

Relation of Postural Instability to Gait Dynamics in Patients with Parkinson's Disease

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Abstract – Rhythm as typified by stride interval is an important factor in walking. The stride interval of patients with Parkinson's disease (PD) randomly fluctuates, and the stride interval variability is large. However, the relationship between gait rhythm dynamics and motor symptoms in PD patients has not been determined. The purpose of this study is to examine the relationship between one of the motor symptoms—postural instability—and the gait dynamics in PD patients. The stride interval variability was quantified using the coefficient of variation (CV) and the fluctuation property of stride interval is quantified as the scaling exponent α using detrended fluctuation analysis. We used multiple test and receiver operator characteristic (ROC) analysis to examine the relationship between severity of postural instability and gait dynamics. We divided PD patients into 3 groups: no postural instability, mild postural instability and obvious postural instability group. We compared the distribution of CV and α among the groups. Then, we compared the performance of the classification by CV with that by α . Forty-five patients with PD and 17 healthy elderly people walked around 200m without any support. The severity of postural instability was determined using the modified Hoehn-Yahr scale (mH-Y). Patients with mH-Y 2.5 have mild postural instability, and patients with mH-Y 3 and more than 3 have obvious postural instability. As a result, the classification by CV has a high performance when we differentiate between the presence and absence of postural instability. Also, the classification by α has a high performance when we differentiate between mild postural instability and obvious postural instability. These results suggest that CV and α can be used to differentiate severity of motor symptoms in patients with PD.

Index Terms – Gait rhythm, Postural instability, Coefficient of variation, Detrended fluctuation analysis.

I. INTRODUCTION

Walking is one of the most fundamental factors in our daily lives. We can walk stably even when the environment changes. The reason is that walking is a rhythmic movement. Therefore, gait rhythm is an important factor in walking. Gait rhythm is not constant but changes subtly. This change can be quantified by a pair of physical measures. One is the coefficient of variation (CV), which represents the magnitude of gait rhythm variability. The other is the scaling exponent α , which represents the fluctuation property of gait rhythm and which can be calculated by detrended fluctuation analysis (DFA). In particular, the fluctuation in gait rhythm is an

important feature of walking. In healthy young people, the gait rhythm has small variation and $1/f$ -like fluctuation properties [1].

Parkinson's disease (PD) causes disorders related to gait dynamics, which generate more variable gait rhythm, and changes the $1/f$ -like fluctuation property. This disorder which effects on gait dynamics are referred to as gait rhythm generation disorder.

Two symptoms have been reported regarding gait rhythm generation disorder in PD patients. One symptom is an increase in gait rhythm variability [2,3], and the other is a change in the fluctuation property of gait rhythm from the normal $1/f$ -like fluctuation property [4-6]. Two types of rehabilitation for gait rhythm generation disorders in PD are used. One is rhythmic auditory stimulation (RAS) gait training [7], and the other is Walk-Mate gait training [8]. In RAS gait training, fixed-tempo rhythmic auditory stimuli are input to PD patients [7]. This type of rehabilitation improves mainly the gait rhythm variability; in other words, RAS gait training decreases CV but does not change α much [6,9]. We have been developing the Walk-Mate system [8]. In Walk-Mate gait training, rhythmic auditory stimuli mutually entrained with the gait rhythm of the PD patient [10]. This type of rehabilitation improves mainly the fluctuation property of gait rhythm [10]. In one study, α improved sustainably, but CV did not change much after four consecutive days of Walk-Mate gait training [11].

These findings suggest that RAS gait training and Walk-Mate gait training might improve different aspects of gait rhythm generation disorder in PD patients. A comprehensive evaluation platform for gait rhythm could be established by combining CV and α . However, it is not clear whether CV and α , which evaluate the individual dynamics of gait rhythm, are related to the clinical symptoms of motor symptoms.

The purpose of this study is to examine whether the feature values of gait dynamics is effective for evaluating the severity of motor symptoms in PD patients. As a dynamic indicator, we focused on two quantities: CV and α because the quantities can be considered as important features that represent the gait dynamics of an individual's gait rhythm. We therefore examined whether and how the CV and α are related to the severity of motor symptoms in PD patients.

This study focused in particular on postural instability (PI) as an example motor symptoms in PD patients, and we classified the subjects according to its presence or absence. Furthermore, the severity of PI in a group of PD patients was classified. The modified Hoehn–Yahr (mH-Y) scale [12,13] was used as the evaluation criterion of the severity of motor symptoms, and it was verified whether the CV and α could be used to classify the motor symptoms.

II. METHODS

A. Participants

Forty-five patients (21 men, 24 women; mean age \pm SD 69.8 ± 8.2 years) with PD and 17 age-matched healthy people (10 men, 7 women; mean age 70.2 ± 2.8 years) participated in this study. The mean disease duration (\pm SD) was 4.7 ± 3.9 years. The mH-Y classifications (and number of subjects) were mH-Y 1–2 ($n=19$), mH-Y 2.5 ($n=11$), and mH-Y 3 ($n=15$). All patients were “on” state of dopaminergic medication during the experiment. All participants could walk without a cane or walker. These experimental procedures were approved by Kanto Central Hospital Ethics Committee. Before the experiment, we obtained participants’ written informed consent.

B. Gait Tasks and Measurement of Stride Interval

Participants walked at their preferred pace along around 200m course. We collected the stride interval time series using foot switches (OT-21BP-G, Ojiden, Japan) attached under participants’ shoes. Stride interval is defined as the time duration between two consecutive foot contacts on the same side. The mean number (\pm SD) of stride intervals was 154 ± 23 strides for the 200 m. Data for foot contact timing were sent to a laptop PC (CF-W5AWDBJR, Panasonic, Japan) by wireless transmitter (S-1019M1F, Smart Sensor Technology, Japan). The sampling frequency was 100 Hz. We used only the data for the left side because no significant differences between stride interval were observed between the left and right sides (left side: mean = 1.06 ± 0.09 s, CV = $2.73\% \pm 1.09\%$, $\alpha = 0.80 \pm 0.21$; right side: mean = 1.06 ± 0.09 s; CV = $2.78\% \pm 1.62\%$; $\alpha = 0.81 \pm 0.22$; p -values based on Welch’s two-sample t test: $p = 0.97$ for mean, $p = 0.82$ for CV, $p = 0.92$ for α). We analysed the data for the right side in only one patient because high noise level in the data for the left side. To analyse only the stable stride interval phase, the first 10 strides and last five strides (i.e., transient stride interval phase) were not analysed.

C. Coefficient of Variation (CV)

We focused on the coefficient of variation CV as a dynamic indicator to evaluate the stride interval variability of participants. CV represents the variability of time series data. It is the standard deviation normalized by mean value, $CV = SD/Mean \times 100$ [%]. The CV of stride intervals is within a range from 1% to 2.5% in healthy people, and CV from 2.5% to 4% in PD patients [2].

D. Detrended Fluctuation Analysis (DFA)

We focused on the scaling exponent α as the other dynamic indicator to evaluate the fluctuation property. α can be quantified by DFA as long-range correlations in time series data [14,15]. We selected this method because it can also be applied for relatively short intervals [16].

If α is near 0.5, the original time series includes white noise. On the other hand, if α is nearly equal to 1.0, the time series is characterized by $1/f$ fluctuation and is thought to be generated by chaos dynamics or limit cycle dynamics with noise [17–20]. The α of the stride interval at the preferred pace has been reported as 0.50–0.85 in PD patients [4,6] and as 0.8–1.2 in healthy young people [21,22]. The α of healthy elderly people’s stride interval decreases to 0.7–0.9, although the CV remains unchanged [5,22,23].

E. Statistical Analysis

Kruskal-Wallis rank sum test was used to examine whether samples of each group originate from the same distribution because there is a bias in the distribution. This is a nonparametric method about one-way analysis of variance. Multiple comparison were done using Holm’s adjustment method. The level of significance was $p = 0.05$. The level of significant tendency was $p = 0.10$.

Receiver Operator Characteristic (ROC) analysis was used to measure the classification performance [24]. ROC curves were generated by SPSS Statics (IBM, New York, USA). The area under the ROC curve (A_C) was calculated to measure sensitivity unaffected by response bias. If A_C is equal to 0.5, the classification is random. By contrast, if A_C is equal to 1.0, the classification is complete. The larger A_C is, the higher classification performance is. From these findings, we compare the performance of CV to that of α . 95% confidence interval of A_C was reported.

F. Relationship between mH-Y and PI in PD patients

Walking is related to posture and muscle tone control [25–29]. In PD patients, gait disorders such as propulsion and festination are often involved in PI. Therefore, we focused on the result of the pull test (30th item in the Unified Parkinson’s Disease Rating Scale) to identify the presence or absence of PI. In this test, the shoulder of the PD patient is pulled backward while the patient remains standing. Performance on the pull test is associated with mH-Y, one of the clinical indicators for assessment of motor symptoms of PD [13].

We focused on mH-Y scale. The scores in the original H-Y takes an integer value from 1 to 5. The mH-Y further includes values of 1.5 and 2.5 [13]. We separated the participants into three groups based on their mH-Y scores and performance on the pull test: mH-Y score of 2 or less with no problems (no-PI), mH-Y = 2.5 with signs of mild disorder (mild-PI), and mH-Y = 3 with obvious signs of disorder (obvious-PI). At first, ROC curve according to the presence or absence of PI was generated. The no-PI group consists of 17 healthy elderly people and 19 PD patients with mH-Y 1–2 (including one with mH-Y score of 1 and one with mH-Y 1.5), and the PI group consists of 26 PD patients with mH-Y 2.5–3. We then

separated the PI group of patients into the mild-PI (mH-Y 2.5) and obvious-PI groups (mH-Y 3).

III. RESULTS & DISCUSSION

Figs. 1-4 show samples of the gait analysis, including the time series of stride interval and the result of DFA. The CV of the stride interval was larger in PD patients with PI (Fig. 1, 2) than in PD patients with no-PI (Fig. 3) or in healthy elderly people (Fig. 4). The α of the stride interval (Fig. 1) was lower in PD patients with obvious-PI than in PD patients with mild-PRD (Fig. 2), in PD patients with no-PI (Fig. 3), or in healthy elderly people (Fig. 4).

Using Kruskal-Wallis rank sum test, the significant difference of CV among healthy elderly, mH-Y1-2, mH-Y2.5 and mH-Y3 group was shown ($\chi^2(3) = 19.3, p = 0.0002$). Comparing these five data, the CV of stride time of healthy elderly were significantly smaller than that of mH-Y2.5 and that of mH-Y3 (Fig. 5A, $p = 0.022, p = 0.001$). Patients with mH-Y2.5 and mH-Y3 shows PI. Because the difference between mH-Y2.5 and mH-Y3 group is subtle, we create two groups: no-PI group by mixing the healthy elderly people and the PD patients with mH-Y1-2 and PI group by mixing the PD patients with mH-Y2.5 (mild-PI) and mH-Y3 (obvious-PI).

As an additional result, we compared the distributions of CV between 3 groups (Fig. 5B). The distributions were significantly different ($\chi^2(2) = 14.9, p = 0.001$). The CV in no-PI was significantly lower than mild-PI or obvious-PI ($p = 0.049, p = 0.002$).

The significant difference of α between the four groups was shown ($\chi^2(3) = 8.22, p = 0.042$). The α of PD patients distributed in wide area, and it overlapped to healthy people (Fig. 6A). However, the α of the PD patients with mH-Y3 was significantly lower than that of mH-Y2.5 ($p = 0.027$). The PD patients with mH-Y2.5 shows mild PI, and the patients with mH-Y3 shows obvious PI. This result therefore suggests that the α mainly differentiate the severity of PI.

We also compared the distribution of α between 3 groups (Fig. 6B). The distributions of α were significantly different ($\chi^2(2) = 7.2, p = 0.028$). The α of obvious-PI was significantly lower than that of mild-PI ($p = 0.013$). The tendency of significant difference between no-PI and mild-PI in α was observed ($p = 0.079$).

Fig. 7 shows the ROC curve of classification between no-PI and PI groups. The area under the ROC curve A_C was 0.779 for CV (95% confidence interval was from 0.664 to 0.893, Fig. 7A). The A_C was 0.493 for α (95% confidence interval was from 0.342 to 0.644, Fig. 7B). This result suggests that the CV mainly differentiate the presence and absence of PI because the A_C for CV is larger than that of α .

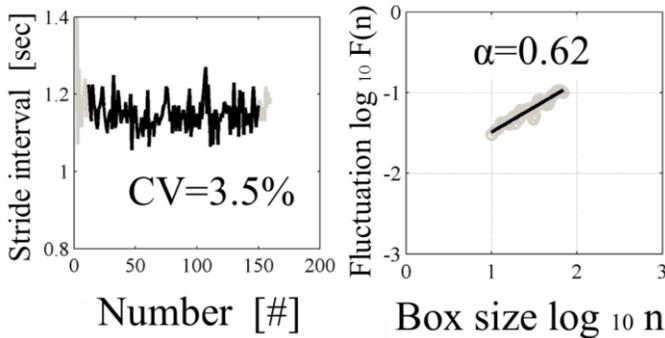


Fig. 1. A sample of stride interval and the fluctuation relative to box size: a PD patient with obvious postural instability (mH-Y 3, age: 76 year of age, male).

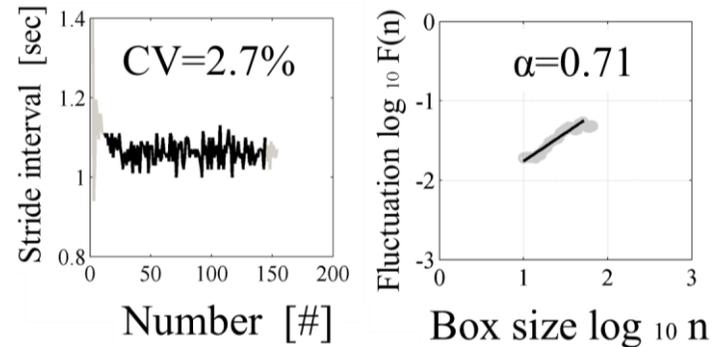


Fig. 3. A sample of stride interval and the fluctuation relative to box size: a PD patient with no postural instability (mH-Y 2, 76 years of age, male).

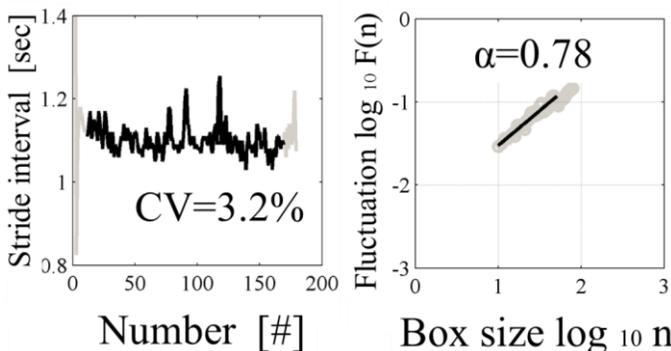


Fig. 2. A sample of stride interval and the fluctuation relative to box size: a PD patient with mild postural instability (mH-Y 2.5, 70 year of age, male).

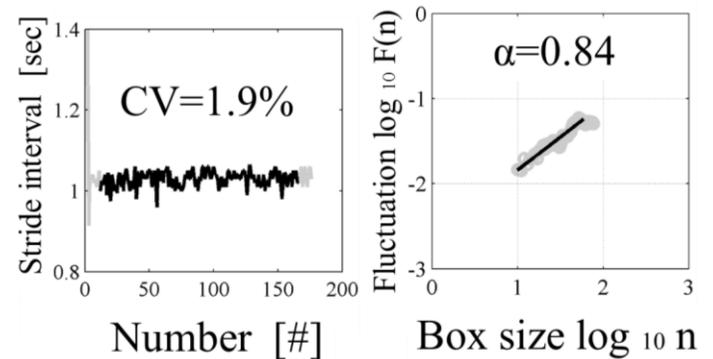


Fig. 4. A sample of stride interval and the fluctuation relative to box size: a Healthy elderly person (71 years of age, male).

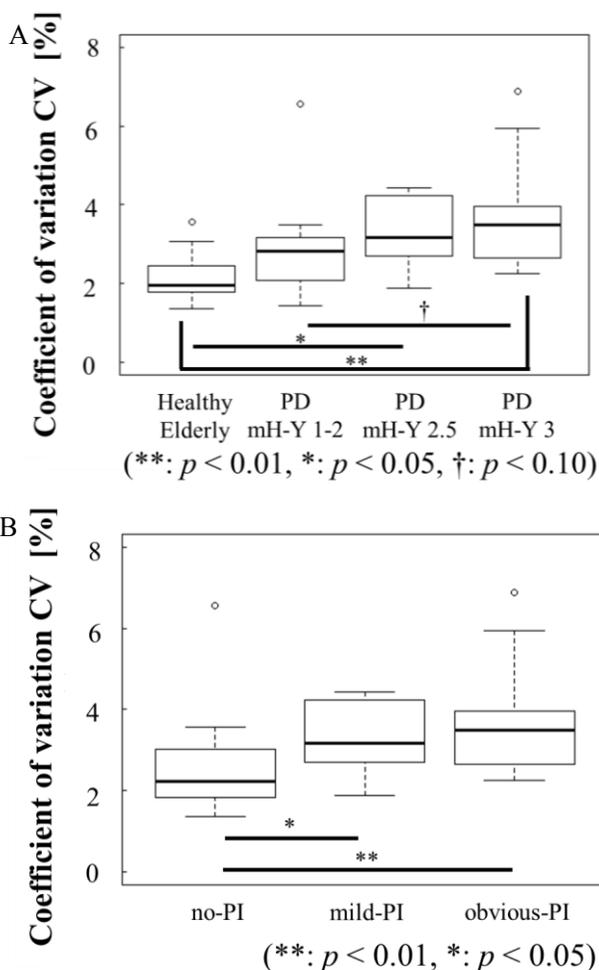


Fig. 5. Distribution of coefficient of variation CV. (A) Multiple comparison between 4 groups. (B) Multiple comparison between 3 groups. The no-PI group consists of healthy elderly people and the PD patients with mH-Y 1-2. The mild-PI consists of the PD patients with mH-Y2.5, and obvious-PI consists of the PD patients with mH-Y3.

Fig. 8 shows the ROC curve of classification between mild-PI and obvious-PI groups. The area under the ROC curve A_C was 0.509 for CV (95% confidence interval was from 0.279 to 0.739, Fig. 8A). The A_C was 0.758 for α (95% confidence interval was from 0.549 to 0.966, Fig. 8B). This result suggests that the α mainly differentiate the presence and absence of PI because the A_C for α is larger than that of CV.

The healthy elderly people and the PD patients with lower mH-Y scores (1, 1.5, or 2) are placed in low CV area. The patients who appear in this area have mild symptoms of PI. By contrast, from the aspect of gait dynamics, the gait rhythm variability of patients in this area is small. The participants with higher mH-Y score (3) are placed in large CV area and low α area. These patients have obvious PI. By contrast, from the aspect of gait dynamics, the gait rhythm variability of patients in this area is large, and the $1/f$ -like fluctuation property of patients in this area is not observed.

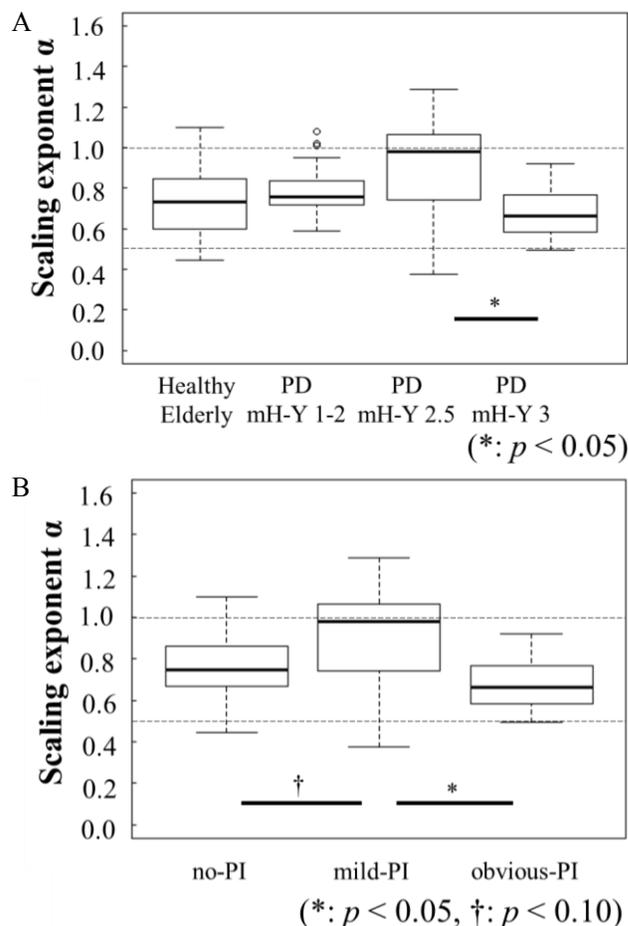


Fig. 6. Distribution of scaling exponent α . (A) Multiple comparison between 4 groups. (B) Multiple comparison between 3 groups.

The patients with a moderate mH-Y score (2.5) are placed in high CV and high α area. These patients have mild PI, and the evaluation of these patients can be difficult. However, this study shows that the two dynamic indicators of the CV and α of gait dynamics can be used to clearly separate patients with mild-PI from other severity levels. From the perspective of gait dynamics, the gait rhythm of the PD patients in this region maintains the $1/f$ -like fluctuation property, but the gait rhythm variability increases. Therefore, CV and α can be used to classify patients according to the presence or absence of PI and the severity of PI, respectively.

From these results, it can be considered how gait dynamics progress during the transition from the healthy state to obvious-PI in PD patients, as follows. The mechanism involved in human walking is a complex dynamic system comprising the interaction between the brain and nervous system, musculoskeletal system, and environment [30]. The characteristics of behaviour generated by such dynamics include the rhythm variability and the $1/f$ -like fluctuation property of rhythm. Our findings suggest that it is possible to use these dynamic indicators to evaluate the progression of movement disorders.

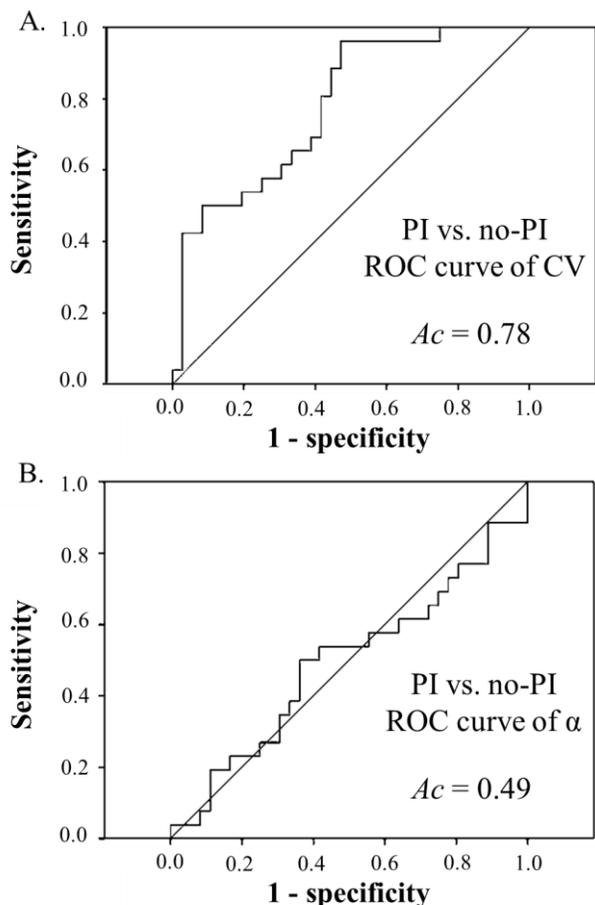


Fig. 7. ROC curve of classification between no-PI and PI. (A) ROC curve of CV. (B) ROC curve of α . The PI group consists of mild-PI and obvious-PI.

In this study, we focused on the presence or absence of PI and the severity of PI as indicators of the progression of motor symptoms. As a speculation, it appears that this evaluation platform based on both the CV and α may be applied to the comprehensive evaluation of rehabilitation in PD patients. For example, the balance between gait rhythm variability and the fluctuation property of gait rhythm may be quantified by following the disease transition using this evaluation platform. Clinician can then use this information to match the rehabilitation to the two aspects of the gait rhythm generation disorder by following the changes in gait dynamics. PD is a progressive neurodegenerative disease, and patients with PD often have gait disorders such as festination. Currently, the estimated number of patients with PD worldwide is about 4 million, and a further increase in this number is estimated with further increases in the aging population [31]. The more PD patients have severe symptoms, the more medicine is expensed. Therefore, effective rehabilitation and further progress of the evaluation of practical aspects of rehabilitation for diseases such as PD comes to be more important.

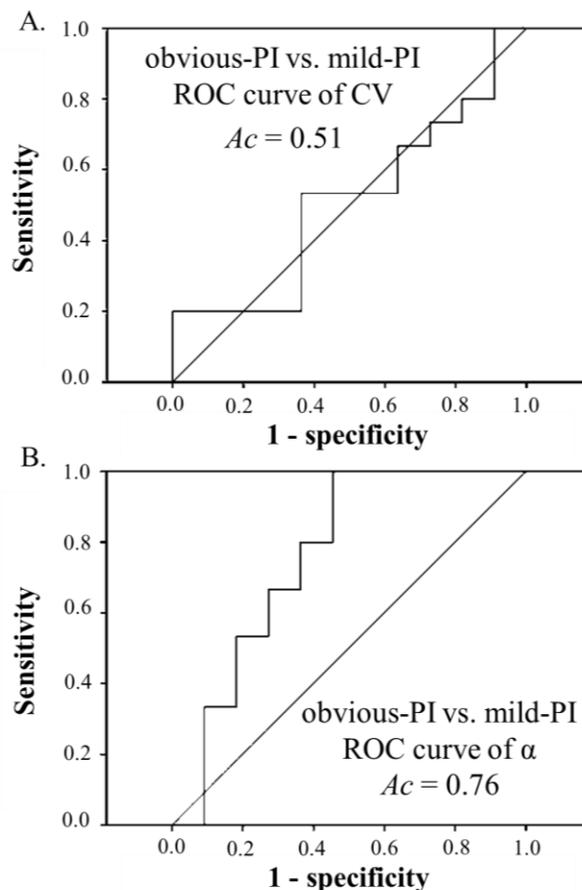


Fig. 8. ROC curve of classification between mild-PI and obvious-PI. (A) ROC curve of CV. (B) ROC curve of α .

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