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Improving Gait Performance in Parkinson's Disease by Interpersonal Synchrony-based Dynamic Stabilization

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***Abstract* - Previously, research on gait control has mainly focused on interpersonal synchrony and locomotor control. However their intersection, the interpersonal synchronization of stepping rhythms which is widely observed in our daily life, remains relatively unexplored, despite being a common phenomenon that has considerable rehabilitation potential. Therefore, from the perspective of mutual entrainment of gait rhythms, we have constructed an interpersonal synchrony emulation system between a human subject and a biped virtual robot that generates pacing signal cues using nonlinear oscillators. This system synchronizes the stride interval times of a human and the robot in a cross-feedback manner; by presenting auditory stimulation that indicates the timing of the partner's foot contacting the ground. Here, we evaluated the effectiveness of the system in gait stabilization of twenty-one Parkinson's disease (PD) patients, who previously displayed disturbances in rhythm formation and festinating gait (accelerating steps). The results showed that the festinating gait, as measured as stride time reduction rate, significantly stabilized and accelerated less with the system compared to unassisted walking. Additionally, significant carry-over effects were observed. After termination of the auditory stimulation, the gait remained stabilized. Our previous pilot study suggested that the gait of PD patients was dynamically stabilized by applying the inter personal synchrony process between the timing of human's gait and of external auditory cues. In this paper, we showed significant improvement for the festinating gait in twenty one PD patients.**

Index Terms - Parkinson's disease (PD), Festinating gait, Stride interval time, synchronization, Interpersonal synchrony emulation system.

I. INTRODUCTION

Parkinson's disease (PD) is one of the neurodegenerative diseases affecting dopaminergic and non-dopaminergic neurons. Degeneration of dopaminergic neurons in the substantia nigra causes reduced level of dopamine in the basal ganglia, resulting in dysfunction of the basal ganglia and their associated networks. PD patients have difficulty starting, stopping, or sustaining movement. Rhythm generation and the timing of repeating movements are also disturbed in PD[1], [2]. These disturbances are related to the disorders of the basal ganglia and the projection path from the brainstem to the spinal cord[3]–[6]. For example, PD scrambles gait rhythm, stride interval time, and gait pattern of the patient[7]–[9]. Because PD causes the movement disorder associated with the patient's daily life like as gait function, PD is treated with not only special medical treatments that are, for instance, dopaminergic medication and deep brain stimulation but also physical trainings like as behavioural therapy and rehabilitation. Moreover, the treatment methods can be applied to the various severity levels of PD patients because it is the cure methods without medicament or surgery. Therefore, it is important to improve the movement function disorder of PD patients effectively[13].

Focusing on the studies of human movement, many researchers make an effort to clarify the mechanisms of human's movements from view point of the dynamic aspect. For instance, there are passive gait[35], cooperative gait[36], and gait simulation based on the hypothesis of the global entrainment among a cranial nerves system, a musculoskeletal system, and an environment[37]. Additionally, the gait evaluation methods using dynamic properties are being developed. A previous study reported that the stride interval time of healthy persons showed 1/f fluctuation characteristic, and the stride interval time of healthy persons, on the other hand, showed random fluctuation characteristic[7],[34]. The evidence indicated that it was significant to evaluate the dynamic aspects of gait disorders.

Based on the dynamics of cooperative gait between humans, our research group developed an interpersonal synchrony emulation system for supporting patients with gait disorders[14],[19]-[22]. The system created interaction between patient's gait timing and an auditory rhythmic beep and these two rhythms were synchronized. A previous study compared this gait support system to another one method having no interaction with patients, which was provided fixed-tempo rhythmic auditory stimulation[16]. The results suggested that the interpersonal synchrony process was effective to improve gait dynamics of PD patients with motor symptoms.

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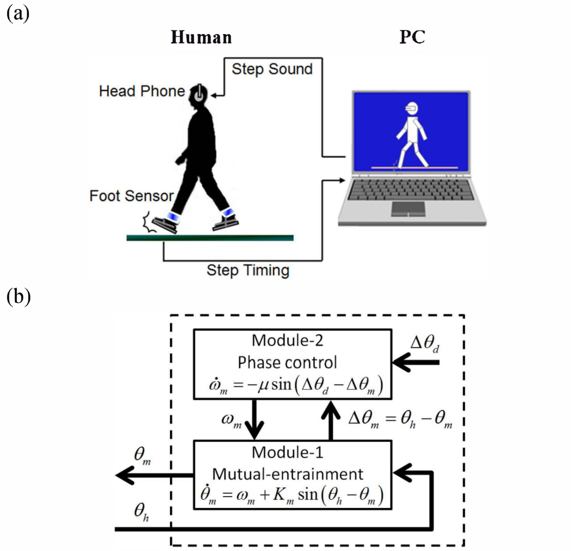

Fig.1 An outline of an experimental system. (a) Depiction of an interpersonal synchrony emulation system. (b) The computer's timing system used nonlinear oscillators and was organized hierarchically in two modules. Module 1 mutually entrained the gait frequencies of the computer and the participant. Module 2 adjusted the relative phase difference between the computer's auditory onset and the participant's step contact to a target phase difference.

From this background, we hypothesized that an interpersonal synchrony process has potential to improve gait performances disturbed by neurodegenerative disease, such as PD. To investigate the hypothesis, we focused on the festinating gait that is one of the particular PD symptoms. The festinating gait is an alteration in gait pattern characterized by a quickening and shortening of normal strides. Because the gait speed accelerates involuntarily, the symptom shows dynamically destabilized gait. We expect that the interpersonal synchrony emulation system has potential for mitigating the festinating gait by dynamically stabilizing gait. Therefore, the purpose of this study is to investigate the effectiveness on improving the PD patients' festinating gait to apply the function which the interpersonal synchrony emulation system generates of dynamically stabilizing gait.

Previously, we reported a pilot study using our interpersonal synchrony system for the festinatimg gait of the small number of PD patients[33]. The study suggested dynamical improvement of the gait. In this study, we applied the system for many PD patients to verify the effectiveness.

II. Materials and Methods

A. Experimental System

An outline of our experimental system is illustrated in Figure 1. Figure 1 (a) shows an interpersonal synchrony emulation system, included a cross-feedback process, whereby the biped virtual robot's timing of ground contact was given as an input signal to the subject, while the robot was provided with the subject's heel strike timing. The rhythm generator model in the robot had a hierarchical structure, as shown in

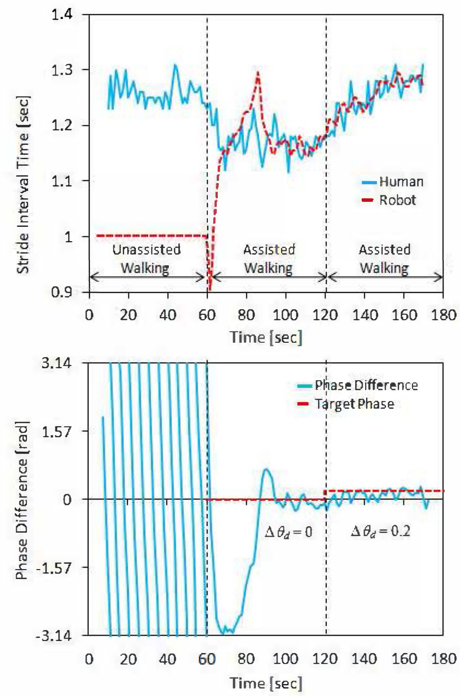

Fig.2 An example of time-course changes in the stride time and phase difference of a healthy subject, achieved by the interpersonal synchrony emulation system.

Figure 1 (b). Module 1 was responsible for mutual entrainment between the human stepping rhythms and the virtual robot's gait pattern, and Module 2 controlled the phase difference (shift in timing) between the sensory input (the subject's foot contact with the ground) and the motor output (production of robot footstep sound stimuli to the subject) to a targeted value. More specifically, Module 1 involved the use of a phase oscillator[18], which has been shown to be effective for simulating CPGs[23], and Module 2 implemented feedback control for the difference (phase difference) in the timing of input and output of Module 1.

The relevance of this model is supported by the finding that human locomotor behaviors were hierarchically governed by spinal CPG-dependent rhythm modulation and by cerebellar and brainstem feedback control systems[25], [26]. It was further supported by the dual process model[27] and our experimental results in synchronization tapping[28], [29].

Figure 2 shows an example of time-course changes in the stride interval time and phase difference achieved by this system. First, a healthy subject was instructed to walk down a straight corridor. The subject walked without exposure to the tones in the first 60 seconds, followed by another 60 seconds during which the cross-feedback of the walking signals was conducted with a targeted phase difference of 0 rad, followed by another 60 seconds interval during which the gaits were synchronized with the targeted phase shift of 0.2 rad (a slight delay in presentation of the auditory stimuli relative to the time point of the subject's heel strike).

During the unassisted walking condition (0-60 sec), the subject and the virtual robot walked at different stride interval time. During the assisted walking condition (60-120 sec), their stride interval time drew closer to each other via mutual entrainment, with the phase difference stably converging to the target value of 0 rad. During the condition when the target phase difference was set to 0.2 rad (120-180 sec), the subjects' walking slowed down; their stride interval times increased automatically without being aware of the phase difference.

This phenomenon is thought to be useful to stabilize festinating gait of PD. These results showed that the stride interval time could be manipulated by controlling the target phase difference in mutual synchrony.

B. *Subjects*

Twenty one normal-hearing and non-demented patients with PD were recruited. There were eight men and thirteen women. The subjects' average age was 75.3±7.62 years. Average disease duration was 5.71±3.65 years. The modified Hoehn and Yahr stage (modified HY) was 2.83±0.29; part 2 of Unified Parkinson's Disease Rating Scale (UPDRS) was 9.76±4.52; and part 3 of UPDRS was 22.4±6.77 (Mean±S.D.). Table I shows details of the subjects' characteristics. Here, Modified HY and UPDRS (part 2 and part 3) are the representative severity indicators of PD.

The subjects exhibited festinating gait during a prescreening interview with the physician, and were receiving medication for treatment of PD. Their modified HY (range: 0-5) were 2 or 3, indicating independent ambulation. All subjects provided written informed consent before participation.

C. *Task*

Subjects were instructed to walk along the path in the corridor; at predefined intervals, they were exposed to rhythmic tones presented by the interpersonal synchrony emulation system, which they were carrying. The corridor was flat and straight, with the ambient temperature and light intensity adjusted to the comfort of the subjects. The walking distance was set at 80 m. Subjects were instructed to make a pretest walk for 80 m to familiarize with the system and environment, without presentation of rhythmic sound stimuli (unassisted condition). Then, after a 5 minutes rest, they were given the following task. One round of the 80 m walking task included a sequence of unassisted walk, synchronized walk (with presentation of step-guiding tones), and unassisted walk. This study was approved by the Kanto Central Hospital Ethics Committee.

D. *Experimental Setup*

In specific terms, the timing of the virtual robot's ground contact was presented to the subject as an auditory stimulus (combination of F5 and C5 notes, 10 ms duration) via headphone (HP-RX500, Victor, Japan). The subject's foot-ground contact was detected by a pressure sensor (OT-21BPG, Ojiden, Japan) fixed underneath the shoe. The detected signals were transmitted to the gait simulation software program running on a portable PC (CF-W5, Panasonic, Japan). The measurement, calculation, and recording of the heel strike timing were performed in real time at 10 ms intervals. The interpersonal synchrony emulation system was intended to achieve interpersonal gait synchrony between the subject and the biped virtual robot.

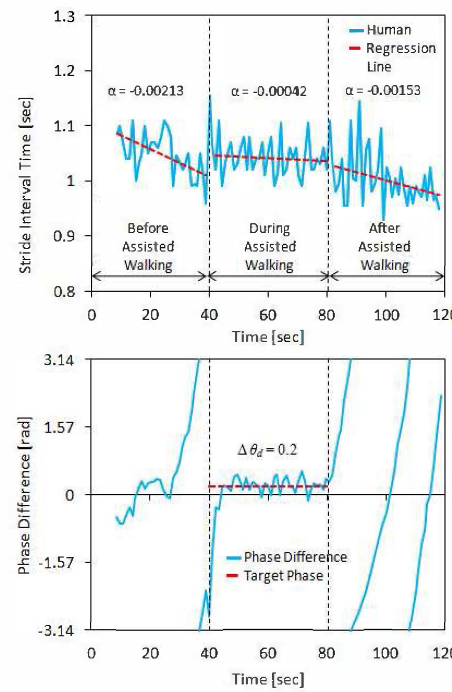

Fig.3 An example of a result of the time-course changes in stride time and phase difference of the subject No. 21, achieved by the interpersonal synchrony emulation system. This result obtained in the before assisted walking, the assisted walking and the after assisted walking are compared. Every these three sections, each gradient of the regression line α was calculated. The festinating gait was defined as α < -0.001.

E. *Analysis of stride interval time and phase difference*

In order to evaluate the festinating gait, we focused on human stride interval time. The human stride interval time, T_h, is shown in equation (1), in which T_h is defined as the difference between the ground-contact timing $t_h(i+1)$ for the $(i+1)$-*th* step and $t_h(i)$ for the *i-th* step of the same leg. Equation (1) is applicable to the virtual robot as well, by replacing the suffix *h* (for human) with *m* (for robot).

$$T_h(i) = t_h(i+1) - t_h(i) \qquad (1)$$

Here, the subject's phase difference $\Delta\theta_h(i)$ for the *i-th* step is determined based on the difference between $t_h(i)$ (i.e., the time at which the subject's foot makes the *i-th* ground contact) and $t_m(i)$ (i.e., the time at which the auditory stimulus is presented in response to the *i-th* ground contact), as shown in equation (2). In this equation, $t_m(i)$, which is defined as the time at which the virtual robot makes the *i-th* ground contact, provides the time at which the auditory stimulus is provided to the subject, because these timings are identical. This equation may also be understood to indicate the phase difference between the times at which the subject and the virtual robot make the *i-th* ground contact.

$$\Delta\theta_h(i) = \left(t_h(i) - t_m(i)\right)\frac{2\pi}{T_h(i)} \qquad (2)$$

F. Quantification of festinating gait

Festinating gait refers to a clinical manifestation in which both the stride interval times and the stride length decrease over time during walking. In this study, we paid attention to stride interval time decrease and conducted least-squares linear regression analysis to estimate the temporal change in stride interval time; the gradient of the regression line, α, was used to evaluate the stride time reduction rate. The gradient, α, which is calculated by equation (3), relates to decrease in stride time per second. In this analysis, based on preliminary analysis results (Mean±S.D. of α: 0.00005±0.00012) obtained from 10 healthy subjects (9 males and 1 females, mean age: 24.3 years) under the same experimental conditions, we defined festinating gait as α < -0.001.

$$\alpha = \frac{n\sum_{i=1}^{n} t_h(i)T_h(i) - \sum_{i=1}^{n} t_h(i)\sum_{i=1}^{n} T_h(i)}{n\sum_{i=1}^{n} t_h^{\,2}(i) - \left(\sum_{i=1}^{n} t_h(i)\right)^2} \qquad (3)$$

III. Results and Discussion

Figure 3 provides an example result of the time-course changes in stride interval time and phase difference in subject No.21 equipped with the system. In the first 40 second period, the subjects walked unassisted (i.e., before assisted walking). The downward-sloping curve demonstrates the characteristic aspect of festinating gait, with the gait gradually accelerating.

However, after the initiation of the auditory stimuli with the targeted phase difference of 0.2 rad (i.e., during assisted walking), the subject's festinating gait decreased, indicating dynamic stabilization of the walking rhythm. The observed phase difference values centered around the target phase difference, suggesting that the walking rhythms of the subject and the virtual robot were stably synchronized with a slight delay in presentation of the auditory stimuli relative to the timing of the subject's heel strike. Stride time reduction rate (decrease in stride time per second) was newly defined as the gradient, , of the regression line for the graph of stride time versus elapsed time. When α was calculated for the subject, we noted a marked improvement (81.0%) from before assisted walking (α = -0.00213) to assisted walking (α = -0.00042). In addition, the mean phase difference for the 40 seconds of assisted walking is near the target phase difference.

After termination of the auditory stimuli (i.e., after assisted walking), the festinating gait returned. However, the stride time reduction rate after assisted walking became closer to zero than before assisted walking. When α was calculated, we noted a marked improvement (28.2%) between the before assisted walking (α = -0.00213) and the after assisted walking (α = -0.00153).

Table I provides *α* values (stride time reduction rate) for all twenty-one subjects and the results of the statistical analysis are graphically summarized in Figure 4. Based on preliminary analysis results (mean ± SD of *α*: 0.00005 ± 0.00012) obtained from 10 normal healthy subjects (9 males and 1 females, mean age: 24.3 years) under the same experimental conditions, we defined festinating gait as *α* < -0.001. Nineteen of the 21 subjects showed a festinating gait (with the exceptions of subject Nos. 13 and 17); and were chosen as the study cohort, because this subgroup demonstrated a significant difference in *α* relative to the normal subjects that participated in this study [two-tailed t-test, $p < 0.001$, $t(27) = 7.49$].

TABLE I
CHARACTERISTICS AND EXPERIMENTAL RESULTS OF SUBJECTS WITH PARKINSON'S DISEASES

Subject No.	Age	Sex	Disease Duration	Modified HY	UPDRS		Stride Time Reduction Rate ($\times 10^{-3}$)		
					Part2	Part3	Before Assisted Walking	Assisted Walking	After Assisted Walking
1	68	Male	13	3	6	29	-1.38	0.13	-
2	75	Male	12	3	15	31	-4.00	-1.41	-
3	75	Male	6	3	10	22	-2.46	-2.69	0.02
4	83	Female	12	3	10	26	-1.09	-2.25	-1.02
5	78	Female	9	3	12	29	-3.44	-2.76	-1.34
6	76	Female	9	3	15	37	-2.12	-0.20	-1.00
7	82	Female	7	3	14	14	-4.07	0.11	-
8	80	Female	7.5	3	13	24	-2.27	-3.31	-0.15
9	73	Female	6.5	2.5	5	22	-2.76	1.17	-
10	76	Male	0.9	3	12	23	-1.35	1.39	0.10
11	72	Female	6	3	10	28	-4.55	-1.27	0.85
12	52	Female	4	2	6	13	-2.13	0.43	-
*13	72	Female	2	2.5	11	15	-0.86	-	-
14	79	Female	3	2.5	3	21	-4.03	-0.12	-
15	75	Male	5	2.5	6	16	-5.34	-1.13	-
16	77	Male	1	2.5	5	21	-1.79	-0.01	-
*17	67	Female	5	3	5	9	0.32	-	-
18	72	Female	3	3	8	19	-2.55	0.01	-
19	79	Female	3	3	8	22	-3.28	-0.52	-1.14
20	79	Male	3	3	9	21	-2.02	-0.16	0.56
21	92	Male	2	3	22	29	-2.13	-0.42	-1.53

*Subjects who did not show festinating gait

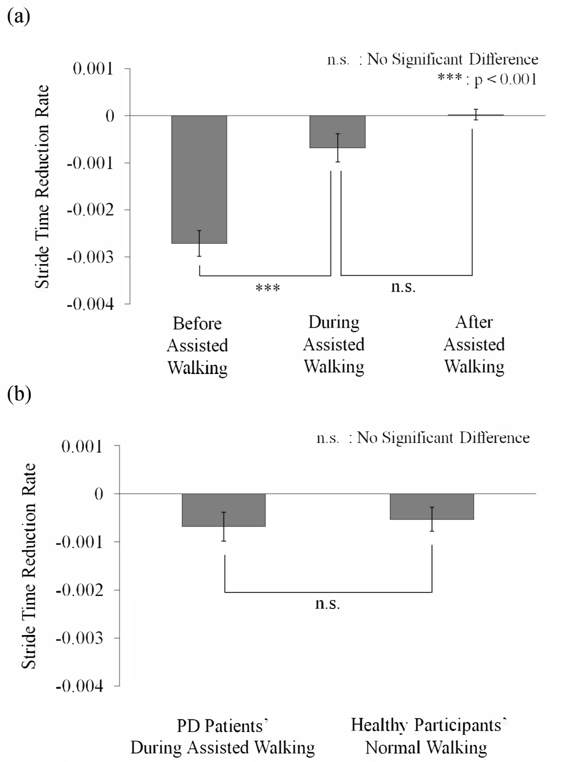

Fig.4 Statistical analysis of stride time reduction rate. (a) Results obtained in the before assisted walk, assisted walk and healthy walk are compared. (b) Results obtained in the assisted walk, after assisted walk and healthy walk are compared. Gradient values for the regression lines representing time-dependent reduction in stride interval time. Error bars indicate standard deviations.

The experimental cohort demonstrated less festinating gait in the assisted walk (mean α = -0.00068) compared to the before assisted walk (mean α = -0.00278), as indicated by a significant difference in α [two-tailed paired t-test, $p < 0.001$, $t(18) = 5.65$]. Sixteen subjects of this study cohort (N=19) showed an improvement (with the exceptions of subject Nos. 3, 4 and 8). Additionally, the α value for the assisted walk of these PD patients was not significantly different from that of the normal healthy group of subjects (mean α = 0.00005) [two-tailed t-test, $p > 0.05$, $t(27) = 1.77$]. As shown in Figure 4, these results indicate a remarkable alleviation of festinating gait for the study cohort (N = 19) during the assisted walk period, with a mean improvement of 75.3% for the stride time reduction rate. This improvement provides clear evidence for the effectiveness of the interpersonal synchrony emulation system in improving the stability of festinating gait in PD patients.

Furthermore, the α value was calculated in the period following termination of the auditory stimuli in the PD patients in which the duration of the after assisted walk was more than 20 sec. As shown in Table 1, the α value of the after assisted walk was obtained from 10 subjects of the study cohort (N=19). The results show that the mean α value of the after assisted walk (mean α = -0.00046) was not significantly different from that of the assisted walk (mean α = -0.00068) [two-tailed t-test, $p > 0.05$, $t(27) = 0.48$]. These results indicate a remarkable carry-over effect of stabilization in the after assisted walk period as shown in Figure 4, with a mean improvement of 83.5% for the stride time reduction rate. In particular, the α value of the after assisted walk was much larger than that during the assisted walk. Such an over-enhanced carry-over effects of diminished stride time reduction rate was observed in 6 subjects (subject Nos. 3, 4, 5, 8, 11 and 20) of the above 10 subjects.

Previous research has proposed the use of fixed-tempo rhythmic auditory stimulation and floor stripe patterns in gait training for PD patients. However, these studies paid no attention to the dynamic stability of the earlier synchronization between the rhythmic stimulation and the gait rhythm. Our investigation is a prime demonstration of the potential applicability of the interpersonal synchrony process for dynamic stabilization of gait performance.

By focusing on festinating gait in PD patients, this study evaluated the effects of our interpersonal synchrony emulation system on rhythm formation disturbances resulting from the neurodegenerative diseases in basal ganglia. The results showed that the interpersonal synchrony process was quite effective for dynamically stabilizing the festinating gait. In addition, the results indicated the presence of carry-over effects of the gait stabilization, thereby suggesting a possible application for reinforcing the time series processing in the basal ganglia[30]. The evidence enhanced the previous study[33], which showed interpersonal synchrony process restored stride interval time fluctuation dynamically compared to healthy person's gait, and indicated the system is effectiveness for improving clinically important gait disturbances. Follow-up research is warranted to clarify how this interpersonal synchrony emulation system contributes to stabilization and improvement of human gait and other various rhythmic movements.

IV. Conclusion

In this study, we applied an interpersonal synchrony emulation system to Parkinson's disease patients with festinating gait. We tested for improvements in festinating gait and analyzed the stride time reduction rate and phase difference of the subjects. Results indicated that gait significantly stabilized and accelerated less when assisted by the system compared to unassisted walking. Moreover, carry-over effects were significantly observed. After termination of the interactive auditory stimulation assistance, the gait remained stabilized. Festinating gait often causes falling in PD patients. The application of this kind system has a potential to prevent falling in the daily life. Further study for the prevention of falling and carry-over effect will be planned. The results warrant future clinical application of this interpersonal synchrony emulation system for patients with a variety of movement disorders.

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