

Severity Estimation of Finger-Tapping Caused by Parkinson's Disease by Using Linear Discriminant Regression Analysis

Yuko Sano, Akihiko Kandori, Toshinori Miyoshi, Toshio Tsuji, Keisuke Shima, Masaru Yokoe, and Saburo Sakoda

Abstract— We propose a linear discriminant regression analysis (LDRA) that provides an estimated severity marker for discriminating between healthy and patient groups and estimating severities of the patient group simultaneously. This method combines an evaluation function for discriminating between two groups and one for estimating severities of one group. The combined function is optimized to obtain an equation for calculating estimated severities. The method was evaluated with finger-tapping data of healthy and Parkinson's disease (PD) groups and PD severities assessed by a doctor. As a result, the discrimination ability of LDRA (AUC: 0.8835) was higher than that of discriminant analysis (DA. AUC: 0.8442), which is a conventional method for classification, and the regression ability of LDRA (mean square error (MSE): 1.27) was superior to that of multiple regression analysis (MRA. MSE: 1.68), which is a conventional method for regression. The results show that LDRA is an effective method for estimating the presence and severity of Parkinson's disease.

I. INTRODUCTION

Recently, many studies have been making efforts to assist medical diagnoses by the use of multivariable analyses or machine learning techniques. To estimate the presence or severity of a disease, the following two steps are generally carried out.

In the first step, a discriminant method is applied to a database of healthy subjects and that of patients with a certain disease. Then, a discrimination criterion for classifying the two groups is obtained. In the second step, a regression method is applied to the database of patients and its severities marked by a doctor. An estimation criterion for calculating an estimated severity is then obtained. After that, the discrimination criterion is applied to data of a new subject for whom the presence and severity of the disease are unknown to classify the new subject into the healthy group or the patient group. If the new subject is classified into the patient group, the estimation criterion is applied to the new subject's data. Thus, the estimated severity of the new subject is calculated.

The above-described procedure in which the estimated

severity is calculated through the two steps has problems with clinical usability and estimation accuracy. The problem with clinical usability is that when the classification result in the first step differs from the doctor's diagnosis, the estimated severity could not be calculated in the second step. For example, even though a new subject is classified into the healthy group in the first step, a doctor may diagnose the new subject as having the disease. In this case, the doctor wants to know the subject's severity but cannot obtain the estimated severity calculated in the second step because the subject was incorrectly classified into the healthy group in the first step.

The problem with estimation accuracy is caused by a shortage of samples (especially patients). To apply multivariable analyses or machine learning techniques with high accuracy, many samples are necessary. The number of patients with a certain disease in a hospital, however, is usually limited to at most several tens. If the patient database used for learning the estimation model is small, generalization of the model is low. That is, the estimated severity of the patient database for learning an estimation model could be calculated with high accuracy, and conversely the estimated severity of the new subject is calculated with low accuracy.

We therefore propose a new method that provides an estimated severity marker for discriminating between healthy and patient groups and estimating severities of the patient group at the same time (linear discriminant regression analysis). The proposed method is applied to a database of finger tapping of healthy subjects and Parkinson's disease (PD) patients and is proven to be effective in clinical use. Besides, the proposed method is compared with the above-described traditional approach (apply a discrimination method, and then apply a regression method) in terms of discrimination and regression accuracy, and the advantage of the proposed method over the traditional approach is shown.

II. LINEAR DISCRIMINANT REGRESSION ANALYSIS

Linear discriminant regression analysis (LDRA) is proposed as a method for discriminating between healthy and patient groups and estimating severities of the patient group at the same time. The flowchart of LDRA is shown in Fig. 1.

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The equation for calculating an estimated severity is represented by linear combination of characteristics as shown in equation (1). The estimation equation for linear discriminant analysis (LDA) and the one for multiple regression analysis (MRA) are also represented in the same manner.

$$\hat{y} = \mathbf{w}^T \mathbf{x} = w_0 x_0 + w_1 x_1 + w_2 x_2 + \dots + w_p x_p \quad (1)$$

where \mathbf{w} is a weight coefficient vector, \mathbf{x} is a characteristic vector extracted from raw data, and p is a dimension of \mathbf{w} and \mathbf{x} (w_0 is a constant, and $x_0 = 1$). The discriminant evaluation function E_D and the regression evaluation function E_R are defined by equation (1) in the following manner.

The regression evaluation function E_R is identical to the evaluation function defined for MRA, which represents the precision of estimating patient severities. E_R is calculated as the sum of square error between the true severity y_{Ri} marked by a doctor and the estimated severity \hat{y}_i calculated by equation (1). The suffix i of the variables denotes the respective samples.

$$E_R = \frac{1}{2N_d} \sum_i^{N_d} (\hat{y}_i - y_{Ri})^2 = \frac{1}{2N_d} \sum_i^{N_d} (\mathbf{w}^T \mathbf{x}_i - y_{Ri})^2 \quad (2)$$

where N_d is the number of the patient group.

E_R represents the difference between the estimated severity \hat{y}_i and the true severity y_{Ri} . Thus, to improve regression accuracy, it is necessary to minimize E_R .

The true severity y_{Ri} of the patient group must be more than 0. Also y_{Ri} must be larger as the disease becomes severer. This is because the estimated severity \hat{y}_i also plays a role as a marker for discrimination, so \hat{y}_i should meet the following requirement for LDA: the subject is classified into the patient group when $\hat{y}_i > 0$ and is classified into the

healthy group when $\hat{y}_i < 0$.

The discriminant evaluation function E_D is explained below. Even if E_R is minimized and the regression accuracy of estimating the severity is improved, the discrimination accuracy may not necessarily be improved at the same time. E_D is adopted in order that the estimated severity \hat{y}_i can also act as an effective discriminant marker.

E_D is designed by reference to the evaluation function for LDA and expressed by equation (3).

$$E_D = \frac{1}{2(N_d + N_h)} \sum_i^{N_d + N_h} (\hat{y}_i - y_{Di})^2 \quad (3)$$

$$= \frac{1}{2(N_d + N_h)} \sum_i^{N_d + N_h} (\mathbf{w}^T \mathbf{x}_i - y_{Di})^2$$

where

$$y_{Di} = \begin{cases} -\frac{N_h + N_d}{N_h} & (i \in \text{healthy subjects}) \\ \frac{N_h + N_d}{N_d} & (i \in \text{patients}) \end{cases}$$

and where N_h is the number of the healthy group and N_d is the number of the patient group. The estimated severity \hat{y}_i is the same as \hat{y}_i in equation (2).

E_D represents the gap between the estimated severity \hat{y}_i and the representative severity value y_{Di} of each group. Thus, E_D should be minimized to improve the [discrimination ability/ability to discriminate?] between the healthy and the patient groups. If E_D is minimized, the estimated severity \hat{y}_i of the patient group becomes close to the representative severity $y_{Di} = (N_h + N_d)/N_d$, which meets the condition $\hat{y}_i > 0$. On the other hand, the estimated severity \hat{y}_i of the healthy group becomes close to the representative severity $y_{Di} = -(N_h + N_d)/N_h$, which meets the condition $\hat{y}_i < 0$.

As stated above, E_R and E_D should be minimized. However, E_R and E_D cannot be minimized simultaneously because \mathbf{w} that minimizes E_D and \mathbf{w} that minimizes E_R are not necessarily equal. Therefore, a combined evaluation function E is defined by combining E_R and E_D using the priority constant c . This constant c represents a trade-off between E_R and E_D . E is minimized instead of E_R and E_D .

$$E = cE_R + (1 - c)E_D \quad (4)$$

where the range of c is $0 \leq c \leq 1$. If the estimation accuracy of the patient's severity is considered important, c should be high. On the other hand, if the discrimination ability between the healthy and the patient groups is regarded as important, c should be low. To obtain the most appropriate c value, it is necessary to explore the value of c that maximizes the regression accuracy or the discrimination accuracy.

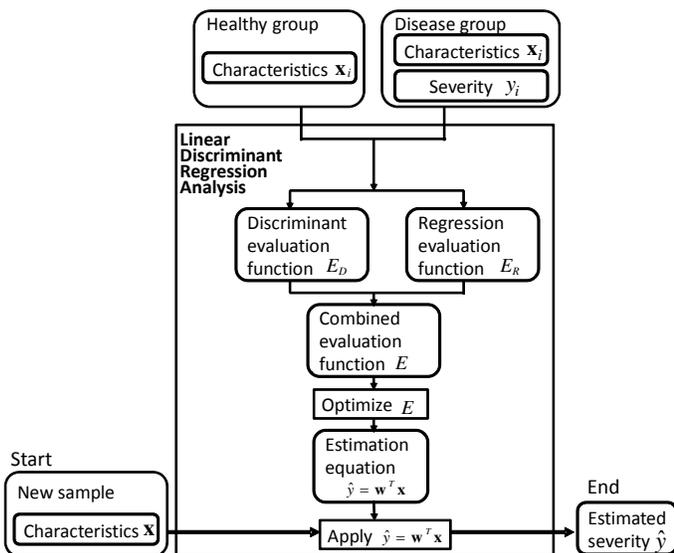


Fig. 1 Flowchart of Linear Discriminant Regression Analysis

To minimize E , it is necessary to take the derivative of E with respect to w and solve the derivative for w . The following equation (5) thereby is calculated.

$$w = (A^T)^{-1} B^T \quad (5)$$

where A and B are defined as follows.

$$A = \frac{c}{N_d} \sum_i x_i x_i^T + \frac{1-c}{N_n + N_d} \sum_i x_i x_i^T \quad (6)$$

$$B = \frac{c}{N_d} \sum_i x_i^T y_{Ri} + \frac{1-c}{N_n + N_d} \sum_i x_i^T y_{Di} \quad (7)$$

w , which is calculated by equation (5) is substituted into equation (1). Accordingly, the equation for estimating a severity is derived.

III. EXPERIMENT WITH FINGER-TAPPING DATA

A. MEASUREMENT TARGET

The proposed method, LDRA, is applied to a finger-tapping movement database of healthy subjects and Parkinson's disease (PD) patients. The finger-tapping movement is opening and closing thumb and index fingers repeatedly. A conventional PD diagnosis method is to observe a patient's finger tapping and grade the degree of motor deterioration. The diagnoses, however, are different among doctors, so an objective evaluation method is required. Therefore, we developed a finger-tapping device with magnetic sensors as shown in Fig. 2(a) and have studied the method of quantifying PD severity by finger-tapping measurement [1, 2].

196 healthy subjects and 26 PD patients as shown in Table 1 are measured with the finger-tapping device. The number of PD patients is relatively small because patient data are difficult to obtain as mentioned in the introduction.

UPDRSft is a PD severity score, which a doctor determines by observing the patient's finger-tapping in accordance with UPDRS (Unified Parkinson's Disease Rating Scale) [3]. UPDRSft is an integer from 0 to 4. UPDRSft = 0 means that the patient's finger tapping is normal, and a larger UPDRSft means severer motor deterioration.

Typical waveforms of a healthy subject and a PD patient are shown in Fig. 3. The upper graph is a distance waveform obtained directly from the finger-tapping device, and the middle and lower graphs are velocity and acceleration waveforms obtained by differentiating a distance waveform. The healthy subject executes finger tapping smoothly (Fig. 3(a)). In contrast, the PD patient performs a quite different movement from the healthy subject's movement due to muscle

rigidity and rhythm disorder (Fig. 3(b)). 21 characteristics are extracted from these waveforms [4].

Table 1 Database for finger-tapping measurement

Group	Total	Male	Female	Age	UPDRSft
Healthy subjects	196	154	42	58.8 ±6.4	—
PD patients	26	14	12	70.3 ±6.17	1 - 3

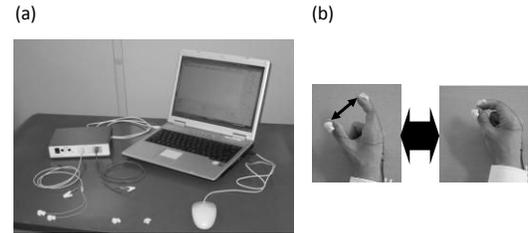


Fig. 2 Finger-tapping device with magnetic sensors (a) Overall view, (b) Finger tapping movement

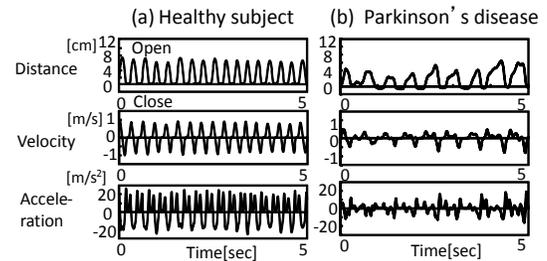


Fig. 3 Typical waveforms of finger-tapping movement (a) Healthy subject, (b) Parkinson's disease patient

B. METHOD FOR APPLYING LDRA

To evaluate LDRA, the discrimination accuracy between the healthy subjects and PD patients and the regression accuracy for estimating the severities of PD patients are calculated using the leave-one-out (LOO) cross-validation method. The discrimination accuracy is evaluated by the area under the ROC curve (AUC). The regression accuracy is evaluated by mean square error (MSE) between true severities by a doctor and the estimated severities calculated by LDRA.

To explore the most appropriate priority constant c that maximizes the discrimination accuracy, c is varied from 0.0 to 1.0 by steps of 0.1, and the value of c that maximizes AUC is selected. Besides, the discrimination accuracy of DA and regression accuracy of MRA are calculated to be compared with those of LDRA.

C. EVALUATION RESULTS

The result of applying LDRA to the finger-tapping data of healthy subjects and PD patients is shown in Fig. 4. The horizontal axis of the graph is UPDRSft marked by a doctor, and the vertical axis is the estimated severity of LDRA. The symbol “○” means a healthy subject, and the symbol “▲” means a PD patient. The healthy subjects are plotted on the

assumption that UPDRSft equals zero because it is not given by a doctor. The result in Fig. 4 is calculated under the condition that the priority constant $c = 0.6$, which maximizes AUC. Each estimated severity in this figure is calculated by the LOO method. In other words, one of the samples is applied to a model learned by the other samples, and the estimated severities of the respective samples are plotted repeatedly.

The discrimination accuracy and the regression accuracy of LDRA ($c = 0.6$) and the traditional methods are shown in Table 2. They are calculated by the LOO method. The AUC of LDRA is 0.8835, which is higher than that of DA (0.8442). The MSE of LDRA is 1.27, which is superior to that of MRA (1.68).

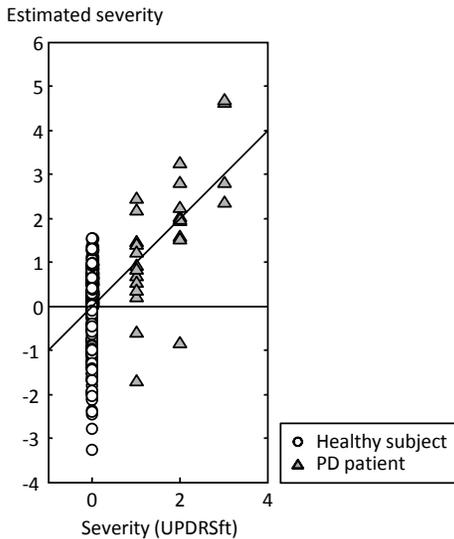


Fig. 4 Distribution of estimated severities calculated by LDRA (Priority constant $c = 0.6$)

Table 2 Comparison of discrimination and regression accuracy between LDRA and the traditional approach

	AUC	MSE
LDRA ($c = 0.6$)	0.8835	1.27
Traditional methods	<DA> 0.8442	<MRA> 1.68

IV. DISCUSSION

Figure 4 and Table 2 reveal that LDRA has a higher discrimination ability than DA and a higher regression ability than MRA. When there are few healthy subjects and patients for learning an estimation model like in this experiment, traditional methods for discrimination and regression (DA and MRA) do not work effectively due to low generalization. They can only provide inaccurate axes of an estimated severity. LDRA can search for the most appropriate axis from that of DA to that of MRA by changing the priority constant c from 0.0 to 1.0.

We previously stated that the true severity y_{Ri} of the patient group marked by a doctor should be more than 0 and y_{Ri} should also be larger as the disease becomes severe. Many severity rating scales meet these requirements, for example, UHDRS (Unified Huntington's Disease Rating Scale) [5] and MMSE (Mini-Mental State Examination) [6] for dementia. Thus, LDRA can be applied to severity scales other than just UPDRS.

LDRA also has a merit with clinical usability. LDRA can provide an estimated severity regardless of the presence or absence of a disease. Thus, the result does not conflict with the doctor's diagnosis, and the doctor can easily monitor the severity of a patient who recovers from the disease over time.

V. CONCLUSION

In this study, we proposed linear discriminant regression analysis (LDRA) that provides an estimated severity index for discriminating between healthy and patient groups and estimating severities of the patient group simultaneously. The effectiveness of LDRA was evaluated by using finger-tapping data of 196 healthy subjects and 26 Parkinson's disease patients. Besides, LDRA and the traditional method (DA and MRA) were compared in terms of discrimination accuracy and regression accuracy.

As a result, LDRA has both the discrimination ability (AUC: 0.8835) that exceeds the discrimination ability of DA (AUC: 0.8442) and the regression ability (MSE: 1.27) that exceeds the regression ability of MRA (MSE: 1.68). The results show that LDRA is an effective method for estimating the presence and severity of Parkinson's disease.

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