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Co-creative Rehabilitation: Effect of Rhythmic Auditory Stimulus on Gait Cycle Fluctuation in Parkinson's Disease Patients

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Abstract: The purpose of this study was to investigate the influence of interactive and non-interactive rhythmic auditory stimulation (RAS) on gait cycle fluctuation in Parkinson’s disease (PD) patients. WalkMate and fixed-tempo RAS were used as interactive and non-interactive RASs that the participants walked with. In the results, 1/f structure of the fluctuation was restored and carry-over effect was shown by interactive RAS, compared to non-interactive RAS. The experiment demonstrated that interaction is important in the (re)emergence of 1/f structure in human behavior and that interactive RAS is a promising therapeutic tool for improving gait of PD patients.

Keywords: Parkinson’s Disease; Gait; Stride interval time; Rhythm; 1/f structure; Interaction; Entrainment; WalkMate

1. INTRODUCTION

Parkinson’s disease (PD) is one of the neurodegenerative diseases in substantia nigra. This disease decreases dopamine in the basal ganglia, and causes dysfunction, in and around the basal ganglia. Parkinson’s disease patients have difficulty starting, stopping, or sustaining movement. It is difficult for a PD patient to generate the rhythm and the timing of repetitive movements [1,2]. These problems are thought to relate to the disorders of the basal ganglia and the projection path from the brainstem to the spinal cord [3-6]. For example, influence of PD such as a lack of balance and strength contribute to an unsteady, stooped gait. [7-9].

PD is treated with not only dopaminergic medication and deep brain stimulation, but also behavioral therapy. Behavioral therapy is one of the rehabilitation methods. This is applied to the PD patients of various levels because this is the cure without medication or surgery. In behavioral therapy for gait disorder, there are two main methods. One is fixed-tempo rhythmic auditory stimulation (RAS). The other is WalkMate, an interactive rhythmic auditory stimulation system.

Fixed-tempo RAS uses rhythmic sounds presented at a fixed tempo. In fixed-tempo RAS, the gait disorder is improved by the patient trying to synchronize with the rhythmic sounds. Previous studies showed that rhythmic sounds with fixed tempo or music were effective in behavioral therapy [10-13]. For example, previous work indicates that Parkinson’s gait was improved by applying fixed-tempo RAS [13].

WalkMate makes the tempo of rhythmic sounds interact with the tempo of the patient’s gait [14]. This system helps the patient to walk stably through the mutual tempo entrainment between the patient’s gait rhythm and rhythmic sounds. Our previous study reported that WalkMate mitigated festinating gait of PD patients significantly [15]. Here, the festinating gait was one of the gait disorders of PD, that was first associated with Parkinsonism. The festinating gait was an alteration in gait pattern characterized by a quickening and shortening of normal strides.

Thus, previous research suggested the effectiveness of both WalkMate and fixed-tempo RAS each on the PD patients’ gait disorders. However, WalkMate and fixed-tempo RAS were not compared by a common evaluation method. Therefore, it is necessary to investigate the influence of the rhythmic sounds of WalkMate and fixed-tempo RAS. Moreover, it is needed to consider that PD connects with the disorder of generating rhythm and timing. In these respects, the index related to dynamics of rhythm is appropriate in an evaluation method.

Regarding the evaluation index, Hausdorff et al. evaluated gait using gait cycle fluctuation, from techniques of complex systems. They reported that the gait cycle fluctuation of a healthy person had 1/f characteristic and self-similarity [16]. This meant that the fluctuation was not random. On the other hand, they also reported that the gait cycle fluctuation of a patient with PD showed highly random characteristics [9,17,18]. Another study indicated that the gait with high randomness tended to have low gait flexibility and to have the high danger of falling [19]. Thus, methodology to judge whether a walk was normal or not was researched from the viewpoint of the dynamics focused on the gait cycle fluctuation. And we made use of the methodology.

From the above, the aim of this study was to investigate the influence of WalkMate and fixed-tempo RAS on the gait of the PD patient from the aspect of dynamics focused on 1/f characteristic. As a concrete strategy, we evaluated the gait cycle fluctuation of the

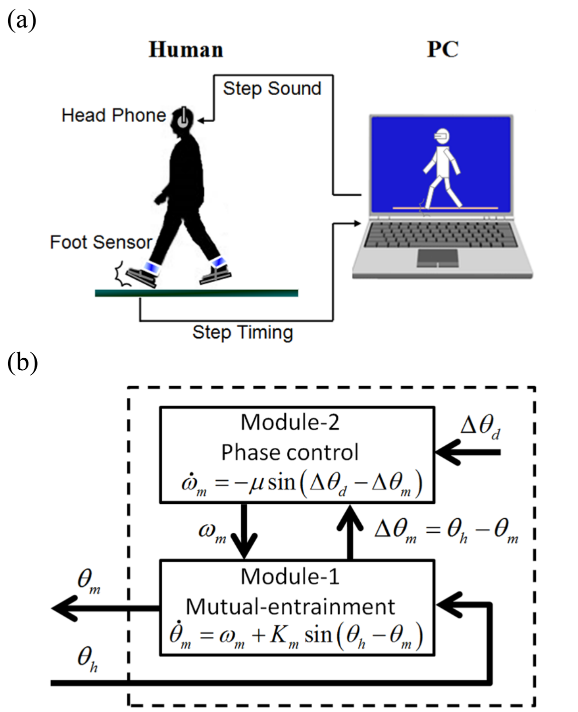

Fig.1 (a) Depiction of WalkMate system. (b) The computer's timing system used nonlinear oscillators and was organized hierarchically in two modules. Module 1 mutually entrained the gait frequencies of the computer and the participant. Module 2 adjusted the relative phase difference between the computer's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

PD patient applied WalkMate or fixed-tempo RAS. In addition, we compared these results. It seems to clarify the meaning of the interactive component on Parkinson's gait rehabilitation.

2. MATERIALS AND METHOD

2.1 Participants

Twenty normal-hearing and non-demented patients with PD were recruited. Eight of the twenty patients were males and twelve of them were females. The average age of the twenty patients is 69.2±7.7 (mean±S.D.) years old. The disease duration of them is 3.64±3.58 (mean±S.D.) years. They belonged Modified Hoehn and Yahr Stage from one to three, 2.40±0.576 (mean±S.D.). They took the medication for PD, and could walk alone without a cane or a walker.

Additionally, eighteen healthy participants were recruited. Sixteen of the eighteen participants were males. The average age of the eighteen participants is 24.7±2.7 (mean±S.D.) years old.

This experiment obtained the certification of ethics committee on Kanto Central Hospital of the Mutual Aid Association of Public School Teachers, in Japan. All participants provided written informed consent before participation.

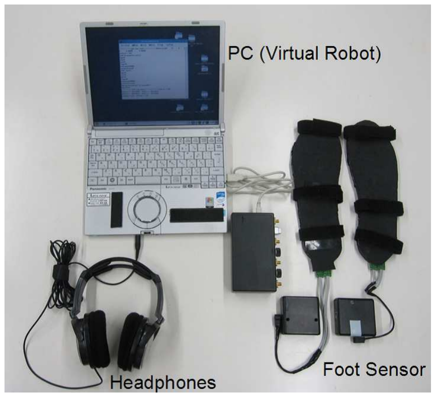

Fig.2 Experimental devices consisted of PC (virtual robot), Headphones, and foot sensors.

2.2 Tasks and experimental procedures

The participants wore headphones and two foot sensors attached to their shoes. The headphones provided rhythmic auditory stimulation. The foot sensors detected the participants' step timings. Each participant walked a flat corridor of 200m every trial.

Our experiment had three experimental conditions. These are WalkMate condition, fixed-tempo RAS condition, and Silent Control condition. Here, under Silent Control condition, the participants walked alone as usual with no sound. The order of the experimental conditions was counterbalanced. Between each condition, the participants took a break for thirty minutes because of removing influence of fatigue of the last condition.

Each experimental condition had three trials. Firstly, the participants walked alone. Secondly, they walked with rhythmic auditory stimulation under a condition. Finally, they walked alone again. Here, under Silent Control condition, they walked alone three times serially. Between each trial, the participants took a break for five minutes because of removing influence of fatigue of the last condition. Therefore, in total each participant walked the corridor nine times.

2.3WalkMate

WalkMate is an interpersonal synchrony emulation system (figure 1). The system [11] used in this study exchanged information on the timing of foot-ground contact between the user and the virtual robot. This system had a hierarchical structure consisting of two modules named Module 1 and Module 2. 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 user's foot contact with the ground) and the motor output (production of robot footstep sound stimuli to the user) to a targeted value.

Phase oscillators [5], which have been successfully used for simulating CPG's function of generating walking patterns [17, 20], were applied to express the control law for Module 1, as shown by equation (1).

Here, θ_m represents the virtual robot's phase of the gait cycle, and ω_m designates the natural frequency (reciprocal of the natural period) for the walking cycle. When θ_m in equation (1) attained an integer multiple of 2π, Module 1 transmitted a tone signal to the user, interpreting it as an indication of the virtual robot's foot making contact with the ground. The input variable of this equation, θ_h, presents the phase of the user's gait cycle, estimated from the discontinuous timing of the user's heel strike; K_m (> 0) designates the coupling constant.

$$\dot{\theta}_m = \omega_m + K_m \sin(\theta_h - \theta_m) \tag{1}$$

The control law for Module 2 was derived based on the following considerations. In a stable state in which two coupled rhythmic oscillators are synchronized through mutual entrainment, the relative phase advances for the oscillator with the larger natural frequency. This finding enabled implementation of a feedback control for the difference in the timing of input and output of Module 1 (equivalent to $\Delta\theta_m = \theta_h - \theta_m$). The control law for Module 2 could then be presented as in equation (2), in which $\Delta\theta_m$, $\Delta\theta_d$, and μ denote the Module 1 phase difference, the target phase difference, and the control gain, respectively.

$$\dot{\omega}_m = -\mu \sin(\Delta\theta_d - \Delta\theta_m) \tag{2}$$

The above equations can be applied for both the right and left legs, with a phase shift of π. In this study, values of *0.5* and *0.32* were used for K_m and μ, respectively.

In specific terms, the timing of the virtual robot's ground contact was presented to the user as an auditory stimulus (alternating between F5 and C5 notes, 200 ms duration) via headphone. The user's foot-ground contact was detected by the pressure sensor fixed underneath the shoe. The detected signals were transmitted to the gait simulation software program running on a portable PC. The measurement, calculation, and recording of the heel strike timing were performed in real time at 10 ms intervals. This WalkMate system was intended to achieve interpersonal gait synchrony between the user and the virtual bipedal robot.

2.4 Fixed-tempo RAS

Fixed-tempo RAS provided rhythmic auditory stimulation having constant tempo to the user. The user walked hearing the sound. This is one of the behavioral therapeutic methods. Here, initial tempo was determined as follows. Firstly, five stride interval times were detected before starting rhythmic auditory stimulation. Secondly, three data without the maximum and the minimum of the five data were averaged. Finally, the average value was set in the initial tempo.

2.5 Experimental setups

Experimental devices consisted of the equipment shown in Figure 2. WalkMate and fixed-tempo RAS were implemented in mobile PC (Panasonic, CF-W5AWDBJR). Foot sensors (OJIDEN, OT-21BP-G) detected a foot-to-ground contact timing. The portable headphone of the high sound quality design by an excellent encapsulated type (Bose, Triport Headphones) provided auditory rhythmic sounds. The radio transmitter (Smart Sensor Technology, S-1019M1F) transmitted data from the food sensors. The radio receiver (Smart Sensor Technology, WM-1019M1F) received these data.

2.6 Analysis Methods

We focused on time series of participants' stride interval time, in order to investigate the influences of WalkMate and fixed-tempo RAS on their gait.

The stride interval time (gait cycle time) T_h is shown in equation (3), 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 (3) is applicable to the virtual robot as well, by replacing the suffix *h* (for human) with m (for robot). In this study, no significant difference was noted in the stride interval time between the legs of the participants. Therefore, data on the right leg were used in further analysis, unless otherwise noted.

$$T_h(i) = t_h(i+1) - t_h(i) \tag{3}$$

We analyzed fluctuation of stride interval time. A previous study developed Detrended Fluctuation Analysis (DFA). This is one of the techniques to analyze the long-term correlative characteristic of time series data. Unsteady data like as biomedical signal often analyzes using DFA. Thus, we judged that DFA was suitable for the analysis of our study.

(i) Starting with a correlated signal *u(i)*, where *i*=1, . . . , N_{max}, and N_{max} is the length of the signal, we first integrate the signal *u(i)* and obtain equation (4).

$$y(k) \equiv \sum_{i=1}^{k} \left[\, u(i) - \langle u(i) \rangle \,\right] \tag{4}$$

Where $\langle u(i) \rangle$ is the mean, and *u(i)* equals $T_h(i)$.

(ii) The integrated signal *y(k)* is divided into boxes of equal length *n*.

(iii) In each box of length *n*, we fit *y(k)*, using a polynomial function of first degree, which represents the trend in that box. The y coordinate of the fit line in each box is denoted by $y_n(k)$.

(iv) The integrated signal *y(k)* is detrended by subtracting the local trend $y_n(k)$ in each box of length *n*.

(v) For a given box size *n*, the root-mean-square (RMS) function for this integrated and detrended signal is calculated by equation (5).

$$F(n) \equiv \sqrt{\frac{1}{N_{\max}} \sum_{k=1}^{N_{\max}} \left[\, y(k) - y_n(k) \,\right]^2} \tag{5}$$

(vi) The above computation is repeated for a broad range of scales (box size *n*) to provide a relationship between *F(n)* and the box size *n*.

A power-law relation between the average root-mean-square fluctuation function *F(n)* and box size *n* indicates the presence of scaling: $F(n) \sim n^{\alpha}$. The fluctuation can be characterized by a scaling exponent α, a self-similarity parameter that represents the long-range power-law correlation properties of the signal. If $\alpha=1$, there is 1/f characteristic (pink noise). If $\alpha=0.5$, there is

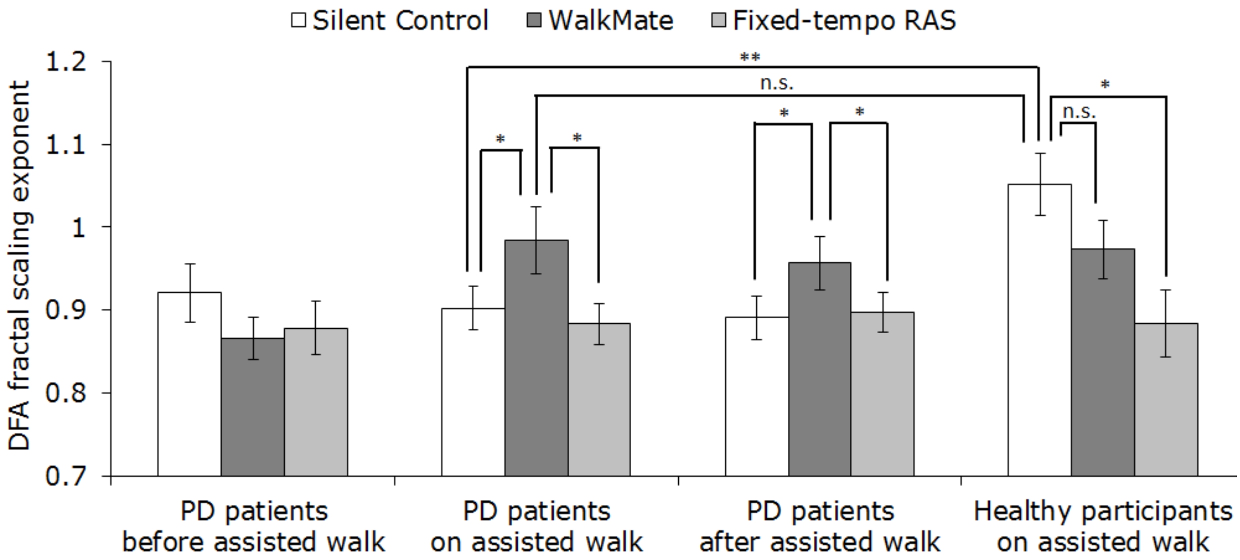

Fig.3 DFA fractal-scaling exponent for Parkinson's disease (PD) patients before assisted walk, on assisted walk, after assisted walk, and healthy participants on assisted walk. The cueing conditions are unassisted Silent Control, interactive WalkMate rhythmic auditory stimulation, and Fixed-tempo rhythmic auditory stimulation (Fixed-tempo RAS). Error bars represent ± SEM. **p < .01, *p < .05, n.s. = no significant difference.

no correlation and the signal is uncorrelated (white noise); is $\alpha<0.5$, the signal is anti-correlated [21].

3. RESULTS

As shown in the figure 3, before walking assisted by rhythmic stimulation, the stride interval time DFA fractal-scaling exponent for PD patients was significantly lower than for healthy participants, $t(36) = 2.60$, $p < 0.01$). This reduced fractal scaling for PD patients away from healthy 1/f structure is indicative of impaired gait. There were three experimental conditions. They were WalkMate, fixed-tempo RAS, and Silent Control. Before assisted walking, the fractal scaling for PD patients did not differ among the three conditions. This evidenced PD patients had same state before assisted walking.

On assisted walking, rhythmic stimulation affected fractal scaling for PD patients, $F(2, 38) = 4.51$, $p < 0.05$. The interactive WalkMate auditory stimulation lead to significantly higher fractal scaling for PD patients compared to unassisted Silent Control and fixed-tempo RAS ($ps < 0.05$). The mean and standard deviation of stride times did not differ among the three conditions, nor did they correlate with fractal scaling; thus dynamic analyses can capture important signals in gait not revealed with more conventional analyses [23]. Moreover, no difference of fractal scaling was observed between unassisted Silent Control and fixed-tempo RAS ($p > 0.05$). Remarkably, fractal scaling for PD patients with WalkMate was not different from fractal scaling of healthy participants' normal walking, $t(36) = 1.23$, $p > 0.05$. This suggested that for PD patients interacting with the WalkMate system could reinstate healthy gait dynamics.

After end of assistance, rhythmic stimulation also affected fractal scaling for PD patients, $F(2, 38) = 4.68$, $p < 0.05$. After assisted walking, fractal scaling for PD patients with interactive WalkMate auditory stimulation was maintained significantly higher compared to unassisted Silent Control and fixed-tempo RAS ($ps < 0.05$). Moreover, no difference of fractal scaling was observed between unassisted Silent Control and fixed-tempo RAS ($p > 0.05$). Importantly, fractal scaling for PD patients after walking assisted by WalkMate did not differ from fractal scaling of healthy participants' normal walking, $t(36) = 1.12$, $p > 0.05$. This effect showed that the WalkMate system had potential to carry-over effect of rhythmic stabilization into short term.

4. DISCUSSION

In the silent control condition, the PD patients' fractal scaling of stride interval time was lower (higher randomness) than healthy participants. This has been associated with impaired gait and basal ganglia dysfunction [17].

Walking assisted by tones in the WalkMate condition, the PD patients' fractal scaling increased significantly compared to before walking assisted by WalkMate. The PD patients' fractal scaling approached the healthy participants' fractal scaling. Thus, the stride interval time of PD patients was improved compared to that before assisted walking. The WalkMate system took over the mutual entrainment by correcting a portion of the relative phase difference and adjusting its period (frequency) to complement the human's timing.

On the other hand, in the fixed-tempo RAS condition, the PD patients' fractal scaling had no significant difference from that before walking assisted by fixed-tempo RAS. Hence, the PD patients' fractal scaling wasn't improved by fixed-tempo RAS, compared to WalkMate. The difference between WalkMate and fixed-tempo RAS was with the interaction consisted of mutual entrainment and phase control or not. These suggested that the interaction had the potential of improving the rhythm structure of stride interval time in PD patients related to rhythm disturbance.

Walking after assistance by tones in the WalkMate condition, the PD patients' fractal scaling had no significant difference from that during assisted walking and had significant difference from that before assisted walking. This meant that the results of the fractal scaling showed residual effect when the PD patients walked with interactive WalkMate rhythmic auditory stimulation. Thus, this suggested that the improvement effect of their gait was maintained after assistance by interactive WalkMate rhythmic auditory stimulation.

On the other hand, in the fixed-tempo RAS condition, the PD patients' fractal scaling had no significant difference from that during assisted walking or before assisted walking. This meant that the low fractal scaling that was shown before assisted walking was maintained through the three conditions. Therefore, the fractal scaling of the stride interval time of PD patients wasn't restored by fixed-tempo RAS. The carry-over effect of higher fractal scaling after rhythmic stimulation including mutual entrainment suggested that rhythmic auditory stimulation is not simply an external pacemaker driving motor system, but that it influences the neural time-keeping circuitry [12]. The basal ganglia SMA circuit supports synchronizing internal oscillations with external events [22], and these oscillations continue after removing the external stimulation. Internal rhythmicity can be reestablished in basal ganglia impairments [22], and a similar reestablishment of the basal ganglia oscillations likely occurs in the short-term after interactive rhythmic stimulation.

The 1/f structure is not merely an epiphenomenal by-product of healthy gait or reintegrated timing circuits, but it could serve to increase flexibility, predictability, and stability. The fractal scaling in healthy gait (as well as in healthy heart beat time-series) might benefit the system by avoiding "mode locking" to a single local tempo, thereby increasing flexibility and responsiveness to environmental demands [23,24]. Additionally, the strong association between low fractal scaling and falling [25] might relate to decreased predictability: Highly random stride times undermine the temporal predictability of an upcoming stride time, which in turn would hinder corrective movement, balance, and stability. In a 1/f time series, the upcoming stride-time is more predictable than in a random series, because short-range correlations have a more circumscribed set of temporal probabilities, and due to scale-invariance, the long-range correlations can be used to predict the short-range ones and vice-versa (similarly, fractal structure in music improves predictability of tempo changes, [26]. This increased predictability might explain the patients' higher perceived movement stability.

In sum, fractal scaling analyses provide a strong diagnostic tool for identifying gait impairment [23,24]. When PD patients' oscillation frequencies mutually entrained with the interactive rhythmic system, their fractal scaling increased back to healthy 1/f levels, and their perceived stability improved. Elevated fractal scaling persisted 5 minutes after removing the interactive stimulation. This human-machine interaction provides a good example of coupling internal and external systems through dynamic feedback [27,28] and is a promising rehabilitation tool. Previous work showed that the interactive system can stabilize gait in hemiparetic stroke patients [29] and in Parkinson's patients with strongly accelerating gait [14]. Future work should investigate effectiveness in patients "off" or with reduced dopaminergic medication. Additionally the carry-over effect of improved rhythmicity post-WalkMate suggests potential in a long-term rehabilitation program. Interactive rhythmic auditory stimulation offers a flexible, portable, low-cost, non-invasive therapeutic intervention that can improve the mobility, stability, and quality of life of Parkinson's Diseases patients.

5. CONCLUSION

In this study, we evaluated the gait cycle fluctuation of Parkinson's disease patients with WalkMate and fixed-tempo RAS. We also compared these results. The comparison showed that WalkMate improved the gait cycle fluctuation. The gait was the same as the normal gait of healthy persons. Moreover, the effectiveness continued after assistance by WalkMate. On the other hand, the gait cycle fluctuation was not changed significantly by using fixed-tempo RAS. Therefore, it was indicated that WalkMate made the gait of Parkinson's disease patients be nearer to the normal gait than RAS, and it had the potential of improving gait disorder of Parkinson's disease patients.

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