzing the sympathetic state at 1, 5, and 10-minute intervals provided a detailed understanding of how an individual's mental state evolves over time. This approach allowed for a closer examination of temporal changes in mental state, offering insights into how emotions or perceptions may fluctuate rapidly. Additionally, it helped in observing the dynamics of an individual's responses, revealing whether their state of mind shifted quickly or gradually in response to various internal stimuli. Our method enabled the identification of patterns or trends in mental states, such as a gradual increase in relaxation or a sudden spike in arousal. Thus, the choice of time intervals—1, 5, and 10 minutes—ensured that both immediate reactions and slightly longer-term trends are captured, allowing for a more comprehensive understanding of the individual's mental state in different contexts.

In the context of our study, H-SNS indicate when the short-term behavior of the EDA signal aligns with its normal, long-term trend, while L-SNS indicate when the short-term EDA signal dips below its extended, overall trend. This signifies that if a subject is experiencing increased restfulness compared to the baseline or any previous minute, the short-term EDA signal for the current time will diminish compared to the long-term signal representing the mental state.

Figure 1 shows the concept of STPs, which are bound by a green vertical line showing the start of a segment and a red vertical line showing the end of a segment. The Non-STP segments are found on either side of an STP segment.

Figure 1: STP and Non-STP Segments



There could be several H-SNS and L-SNS segments on an EDA signal. A low point is the start of a segment, while a corresponding high point is the end of that particular segment. The formula for creating H-SNS and L-SNS segments are given below:

We calculated Signal A by subtracting a 10-min exponential moving average (EMA) from a 1-min EMA, of EDA (μS). Mathematically Signal A and EMA are expressed in Eq. (1) and Eq. (2):

$$Signal\ A\ =\ EMA_1(EDA)\ -\ EMA_{10}(EDA) \tag{1}$$

$$EMA[n] = \alpha\ EDA[n]\ +\ \sum_{i=1}^{n}(1-\alpha)^i\ EMA[n-i] \tag{2}$$

Where the smoothing factor α is defined as:

$$\alpha = \left(\frac{2}{1+m}\right) \tag{3}$$

Where m is span in minutes.

The H-SNS and L-SNS can be observed by comparing Signal A and Signal B which is a 5 min EMA of EDA. The mathematical expression of Signal B is expressed in Eq. (4)

$$Signal\ B = EMA_5\ (EDA) \tag{4}$$

3 Experiment design

Our experiment had two objectives. Firstly, it aimed to objectively differentiate between states of anxiety and depression compared to a 'neutral' state. A 'neutral' mental state is a baseline of functioning where an individual is not significantly affected by distortions in cognition or experiencing overwhelming emotional distress. This state contrasts with anxiety, where individuals may experience heightened arousal, and depression, where there might be a blunting of positive affect.

Secondly, we sought to capture the dynamic shifts in mental states, seeking to understand movement towards states of either stress or calmness in individuals.

Generally, during studies on moods and emotions, stress is induced in subjects to elicit the appropriate sympathetic and the parasympathetic responses, which are then measured and reported.[106] [107] In real-world situations, consistently inducing stress, particularly within clinical settings to elicit anxious or depressive responses, is impractical. For practical use, it is also essential to identify different mood states naturally, without the artificial inducement of stress. To ensure clinical applicability, any technological solution aimed at real world implementation needs to operate with a high degree of independence. Thus, we attempted to conduct our experiment in a real-life setting, without relying on explicit provocations to induce varying states of stress in the subjects. Further, building on Bernard's views that stress is mostly induced internally, we decided to study the three groups of subjects enrolled in our study without imposing any artificial stressors on them, and observe whether the groups showed statistically significant differences in attributes.

3.1 Subject enrolment

For the experimental study, we used data of 231 subjects (109 females and 122 males), from a total batch of 300 individuals, between the ages of 18-65 years. See Supplementary for demographic details. Data was collected at Bangalore (TerraBlue XT Lab) and Hyderabad (Heartfulness Ashram), India and the experiment was approved by the local ethical committee. Subjects were enrolled through advertisements via phone groups and posters at office premises. All subjects signed an informed consent form before being enrolled. Standardized self-ratings were obtained before data acquisition. Subjects that did not meet the Anxiety (based on GAD 7[108]) or Depression (based on PHQ 9[109]) criteria set for the study, apart from not meeting clinical standards for severity as per clinician assessment, and the meditators that exceeded the GAD 7 and PHQ 9 criteria were dropped from the study.

Of the total sample finally enrolled, 60 subjects were meditators with greater than 5 years of meditation experience (mean 7 years). The meditators were trained in Sahaj Marg or Heartfulness meditation - a form of concentrative meditation technique where the focus of attention is the heart. The meditators enrolled in the study scored less than 8 in GAD-7and PHQ-9 and they were placed in the Neutral group. 110 subjects with a clinical diagnosis of anxiety and score greater than 12 (moderate-severe) on GAD-7 were enrolled in the Anxiety group, while 60 subjects with clinical depression, and scores greater than 15 (moderate-severe) on PHQ-9 were enrolled in the Depression group.

3.2 Experimental task

We chose relaxation as the experimental task to collect data from subjects. All subjects were required to wear the data collection unit and sit, either on the floor or on a chair, for a duration of 45 minutes, in a designated place. Subjects were asked to relax, without sleeping. They were also given the flexibility to either stop their activity if they were uncomfortable or extend their session beyond the allocated time.

3.3 Data acquisition and pre-processing

We extracted BVP and EDA data using devices from BioSignal Plux. Data was sampled at 250 Hz for both EDA and BVP, which were extracted from the distal and proximal phalanges of the non-dominant hand. We analyzed continuous, non-overlapping per 10-millisecond segments of data. During pre-processing, data was converted from raw form to their respective units, filtering and smoothening were done, along with timestamp insertion and artefact detection and removal. We used cvxEDA[110] for EDA processing and decomposition, while BVP data was processed using NeuroKit2[111]. Feature extraction of EDA and BVP were done using NeuroKit2 and Python programming. See Supplementary for list of features.

3.4 Data analysis

We performed exploratory data analysis on the groups to understand the distribution of the data extracted from subjects. The upper and lower boundaries of the values of each feature was decided using the Interquartile Range (IQR) technique. The data points outside the lower and the upper boundaries were considered outliers, while the data inside, encapsulated within the respective boundaries of each feature was used in the study.

3.4.1 Data labelling

For each subject, after calculating the difference between trends, we labelled segments of data as STP (data that will be encapsulated with STP segments) and Non-STP (data that will be outside of the STP segments).

The conditions for labelling the segments is shown in Eq. (5):

$$Segment[n] = \begin{cases} H - SNS, if\ Signal\ B\ [n] > Signal\ A\ [n] \\ L - SNS, if\ Signal\ B\ [n] \leq SignalA\ [n] \end{cases} \quad (5)$$

Following segmentation, STP and Non-STP segments were stacked for each experimental group, facilitating the computation of relevant features to understand dynamic alterations in signal dynamics.

The computed data was fed into multiple machine learning algorithms for automatic classification of groups.

4 Result and analysis

We analyzed the groups both within and outside of the STP segments in order to assess the behavior of each group in both the short-term and long-term contexts. We used the Mann-Whitney (MW) U Test to compare outcomes between the STP and the Non-STP segments, as the test of normality (Shapiro Wilk) and homogeneity of variance (Levene's) showed that the samples were not normally distributed and non-homogeneous. Table 1 shows the comparisons of the Anxiety, Depression and Neutral Groups, within and outside the STP segments.

Table 1: Mean and STD of Features of Anxiety, Depression and Neutral Groups, Across STP & Non-STP

	Anxiety				**Depression**				**Neutral**			
Feature	STP	Non-STP	MW	D	STP	Non-STP	MW	D	STP	Non-STP	MW	D
EDA (μS)	1.9771 ± 2.3588	2.0149 ± 2.4153	0.461	-0.0158	0.299 ± 0.2139	0.3012 ± 0.226	0.919	-0.0100	0.3985 ± 0.2959	0.3719 ± 0.2652	0.030	0.0948
Tonic (μS)	1.9205 ± 2.2756	1.9177 ± 2.2617	0.738	0.0012	0.2987 ± 0.2137	0.3007 ± 0.2257	0.906	-0.0092	0.3982 ± 0.2958	0.3717 ± 0.265	0.031	0.0943
Phasic (μS)	0.0706 ± 0.4006	0.1072 ± 0.3718	0.000	-0.0947	0.0003 ± 0.0008	0.0005 ± 0.001	0.000	-0.1779	0.0003 ± 0.0009	0.0002 ± 0.0006	0.000	0.2054
SMNA (μS)	0.0565 ± 0.3238	0.0845 ± 0.2946	0.000	-0.0904	0.0002 ± 0.0006	0.0003 ± 0.0007	0.000	-0.1618	0.0002 ± 0.0007	0.0001 ± 0.0004	0.000	0.1838
Amplitude (μS)	0.1091 ± 0.2572	0.1531 ± 0.2949	0.000	-0.1590	0.0014 ± 0.0033	0.0019 ± 0.0036	0.000	-0.1360	0.0013 ± 0.0032	0.0008 ± 0.0022	0.000	0.1907
Rise Time (sec)	2.0702 ± 1.2188	2.106 ± 0.8746	0.006	-0.0337	1.989 ± 2.6522	1.8434 ± 2.2776	0.495	0.0589	1.7978 ± 2.335	2.0874 ± 2.7539	0.530	-0.1134
Recovery Time(sec)	1.9488 ± 0.9268	2.0063 ± 0.8126	0.903	-0.0659	1.1711 ± 1.1418	1.3168 ± 1.1789	0.047	-0.1256	1.1894 ± 1.15	1.2083 ± 1.2262	0.535	-0.0159
EDA Standard Deviation	0.1062 ± 0.1895	0.1537 ± 0.2719	0.000	-0.2028	0.0025 ± 0.0026	0.003 ± 0.0028	0.000	-0.2053	0.0034 ± 0.0028	0.0024 ± 0.0021	0.000	0.4264
Inter Beat Interval (IBI)	755.663 ± 98.07	746.3925 ± 96.8143	0.002	0.0951	778.4079 ± 109.3663	777.296 ± 103.8437	0.921	0.0104	767.4781 ± 101.526	797.4864 ± 105.5743	0.000	-0.2897
Respiratory Rate	22.6988 ± 9.6576	23.1151 ± 9.2603	0.002	-0.0440	20.0159 ± 7.3873	19.9642 ± 7.8005	0.590	0.0068	20.0086 ± 7.9233	19.4786 ± 8.2507	0.006	0.0655
Heart Rate (BPM)	82.1588 ± 11.6586	83.3742 ± 11.3939	0.000	-0.1054	79.5818 ± 11.8384	79.613 ± 11.5832	0.956	-0.0027	80.5568 ± 11.4566	77.6309 ± 11.8057	0.000	0.2515
RMSSD (ms)	71.2365 ± 75.5941	80.4533 ± 80.6766	0.001	-0.1179	61.3859 ± 68.2239	62.4129 ± 68.3464	0.423	-0.0150	65.5579 ± 64.5338	64.724 ± 65.7565	0.748	0.0128
SDNN (ms)	69.1643 ± 53.9154	78.5172 ± 55.1334	0.000	-0.1715	55.4674 ± 50.8107	57.2077 ± 49.7087	0.114	-0.0346	57.4131 ± 45.5111	57.0729 ± 46.5492	0.667	0.0074
PNN50 (%)	21.9235 ± 25.4496	24.0047 ± 26.416	0.006	-0.0802	16.0028 ± 21.9037	17.2554 ± 22.4916	0.079	-0.0564	20.3974 ± 23.7261	19.9145 ± 22.7231	0.553	0.0208
SD1 (ms)	50.3718 ± 53.4531	56.889 ± 57.0469	0.001	-0.1179	43.4063 ± 48.2416	44.1328 ± 48.3282	0.423	-0.0150	46.3565 ± 45.6322	45.7668 ± 46.4967	0.748	0.0128
SD2 (ms)	81.6056 ± 57.6831	92.4788 ± 58.0223	0.000	-0.1879	63.6756 ± 55.2371	65.8541 ± 53.549	0.112	-0.0400	64.8148 ± 47.9906	64.7962 ± 48.9229	0.763	0.0004
SD1:SD2	0.5607 ± 0.267	0.551 ± 0.2856	0.014	0.0353	0.6233 ± 0.2941	0.6192 ± 0.3132	0.308	0.0136	0.6626 ± 0.3099	0.657 ± 0.2746	0.366	0.0192
Total Power (ms2/Hz)	4615.926 ± 7358.2994	5541.6029 ± 8009.8187	0.000	-0.1204	3489.546 ± 7427.7845	3430.262 ± 6807.4137	0.098	0.0083	3032.5636 ± 5642.094	3115.3342 ± 5595.0296	0.731	-0.0147
LF:HF Ratio	1.6537 ± 2.0071	1.8218 ± 2.1798	0.014	-0.0802	1.3801 ± 1.8334	1.3702 ± 1.9655	0.231	0.0052	1.1731 ± 1.6079	0.8966 ± 1.2102	0.001	0.1943
LF Power (ms2/Hz)	1644.0162 ± 2612.1797	1957.3511 ± 2862.3916	0.000	-0.1143	1057.3476 ± 2477.8076	1014.2917 ± 1950.2964	0.697	0.0193	921.6986 ± 1885.186	864.9874 ± 1493.7703	0.287	0.0333
HF Power (ms2/Hz)	2448.1699 ± 4987.0476	2855.8083 ± 5341.1185	0.002	-0.0789	2008.419 ± 4593.9679	1997.1085 ± 4585.7597	0.083	0.0025	1785.0105 ± 3648.4816	1923.4523 ± 3948.0092	0.110	-0.0364
VLF Power (ms2/Hz)	523.7253 ± 865.7345	728.436 ± 1033.5188	0.000	-0.2147	423.7774 ± 1191.7155	418.8655 ± 1085.8454	0.212	0.0043	325.8615 ± 777.0188	326.874 ± 758.1008	0.685	-0.0013

In periods of low points or within the STP segment, the Anxiety group exhibited certain characteristic indications of sympatovagal balance,[112] with numerous EDA and HRV features displaying pertinent patterns.

Electrodermal activity (EDA), indicative of sympathetic arousal, displayed no significant change between STP and Non-STP conditions (EDA μS: Cohen's D = -0.016; Tonic μS: Cohen's D = 0.002), suggesting a stable sympathetic tone during the measurement periods.

However, variables associated with transient sympathetic responses, such as Phasic EDA (Cohen's D = -0.095), Skin Conductance Response to Non-specific Activation (SMNA) (Cohen's D = -0.090), and Amplitude (Cohen's D = -0.159), demonstrated a significant decrease during STP. This decrease reflects a reduction in the responsiveness of the sympathetic nervous system or an adaptation to the task over time.

Cardiovascular indices, including the Inter Beat Interval (IBI) showed a slight but significant increase (Cohen's D = 0.093), suggesting a small rise in parasympathetic activity. Conversely, Heart Rate exhibited a small decrease (Cohen's D = -0.104), alongside other heart rate variability (HRV) metrics such as RMSSD (Cohen's D = -0.119) and SDNN (Cohen's D = -0.172), which typically indicate decreased autonomic regulation and increased stress. The PNN50 (Cohen's D = -0.080), SD1 (Cohen's D = -0.119), and SD2 (Cohen's D = -0.188) further support this trend of reduced parasympathetic and increased sympathetic activity.

The Total Power (TP) of HRV significantly decreased (Cohen's D = -0.121), as did the Low-Frequency (LF) Power (Cohen's D = -0.114) and High-Frequency (HF) Power (Cohen's D = -0.079), with the Very Low-Frequency (VLF) Power showing the largest decrease (Cohen's D = -0.215). These reductions in HRV power spectral components suggest diminished autonomic nervous system resilience. Notably, the LF:HF Ratio, a marker of sympathovagal balance, also decreased (Cohen's D = -0.082), indicating a shift towards parasympathetic dominance or a decrease in sympathetic tone. The findings align with existing literature that posits anxiety disorders are associated with diminished HRV, reflecting a less adaptive autonomic nervous system. [113] [114]

The analysis of the Depression group reveal that within the STP segment, the majority of the features showed a declining trend, which included a reduction in all the EDA-related features except for Rise Time. This general decrease suggests that the relaxation task induced a reduction in autonomic arousal. However, the fact that not all features declined, notably Rise Time, which showed an increasing trend, might indicate the presence of residual stress and ruminations that are characteristic of depression. The HRV analysis within STP revealed reductions in LF Power and other metrics associated with both sympathetic and parasympathetic activity (RMSSD, SDNN, PPN50, SD1, and SD2). These findings typically suggest a calm and relaxed state, yet the complexity of changes across both autonomic branches could also reflect the struggle individuals with depression might face in achieving a fully relaxed state.

Comparison of the features between STP and Non-STP segments revealed significant differences in specific EDA-related features, such as Phasic (Cohen's D = -0.196), SMNA (Cohen's D = -0.142), and Amplitude (Cohen's D = -0.122). These differences, along with the significant change in Recovery Time (Cohen's D = 0. -0.113) and EDA STD (Cohen's D = -0.180), suggest that these individuals experience significant physiological shifts when attempting to relax.

The HRV indices, such as RMSSD and SDNN, also did not show significant changes (RMSSD: Cohen's D = 0.010; SDNN: Cohen's D = -0.012), indicating a preservation of cardiac autonomic modulation across the STP and Non-STP segments. The lack of significant change in PNN50 (Cohen's D = -0.034) and the ratio between short-term and long-term variability (SD1:SD2, Cohen's D = 0.040) further reflects this stability. The reduced variability in these measures might reflect a diminished autonomic response to relaxation, which aligns with the impaired mood homeostasis commonly observed in depression. [115] The Total Power (TP) and High-Frequency (HF) Power also decreased, albeit slightly (TP: Mean difference = 183.226, Cohen's D = -0.027; HF: Mean difference = 131.764, Cohen's D = -0.029), further illustrating the challenges individuals with depression may face in achieving the parasympathetic activation that characterizes a relaxed state.

For the Neutral group, the EDA parameters showed a statistically significant yet modest increase in the STP compared to the Non-STP segment, with small effect sizes (EDA: Cohen's D = 0.096; Tonic: Cohen's D = 0.095). These findings suggest a slight elevation in sympathetic arousal during task engagement within the Neutral group. Interestingly, the phasic component of EDA, along with SMNA and Amplitude, revealed more pronounced decreases during the STP (Phasic: Cohen's D = 0.206; SMNA: Cohen's D = 0.187; Amplitude: Cohen's D = 0.200), indicating a reduced transient sympathetic response, which may reflect a habituation effect or an adaptive attenuation in response to the task.

The cardiovascular measures provided additional insights. Although the Inter Beat Interval (IBI) showed a significant decrease (Cohen's D = -0.286), suggesting an increased heart rate during the STP, the Heart Rate itself showed a significant but small increase (Cohen's D = 0.249). The respiratory rate also increased slightly (Cohen's D = 0.082), which could be interpreted as a subtle autonomic response to the demands of the task.

The EDA Standard Deviation, a measure of variability in skin conductance, demonstrated a significant decrease (Cohen's D = 0.433), implying less variability in autonomic response during the STP. This is in line with the concept that a neutral affective state may be associated with a more stable pattern of autonomic activity.[116]

The heart rate variability (HRV) indices such as RMSSD, SDNN, and the PNN50 did not show significant changes, which suggests a stable cardiac autonomic modulation across the STP and Non-STP. The ratio of low-frequency to high-frequency power (LF:HF Ratio) saw a small increase (Cohen's D = 0.194), hinting at a subtle shift towards sympathetic dominance during the STP.

Taken together, these results illustrate that the Neutral group's ANS maintained a stable yet responsive state during the task condition. The slight increases in sympathetic measures during the STP, coupled with the stability of the HRV indices, underscore the dynamic yet balanced nature of the autonomic response to cognitive demands in the absence of emotional or stress-induced arousal. These transient changes eventually contribute to an overall smoother trend, emphasizing the intricate dynamics influenced by both meditation type and subjects' meditation experience levels. This balanced autonomic activity observed in this group could potentially serve as a baseline for comparative studies of ANS reactivity in clinical populations.

5 Machine learning implementation

Following the manual analysis of the data, we used machine learning to automate the classification of mental states into anxiety, depression, and neutral categories. Feature engineering was employed to enhance the predictive models, which were trained on a split of 70% of the data, with the remaining 30% reserved for testing. This test set was isolated from the training process to ensure the integrity of model evaluation.

We employed five distinct machine learning classifiers - XG-Boost, Random Forest, Light Gradient Boosting Machine (Light-GBM), Gradient Boosting, and a Voting Classifier integrating Random Forest, XG-Boost, and Light-GBM. These classifiers were optimized through a Randomized Cross Validation Search algorithm, leveraging a randomized fivefold validation technique for model training. This approach allowed for an extensive search of the hyperparameter space to ascertain the most effective configuration for each model.

Among the classifiers, Random Forest emerged as the most effective, confirming its ability to handle data variance and reduce overfitting through its ensemble of decision trees.

To assess the generalizability of the models, predictions were generated on the held-out test set. The evaluation of model performance was based on several metrics, including accuracy, precision, recall, F1 score, specificity, Receiver Operating Characteristic - Area Under the Curve (ROC-AUC), and the Matthews Correlation Coefficient (MCC). See Supplementary for definitions. These metrics collectively provided a multi-faceted view of the models' predictive capabilities, ensuring that the results were not only statistically significant but also clinically relevant and generalizable to real-world scenarios.

Table 2: Performance Metrics of ML Models

Model	F1 (Macro)	Precision (Macro)	Recall (Macro)	Specificity (Macro)	MCC	ROC-AUC (Average)	Accuracy
Random Forest	0.994	0.995	0.993	0.997	0.991	1	0.994
Voting Classifier	0.994	0.994	0.993	0.996	0.99	1	0.994
Gradient Boosting	0.993	0.993	0.992	0.996	0.988	1	0.993
LightGBM	0.992	0.993	0.993	0.995	0.988	1	0.992
XGBoost	0.992	0.992	0.992	0.996	0.987	1	0.992

Table 2 presents the performance metrics of different machine learning models for classifying anxiety, depression, and neutral groups automatically. The Random Forest model achieved the highest F1 score of 0.994, indicating strong performance in terms of precision and recall. Similarly, other models such as Gradient Boosting, LightGBM, XGBoost, and the Voting Classifier also demonstrated high F1 scores above 0.990, highlighting their efficacy in classification tasks. Moreover, all models exhibited excellent precision, recall, specificity, Matthews correlation coefficient (MCC), and area under the receiver operating characteristic curve (ROC-AUC), with scores close to 1.000. This indicates robust performance across various evaluation metrics, suggesting the reliability and consistency of the classification results.

6 Conclusion

Our proposed methodology provides an unbiased and quantitative mechanism to efficiently predict mental states without human bias. To the best of our knowledge, we are the first to show the transition of mental states from one to another.

Our approach brings forth several notable benefits. Firstly, our method enables a comprehensive understanding of shifts in mental states across different time frames. Additionally, our method ensures objectivity through data-driven computations and comparisons, reducing potential subjective biases in identifying mental states.

The ability to classify Anxiety, Depression, and Neutral groups automatically using machine learning models hold significant implications for mental health assessment and intervention. By accurately identifying individuals with anxiety or depression symptoms, our models enable timely interventions and support, potentially reducing the burden on healthcare systems and improving patient outcomes. Additionally, automated classification allows for scalable and efficient screening processes, facilitating early detection and intervention for individuals at risk of developing mental health disorders. The high performance of the models underscores their potential to revolutionize mental health care delivery by providing accurate, objective, and scalable tools for assessment and intervention.

Finally, our approach provides greater temporal resolution, enabling the discernment of even subtle shifts in consciousness over short time intervals.

Our approach may make it possible to provide recovery-focused screening solutions leading to faster diagnosis, followed by timely guidance, tailored cognitive behavioral therapy and tracking of both stressors as well as calmness-inducing factors in the day-to-day lives of people. We hope our work will help foster further exploration in the area and very soon pave the way for diagnostics in the mental health space.

7 Limitations of our work

Though promising in its inceptual form, there are several limitations of our work. Variables like environmental conditions, body position, and other physiological functions may reduce the reliability of EDA and HRV as indices of the ANS.[117] Further experimentation and thorough investigation is required to establish the validity of our work for real-world use. Our experiment was conducted in India with subjects trained in a particular form of meditation. Application of our methodology in other groups and geographies will confirm if our findings apply to the general population. While we acknowledge the shortcomings of our solution, we believe we have laid the foundation to similar studies in the area.

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9 Conflict of interest

This project was funded by TerraBlue XT. TerraBlue XT is responsible for the project design, and collection and analysis of the data. The authors are TerraBlue XT employees, and they were responsible for data interpretation, revising the manuscript for intellectual content, and approving of the manuscript for submission.

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