Original Article

Evaluation of the severity of major depression using a voice index for emotional arousal

Shuji Shinohara [1]*, Hiroyuki Toda [2], Mitsuteru Nakamura [3], Yasuhiro Omiya [4], Masakazu Higuchi [1], Takeshi Takano [4], Taku Saito [2], Masaaki Tanichi [2], Shuken Boku [5], Shunji Mitsuyoshi [1], Mirai So [6], Aihide Yoshino [2], and Shinich Tokuno [1]

[1] Department of Bioengineering, Graduate School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, Japan, 113-8656; S.S.: shinohara@bioeng.t.u-tokyo.ac.jp; M.H.: higuchi@bioeng.t.u-tokyo.ac.jp; S.M.: mitsuyoshi@bioeng.t.u-tokyo.ac.jp; S.T. tokuno@bioeng.t.u-tokyo.ac.jp

[2] Department of Psychiatry, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama, Japan, 359-8513; H.T: toda1973@gmail.com; T.S.: t.saito3025@gmail.com; M.T.: mtanichi@gmail.com; A.Y.: aihide@ndmc.ac.jp

[3] Health Science Center at San Antonio, The University of Texas, San Antonio, TX, USA; M.N: nakamuram@uthscsa.edu

[4] PST Inc., Industry & Trade Center Building 905, 2 Yamashita-cho, Naka-ku, Yokohama, Kanagawa, Japan, 231-0023; Y.O.: omiya@medical-pst.com; T.T: takano@medical-pst.com

[5] Department of Psychiatry, Graduate School of Medicine, Kobe University, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe, Hyogo, Japan, 650-0017; S.B.: shuboku@gmail.com

[6] Department of Psychiatry, Tokyo Dental College, 2-9-18, Misakicho, Chiyoda-ku, Tokyo, Japan, 101-0061; M.S.: somirai@tdc.ac.jp

* Correspondence: shinohara@bioeng.t.u-tokyo.ac.jp; Tel.: +81-3-5841-0439

Abstract: Recently, the relationship between emotional arousal and depression has been studied. Focusing on this relationship, we first developed an arousal level voice index (ALVI) to measure arousal levels using the Interactive Emotional Dyadic Motion Capture database. Then, we calculated ALVI from the voices of depressed patients from two hospitals (Ginza Taimei Clinic [GTC] and National Defense Medical College hospital [NDMC]) and compared them with the severity of depression as measured by the Hamilton Rating Scale for Depression (HAM-D). Depending on the HAM-D score, the datasets were classified into a no depression (HAM-D<8) and a depression group (HAM-D≥8) for each hospital. A comparison of the mean ALVI between the groups was performed using the Wilcoxon rank-sum test and a significant difference at the level of 10% (p = 0.094) at GTC and 1% (p = 0.0038) at NDMC was determined. The area under the curve (AUC) of the receiver operating characteristic was 0.66 when categorizing between the two groups for GTC, and the AUC for NDMC was 0.70. The relationship between arousal level and depression severity was indirectly suggested via ALVI.

Keywords: arousal level; emotion; major depression severity; voice index; Hurst exponent; zero-crossing rate; Hamilton Rating Scale for Depression

1. Introduction

Globally, economic loss due to mental health disorders is an issue that requires immediate and appropriate attention [1,2]. To address this issue, an easily accessible and low-cost mental health screening method is required. The primary mental health assessment tools currently in use include medical interviews by specialists (e.g., the Hamilton Rating Scale for Depression [HAM-D]) [3], self-administered questionnaires (e.g., the general health questionnaire) [4], and the Beck Depression Inventory [5]. However, the practicality of medical interviews by specialists is limited by the restricted number of patients that can be examined, and self-administered questionnaires have

reporting bias issues. Reporting bias refers to participants' intentional disclosure or suppression of certain information (e.g., medical history, smoking history). Further, assessment tools using biomarkers such as saliva and blood, have also been studied [6-8]; however, these tools have drawbacks concerning cost and patient burden.

Meanwhile, with increasing usage of smartphones, a pathological analysis using speech data has attracted attention [9-13]. According to long-established findings, patients with depression have unique speech characteristics [14] and listeners can perceive their distinctive prosody [15,16]. Additionally, speech analysis is non-invasive and can be conveniently and remotely accessed without any dedicated device.

Many recent studies denote that speech characteristics are an effective predictor of the signs and severity of depression [17]. For example, Cannizzaro et al. [18] examined the interdependence between the HAM-D and voice acoustics and found a strong correlation between the HAM-D and speaking rate or pitch variation. Similarly, Hashim et al. [19] determined a mean absolute error of approximately 2 between the predicted HAM-D scores, which were calculated through multiple linear regressions of various audio signal features, and the actual HAM-D scores. Moreover, Yang et al. [16] indicated that changes in the severity of depression, measured by the HAM-D, can be deciphered through a switching pause. They specify switching pause as "the pause duration between the end of one speaker's utterance and the start of an utterance by the other" [16] (p. 145). Notably, Faurholt-Jepsen et al. [20] found that depressive symptoms, which were measured by the HAM-D, and manic symptoms, which were examined through the Young Mania Rating Scale (YMRS) [21], can be classified accurately via audio signal features for patients with bipolar disorder. Additionally, the Mel-frequency cepstral coefficient (MFCC) is often used for voice recognition and Taguchi et al. [22] verified that MFCC 2 (i.e., the second dimension of the MFCC) is efficient in classifying between depressive and healthy individuals.

Although Faurholt-Jepsen et al. [20] indicated a relationship between the HAM-D score and voice index, the issue of overfitting may remain because of the many audio signal features extracted from openSMILE [23]. In contrast, Taguchi et al. [22] showed that healthy individuals and patients with depression could be grouped based only on MFCC 2; however, MFCC 2 did not correlate with the severity of depression.

With the progress of brain science research, the correlation between depression and arousal has been attracting attention in recent years, and many studies using physiological indices, such as electroencephalogram (e.g., late positive potential amplitude), magnetoencephalography (e.g., neuromagnetic oscillatory activity), and skin conductance magnitude, have been conducted [24-26]. Additionally, the methods for assessing emotional arousal from voice have been studied, and the relationship between arousal level, vocal intensity, and pitch has been validated [27, 28].

In this paper, we examined the possibility of detecting depression using a voice index that estimates the arousal level. First, we constructed an algorithm for calculating arousal levels from voices by integrating emotional voices in the Interactive Emotional Dyadic Motion Capture (IEMOCAP) database [29]. We focused on the relationship between the Hurst exponent (HE) and the zero-crossing rate (ZCR) of the speech waveform when formulating the algorithm. Next, we used the algorithm to determine the arousal level from the voice of patients with depression and investigated the relationship between the arousal level and the severity of depression according to HAM-D scores.

2. Materials and Methods

2.1. Acquisition of Data

2.1.1. Data about arousal level

We used the IEMOCAP database [29] to create an algorithm that calculates the arousal level from the acoustic features of a person's voice. The database contains audio recordings of dyadic mixed-gender pairs of actors. There were five sessions in total, that is, the voices of 10 actors were

aggregated and then manually divided into utterance units. Notably, the arousal level of each utterance was gauged by two different annotators on a 5-point scale. Further, the arousal level of each utterance was equal to the average evaluation values given by each evaluator. In total, 10039 utterances were included in this study, and among these utterances, low arousal data with arousal level of 2 or less (n = 1112, mean ± SD = 1.92 ± 0.19) and high arousal data of level 4 or more (n = 1692, mean ± SD = 4.19 ± 0.28) were used.

2.1.2. Data about the severity of depression

The patients' speech data were collected from outpatients with major depressive disorders after acquiring informed consent from participants attending two hospitals, National Defense Medical College hospital (NDMC) and Ginza Taimei Clinic (GTC). The patients were directed to read the 17 Japanese phrases. However, all 17 phrases collected at both hospitals were not the same; 10 among them were common at both hospitals. Therefore, this study elicited the 10 common phrases and Table 1 illustrates them accordingly. Additionally, the speech of the two groups was recorded in a quiet and controlled environment and the voice was recorded using a pin microphone (ME52W, Olympus, Tokyo, Japan) placed on the chest about 15 cm from the mouth. The recording equipment was a portable recorder R-26 (Roland, Shizuoka, Japan) and the record format was linear PCM with the sampling frequency and the number of quantization bits at 11,025 Hz and 16, respectively.

In addition to voice recording, the HAM-D was also used by psychiatrists to appraise the severity of major depression. For each speech data acquisition session, HAM-D data were obtained from each participant and paired with the recorded speech data. Table 2 shows participants' information at each hospital.

Table 1. Ten phrases used for recording.

Phrase	Phrase in Japanese	Purpose (meaning)
P1	I-ro-ha-ni-ho-he-to	Non-emotional (no meaning, similar to "a-b-c")
P2	Honjitsu ha seiten nari	Non-emotional (It is fine today)
P5	Mukashi aru tokoro ni	Non-emotional (Once upon a time, there lived)
P11	Garapagosu shotou	Check pronunciation (Galápagos Islands)
P12	Tsukarete guttari shiteimasu.	Emotional (I am tired/dead tired)
P13	Totemo genki desu	Emotional (I am very cheerful)
P14	Kinou ha yoku nemuremashita	Emotional (I was able to sleep well yesterday)
P15	Shokuyoku ga arimasu	Emotional (I have an appetite)
P16	Okorippoi desu	Emotional (I am irritable)
P17	Kokoroga odayaka desu	Emotional (My heart is calm)

Table 2. Participants' information.

Hospital	Sex	Number of subjects	Mean age ± SD
GTC	Female	55	31.6 ± 8.6
	Male	33	32.5 ± 6.5
	Total	88	32.0 ± 7.9
NDMC	Female	44	62.0 ± 13.1

Male	46	48.8 ± 13.5
Total	90	55.2 ± 14.8

Note: GTC: Ginza Taimei Clinic; NDMC: National Defense Medical College; SD: Standard deviation.

Patients were included if they had been diagnosed with a major depressive disorder according to the DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision) [30] and were over the age of 20 years. However, the participants were excluded if the presence of serious physical disorders or organic brain disease was confirmed. Specifically, the Mini-International Neuropsychiatric Interview [31] was employed by a psychiatrist to evaluate these conditions.

The protocol of this study was designed as per the Declaration of Helsinki and relevant domestic guidelines issued by the concerned authority in Japan. The protocol was approved by the ethics committee of the faculty of medicine, The University of Tokyo (no. 11572) and the ethics committee of National Defense Medical College (no. 2248).

According to Japanese law, the sensitivity of audio files is similar to that of any other personal information and cannot be published without consent. In this research protocol, we did not obtain consent from the subjects to publish the raw audio files as a corpus. Hence, we only published the analysis data and the source code of the analysis program.

2.2. Proposed Method

This study proposes a new voice index for emotional arousal level calculated based on the relationship between two scales, namely HE and ZCR.

HE is an index that is regularly used in stock price analyses and hence it is widely used as a method to measure the characteristics of long-term memory [32]. The following equation was used to obtain the standard deviation (SD) $\sigma(\tau)$ of the difference between signal $x(t)$ at time t and signal $x(t + \tau)$ after τ elapsed (Equation [1]).

$$\sigma(\tau) = \sqrt{\frac{\sum_{t=1}^{n}\left(y(t,\tau) - \overline{y(\tau)}\right)^2}{n-1}}$$
$$y(t,\tau) = x(t+\tau) - x(t) \tag{1}$$
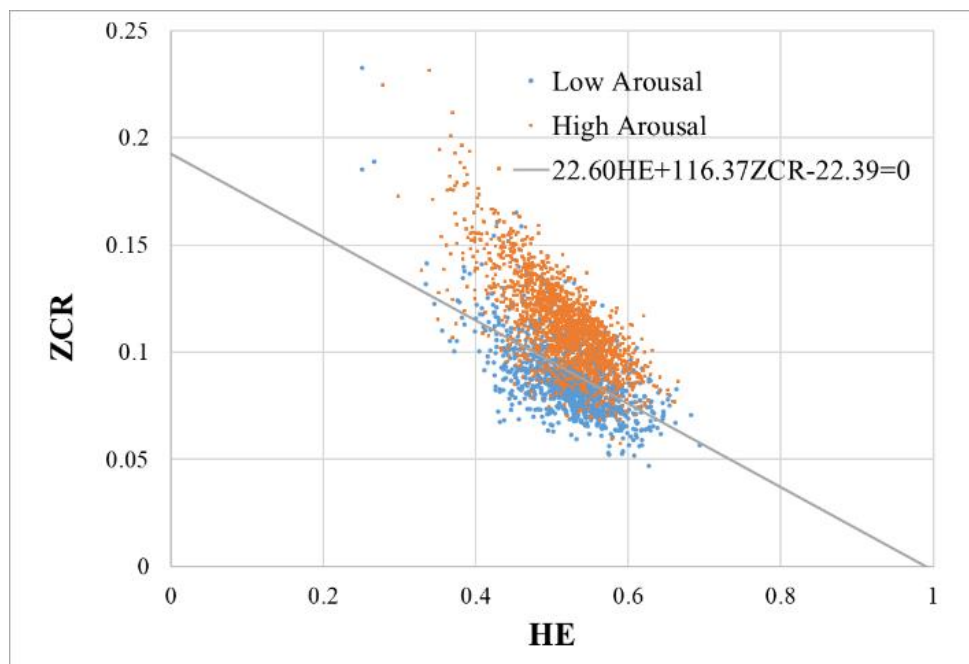$$\overline{y(\tau)} = \frac{\sum_{t=1}^{n} y(t,\tau)}{n}$$

It is known that there is a power law relationship (e.g., $\sigma(\tau) \propto \tau^{\alpha}$) between $\sigma(\tau)$ and τ when τ is a small value. Moreover, α is called a HE and in this research, the range of τ was defined as $\tau \leq 1.45ms$ (16 data points). However, if the coefficient of determination when calculating the regression line between $log(\sigma(\tau))$ and $log(\tau)$ was less than 0.9, it was considered that the power law relationship does not last, and the value of HE is returned as invalid. Thus, HE is an index of displacement from an initial position over time and theoretically, HE = 0.0 is in white noise and HE = 0.5 is in brown noise.

Meanwhile, ZCR is an index often used in studies on voice activity detection and classification of voiced/unvoiced sounds, indicating the rate at which the signal $x(t)$ changes from positive to negative, or conversely, from negative to positive [33-35]. In summary, the rate at which the signal crosses the reference line is denoted. Specifically, the ZCR of signal $x(t)$, which is a signal of length n, is expressed using the following equation (Equation [2]):

$$ZCR = \frac{\sum_{t=1}^{n-1} I\big(x(t)\,x(t+1)\big)}{n-1}$$

$$I(y) = \begin{cases} 1 & if \ y < 0 \\ 0 & else \end{cases} \tag{2}$$

Notably, the relationship between HE and ZCR as a voice index of arousal was examined. First, each speech phrase was separated into frames of length L where individual frame lengths were set with an overlap of L/4. In this study, L was set to 46.44 ms (i.e., 512 data points). Second, HE and ZCR were calculated for each frame. Then, among the frames contained in the utterance, the frames with valid HE values were selected. The mean value of HE of those frames was set as HE of the utterance and the same applied to ZCR.
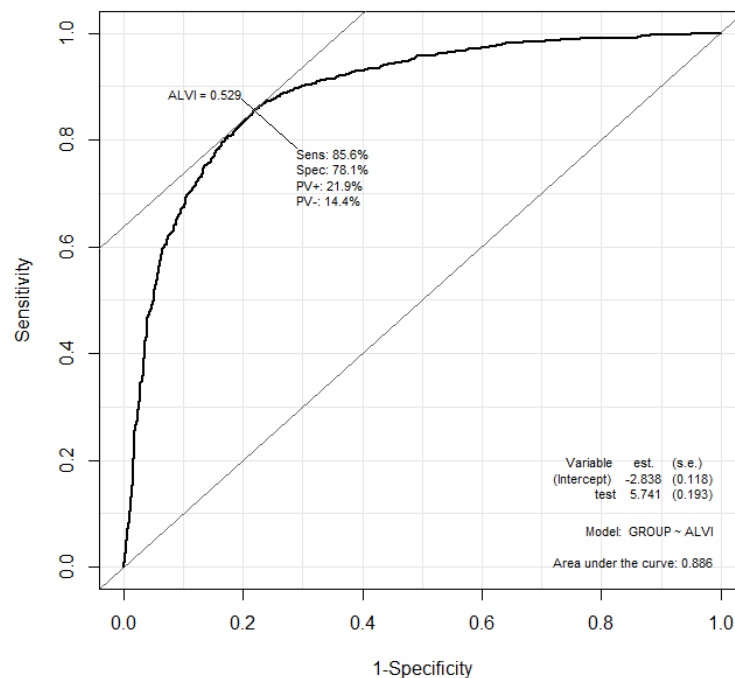

Note. ZCR: zero-crossing rate; HE: Hurst exponent; IEMOCAP: Interactive Emotional Dyadic Motion Capture.

Figure 1. A scatter plot between Hurst exponent and zero-crossing rate calculated from the utterances in the Interactive Emotional Dyadic Motion Capture database. Each data point represents data for each utterance. The low arousal level data are shown in blue and the high arousal level data are shown in orange.

Figure 1 shows a scatter plot between HE and ZCR calculated from the utterances in the IEMOCAP database. We performed a logistic regression analysis wherein HE and ZCR were used as explanatory variables. Alternatively, data with an arousal level of 2 or less were set to 0, and data of 4 or more were set to 1. These binary values (0, 1) were used as levels of an objective variable and the discrimination score was termed the arousal level voice index (ALVI) expressed by the following formula.

$$ALVI = \frac{1}{1 + \exp\big[-(21.60HE + 116.37ZCR - 22.39)\big]} \tag{3}$$

ALVI takes values in the range [0.0, 1.0]. Figure 1 also shows a straight line $21.60HE + 116.37ZCR - 22.39 = 0$ that aligns a set of points where ALVI = 0.5. The mean ALVI values for the low and high arousal groups were 0.33 ± 0.26 and 0.78 ± 0.22, respectively. Figure 2 shows the receiver operating characteristic (ROC) curve when the utterance data of low and high arousal levels are classified by ALVI.

Note. ALVI: arousal level voice index

Figure 2. Receiver operating characteristic curve when arousal level voice index identifies utterance data of low arousal level and high arousal level in the Interactive Emotional Dyadic Motion Capture database. The horizontal and vertical axes represent 1-specificity (false positive rate) and sensitivity (positive rate), respectively.

The area under the curve (AUC) of the ROC was 0.89. The cut-off value was ALVI = 0.53 and the sensitivity and specificity at the time were 0.86 and 0.78, respectively. The above analysis was performed using the statistical software R [36]. The following analysis was also performed using R unless otherwise specified.

3. Results

3.1. HAM-D score

Although there are various arguments about severity classification using the HAM-D [37], by using Hashim's method in this study, patients' data were divided into two groups based on HAM-D scores: a no depression group with a HAM-D score of <8 and a depression group with a HAM-D score of ≥8 [19]. Table 3 displays the mean HAM-D for each group per hospital.

As a result of the Wilcoxon rank-sum test, significant differences in the HAM-D score were observed between the groups at GTC ($p = 1.22 \times 10^{-8}$). Similarly, there was a significant difference at NDMC as well ($p = 1.56 \times 10^{-13}$).

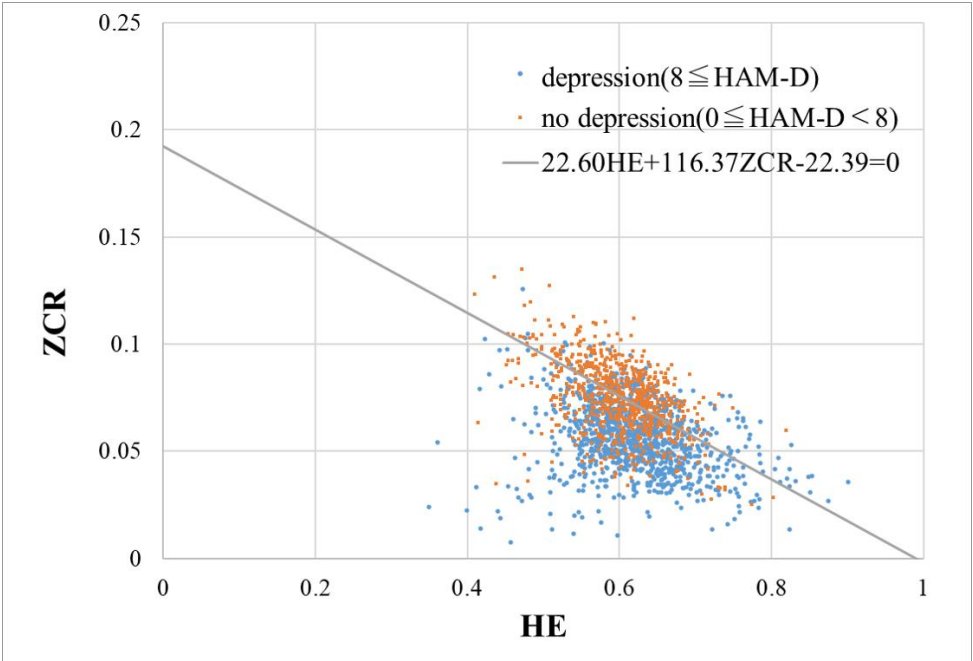**Table 3.** Mean scores on the Hamilton Rating Scale for Depression

Hospital	Group	Number of subjects	Mean HAM-D Score ± SD
GTC	No depression (HAM-D < 8)	10	4.8 ±1.3

	Depression (HAM-D ≧ 8)	78	24.4±8.5
	Total	88	22.2±10.1
NDMC	No depression (HAM-D < 8)	65	2.2 ±2.2
	Depression (HAM-D ≧ 8)	25	15.3±7.2
	Total	90	5.8±7.2

Note. HAM-D: Hamilton Rating Scale for Depression; SD: Standard deviation.

3.2. Performance Evaluation of ALVI

In this section, the results of applying ALVI to the voice of patients with depression are outlined. Figure 3 shows a scatter diagram of HE and ZCR calculated from each utterance (n = 1780) of depressed patients, and a straight line $21.60HE + 116.37ZCR - 22.39 = 0$ is also shown, as in Figure 2.
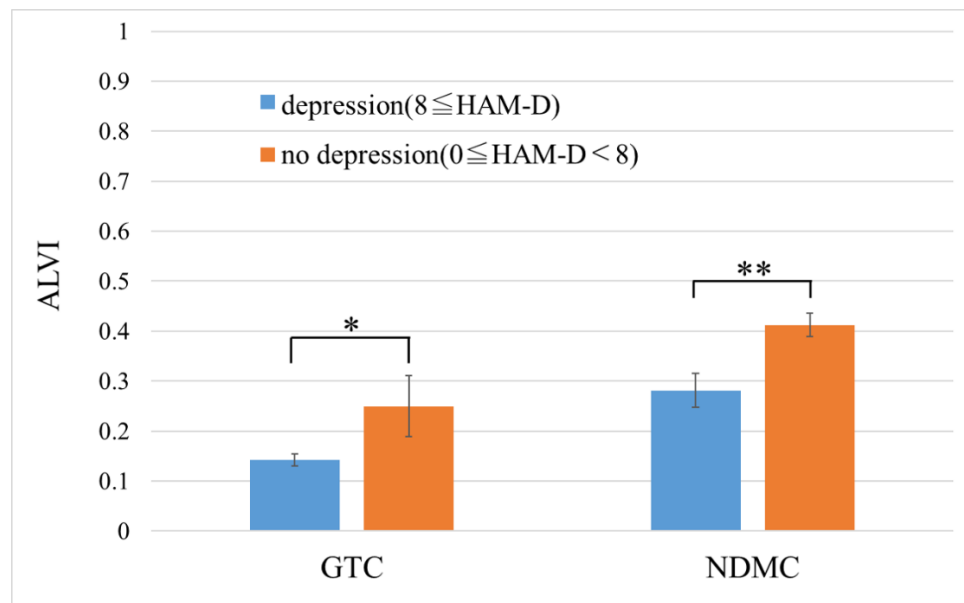

Note. HAM-D: Hamilton Rating Scale for Depression; HE: Hurst exponent; ZCR: zero crossing rate

Figure 3. A scatter diagram of the Hurst exponent and zero crossing-rate calculated from each utterance (n = 1780) of depressed patients. The data of the no depression group and the depression group are shown in orange and blue, respectively.

Depressed patient voices were collected at two hospitals, GTC and NDMC. As shown in Table 2, the age groups of the patients are quite different. Likewise, the sound field environment may also vary. Therefore, an analysis has been performed for each hospital.

Figure 4 shows the mean ALVI for each group per hospital. However, the ALVI value of each patient was the mean value of ALVI of each phrase. At GTC, the ALVI mean values of the no depression group and depression group were 0.25 ± 0.19 (n = 10) and 0.14 ± 0.10 (n = 78), respectively. At NDMC, the ALVI mean values of the no depression group and depression group were 0.41±0.18 (n = 65) and 0.28 ±0.17 (n = 25), respectively.
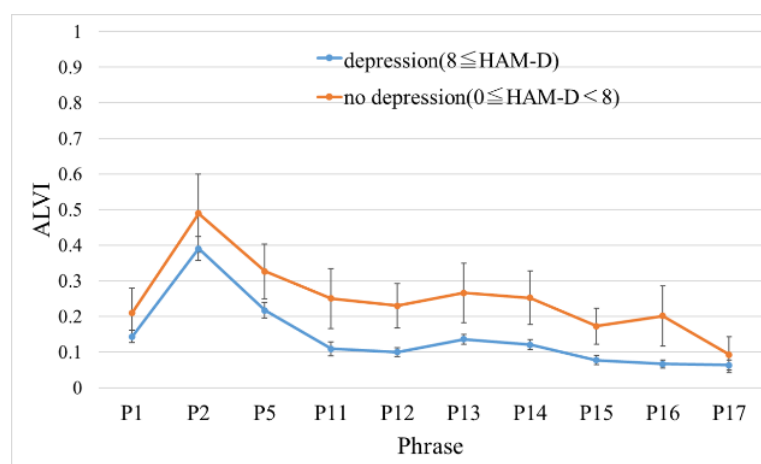
Note. HAM-D: Hamilton Rating Scale for Depression; GTC: Ginza Taimei Clinic; NDMC: National
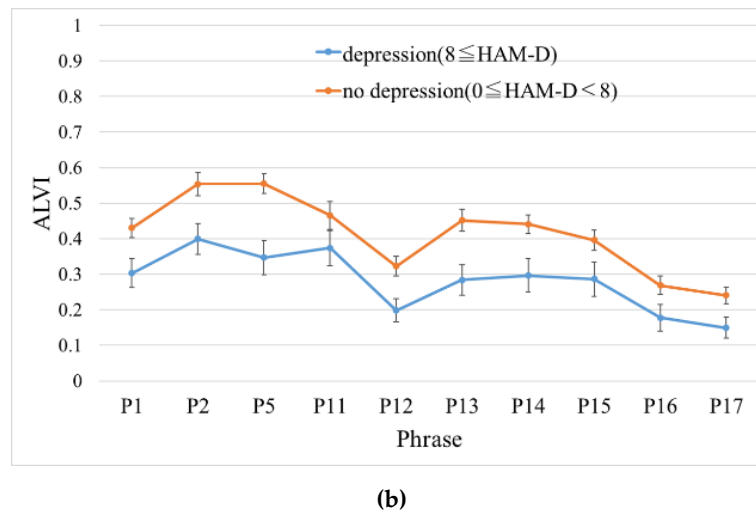Defense Medical College; ALVI: arousal level voice index.

Figure 4. The mean arousal level voice index for depression and no depression groups per hospital.
Error bars represent standard error. ** (p <0.01), * (p <0.1).

A comparison between the groups was performed using the Wilcoxon rank-sum test, and it determined a significant difference at the level of 10% (p = 0.094) at GTC and 1% (p = 0.0038) at NDMC. The AUC, at the moment when the groups were identified using ALVI, was 0.66 for GTC (cutoff point = 0.20, sensitivity = 0.60, specificity= 0.78) and 0.70 for NDMC (cutoff point = 0.23, sensitivity = 0.85, specificity = 0.56).

Next, we inspected the effect of different phrases on the ALVI for each hospital. Two-way ANOVA of ALVI was conducted for two factors, groups (i.e., no depression or depression) and phrases (i.e., 10 phrases). At GTC, significant differences in both group and phrase factors ($F_{(1, 860)}$ = 33.52, p = 9.87×10^{-9}, $F_{(9,860)}$ = 28.26, p<2.00×10^{-16}) were noted; however, there was no interaction between them ($F_{(9, 860)}$ = 0.375, p = 0.95). Similarly, at NDMC, there were significant differences in the factors of both groups and phrases ($F_{(1, 880)}$ = 57.09, p = 1.04×10^{-13}, $F_{(9,880)}$ = 16.56, p<2.00×10^{-16}) and no interaction was observed again ($F_{(9,880)}$ = 0.488, p = 0.88). Figure 5 shows the mean ALVI for each phrase in the no depression and depression groups. Finally, in all phrases, the ALVI of the no depression group was higher than that of the depression group in both hospitals.

(a)

(b)

Note. ALVI: arousal level voice index; HAM-D: Hamilton Rating Scale for Depression

Figure 5. The mean of arousal level voice index of the no depression and depression groups for each phrase. **(a)** represents Ginza Taimei Clinic and **(b)** represents National Defense Medical College. Error bars represent standard error.

Table 4 highlights the classification performance between the no depression and depression groups through ALVI. The table shows the results of comparing the mean ALVI of each group using the Wilcoxon rank-sum test and the AUC for each phrase. In the table, the minimum p-value and maximum AUC for each hospital are shown in bold type. At GTC, the discrimination performance for phrase 12 was the highest, and the AUC was 0.70 (cutoff point = 0.14, sensitivity = 0.70, specificity = 0.73). In contrast, at NDMC, the discrimination performance for phrase 5 was the highest, and AUC was 0.74 (cutoff point = 0.30, sensitivity = 0.85, specificity = 0.60).

Table 4. A summary of classification performance between the no depression and depression groups through arousal level voice index.

Phrase	p-value[a]		AUC	
	GTC	NDMC	GTC	NDMC
P1	0.33	0.027*	0.60	0.65
P2	0.30	0.0092**	0.60	0.68
P5	0.20	**0.00060***	0.63	**0.74**
P11	0.096*	0.29	0.66	0.57
P12	**0.040***	0.016*	**0.70**	0.67
P13	0.17	0.0047**	0.63	0.69
P14	0.096*	0.0062**	0.66	0.69
P15	0.099*	0.040*	0.66	0.64
P16	0.19	0.022*	0.63	0.68
P17	0.28	0.028*	0.61	0.65

Note. GTC: Ginza Taimei Clinic; NDMC: National Defense Medical College; AUC: Area under the curve.

*** (p <0.001), ** (p <0.01), * (p <0.1). [a] by Wilcoxon rank sum test.

4. Discussion

First, we focused on the relationship between the HE and the ZCR and developed a voice index (i.e., ALVI) for arousal. Next, ALVI was derived from the voices of depressed patients and applied for the identification of severity-based groups. Consequently, the ALVI of the no depression group

was significantly higher than that of the depression group. In other words, the association between arousal level and depression severity was indirectly suggested via the voice index ALVI. However, the arousal level used in the development of ALVI was an evaluation value given by the annotator, and not based on the subject's evaluation. Hence, in the future, it is imperative to investigate the relationship between ALVI and physiological indicators.

The AUC of ALVI was about 0.7 in the highest phrase. Comparably, Taguchi et al. [22] presented the AUC of MFCC 2 as 0.88 when classifying between patients with depression and healthy individuals. In our study, we did not compare healthy individuals with depressed patients as in Taguchi et al. Instead, we compared patients with mild depression with severely depressed patients. In other words, we compared two patient groups. This may be the reason why the AUC of our ALVI became lower. We plan to compare healthy individuals with depressed patients in future studies.

Regarding the severity of depression, the model classifying a depressive state versus a euthymic state had an AUC of 0.78 in the study of Faurholt-Jepsen et al. [20]. Here a depressive state is defined by a HAM-D score ≥13 and YMRS score <13, while a euthymic state is defined as a HAM-D score <13 and YMRS score <13. Even though no simple comparison is viable, the AUC shown here is higher than that of ALVI. However, it may be advantageous because the ALVI is unlikely to be overfitted. After all, it consists of only two indices, HE and ZCR.

Moreover, the voices of patients with depression have been reported to be dull, monotonous, and lifeless based on a qualitative point of view [14]. As seen in Equation [3], ALVI increases as both HE and ZCR increase. Notably, HE is represented by HE = 2-D where D is the fractal dimension. Therefore, HE can be regarded as an index representing waveform smoothness (i.e., the opposite of fractal dimension). Plus, as described in the definition, ZCR is higher in white noise and lower in smooth waveforms. Therefore, there may be a negative relationship between HE and ZCR.

In general, unvoiced sounds, such as "s," have a higher frequency and ZCR. Previous findings have shown that voices with lower short-time energy and higher ZCR are likely to be unvoiced sounds [33-35]. Furthermore, Shinohara et al. [38] proved that the pitch detection rate of patients with depression was lower than that of healthy individuals, where the pitch detection rate can also be defined as the proportion of voice sounds. Perhaps a sound may tend to become an unvoiced sound not only when ZCR is high but also when HE is simultaneously low.

This study has limitations. First, all participants had to use the same phrases for accurate evaluation because the current ALVI values vary depending on the phrase. Our future task is to apply ALVI to spontaneous speech. Future studies should explore the reasons for such differences among phrases.

Second, the sample size of the group was small because we collected voices from two hospitals, GTC and NDMC, where the age groups were very different. The reason for this may be that GTC is located in the city center and most of the patients are young workers who commute to the city center, while NDMC is located in the suburbs where many retired local residents live. Depression severity was uneven at both hospitals. The reason for this may be that NDMC is a university hospital and there are many patients that have been treated in another hospital. Therefore, future studies should include a bigger sample acquired in the same environment.

By daily monitoring the severity of depression using ALVI, we can encourage people to visit a hospital before they become depressed or during the early stages of depression. This may lead to reduced economic loss due to treatment costs and interference with work.

Conflicts of Interest: MH, MN, and ST received financial support from PST Inc until 2019 and currently report no financial support from the company. All other authors declare no conflicts of interest.

References

1. Kessler, R.C.; Akiskal, H.S.; Ames, M.; Birnbaum, H.; Greenberg, P.; Hirschfeld, R.M.A.; Jin, R.; Merikangas, K.R.; Simon, G.E.; Wang, P.S. Prevalence and effects of mood disorders on work performance in a nationally representative sample of U.S. workers. *Am J Psychiatry* **2006**, *163*, 1561–1568. https:doi.org/10.1176/appi.ajp.163.9.1561

2. World Health Organization. *The Global Burden of Disease: 2004 Update*; WHO Press: Geneva, Switzerland, 2004; pp. 46–49.

3. Hamilton, M. Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychol* **1967**, *6*, 278–296. https://doi.org/10.1111/j.2044-8260.1967.tb00530.x

4. Goldberg, D.P. *Manual of the General Health Questionnaire*; NFER Publishing: Windsor, England, 1978.

5. Beck, A.T.; Ward C.H.; Mendelson, M.; Mock, J.; Erbaugh, J. An inventory for measuring depression. *Arch Gen Psychiatry* **1961**, *4*, 561–571. https://doi.org/10.1001/archpsyc.1961.01710120031004

6. Izawa, S.; Sugaya, N.; Shirotsuki, K.; Yamada, K.C.; Ogawa, N.; Ouchi, Y.; Nagano Y.; Suzuki, K.; Nomura, S. Salivary dehydroepiandrosterone secretion in response to acute psychosocial stress and its correlations with biological and psychological changes. *Biol Psychol* **2008**, *79*, 294–298. https://doi.org/10.1016/j.biopsycho.2008.07.003

7. Suzuki, G.; Tokuno, S.; Nibuya, M.; Ishida, T.; Yamamoto, T.; Mukai, Y.; Mitani, K.; Tsumatori, G.; Scott, D.; Shimizu, K. Decreased plasma brain-derived neurotrophic factor and vascular endothelial growth factor concentrations during military training. *PloS One* **2014**, *9*, e89455. https://doi.org/10.1371/journal.pone.0089455

8. Takai, N.; Yamaguchi, M.; Aragaki, T.; Eto, K.; Uchihashi, K.; Nishikawa, Y. Effect of psychological stress on the salivary cortisol and amylase levels in healthy young adults. *Arch Oral Biol* **2004**, *49*, 963–968. https://doi.org/10.1016/j.archoralbio.2004.06.007

9. Arora, S.; Venkataraman, V.; Zhan, A.; Donohue, S.; Biglan, K.M.; Dorsey, E.R.; Little, M.A. Detecting and monitoring the symptoms of Parkinson's disease using smartphones: A pilot study. *Parkinsonism Relat D* **2015**, *21*, 650–653. https://doi.org/10.1016/j.parkreldis.2015.02.026

10. Rachuri, K.K.; Musolesi, M.; Mascolo, C.; Rentfrow, P.J.; Longworth, C.; Aucinas, A. EmotionSense: A mobile phones based adaptive platform for experimental social psychology research. In *Proceedings of the 12th ACM International Conference on Ubiquitous Computing*, *Copenhagen, Denmark, 26–29 September, 2010*; ACM: New York, 2010; pp. 281–290.

11. Lu, H.; Rabbi, M.; Chittaranjan, G.T.; Frauendorfer, D.; Mast, M.S.; Campbell, A.T.; Gatica-Perez, D.; Choudhury, T. StressSense: Detecting stress in unconstrained acoustic environments using smartphones. In *Proceedings of the 2012 ACM Conference on Ubiquitous Computing*; ACM: New York, USA, 2012; pp. 351–360.

12. Byrom, B.; McCarthy, M.; Schueler, P.; Muehlhausen, W. Brain monitoring devices in neuroscience clinical research: The potential of remote monitoring using sensors, wearables, and mobile devices. *Clin Pharmacol Ther* **2018**, *104*, 59–71. https:doi.org/10.1002/cpt.1077.

13. Haihua, J.; Bin, H.; Zhenyu, L.; Lihua, Y.; Tianyang, W.; Fei, L.; Kang H.; Li X. Investigation of different speech types and emotions for detecting depression using different classifiers. *Speech Commun* **2017**, *90*, 39–46. https://doi.org/10.1016/j.specom.2017.04.001.

14. Sobin, C.; Sackeim, H.A. Psychomotor symptoms of depression. *Am J Psychiatry* **1997**, *154*, 4–17.

15. Darby, J.K.; Hollien, H. Vocal and speech patterns of depressive patients. *Folia Phoniatr* **1977**, *29*, 279–291.

16. Yang, Y.; Fairbairn, C.; Cohn, J.F. Detecting depression severity from vocal prosody. *IEEE Trans Affect Comput* **2013**, *4*, 142–150 (2013). https://doi.org/10.1109/T-AFFC.2012.38

17. Mundt, J.C.; Vogel, A.P.; Feltner, D.E.; Lenderking, W.R. Vocal acoustic biomarkers of depression severity and treatment response. *Biol Psychiatry* **2012**, *72*, 580–587. https://doi.org/10.1016/j.biopsych.2012.03.015

18. Cannizzaro, M.; Harel, B.; Reilly, N.; Chappell, P.; Snyder, P.J. Voice acoustical measurement of the severity of major depression. *Brain Cogn* **2004**, *56*, 30–35. https://doi.org/10.1016/j.bandc.2004.05.003

19. Hashim, N.W.; Wilkes, M.; Salomon, R.; Meggs, J.; France, D.J. Evaluation of voice acoustics as predictors of clinical depression scores. *J Voice* **2017**, *31*, 256.e1–256.e6. https://doi.org/10.1016/j.jvoice.2016.06.006.

20. Faurholt-Jepsen, M.; Busk, J.; Frost, M.; Vinberg, M.; Christensen, E.M.; Winther, O.; Bardram, J.K.; Kessing, L.V. Voice analysis as an objective state marker in bipolar disorder. *Transl Psychiatry* **2016**, *6*, e856. https://doi.org/10.1038/tp.2016.123

21. Young, R.C.; Biggs, J.T.; Ziegler, V.E.; Meyer, D.A. A rating scale for mania: reliability, validity and sensitivity. *Br J Psychiatry* **1978**, *133*, 429–435. https:doi.org/10.1192/bjp.133.5.429

22. Taguchi, T.; Tachikawa, H.; Nemoto, K.; Suzuki, M.; Nagano, T.; Tachibana, R; Nishimura, M.; Arai, T. Major depressive disorder discrimination using vocal acoustic features. *J Affect Disord* **2018**, *225*, 214–220. https://doi.org/10.1016/j.jad.2017.08.038.

23. Eyben, F.; Wöllmer, M.; Schuller, B. OpenSMILe—The Munich Versatile and Fast OpenSource Audio Feature Extractor, In *Proceedings of the 18th ACM international conference on Multimedia, Firenze, Italy, October 2010*; ACM: New York, USA, 2010; pp. 1459–1462.

24. Schmidt, F.; Sander, C.; Dietz, M.; Nowak, C.; Schröder, T.; Mergl, R.; Schönknecht, P.; Himmerich, H.; Hegerl, U. Brain arousal regulation as response predictor for antidepressant therapy in major depression. *Sci Rep* **2017**, *7*, 45187. https://doi.org/10.1038/srep45187

25. Moratti, S.; Rubio, G.; Campo, P.; Keil, A.; Ortiz, T. Hypofunction of right temporoparietal cortex during emotional arousal in depression. *Arch Gen Psychiatry.* **2008**, *65*, 532-541. https://doi.org/10.1001/archpsyc.65.5.532.

26. Benning, S.D.; Ait Oumeziane, B. Reduced positive emotion and underarousal are uniquely associated with subclinical depression symptoms: Evidence from psychophysiology, self-report, and symptom clusters. *Psychophysiology.* **2017**, *54*, 1010-1030. https://doi.org/10.1111/psyp.12853.

27. Bone, D.; Lee, C. C.; Narayanan, S. Robust unsupervised arousal rating: A rule-based framework with knowledge-inspired vocal features. *IEEE T Affect Comput.* **2014**, *5*, 201–213. https://doi.org/10.1109/TAFFC.2014.2326393.

28. Schmidt, J.; Janse, E.; Scharenborg, O. Perception of emotion in conversational speech by younger and older listeners. *Front Psychol.* **2016**, *7*, 781. https://doi.org/10.3389/fpsyg.2016.00781.

29. Busso, C.; Bulut, M.; Lee, C.; Kazemzadeh, A.; Mower, E.; Kim, S.; Chang, J.N.; Lee, S.; Narayanan, S.S. IEMOCAP: Interactive emotional dyadic motion capture database. *Lang Resources & Evaluation* **2008**, *42*, 335 https://doi.org/10.1007/s10579-008-9076-6.

30. American Psychiatric Association. *Steering Committee on Practice Guidelines, American Psychiatric Association Practice Guidelines for the Treatment of Psychiatric Disorders: Compendium 2000*; American Psychiatric Association: Arlington, VA, US; 2000.

31. Otsubo, T.; Tanaka, K.; Koda, R.; Shinoda, J.; Sano, N.; Tanaka, S.; Aoyama, H.; Mimura, M.; Kamijima, K. Reliability and validity of Japanese version of the Mini-International Neuropsychiatric Interview. *Psychiatry Clin. Neurosci.* **2005**, *59*, 517-526. https://doi.org/10.1111/j.1440-1819.2005.01408.x

32. Eom, C.; Choi, S.; Oh, G.; Jung, W.S. Hurst exponent and prediction based on weak-form efficient market hypothesis of stock markets. *Physica A* **2008**, *387*, 4630–4636. https://doi.org/10.1016/j.physa.2008.03.035.

33. Jalil, M.; Butt, F.A.; Malik, A. Short-time energy, magnitude, zero-crossing rate and autocorrelation measurement for discriminating voiced and unvoiced segments of speech signals. In: *2013 International Conference on Technological Advances in Electrical, Electronics and Computer Engineering (TAEECE)*; IEEE: Konya, 2013, pp. 208–212. https://doi.org/10.1109/TAEECE.2013.6557272.

34. Bachu, R.; Kopparthi, S.; Adapa, B.; Barkana, B. Voiced/unvoiced decision for speech signals based on zero-crossing rate and energy. In *Advanced Techniques in Computing Sciences and Software Engineering*, Elleithy, K., ed.; Springer: Dordrecht, 2010; pp. 279-282.

35. Kazi, M.H.; Ekramul, H.; Khademul, I.M.A. method for voiced/unvoiced classification of noisy speech by analyzing time-domain features of spectrogram image. *Sci J Circuits Syst Signal Processing* **2017**, *6*, 11–17. https://doi.org/10.11648/j.cssp.20170602.12.

36. R Core Team. R: *A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria, 2019. Available online: https://www.R-project.org/

37. Zimmerman, M.; Martinez, J.H.; Young, D.; Chelminski, I.; Dalrymple, K. Severity classification on the Hamilton Depression Rating Scale. *J Affect Disord* **2013**, *150*, 384–388. https://doi.org/10.1016/j.jad.2013.04.028

38. Shinohara, S.; Omiya, Y.; Nakamura, M.; Hagiwara, N.; Higuchi, M.; Mitsuyoshi, S.; Tokuna, S. Multilingual evaluation of voice disability index using pitch rate. *Adv Sci Technol Eng Syst J* **2017**, *2*, 765–772. https://doi.org/10.25046/aj020397