Different Parameters for Computational Depression Analysis: A Review

Shamla Mantri, Mrunalini Kulkarni, Mugdha Joglekar, Sharwin Bobde

Abstract— Depression is a mental disorder that affects not only the thoughts but also the body and behavior of the person suffering from it. Depression detection, as of today, is limited to analysis of the patient by the psychologist, which is prone to subjective bias. Although depression is a mental disorder, it affects various physical attributes like eye movements, voice modulation, urine, saliva, etc. These effects, if observed and analyzed, can be used for designing tests wherein the physiological parameters are observed and depression is detected objectively, thus reducing the burden on psychologists. This paper gives a systematic review of the studies undertaken for analyzing the effects of depression on different physical attributes.

Index Terms— Active Appearance Models, Biomarkers, Gaussian Mixture Model, Major Depressive Disorder, Multivariate Pattern Recognition, NMR Spectroscopy, Neurotransmitters.

I. INTRODUCTION

Depression is a serious mental disorder that leads to partial disability in emotional control. Efforts are being undertaken for detecting depression objectively through the testing of physiological parameters instead of depending solely upon the patients' subjective analysis about themselves. This makes the detection process unbiased.Objective detection of depression is possible only when we know the effects of depression on different physical attributes such as eye movements, saliva, urine, brain functioning, voice modulation, etc. This paper gives a systematic review of the studies undertaken for analyzing the effects of depression on these parameters.

Depression is associated with lack of cognitive inhibition [2]. This is reflected directly through saccadic, anti-saccadic and smooth pursuit eye movements as well as the pause ratio in voice modulation [1], [3], [4], [5]. The testing of saliva samples of depressed and healthy individuals established that the cortisol level in depressed individuals was significantly high and melatonin level was significantly low as compared to the controls [6]. Neurotransmitters can be tested by taking urine as a parameter. It was also observed from urine testing that the levels of certain metabolites in urine were significantly reduced in depressed individuals.

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This paper gives a review of the methods and studies undertaken to analyze the effects of depression on eye movements, urine, saliva, voice modulation and brain functioning.

II. LITERATURE REVIEW

Existing studies have found that clinical depression is associated with changes in physiological parameters. Darby and Hollien found that listeners of people suffering from depression could notice difference in pitch, loudness, speaking rate and other acoustical parameters in recordings before and after the treatment [1]. JuttaJoorman and Ian Gotlib put forth the relation between depression and cognitive inhibition [2]. Independent studies were conducted by SharifaAlghowinem and Yu Li et.al. to observe how clinically depressed individuals react to positive and negative stimuli [3], [4]. It was found that depressed individuals have difficulty in inhibition of negative emotions. Duque A. et.al. further concluded that depressed individuals suffer double attention bias- difficulty in masking negative emotions and difficulty in focusing on positive emotions [5]. Cognitive deficit can also be detected through saliva samples. Rowena Gomez et.al. concluded that higher cortisol levels in saliva are associated with greater cognitive deficit[6]. It was asserted by independent studies by Takashi Yonekura et.al. [7], ZubinBhagwagar et.al. [8] and EsinKasap et.al. [9] that depressed individuals have higher level of cortisol. Studies were undertaken to identify the metabolites whose levels vary significantly in the urine samples of depressed individuals as compared to the healthy individuals. Donald H. Macknew et.al. observed that the level of 3-methoxy-4-hydroxyphenylethylengelycol(MHPG) was higher in depressed individuals as compared to the controls[10]. Paige LA et.al. observed that the levels of several fatty acids, glycerol, gamma-aminobutyric acid (GABA) and ketone 3-hydroxybutanoic acid were different in depressed individuals as compared to healthy individuals [11].

III. METHODS

Depression has an effect on various physiological parameters. These effects are observed using scientific equipment and analyzed using statistical analysis techniques so as to identify the potential markers for Major Depressive Disorder. The physiological parameters assessed include urine, saliva, brain, voice modulation and eye movements. Some of the methods used for analysis are as follows:

A. URINE

A study [13] was conducted by The American Society for Biochemistry and Molecular Biology, Inc for identifying and validating urinary metabolite biomarkers for Major

Depressive Disorder [14],[15]. NMR spectroscopy was conducted where 82 healthy people and 82 people suffering from psychiatric diseases were selected. Multivariate pattern recognition techniques were used to identify potential metabolite biomarkers for Major Depressive Disorder. After an overnight of fasting, urine samples of the subjects were collected and they were thawed and centrifuged for the NMR analysis. Stepwise algorithm for optimization was performed based on Akaike's information criterion. Most prominent differences between normal and Major Depressive Disorder patients were observed in five following metabolites: malonate, formate, N-methylnicotinamide, m-hydroxyphenyl acetate, and alanine. Urinary levels of the following metabolites - m-hydroxyphenylacetate, hippurate, dimethylamine, dimethylglycine, and trimethylamine-N-oxide are significantly decreased in Major Depressive Disorder subjects in comparison with the normal people. They are uniquely produced in the intestinal tract by the bacterial metabolism. This is an indication that Major Depressive Disorder can be associated with changes in the intestinal microflora. IBS-irritable bowel syndrome was observed in these Major Depressive Disorder subjects which is related to the microflora.

A study was conducted by Gottfried Kellermanna to check the impact that the neurotransmitters are having on depression using urine as the parameter [12]. Neurotransmitters change in a predictable manner and they are prominent markers for the various processes in our body. According to this study there is a significant relation between a subject's mental health and his neurotransmitter level. Patients suffering from depression have low urinary serotonin and dopamine but increased levels of norepinephrine. A survey of patients after severe traumatic incidents was taken and it was observed that they have surged urinary catecholamines. The neurotransmitters in our brain are the ones that make humans happy, so technically getting them checked is an effective way of analyzing depression disorders among people.

B. SALIVA

A study was conducted by Brandon N. Peacock, David J. Scheiderer and Gottfried H. Kellermanna to find a way of differentiating Major Depressive Disorder patients from normal people by analyzing their saliva samples [16]. A statistical and clinical analysis of the salivary hormones (peripheral cortisol and melatonin) was done. Samples of saliva were collected early in the morning before brushing and the next samples were collected after an interval of 5 hours every time. An electro chemiluminescence kit was used to measure the cortisol levels in the samples. Radioimmunoassay Kit was used to analyze melatonin levels. All the samples were stored at −20 °C and they were stabilized for a month. A Mann-Whitney test was used to compare the p values in the saliva samples. A linear regression analysis between BMI of the subject and p values was done. The study of cortisol samples showed that there was a great rise in the values in the morning and the values stabilized as the day progressed. But the values for the depressed group deviated during the fall and there was a vast difference in the output as well. It was also found that there is decreased level of melatonin and increased level of cortisol in the depressed patients. Along with this the subjects were made to converse and it was found that 90-95% of depressed

patients were restless, felt fidgety and angry a lot many times. Around 15% of them were detected with the Irritable Bowel Syndrome [18].

Unstimulated salivary flow is influenced by many different factors. A study was conducted to observe the effect of stress, anxiety and depression on unstimulated salivary flow rate and xerostomia on 122 depressed and non-depressed individuals [17]. The sample collection was done in the morning where the subjects were asked to collect their own spit samples after a gap of 1 minute for 5 times. The subjects were divided into 4 groups as given in table 3.2.

TABLE 3.2
GROUPS OF SUBJECTS

Sr No.	Saliva flow	Dry mouth(Yes/No)	No. of subjects
1	<0.1ml	Yes	30
2	>0.1ml	Yes	28
3	<0.1ml	No	30
4	>0.1ml	No	34

The subjects were made to fill the Depression Anxiety Stress Scale questionnaire to map the levels of stress they were undergoing. Group 1 had low saliva flow and xerostomia, group 2 had normal saliva flow and xerostomia, group 3 had low saliva flow and no xerostomia and group 4 had normal saliva flow and no xerostomia. For the statistical and analytical management of this available data means and chi square methods were used. Borhan et.al. conducted a similar study with smaller number of people[19]. He stated that depression plays a major role in reduction of flow of saliva and rise in the occurrences of getting dry mouth. In another study Scarablot et.al. observed a significant relation between depression, reduced saliva and reduced sleep among people [20]. Another survey was done consisting of 38 students. It was observed that 45% of them suffered from oral dryness and suffered from sleep disorders and depression.

C. BRAIN IMAGING

The functional connectivity of brain was analysed using Magnetic Resonance Imaging for detection of Major Depressive Disorder [21]. The study was helpful in understanding the neural mechanisms underlying behavioral symptoms of depression [23]. 32 patients diagnosed with MDD and 33 healthy subjects were considered for the survey. Functional MRI images were collected using a gradient-echo planar imaging sequence. These images were then smoothened to obtain a linear trend and then they were filtered by using Chebyshev band-pass filter (0.01–0.08 Hz). 116 parts of these registered functional MRI volumes were made in accordance to the labelling atlas [25], which divides cerebellum [22] into 26 regions and cerebrum into 90 regions. The regional mean time series was obtained for every individual by averaging the functional MRI series of 116 regions. The observations obtained with global signal regression technique were made clear by using global signal regression [24]. Hence changes were made in each regional mean time series to improve results by regressing out head motion and the global signals. The set of regional mean time

series which were the residuals were used for survey of the functional connectivity. For each subject, a 116 × 116 resting state functional symmetric matrix was derived. 116 diagonal elements were removed and the upper triangular elements of the functional connectivity matrix were taken out. Thus this study relatively managed to differentiate between depressed patients and normal people [26]. The results show that the linear vector support machine was useful in finding out the relationship between brain images and depression with probability of being wrong was negligible.

D. VOICE MODULATION

A six week long study was conducted to record and analyze the voice samples of depressed patients. The aim was to investigate their voice patterns and find out the severity [27]. 35 subjects consisting of both men and women were taken under consideration. The method of assessing depression longitudinally was used and around 66% of the patients had Hamilton Criteria score greater than 17. Subjects were asked to explain how they were feeling in the past week, how are they physically feeling, their leisure activities etc. Some of the other tasks included counting numbers from 1-20 and saying various vowels. The following parameters were noted during the speech test:(1)Rate of speaking(2)Number of pauses(3)Ratio of pauses(4)Total recording duration(5)Vocalization time. It was observed that the pause ratio had a positive correlation with the seriousness of depression.

In another study [28] patients completed a weekly HAMD (Hamilton Depression Rating Scale) and Quick Inventory of Depressive Symptomatology (QIDS) by IVR [29], [30]. These tests used touch tone inputs for obtaining caller responses to some standard queries according to the clinical format. These scales have been decided after performing many clinical trials [31]. The observations of these clinical trials show that there is a decrease in the severity of depression over a period of time. The vocalization to number of pauses ratio as well as the speaking rates in all the speech samples are very closely related to the HAMD observations.

E. EYE MOVEMENTS

Depression related studies have found that cognitive inhibition is suppressed in clinically depressed individuals as compared to healthy individuals [2], [32], [34]. Eye movements give an insight into cognitive inhibition of brain.

SharifaAlghowinem et.al. [3] conducted a study wherein distance between eyelids was used as a parameter for depression detection. 30 depressed and 30 healthy individuals were selected as a sample. Questions invoking positive and negative emotions were asked and a comparison of spontaneous eye movements were noted for bad news and good news (bad news is related to a negative incident and good news to a positive incident). 45 images per person were manually selected from the interview videos, with different eye distances between eyelids, like half open, half closed and completely closed. These images were further explained using 74 points for both eyes. These points are used to create subject-specific eye AAM (active appearance model).The horizontal, vertical features and eyelid movements for each eye were noted. The horizontal distance of the eye was calculated by taking the length from the inner corner of the eye to the centre of the iris, 'A'. This was standardized based on the line connecting the eye corners, 'B'. The vertical distance was measured by considering the angle between the

lines 'A' and 'B' mentioned previously. The distance between the eyelids was computed using the line connecting the centre of both the eyelids. These features were further classified using the Gaussian mixture models and Support vector machines [3]. It was found that there was deformity in the ocular movement system of the patients. It was also observed that the average eye opening was smaller and the average span of blinks was longer in the depressed patients than the normal patients. It was also observed that depressed individuals find it difficult to mask negative emotions. It is worth noting that another independent study conducted on the double attention bias in depressed individuals also came to the same conclusion [36].

Two independent studies [4], [35] were conducted that used saccadic and anti-saccadic eye movements as a parameter for analyzing depression. The study [35] by Nicholas Carvalho et.al. was conducted to characterize oculomotor performances in elderly depressed patients. The sample set comprised of 47 healthy patients and 20 clinically depressed patients. Both the sets of individuals were asked to perform one pro-saccadic task first and one anti-saccadic task later. In the pro-saccade task the patients were asked to fix their gaze on the red dot on a screen. In the anti-saccade task the patients were in turn asked to fix their gaze on the corner opposite to the red dot. Video-occulography techniques that were based on the corneal reflection of infrared light were used to record their eye movements. In the prosaccade task, reaction time was recorded, whereas in the anti-saccade task reaction time, error rate and correlation factor were recorded. Shapiro-Wilk test and Fisher-Snedecor test were used for statistical analysis. Evaluation of the differences between both the groups was done using Analysis of co-variants (ANCOVA), taking depressed vs control as a group and neuropsychological and psychiatric scores as variates. It was found that the depressed individuals showed higher reaction time in both the pro-saccade and the anti-saccade tasks and higher error rates in the anti-saccade task than the healthy patients.

The study conducted by Yu Li et.al. aimed to find whether eye movement indices of the depressed patients were different from those of healthy patients [4]. A sample of sixty healthy patients and sixty depressed patients was considered for this study. Each volunteer was given three tasks to perform. A desktop based eye tracking device was used for the analysis of eye movements. The experiment consisted of one fixation task, one saccade task and one free view task. The first task was the fixation task. Each participant was asked to fix his gaze on the stationary black '+' on a white screen. While doing so, the participant had to ignore all the '*' symbols that were moving near the '+' symbol. In the saccade task, the stimulated target was either a hollow dot or a solid dot. The participants had to move their gaze along the dot if it was solid and away from it when it was hollow. There were a total of 8 pro-saccade and anti-saccade tasks each. In the free view task, the participants were asked to view a set of black and white pictures freely. It was found that the pro-saccade amplitude and anxiety symptoms were negatively correlated and the anti-saccade latency and anxiety symptoms were positively correlated. The depression symptoms were negatively correlated with fixation times, saccades, and saccadic paths respectively in the free-view task; while the mean fixation duration and depression symptoms showed a positive correlation. This study further

helped to prove that anxiety and depression can be detected using saccadic eye movements.

Apart from the above ,studies have also concluded that depressed individuals exhibit abnormality in smooth pursuit eye movements[33] and depressed patients have very low rapid eye movement(REM) latency (70.9 min on average) as compared to controls(122.5 min average).

IV. CONCLUSION

Physiological parameters can be used to predict mental state with considerable accuracy. Depression is associated with deficit in cognitive inhibition and reduced attention. This is reflected through the higher saccade latency and error rates in eye movements, hyper secretion of cortisol in saliva and pause ratio in voice modulation. Similarly, effects of neurotransmitters which are primarily responsible for happiness of human beings can be studied 6 using urinary samples. The levels of malonate, formate, N-methylnicotinamide, m-hydroxyphenyl acetate, and alanine differ significantly between depressed and non-depressed individuals. Irritable Bowel Syndrome is observed in depressed individuals. Thus depression, which is a mental disorder, has an effect on various physiological parameters. However since the physiological effects of depression, bipolar disorder and Alzheimer's disease are similar, testing only one parameter cannot give accurate results. Clinical depression can be diagnosed accurately if a combination of all these parameters is used as a test, thus paving way for objective detection of depression as opposed to the prevailing subjective detection of depression.

V. FUTURE WORK

Diagnosis of mental disorders like depression is much more difficult than the diagnosis of physical disorders because there are no direct techniques like MRI or X rays to identify the exact ailment. Another major difficulty is that the symptoms of mental disorders like major depressive disorder, bipolar disorder and Alzheimer's disease are similar, which causes errors in diagnosis. Our future aim is to conceive a test which takes into account the effects of depression on various physiological parameters for detecting clinical depression accurately, objectively and without much of human intervention.

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