Lyfas, A Smartphone-Based Subclinical Depression Tracker

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ABSTRACT

Background: Subclinical traces of depression are difficult to diagnose; although, it influences other mental faculties. Lyfas is a smartphone-based ubiquitous and non-invasive biomedical application that captures Heart Rate Variability (HRV) and its associated Cardiovascular biomarkers (CVb), which might help detect such traces as mind and body are intertwined through autonomic modulation.

Aim: Using Lyfas, an attempt has been made to (i) screen Subclinical depression states in adults by assessing the CVb scores, and (ii) analyze the psychophysiological effects of Subclinical depression on other mental faculties for establishing a correlation.

Methods: The paper presents a retrospective observational study of 86 adults, comprised of 52 males and 36 females who took the Lyfas test. Lyfas findings are validated by an established questionnaire-based instrument under the supervision of a senior psychiatrist.

Results: The study found that 77% of the subjects (84% females and 72% males) showed traces of Subclinical depression, further validated by a senior psychiatrist through a series of consultations. 'Insomnia' (males 36% and females 71%) and 'Negative thoughts' (males 36% and females 46%) were the two correlated high-rank effects of the Subclinical depression in the sample.

Conclusion: The paper proposes that Lyfas can detect the traces of Subclinical depression in adults by capturing and interpreting CVb scores that surrogate for the Cardiac Autonomic Modulation (CAM) and provide the snapshot of the mind-body state of homeostasis.

Introduction

Smartphone-based mobile healthcare (popularly termed as *mHealth*) is gaining importance to connect the medical doctors with the patients, keeping patients' privacy and confidentiality intact. The ubiquitous, non-invasive, and personalized features of mHealth could be a useful connector between the patient pool and the psychiatrists to facilitate and support high-quality mental healthcare globally through proper screening and monitoring of patients.

Mental health has been grossly underrated and overlooked across the world [1]. Depression is one of the most common debilitating mental illnesses as per the World Health Organization (WHO) and its data shows that about 264 million people suffer from depression worldwide [2]. The consequences of depression range from the loss of meaning to the deliberate ending of one's life [3]. In the developing nations, e.g. in India, about 45.7 million people are affected with depression of various grades and pose to be a major contributor of Disability Adjusted Life Years (DALY) [4] and the post-pubertal age group is currently the most vulnerable population in the Indian context [5]. This is the data of overt depression cases and is the

tip of the iceberg, where the number of subclinical depression cases is unknown to us.

Depression presents in various ways, which differ from one patient to another patient. In many cases, there is no obvious symptom and hence called 'subclinical' depression [6] that is because the symptoms, some of which might be quite similar to major depression, reside inside the anterior cingulate cortex, hippocampus, and anterior cingula of the brain, which is quite similar to the involvement of the amygdala in cases of major anxiety disorders, but remain subclinical [7]. There is also no objective tool to measure the degree of subclinical depression in the population. Screening and grading are majorly done in mental health set up subjectively, often questionnaire-based and through a series of interviews by the psychiatrists. The interpretation of the symptoms largely depends on the patients' history, stated by the patients or their relatives, which may be flawed [8]. Current data shows that depression often overlaps with other mental illnesses, such as schizophrenia, anxiety disorders, obsessive-compulsive disorders, personality disorders, and so forth [9]. Hence, detecting depression as singleton morbidity at its subclinical state is not an easy task.

Digital smart home health methods are aimed at patients' privacy, assisting in the screening and monitoring of the patients by the psychiatrists seamlessly at any time from anywhere due to wide network coverage by the mobile data service providers [10]. The advantage is that it enables a higher number of patients to reach out to the psychiatrists through early screening and psychiatrists can retain them through continuous monitoring. Smartphones play a significant role to cater to digital home-healthcare due to the higher number of smartphone users globally. The in-built camera with an optical sensor and the LED light that the phone possesses is key to capturing the peripheral capillary blood flow, rate, and volume. By further evaluating with the principles of signal processing and noise filtering, it captures the Heart Rate Variability (HRV) and its various other biomarker correlates in assessing the mind-body physiology of the body.

HRV surrogates for Cardiac Autonomic Modulation (CAM), which is influenced by the state of mind. Depression is a mental state in which a person feels dejected and lonely. The individual avoids social contact and the usual physical activity becomes restricted. A lot of energy is wasted in overthinking and therefore the body goes into a state of catabolism midst apparent laziness [11]. The autonomic system, especially the sympathetic system slows down significantly, compared to individuals without depression [12]. It is reflected in HRV and its correlates together called Cardiovascular biomarkers (CVb) [13]. The authors propose that such CVb-based parameters help identify depression as early as its subclinical state.

Given this scenario, Acculi Labs Pvt. Ltd., which is an Indian organization, has developed *Lyfas*, which is a non-invasive smartphone-based home health application that can capture several digital biomarkers and give the analytics of 'mind-body' coordination [14]. It is important to note that Lyfas is ISO

and CE India certified smart home-health gadget and hence a standardized biomedical instrument. The contribution of *Lyfas* is that by correlating the digital biomarkers of multiple systems such as cardiovascular system, endocrine system, sleep, and various cognitive conditions (i.e., the differential diagnosis), which are interconnected, using its heuristics and AI-enabled analytics, it can give a comprehensive visual snapshot of the mind-body homeostasis. A detail of *Lyfas* application has been mentioned below.

The *objective* of this paper is to study how *Lyfas* can
(i) *Screen* subclinical depression states in adults by capturing and assessing the CVb scores and
(ii) *Evaluate* the psychophysiological effects of depression traces in other mental faculties.
the *purpose* of the study is to provide a novel seamless, noninvasive, and ubiquitous technology for the psychiatrists and the patient population.

The rest of the paper is structured as follows. The next section discusses the Methodology, followed by Results, and the elaborated Discussion of the result. Finally, the paper is concluded with the contributions, limitations, and extended research possibilities in the future.

Methodology
In this section, the authors have discussed the *study design*, *working principle of Lyfas in detail*, *data capturing (i.e., digital phenotyping)*, and *interpretation* for screening subclinical depression. It is worth noting that the study has been conducted under the expert guidance of a senior *psychiatrist*, who assisted the study by screening the subjects with a published *questionnaire-based interview instrument* [15] post Lyfas test to validate the Lyfas results. According to the instrument, the subjects showing adult depression score <0.3 have been marked as 'suspected' depression cases; whereas scores from 0.31-0.6 are graded as subclinical depression, while scores >0.6 are considered to be overt depression. Such scoring has been conducted by the psychiatrist for the necessary corroboration after the screening made by Lyfas.

Study Design
Recruitment of the subjects
The authors invited adult volunteers to take the Lyfas test through its web community. There was a total of 209 respondents, out of which, for the study, 86 were chosen comprising of 54 males (*Age*: min 20 years, max 24 years, and median 22 years; *BMI*: min 18.30, max 28.3, and median 23.3; *Bodyweight*: min 51 Kg, max 79 Kg, and median 65 Kg.) and 32 females (*Age*: min 23 years, max 27 years, and median 25 years; *BMI*: min 25, max 26.6, and median 25.8; *Bodyweight*: min 64 Kg, max 77 Kg, and median 65 Kg.) who took *Lyfas* test at their residences upon installation in their smartphones during December 2020 to March 2021 (i.e., the COVID-19 pandemic period) in four major cities, such as Delhi, Mumbai, Bangalore, and Kolkata in India. None of them

were previously diagnosed with depression or ever presented with any relevant symptoms or were under anti-depressive medications at any time, which they mentioned during the pre-test interview. They also claimed that they were devoid of known mental health issues and had no history of any substance abuse.

Permission and privacy

Informed consent has been taken from each of the participants twice, at first during the pre-test counseling and then as prompted by the smartphone at the start of the test (Figure 1). Names, addresses, and contact numbers of the subjects are kept confidential throughout the study. Moreover, patients' data has been stored in a secured cloud-based repository of the company.

Ethical committee approval

Proper approval had been taken from an external ethical committee (No. ECR/1181/Inst/K.A., 2019, dated 30th January 2020).

Conditions for Lyfas test

- Accurately filling the personal details in the application through the smartphone's keyboard (e.g., medication history, substance abuse, family, and personal histories, etc.) and vitals (BP)
- The relaxed approach of the test taker (at least ten minutes rest should be taken before the start of the test)
- Proper breathing (normal breathing, neither deep nor holding the breath)
- Before the meal is the ideal time or 2 hours post-meal
- Sitting on a sofa or a chair having a backrest for a relaxing posture
- Keeping both hands on the lap to prevent shaking of the hands in holding the mobile
- Avoiding direct exposure to the light source as it may interfere with the optical feature capturing of blood cells and solutes
- Mobile must have over 50% of battery as light flash may consume battery faster
- Mobile storage must be over 200 Mb to accommodate the report
- Avoiding unnecessary thoughts or becoming anxious as it might interfere with HRV and R-R intervals
- Avoiding unnecessary clicking on the screen, which may interfere with test
- Sharing the report to the Lyfas team who are trained to interpret the report, and
- Waiting for certified clinicians for analysis and deciding on management and not to pursue self-diagnosis.

About the Lyfas Application

Lyfas is a smartphone-based non-invasive digital biomarker capturing tool having ISO and CE certifications. It is commercially available and has been used on over a total of 52375 test-takers to assess the psychophysiological snapshots of their state of health. The key objective is to assist the doctors by providing them with the overall information of the test-taker. The tool has been developed using the principle of digital signal processing [14]. It can capture different digital biomarkers in the human body. In this study, however, the authors have evaluated the following biomarkers, surrogates for the mental state of the patients: [16]

(i) Heart Rate Variability (HRV) [17],
(ii) Low frequency (LF) / High Frequency (HF) of R-R intervals [18],
(iii) Left and Right Cardiovascular Coherence (LRCV) [19],
(iv) pNN50 which is a pair of R-R intervals that differs more than 50 milliseconds [20],
(v) Sympathetic Nervous System percentage (SNSPC) [21],
(vi) Parasympathetic Nervous System percentage (PNSPC) [22],
(vii) STRESS [23],
(viii) SDNN, which is the standard deviations of the R-R intervals [24], and
(ix) SD1/SD2 is a ratio of short and long HRV [25].

These digital biomarkers are indicative of the CAM-led physiological, pathological, and psychological homeostasis [14].

Lyfas works on two principles, Photoplethysmography (PPG) and Photochromatography (PCG). PPG measures blood volume changes in the microvasculature, while PCG measures the reflected light of various blood components and solutes [14]. This is carried out using an optical sensor on the camera and the flashlight of a smartphone acting as an information capturing layer [14]. The next layer is a signal processing layer, which consists of the proprietary mathematical modeling and an algorithm, which converts the input signal into actionable metrics, which in turn captures the functional biomarker parameters [14]. These parameters were then validated in clinical settings to reflect several electromechanical and physiological activities, such as cardiovascular mechanics, hemodynamics, hemorheology, indicative hematology, and biochemistry in the test taker [14]. Figure 2 shows how Lyfas works. Figure 3 shows the sample report of one anonymous test taker.

In figure 2, the working principle of Lyfas has been elaborated step-by-step.

Step-1: Placing the index finger on the rear mobile camera of the smartphone (Android version 7 and above), pre-loaded with Lyfas application by sitting in a relaxed position

Step-2: The camera captures the capillary blood volume using the principle of Photoplethysmography (PPG), Arterialplethysmography (APPG), Photochromatography (PCG), Heart Rate Variability (HRV), Mobile Spirometry (SPM), and Maneuvers like Orthostatic homeostasis

Step-3: Grouping of biomarkers into various organ systems

Step-4: AI-enabled analytics of these biomarkers to assess several psychophysiological states of the body, and finally

Step-5: Correlating analytics with clinical conditions.

Lyfas can run the test, interpret, and then generate the report in total 3-5 minutes on physiological biomarkers and depression is one of these. In this study, tracing subclinical depression and how it may affect other mental faculties would be an interesting addition that Lyfas provides. Those are types of Thoughts (positive/ negative), Addiction disorders, Cognitive dissonance, Memory issues, Energy (positive/negative), Anger, Sleep, Anxiety, Emotion, and Mood swings, together called Mind analytics, developed using

Figure 1: Informed consent was taken before (on the right side of the figure) and during the Lyfas test (on the left side of the figure).
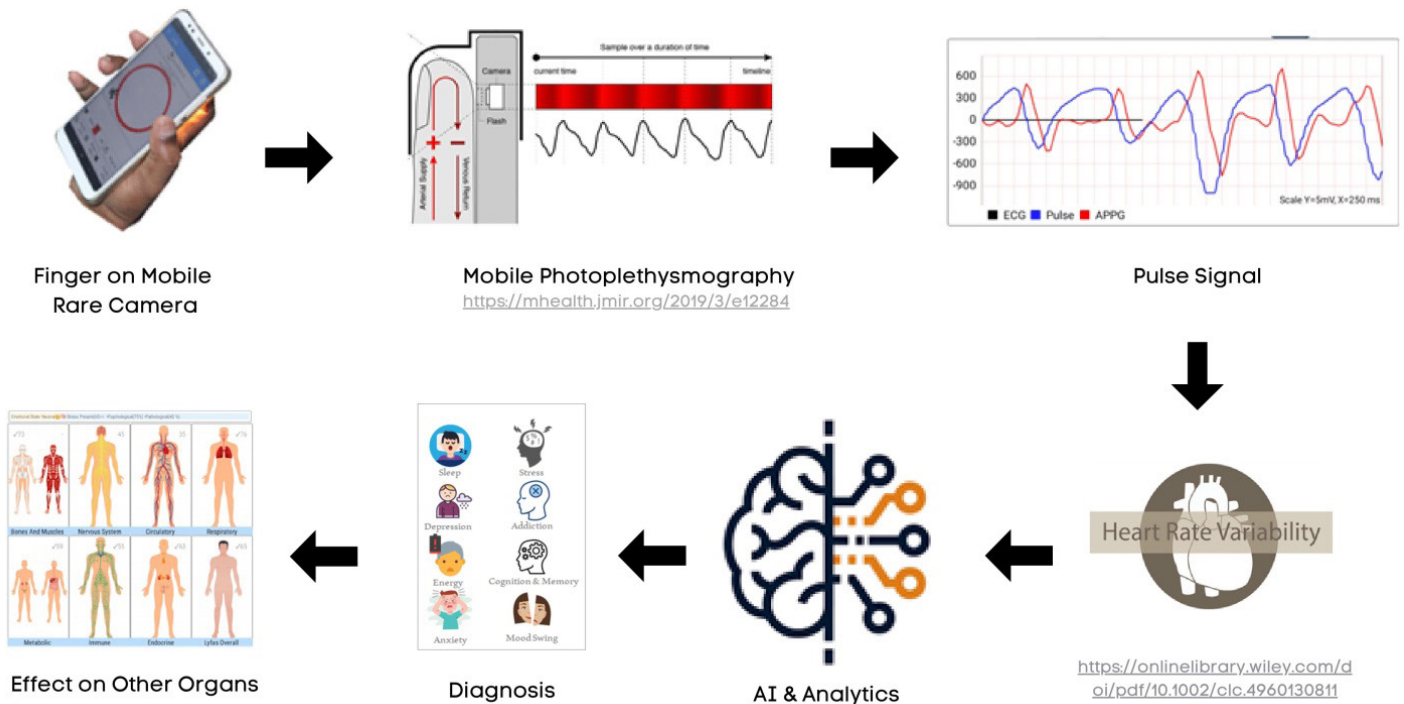

Figure 2: Working principle of *Lyfas*.

its AI algorithms and is purely underlying psychophysiological evidence-based.

Lyfas claims to predict these conditions by using the science behind the above-mentioned digital biomarkers and it appears in a report format throwing lights about the mental and physical health as a bouquet [26], such as gut health e.g., Irritable Bowel Syndrome [27], sleep [28], palpitation [29], and several metabolic disorders due to chronic stress [30]. Later doing teleconsultation and taking personal and family histories of patients, the psychiatrist was able to confirm the state of depression, whether it was subclinical or not as per the questionnaire-based interview instrument [15]. This study was planned to evaluate the capability of *Lyfas* to detect subclinical depression and its psychological and physiological effects by studying the digital biomarkers. The process is termed *digital phenotyping*.

Statistical approach
Basic *descriptive statistics* such as the calculation of the percentage of occurrence, mean, median, standard deviation, maximum and minimum values for each gender their age, and BMI have been calculated in MS Excel.

Results
This section shows how *Lyfas* has mined suspected subclinical depression for one sample subject. Similarly, other subjects have also been studied and could not be presented due to space constraints. Figure 4 (a-f) shows various biomarker-based analytics of how subclinical depression states have been screened. Table 1 in the Discussion section shows the average CVb scores and their interpretation of a sample case based on Lyfas.

In the above figure, among all, section (f) is the most important slider that moves from left (agitation) to right (silence) for the time-series study of mood. The movement of the slider more towards the left side denotes a high possibility that the subject is suffering from depression. Out of 86 patients, in which *Lyfas* has detected subclinical depression, the majority of the patients (n= 67.77%) had confirmed off and on of 'feeling depressed' at a certain time of the day during subsequent consultations with the psychiatrist, which they did not divulge initially during the interview. Out of 54 males, 40 (72%) had confirmed subclinical depression state at some time and out of 32 females, 27 females (84%) were suffering from a confirmed state of subclinical depression during teleconsultations, which had been revalidated by the psychiatrist with the help of the interview-based questionnaire instrument [15]. Table 1 shows various cascading effects (i.e., psychological biomarkers) of the subclinical depression and the respective ranking has been assigned based on the number of males and females affected versus the total numbers of each.

Table 1: Cascading effects of Subclinical depression as the percentage of occurrence.

No.	Parameter	Male(n=54)	Female(n=32)	Rank
1	*Insomnia*	n=20 (36%)	*n=23 (71%)*	*1*
2	*Hypersomnia*	n=18 (32%)	n=7 (21%)	
3	*Negative thoughts*	**n=20 (36%)**	**n=15 (46%)**	*2*
4	*Memory issue*	n=8 (14%)	n=5 (15%)	
5	*Digestion issue*	n=13 (23%)	n=9 (28%)	
6	*Tiredness/Fatigue*	n=8 (15%)	n=5 (15%)	
7	*Metabolic stress*	n=16 (29%)	n=10 (31%)	

Discussions
In this section, the results are discussed, based on the findings in Figure 4. These interpretations are made by *Lyfas* analytics based on its AI algorithms and heuristics, further corroborated by the supervising psychiatrist with the help of the scores that the questionnaire-based subclinical measuring instrument provided. Due to proprietary rights, formulae and calculations of the AI and heuristics cannot be revealed in this paper. Table 2 explains the analytics shown in Figure 4 and the interpretations of the mental state of one subject (male, 36 yrs., 72 Kg. body weight, and BMI 25.8) as a sample report. Similarly, for others, reports were generated and interpreted jointly.

Table 2: Interpretation of the biomarker-based mental state of the sample case shown in Figure 4.

Physiological condition	Biomarker with average score (14)	Interpretation (14)
Emotion (Figure. 4(a))	HRV score (>80)	Positive thoughts
Addiction (Figure 4(b))	SDNN (>40)	No addiction
Cognitive Dissonance (Figure 4(c))	CardioScoreHRV (LSB or Left Side of the Brain – CardioScoreOrtho LSB or Left Side of the Brain) <10	No Cognitive Dissonance, i.e., he is emotionally stable
Memory (Figure 4(d))	CardioScoreHRV >65	Mild memory issues
Energy (Figure 4(e))	Energy >35-75	High positive energy

Insomnia and *Negative thoughts* are found to be associated with depression for 93.4% of the sample (refer to Table 1). This could be due to the devastating second peak of the COVID-19 pandemic in India, which raised the number of hospitalizations and mortalities, loss of jobs, and many biopsychosocial uncertainties. The associations of *Insomnia* and *Negative thoughts* are also supported by other studies on depression [31,32]. Hence, the authors propose that the *Lyfas* results are purely evidence-based and credible. It is also important to note from the sample that, females possessing higher body weight (median 70.5 Kg compared to 65 Kg in males) and the BMI (median 25.8 compared to 23.3) are more prone to get *mood disorders*, which is a major construct for depression and corroborated by the study conducted by [33]. Mood disorders lead to more negative thoughts which results in poor HRV scores [34,35]. Moreover, these are reflected through sleep patterns and hence *Insomnia* and *hypersomnia* pose to be two major attributes to the mood disorder, substantiated by the work of [36] and *Negative thoughts*, as evident in the work of [37] are also found within this group. It can be stated that the COVID-19 pandemic during the time of the study could have played a significant role in the mental states of the test-takers. The findings in Table 2 are quite encouraging vibe of the healthy nature of the mental state of the subject is could be the compensatory mechanism of the brain while coping with the pandemic, although the negative
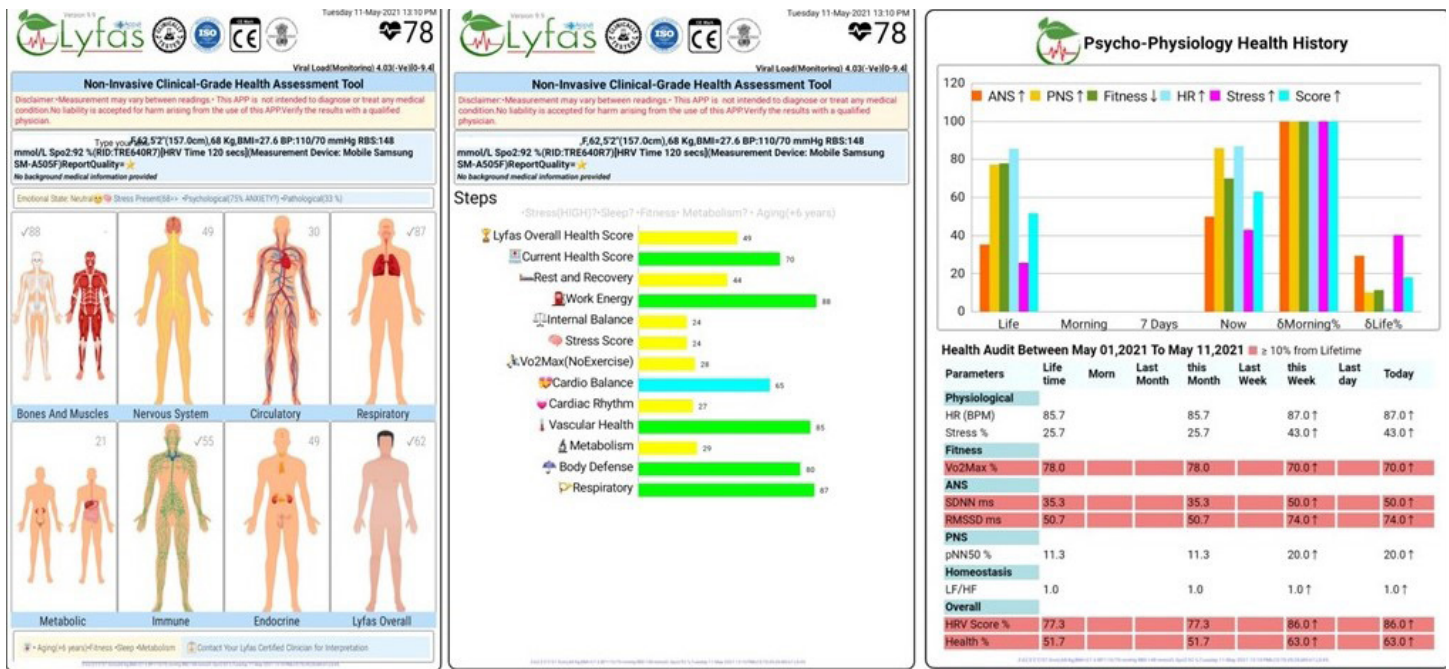
Figure 3: A sample report of *Lyfas*.
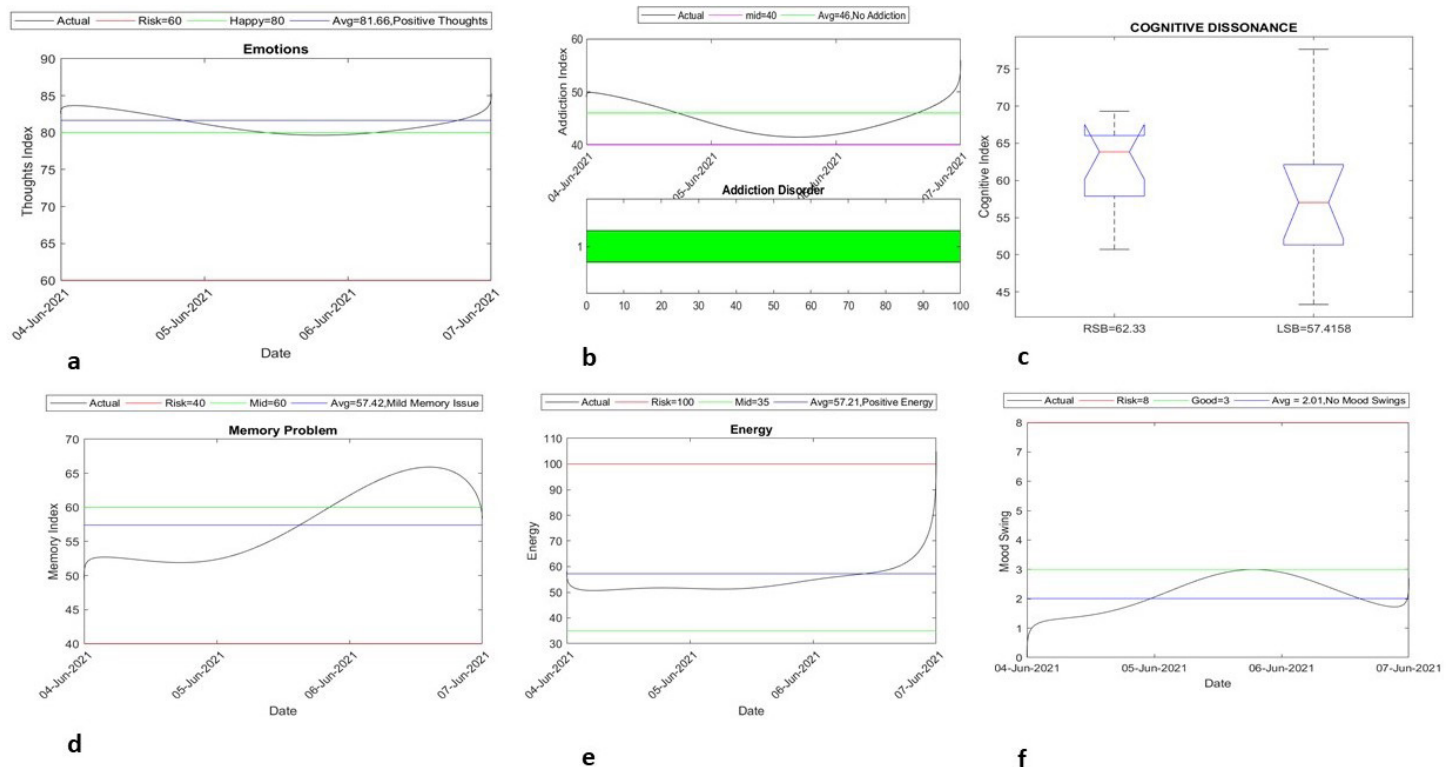
Figure 4: Sample mental mapping through analytics using the *Lyfas* application.

thoughts and for that, lack of sleep was evident in most of the subjects as an overall effect of the pandemic on the psyche of the subjects.

It is important to mention that there are mobile-based digital biomarker detecting tools and several other predicting models to diagnose various mental and physical conditions of the human body, though its number is less. However, all these studies and tools are immensely inspiring and considered to be the precursors of *Lyfas* and those have attempted addressing various challenges of healthcare, most important of which is how mental illness influences the physical systems in real-time and causes discordance has not been studied in any of the following studies.

A rise in the prevalence of depression emphasizes the necessity for accessible and effective interventions, which could be extended by applying smartphones and wearable devices. Below the authors have showcased some useful tools, which is not an exhaustive list though. Studies have been conducted to use wearable devices and smartphones to analyze and predict mental health. Oura ring (wearable device) and Apple iPhone (smartphone) have been used on 60 adults (age: 24 to 68 yrs.) over the two weeks. The smartphone can track the location and usage type (time and frequency), while the Oura ring can capture various digital data of sleep, activity, and Heart Rate Variability (HRV). The study concludes that HRV is an important predictor for assessing mental health status including depression, anxiety, and other mood disorders [38]. In the study conducted by [39], HRV poses to be a potential indicator for assessing mental health. To study the effectiveness of smartphone-based Photoplethysmogram (PPG) HRV analysis, the authors collected data from 93 university students and university employees of China. The study concludes that smartphone-enabled PPG-based indicator is an important factor to assess the mental health of the subjects. Mindfulness Meditation Application (MMA) is a smartphone-based tool in adding value to the practice of mindful breathing [40]. This randomized control trial study assesses the parasympathetic nervous system using HRV, pain, and mood symptoms, such as depression. The study concludes that HRV is a significant biomarker for assessing depression and anxiety. In another study, a mobile-based application, known as 'Psychologist in a Pocket or PiaP' has been developed using the lexical analysis algorithm to predict one's mental health including negative thoughts, schemas, depression, and so on [41]. Based on the keyword-based mapping of language used by the participants, the state of mental health has been assessed (based on DSM-V and ICD-10) by the tool with appreciable accuracy. A mobile cloud-based depression diagnostic tool applying ontology and Bayes' net has been developed [42]. The tool used the cloud technology to create the environment for diagnosis and the Bayesian net has been used for prediction. Ontology has been developed to run the tool in the Android platform. The tool is found to be effective in diagnosing whether a person is depressed or not. In another study, a wearable depression monitoring system has been proposed with an 'application-Specific-system-on-Chip solution (SoC)', which can extract and filter the digital biomarkers, such as HRV and ECG to predict depression using Beck Depression Inventory with 71% accuracy [43]. A similar study has also been reported and found quite encouraging [44].

Conclusions

Lyfas is a non-invasive smartphone-based application that can perform 'digital phenotyping' of the test takers and analyze the interplay of several physiological conditions in an average time of five minutes. It is also able to study the interplay of the mind-body and identify the dissonance if any. In this paper, the authors have showcased how *Lyfas* can mine traces of subclinical depression in the test-takers, who never had any relevant history. In the present study, Females show more traces of depression than males (84% vs. 72%). The key feature of *Lyfas* lies within its validated AI-enabled heuristic and analytics, which provide a comprehensive picture of the mind-body state of the test-takers [45,46]. AI and ML applications in depression have been popular and accepted techniques already [47,48]. While evaluating the effects of depression in other mental health facets, *Lyfas* can mine that *Insomnia* and *Negative thoughts* are two major outcomes in this sample. The COVID-19 pandemic was the plausible external stressors, which might be responsible for *Insomnia* and *Negative thoughts* [47,48] and unveiled the traces of subclinical depression state in Lyfas test-takers who suspected plausible state of underneath depression, further validated by the questionnaire-based instrument [15], used by the supervising senior psychiatrist in this study. These findings are supported by other studies as well in the previous section. In this way, *Lyfas* could be a very handy and reliable tool for the healthcare providers, such as psychiatrists and mental health nurses to get an idea of the overall psychophysiological state of the patients. However, the authors recommend that *Lyfas can only be used under the expert guidance of the psychiatrists* to evaluate (i.e., screen diagnose, and monitor) any mental health-related issue. Its ubiquitous nature, cloud-based data privacy, faster data processing as well as the analysis, and finally validations of the results by a senior psychiatrist are examples of a purely evidence-based new extension to the 21st century's digital healthcare.

The *limitations* of this study are as follows:

i. **Assessment and selection bias:** It lies in its sensitivity to various pre-conditions that should be satisfied during the test. Although due diligence was conducted to identify the presence of any comorbid mental illness in the subjects under the clinical guidance of the senior psychiatrist, still there could be traces of such conditions, which could have been overlooked or missed out during the study.

ii. **Testing bias:** COVID-19 pandemic period was stressful, as many lost the hope of survival. The study was carried during the peak of the second wave. Hence, many who showed the digital sign of subclinical depression could be transient and presented then. The research team is carefully monitoring them to understand how much is this bias.

Scope for the future study:
The authors look forward to conducting multi-centric studies on a larger population for further validation of Lyfas as a subclinical depression tracking tool for adults involving more psychiatrists.

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