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Evaluation of severity of Parkinson's disease using stride interval variability

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***Abstract*—Parkinson's disease (PD) is a neurodegenerative disorder by degeneration of dopamine neurons, affecting motor controls related to basal ganglia. Because severe movement disorders such as gait disturbances are often observed, evaluation from gait analysis is useful. From such a background, Coefficient of Variation (CV) and Detrended Fluctuation Analysis (DFA) comes to be used as one of the methods for analyzing the variability of the stride interval in recent years. However classification of the severity of PD by stride interval variability has not been reached to practical use enough. In this paper, in order to clarify the difference in age and the severity of PD patients, variability of stride interval were analyzed by CV and DFA. As a first step, we performed analysis of stride interval in three minutes' walk of 17 PD patients, 13 healthy elderly and 12 healthy young people. Particularly, we divided PD patients based on the Hoehn and Yahr (HY) scale into an HY2 group (n=9) and an HY3 group (n=8) in order to examine the relation to disease severity. Results indicate that CV seemed to distinguish PD patients from healthy people and that DFA fractal exponent tended to be related to the age and the disease severity. From these results, gait analysis using both CV and DFA is suggested to classify participants into healthy young, healthy elderly, HY2 and HY3 groups. For future direction, there are possibilities for seeing the progression from healthy people to PD patients.**

***Index Terms*—Fractal analysis, gait analysis, stride interval variability, Parkinson's disease and Hoehn and Yahr stage.**

I. Introduction

Parkinson's disease (PD) is a progressive neurological disease caused by degeneration of the dopamine neurons. Due to strong depression of motor control and dysfunction of rhythm generation in basal ganglia, movement disorders such as tremor, akinesia, rigidity, and impairment of postural reflex are typical symptoms of PD [1]. When PD progresses, postural instability or gait disturbances appears in many cases. For example, gait festination, wiggle walk (brachybasia) and freezing of gait are observed.

In recent years, objective measurement of human walking comes to be easy. And biological or physiological time series including gait data is thought to be come from nonlinear dynamics, which is composed from complex interactions. From perspective of nonlinear dynamics, variability of gait cycle is attracted. Magnitude of the stride interval variability of PD patients were bigger than that of healthy people [2]. We can calculate the Magnitude of variability by means of standard deviation or Coefficient of variation (CV). In addition, the fractal property of the gait cycle fluctuation has been reduced by specific disease such as PD or Huntington's disease [3]–[6]. Spectral analysis or Detrended Fluctuation Analysis (DFA) are used to see fractal property. By DFA, we can analyze the fractal properties of non-stationary time series data [7], [8]. Based on these background, there is possibility of diagnosis of the severity of PD using CV or DFA.

There are some scales for severity of PD [9], [10]. Particularly, Hoehn and Yahr (HY) scale is widely used in the clinical field as an index of the severity of the PD, because the number of items that we have to examine is few [10]. Correlation with the severity of PD and CV has been suggested [2]. However, there are some exceptions [6], [11]. Therefore, to classify the severity of PD with only CV is difficult. On the other hand, correlation between the fractal property of the gait cycle fluctuation and the severity of PD is also reported [6]. However fractal property of healthy elderly people is likely to be reduced compared to young people [3]–[5]. Therefore, classifying the gait variability into different age or severity of PD groups using only CV or using only DFA has problems.

In this study, we tried to analyze stride interval variability comprehensively using both the DFA and the CV. Our hypothesis is that we can clarify the difference in age or the severity of PD by combining magnitude of stride interval variability and fractal property of stride interval. In order to verify this hypothesis, we divided participants into healthy young group, healthy elderly people, mild PD patients groups and relatively severe PD patients. Then we compared each group in terms of both CV and DFA.

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II. Material and Method

A. Participants

Seventeen patients (11 women, 6 men) with idiopathic Parkinson's disease participated in the experiment. We recruited the patients whose HY stage is 2 or 3, and they did not exhibit freezing or festinating gait [11]. HY stage 2 (HY2) is defined as bilateral disorder without balance impairment, and HY stage 3 (HY3) is defined as bilateral disorder with balance impairment, but physically independent [10]. These participants were divided into two groups. One group HY2 consisted of 9 patients whose HY stage was 2 (mean age = 65.3 years; s.d. = 6.1 years; see Table III) and the other group HY3 consisted of the patients whose HY stage was 3 (mean age = 70.9 years; s.d. = 8.0 years; see Table IV). Mean duration of disease of HY2 was 3.8 years (s.d. = 3.1 years) and that of HY3 was 4.1 years (s.d.=4.5years). All were tested while on dopaminergic medication. Twelve younger healthy controls (11 men, 1 woman, mean age = 25.0 years; s.d. = 3.2 years; see Table I) and thirteen elderly healthy controls (7 men, 6 woman, mean age = 70.1 years; s.d. = 3.1 years; see Table II) also participated. Informed consent was provided and participants were paid for participating. Experimental procedures were approved by the Kanto Central Hospital Ethics Committee.

B. Task and Experimental setup

Participants were instructed to walk at a natural and comfortable pace around a long corridor. The length of the course was 200m. On average, each trial lasted about 3 minutes and contained approximately 320 footsteps. Foot step timing was collected via foot switches (OT-21BP-G, Ojiden, Japan) attached to participants' shoes, was relayed to a laptop (CF-W5, Panasonic, Japan) via radio frequency every 10 ms, and was processed in real time. Two transceivers (S-1019M1F, Smart Sensor Technology, Japan) and a receiver (WM-1019M1F, Smart Sensor Technology, Japan) were used. Fig. 1 shows a scene of the walking experiments and foot switches. The computer algorithm controlling the above experimental system was run on the laptop.

C. Data Analysis

The stride interval time series were analyzed. The time series data are represented by $u(i)$ in the following (1),

$$u(i) = T(i+1) - T(i), \tag{1}$$

where $u(i)$ is the i-th stride interval, and $T(i)$ represents the i-th step timing (i.e. the time to get the right foot on the ground).

Fluctuation magnitude is evaluated by Coefficient of variation (CV). This is standard deviation (s.d.) normalized by the mean value, as in (2).

$$CV = \frac{u_{s.d.}}{u_{ave}} \times 100 \qquad [\%], \tag{2}$$

(a) *A scene of walking experiment*

(b) *Foot switches for detecting heel contact*

Fig. 1. Experimental scene and experimental setup

where u_{ave} is average of stride interval and $u_{s.d.}$ is standard deviation of stride interval.

We quantified the long-range correlations using Detrended Fluctuation Analysis (DFA). This technique offers certain advantages over other methods (e.g., spectral or Hurst analyses) when dealing with non-stationary time series, for it "avoids spurious detection of apparent long-range correlations that are an artifact of non-stationarity" [7] [8].

First the human's stride interval time series $u(i)$ is integrated as in (3),

$$y(k) = \sum_{i=1}^{k} (u(i) - u_{ave}), \tag{3}$$

where u_{ave} is the average of stride interval time series. Then, this integrated time series $y(k)$ is divided into equal boxes of length, n. In each box of length n, a least-squares line is fit to the data, which represents the trend in each box. The fluctuation $F(n)$ for each box is then calculated as the root-mean-square deviation between the integrated time-series and its local trend $y_n(k)$ as in (4).

$$F(n) = \sqrt{\frac{1}{N} \sum_{k=1}^{N} [y(k) - y_n(k)]^2} \tag{4}$$

This calculation is repeated for all possible time scales (box sizes) to provide a relationship between $F(n)$, the average fluctuation as a function of box size, and the box size n (i.e. the number of stride interval in a box which is the size of the window of observation).

TABLE I
DFA FRACTAL EXPONENTS OF HEALTHY YOUNG PARTICIPANTS (M:*Male*, F:*Female*)

Participants	Sex	Age (years)	Stride interval		
			mean (sec)	CV (%)	fractal exponent
1	M	34	1.07	1.28	1.12
2	M	23	1.23	2.71	1.29
3	M	24	1.21	2.18	0.98
4	M	24	1.08	1.49	0.85
5	M	26	1.06	1.84	0.90
6	F	25	1.07	2.02	1.21
7	M	26	1.14	2.12	0.88
8	M	22	1.09	1.70	1.29
9	M	22	1.19	2.26	1.01
10	M	24	1.07	1.86	0.94
11	M	27	1.18	1.70	0.96
12	M	23	1.22	3.56	1.04
mean	-	25.00	1.13	2.02	1.04
s.d.	-	3.25	0.07	0.57	0.15
median	-	24	1.11	2.13	1.00

TABLE II
DFA FRACTAL EXPONENTS OF HEALTHY ELDERLY PARTICIPANTS (M:*Male*, F:*Female*)

Participants	Sex	Age (years)	Stride interval		
			mean (sec)	CV (%)	fractal exponent
1	F	67	1.03	3.12	0.71
2	M	71	1.03	1.67	0.75
3	M	75	0.98	1.47	0.63
4	M	71	1.01	1.61	1.00
5	F	71	1.04	3.41	0.93
6	F	67	1.06	2.11	0.97
7	M	63	1.09	1.38	0.92
8	F	71	0.94	2.22	0.76
9	M	71	0.97	1.40	0.82
10	M	74	1.07	1.90	0.91
11	F	69	1.02	2.11	0.87
12	F	70	1.14	1.91	0.85
13	M	71	1.29	3.47	0.87
mean	-	70.08	1.05	2.14	0.85
s.d.	-	3.09	0.08	0.74	0.11
median	-	71	1.01	1.91	0.87

Typically, the fluctuation, $F(n)$, will increase with larger box sizes. A linear relationship between n and $F(n)$ on a log-log plot indicates self-similar scaling property, in that fluctuations in the smaller boxes are related to the fluctuations in the larger boxes in a power-law relation. The slope of the line $\log_{10} F(n)$ over $\log_{10} n$ is the fractal exponent α, and gives a measure of the randomness of the original stride interval time series. Using DFA, a fractal scaling exponent $\alpha = 0.5$ corresponds to rough and unpredictable white noise; $\alpha = 1.0$ corresponds to 1/f-like noise and long-range correlations [7] [8], [4]. Because no significant difference were observed between fractal exponent of stride interval of right and left, analyses were performed on the stride interval of the right leg.

TABLE III
DFA FRACTAL EXPONENTS OF HY2 PATIENTS (M:*Male*, F:*Female*)

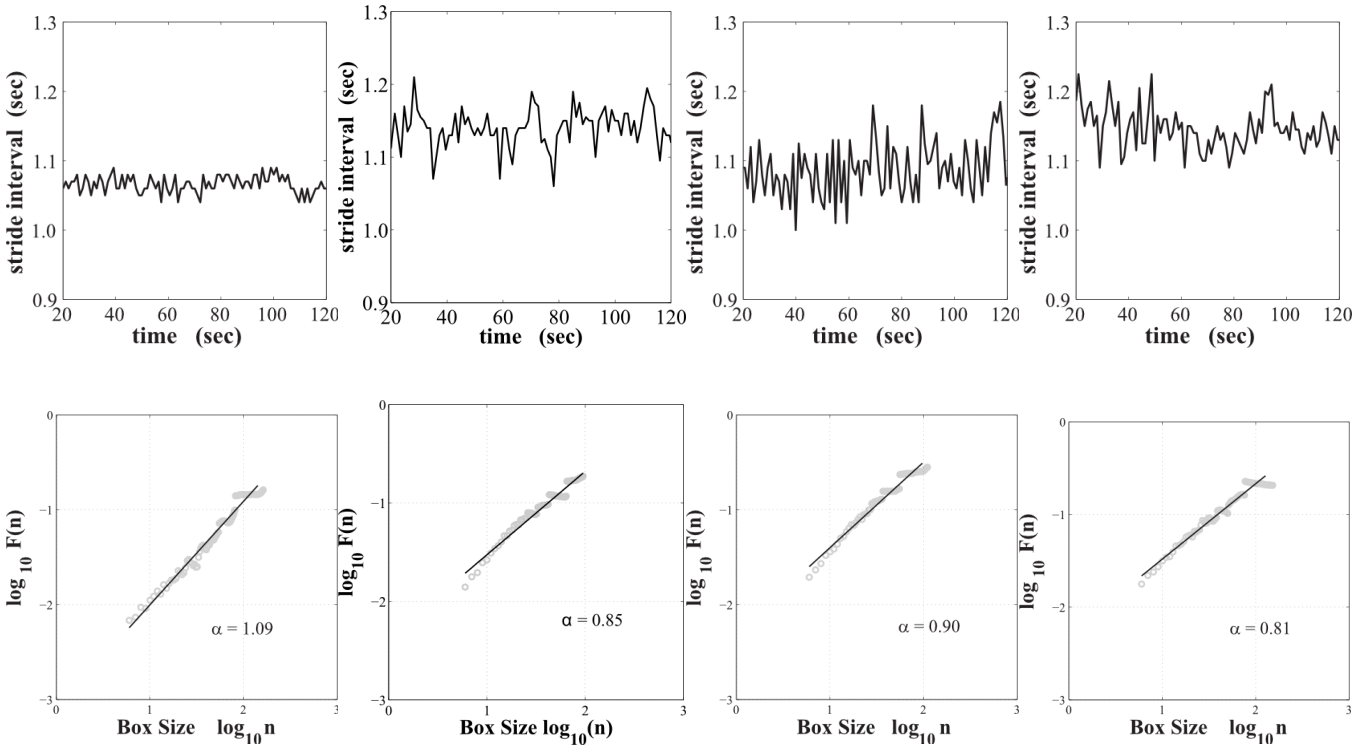
Patients (HY2)	Sex	Age (years)	Disease duration (years)	Stride interval		
				mean (sec)	CV (%)	fractal exponent
1	F	59	0.6	1.01	3.60	0.93
2	F	57	0.5	0.91	1.92	0.91
3	F	76	6	1.01	1.74	0.80
4	F	71	5	0.99	2.22	1.14
5	M	66	0.25	1.00	3.51	0.79
6	F	63	8	1.21	3.35	0.88
7	F	66	2	1.14	3.28	0.99
8	F	61	4	0.95	1.64	0.82
9	F	69	8	1.05	3.35	0.83
mean	-	65.33	3.82	1.03	2.73	0.90
s.d.	-	6.06	3.13	0.09	0.83	0.11
median	-	66	4	1.01	3.28	0.90

III. RESULT AND DISCUSSION

Fig. 2 shows examples of the time series data of stride interval (upper panels) and the DFA plot (lower panels). Fig. 2(a), 2(b), 2(c) and 2(d) correspond to healthy young, healthy elderly, HY2 and HY3 group, respectively. Comparing these four groups, the temporal variation of stride interval of healthy young group and healthy elderly group were shown to be smaller than that of HY2 or HY3. The fractal property of these time series data suggests that the fractal exponent becomes lower in bigger HY stage or older age. Furthermore, all DFA fractal exponents are shown in Table I, II, III and IV. The mean values of each fractal exponent were in the order of disease severity or age. Therefore, the fractal exponent becomes lower in bigger HY stage, suggesting that the higher disease severity means more unpredictable gait.

A. Coefficient of Variation (CV)

Fig. 3 is a box and whisker plot of CV. Using Kruskal-Wallis rank sum test, the significant difference among healthy young, elderly, HY2 and HY3 group was shown ($\chi^2(3) = 10.35$, $p = 0.016$). Furthermore, CV of HY3 ($Mean = 2.88\%$) was significantly higher than that of healthy young participants ($Mean = 2.02\%$), using Holm's method ($p = .044$). Similarly, CV of HY2 ($Mean = 2.73\%$) was also likely to be higher than that of healthy young ($Mean = 2.02\%$) ($p = .092$). In addition, CV of HY3 ($Mean = 2.88\%$) was also likely to be higher than that of healthy elderly ($Mean = 2.14\%$) ($p = .092$). These results suggest that fluctuation amplitude of PD patients' stride interval is higher than that of healthy participants. Here, the result that CV of PD patients were relatively higher than that of healthy participants (young and elderly) is consistent with previous studies [2], [6], [12], [13]. On the other hand, the significant difference of CV between HY2 and HY3 was not observed (using Holm method, $p = .64$). Mean of CV of HY3 ($Mean = 2.88\%$) was similar to that of HY2 ($Mean = 2.73\%$), but median of CV of HY3 ($Median = 2.91\%$) was likely to lower than that of HY2($Median = 3.28\%$). Median



(a) ***Healthy young participant*** **(b)** ***Healthy elderly participant*** **(c)** ***Patient of HY2*** **(d)** ***Patient of HY3***

Fig. 2. Samples of time series data of stride interval (figures above) and DFA fractal exponents (figures below). Stride interval variability of healthy young people tends to be smaller than that of elderly people and PD patients. And the fractal exponent represents the property of stride interval time series structure. Fractal exponent of healthy young people is likely to be higher than that of elderly people and PD patients.

TABLE IV
DFA FRACTAL EXPONENTS OF HY3 PATIENTS (M:*Male*, F:*Female*)

Patients (HY2)	Sex	Age (years)	Disease duration (years)	Stride interval mean (sec)	CV (%)	fractal exponent
1	M	69	14	0.97	2.72	0.85
2	F	74	6	1.05	2.54	0.76
3	M	78	4	0.99	2.42	0.90
4	M	53	4	0.99	2.73	1.02
5	F	69	1	1.07	3.29	0.80
6	M	76	0.25	1.15	2.69	0.77
7	F	77	3.00	1.14	3.74	0.72
8	M	71	0.25	0.95	2.90	0.89
mean	-	70.88	4.06	1.04	2.88	0.84
s.d.	-	8.03	4.51	0.08	0.43	0.10
median	-	72.5	3.5	1.02	2.91	0.80

of CV of healthy young participants ($Median = 2.13\%$) was lower than that of PD patients' groups, and that of healthy elderly participants ($Median = 1.91\%$) was the same as young people. Therefore CV might detect neurodegenerative disease.

From these results, increase in CV of gait cycle seems to be associated with PD. These results suggest that the size of gait cycle fluctuation have potential to diagnose the PD disease, by only measuring some gait cycle information.

B. Detrended Fluctuation Analysis (DFA)

Fig. 4 is a box and whisker plot of DFA fractal exponents. Using Kruskal-Wallis test, the significant difference among healthy, HY2 and HY3 group was shown ($\chi^2(3) = 12.78$, $p = 0.005$). Furthermore, the fractal exponent of HY3 ($Mean = .84$) was significantly lower than that of healthy young participants ($Mean = 1.04$), using Holm's method ($p = .004$). Similarly, the fractal exponent of HY2 ($Mean = .90$) was also lower than that of healthy young ($Mean = 1.04$) ($p = .05$). These results suggest that randomness of PD patients' stride interval is higher than that of healthy participants. The significant difference of fractal exponent between HY2 and HY3 was not observed (using Holm method, $p = .35$), but mean of fractal exponent of HY3 ($Mean = .84$) is likely to be lower than that of HY2 ($Mean = .90$). Here, similar tendency were confirmed in previous studies [5], [14].Moreover, the median of fractal exponent of HY2 ($Median = .90$) was higher than that of HY3 ($Median = .80$). Median of fractal exponent of healthy participants ($Median = 1.00$) was the highest, and the

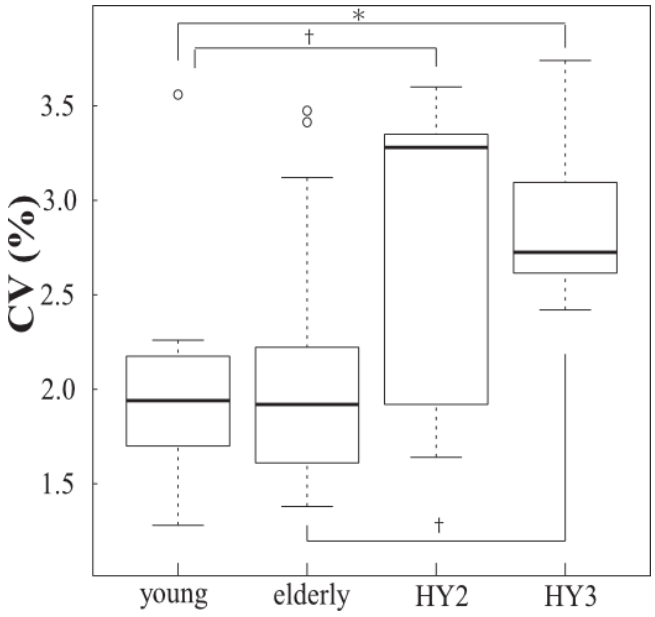


Fig. 3. Comparison of CV of stride interval among healthy younger, healthy elderly, HY2 and HY3 group (*: $p < .05$, †: $p < .10$). Significant difference between healthy young group and HY3 group is observed. And CV of HY2 tends to be higher than that of young people. Furthermore, CV of HY3 tends to be higher than that of healthy elderly people.

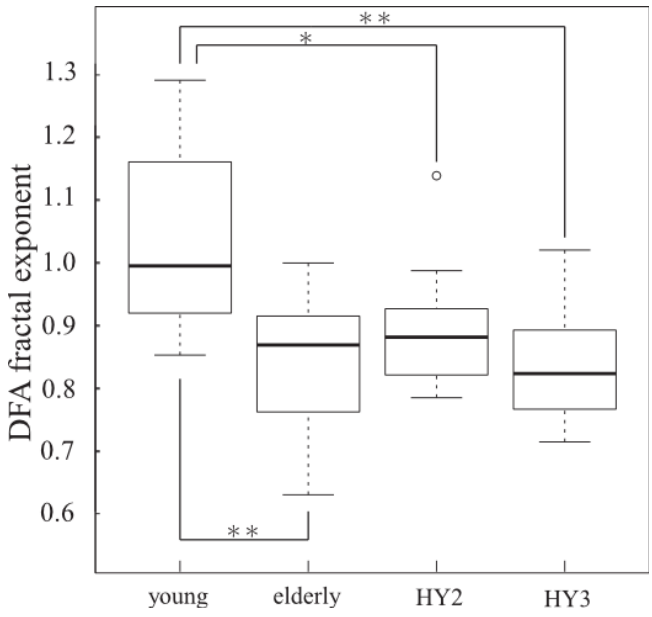


Fig. 4. Comparison of DFA fractal exponent of stride interval among healthy younger, elder, HY2 and HY3 group (**: $p < .01$, *: $p < .05$). Fractal exponent of healthy young people seems to be higher than that of healthy elderly people and PD patients.

magnitude relation in median was consistent to the magnitude relation in mean.

However, the fractal exponent of healthy elderly ($Mean = .85$) was significantly lower than that of healthy young participants ($Mean = 1.04$) ($p = .002$). And median of fractal exponent of healthy elderly participants ($Median = .87$) was the same level as that of HY2. It is suggested that age and neurodegenerative disease might related to fractal property of stride interval. In previous study, relationship between complexity of power spectrum of stride interval and disease severity of PD were reported [6]. In this paper, positive correlation between spectral exponent β and Webster scale. β is determined by culculating the negative slope of the line relating the squared Fourier amplitude$[\log S(f)]$ to frequency$[\log f]$. β is related to DFA fractal exponent α by formula $\beta = 2\alpha - 1$ [15]. However spectral analysis might not be able to avoid spurious detection of long-range correlations as DFA [8]. And they used Webster scale as severity of PD. The range of Webster scale is 0-30, and the score of Webster scale is high when impairment is severe. The Webster includes one disability (self-care) and nine impairment items [9]. There is possibility that the relationship of Webster scale and HY scale is not in direct proportion.

From these results, DFA fractal exponent of gait cycle seems to be associated with HY scale or age compared with CV of gait cycle. These results suggest that the dynamics of gait cycle fluctuation have potential to diagnose the PD disease severity, but the healthy elderly people are likely to be the same level as PD patients.

C. Feature Space Configured with CV and DFA

Based on the observation of CV and DFA, we investigated the relationship between CV and DFA.

Fig. 5 plots the gait patterns associated with the healthy young people, healthy elderly people, PD patients in HY2 group and PD patients in HY3 group, in the feature space that is configured with CV and DFA. It can be observed that patterns healthy people's mainly congregated in the area where $CV < 2.5\%$, whereas most of PD patient's patterns were in the area where $CV > 2.0\%$. Almost all healthy young people's patterns were in the area where $DFA > .85$, in contrast to elderly people's patterns, which mostly were in the area where $DFA < .90$. In PD patient's groups, HY2 patterns were in the area where $DFA > .80$, but HY3 patterns were in the area where $DFA < .85$.

For future direction, to apply the cluster analysis is considered, to distinguish these four groups. For details, to correct more stride interval time series set of participants and to apply canonical discriminant method or extended Support Vector Machine (SVM) is considered.

IV. Conclusion

We evaluated variability of stride interval in a three-minute walk performed by healthy young and elderly participants and PD patients whose HY scale were 2 and 3, using CV and DFA. From CV, the possibility of detecting PD were

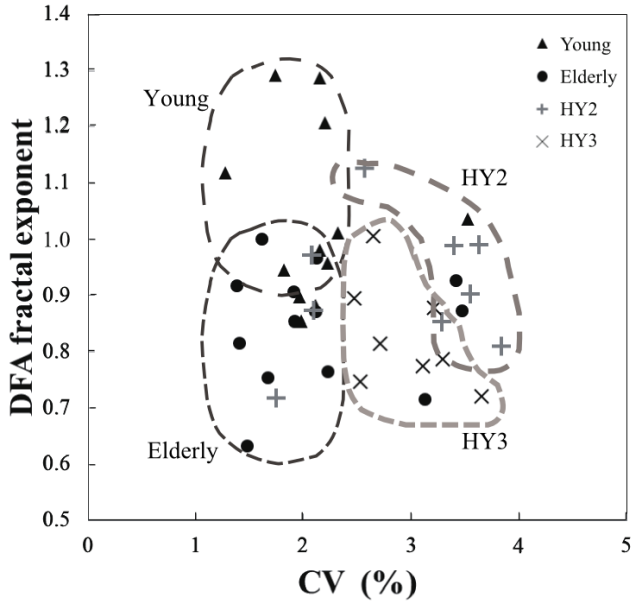


Fig. 5. Scatter plot of the gait patterns of the healthy young people, marked as *triangles*, that of the healthy elderly people, marked as *circle*, that of the HY2 group, marked as $+$, and that of HY3 group, marked as $\times$, in the 2-D feature space that is configured with CV and DFA fractal exponent of stride interval. CV of healthy people including both young and elderly people tends to be lower than CV of PD patients including both HY2 and HY3. In PD groups, HY2's fractal exponent seems to be higher than HY3's fractal exponent.

suggested. But the severity of PD were not detected. On the other hand, DFA seemed to reflect age or severity of PD. From these results, the possibility of clustering 4 group were speculated.

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