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Rhythmic priming across effector systems: A randomized controlled trial with Parkinson's disease patients

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ABSTRACT

This study investigated the immediate effects of auditory-motor entrainment across effector systems by examining whether Rhythmic Auditory Stimulation training of arm or finger movements would modulate gait speed. Forty-one participants with idiopathic Parkinson's Disease were randomly assigned to 3 groups. Participants in the finger-tapping group tapped in synchrony with a metronome set to 20% faster pace than the pre-training walking cadence, whereas participants in the other group were asked to swing both arms in an alternating motion in synchrony with the metronome. Participants in the control condition did not receive training. To assess gait parameters pre- and post-training, participants walked on a 14-meter flat walkway at his/her preferred walking cadence with no auditory cueing. Results indicated that there was a significant increase in gait velocity after the finger tapping training ($p < .005$), whereas no differences were observed in the arm swing ($p = .802$) and in the control conditions ($p = .525$). Similarly, there were significant changes in gait cadence post-training in the finger tapping group ($p < .005$), but not after arm swing training ($p = .879$) or control ($p = .759$). There were no significant changes in stride length post-training in none of the groups. These findings suggest that auditory-motor entrainment in one effector system may prime a second effector system. Interestingly, however, the priming effect on gait was only observed in the finger tapping condition and not with synchronized arm swing movements. These findings have significant implications for motor rehabilitation and open new avenues for further investigation of the mechanisms underlying cross-effector coupling.

1. Introduction

Entrainment is generally defined as the process of temporal alignment between systems. This phenomenon is observed in physical (e.g., pendulum clocks) and biological systems (e.g., fireflies, circadian rhythms) when the motion or signal frequency of one system entrains to the frequency of another system (Pantaleone, 2002; Roenneberg, Daan, & Merrow, 2003; Wilson & Cook, 2016). In the context of human motor behavior, entrainment is generally understood as the temporal coupling between body movements and rhythmic stimuli such as auditory, visual, tactile, multimodal, or social signals (Phillips-Silver, Aktipis, & Bryant, 2010; Ross & Balasubramaniam, 2014). In particular, auditory rhythmic stimuli have a strong effect on motor entrainment. The auditory system is

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well-known for its ability to precisely detect temporal patterns in acoustic signals and rapidly construct stable internal temporal representations (Bizley, 2017; Moore, 2012; Theunissen & Elie, 2014). Moreover, it has been shown that auditory rhythms can prime and alter the timing of spinal motor neuron activity via reticulospinal pathways (Ermolaeva & Borgest, 1980; Paltsev & Elner, 1967; Rossignol & Melvill Jones, 1976). The continuous time reference provided by auditory rhythmic signals prime the motor system in a state of readiness by providing predictable time cues that allow movement anticipation and motor planning to occur based on expectations of the duration of the time cues, thus optimizing all aspects of motor control (Thaut, McIntosh, & Hoemberg, 2015).

However, rhythmic priming extends beyond auditory-motor synchronization. Studies have consistently demonstrated rhythmic priming effects across sensory modalities (for review, Ross & Balasubramaniam, 2014). Recently emerging electrophysiological and behavioral studies have shown, for instance, that perceptual judgements are faster when visual stimuli are presented in synchrony with auditory rhythms as opposed to out of synchrony (Bolger, Trost, & Schön, 2013; Escoffier, Herrmann, & Schirmer, 2015; Feng, Stormer, Martinez, McDonald, & Hillyard, 2014; Miller, Carlson, & McAuley, 2013; Sacrey, Clark, & Whishaw, 2009; Su, 2014). It has also been shown that exposure to auditory rhythms prior to a visual task can prime an internal representation of a beat that interferes with the perception of visual rhythms presented several minutes later (Grahn, Henry, & McAuley, 2011). Collectively, these studies support the notion that the brain uses rhythmic cues (i.e., auditory rhythms) to make predictions and optimize attention and stimulus perception (for review, see Nobre & Van Ede, 2018).

There is also growing evidence of the effect of rhythm priming on speech and language (Cason & Schön, 2012; Cason, Astésano, & Schön, 2015; Falk & Dalla Bella, 2016; Kotz & Gunter, 2015; Parrell, Goldstein, Lee, & Byrd, 2014; Schön & Tillmann, 2015; Tierney & Kraus, 2014). Recent studies have demonstrated that speech processing is significantly enhanced when an auditory rhythmic prime is presented prior to the task (Cason & Schön, 2012; Cason et al., 2015). Falk and Dalla Bella (2016) also found that verbal processing was facilitated when rhythmic movements (e.g., finger tapping) were temporally aligned with the stressed syllable, providing further evidence of cross-modal priming.

However, the effect of rhythmic priming across effector systems remains largely under-explored in research and rehabilitation. Behavioral and functional neuroimaging research suggest that rhythmic priming can have lasting effects in self-paced (e.g., internally-guided) motor behaviors (Jantzen, Oullier, Marshall, Steinberg, & Kelso, 2007; Jantzen, Steinberg, & Kelso, 2002, 2004, 2005; Mayville, Jantzen, Fuchs, Steinberg, & Kelso, 2002; Zelaznik & Rosenbaum, 2010). For instance, it has been demonstrated that performing a finger-tapping task before circle drawing can prime an internal temporal representation that persists over time and over tasks interfering with the execution of subsequent circle-drawing tasks (Studenka, Zelaznik, & Balasubramaniam, 2012; Zelaznik & Rosenbaum, 2010). Recent findings also suggest that priming of a common central timekeeping can influence effectors that rely less on a clock-like mechanism (Cong, Sharikadze, Staude, Deubel, & Wolf, 2010; Richardson, Cluff, Lyons, & Balasubramaniam, 2013; Ross & Balasubramaniam, 2014; Richardson & Balasubramaniam, 2010). Richardson et al. (2013) instructed participants to tap in synchrony with a pacing stimulus while simultaneously making repetitive horizontal saccadic eye movements, and found that finger movements were unintentionally attracted in the direction of the saccades when both movements were planned and timed together.

Auditory rhythms have been extensively used in rehabilitation to prime the motor system in order to facilitate the execution of motor patterns of patients with Parkinson's Disease (McIntosh, Brown, Rice, & Thaut, 1997; Thaut & Abiru, 2010; Thaut & Hoemberg, 2014; Thaut, Miltner, Lange, Hurt, & Hoemberg, 1999). Parkinson's Disease is associated with gait disturbances such as gait shuffling, slowness of movement, freezing of gait, reduced stride length, slower cadence, and asymmetric and reduced arm swing during walking (Huang et al., 2012; Jankovic, 2008; Lewek, Poole, Johnson, Halawa, & Huang, 2010; Morris, Huxham, McGinley, Dodd, & Iansek, 2001; Wood, Bilclough, Bowron, & Walker, 2002). There are strong indications that increased temporal variability in gait kinematics in persons with Parkinson's Disease is associated with compromised internal motor timing mechanisms, which is reflected in difficulties with tasks involving perceptual timing, beat discrimination, self-paced repetitive movements, and sensorimotor synchronization (Bienkiewicz & Craig, 2015; Grahn & Brett, 2009; Nombela, Hughes, Owen, & Grahn, 2013; O'Boyle, Freeman, & Cody, 1996; Pastor, Artieda, Jahanshahi, & Obeso, 1992; Skodda, Flasskamp, & Schlegel, 2010). Thus, therapeutic interventions focusing on internal timing functions underlying temporally stable rhythmic gait kinematics are particularly effective (Hove & Keller, 2015; Nombela et al., 2013; Thaut et al., 2015). Rhythm-based interventions such as the Rhythmic Auditory Stimulation (RAS) involve the utilization of rhythmic cues (metronome or rhythmically accentuated music with embedded metronome clicks) to facilitate gait and improve the kinematic stability of walking movements (Thaut & Hoemberg, 2014). Indeed, there is robust evidence that Rhythmic Auditory Stimulation has immediate effects on gait by increasing velocity, stride length, and by improving symmetry and stability (Arias & Cudeiro, 2010; Ashoori, Eagleman, & Jankovic, 2015; Hausdorff et al., 2007; Hove, Suzuki, Uchitomi, Orimo, & Miyake, 2012; McIntosh et al., 1997; Thaut et al., 1996, 1997, 1999, 2015; for review, see Ghai, Ghai, Schmitz, & Effenberg, 2018). However, it is still unclear whether short-term Rhythmic Auditory Stimulation training of other effectors, such as arm or finger movements, would prime the motor system and induce changes in gait.

Therefore, the present study investigated rhythmic priming across effector systems by examining the immediate effects of Rhythmic Auditory Stimulation training of arm or finger movements in modulating gait kinematics (i.e., velocity, cadence, and stride length) of patients with Parkinson's Disease. For that, participants underwent a 4-minute auditory-motor training whereby they synchronized arm or finger movements with a metronome set to a pace 20% faster than the pre-training walking cadence. We hypothesized that, if rhythmic priming were to occur across effector systems, we would see a significant change in gait kinematics after this short entrainment phase. Arm movements are a crucial part of human bipedal gait. During human walking, the passive pendular motion of arm swing movements are stabilized by rhythmic muscular activation that originate from locomotor networks in the central nervous system that connect cervical and lumbar spinal circuits, such as central pattern generators (Dietz, 2002; Meyns, Bruijn, & Duysens, 2013; Zehr & Duysens, 2004). There are several studies demonstrating that rhythmic arm movements (i.e., alternating or anti-phase arm swing) modulate the pattern of activation of the soleus H-reflex and facilitate leg muscle activity (Balter

& Zehr, 2006; de Kam et al., 2013; Frigon, 2004; Hiraoka et al., 2011; Huang & Ferris, 2004; Knikou, 2007; Massaad et al., 2014; Selionov, Solopova, & Zhvansky, 2016; Sylos-Labini et al., 2014), thus suggesting that merely moving the arms in locomotor-like motion activates spinal networks underlying interlimb coordination during gait. In recent years, studies have examined the effects of simultaneous arm and leg exercises in gait rehabilitation (Ustinova, Langenderfer, & Balendra, 2017; Zhou et al., 2018). However, it is still unclear whether synchronized arm movements alone would prime locomotor networks and modulate gait kinematics. In this study, we also tested a second rhythmic priming condition using finger movements. Rhythmic discrete movements such as finger tapping are thought to rely on a clock-like mechanism (Zelaznik et al., 2005). Based on previous evidence that priming of a common central timekeeping mechanism can have lasting effects (Richardson et al., 2013; Ross & Balasubramaniam, 2014; Studenka et al., 2012; Zelaznik & Rosenbaum, 2010), we also examined whether rhythmic finger movements would prime the motor system and modulate gait.

2. Methods

2.1. Participants

Forty-one patients were recruited through advertisement at community-based Parkinson's Disease support groups, hospitals, and neurology practices. All participants had a primary diagnosis of idiopathic Parkinson's Disease. Inclusion criteria were Hoehn and Yahr (H & Y) Parkinson's scale score of 1–2, ability to ambulate independently without assistive devices for at least 14 meters, and a stable antiparkinsonian medication regime. Subjects were excluded if they had other neurological or orthopedic conditions and severe perceptual deficits such as medically diagnosed hearing loss. The study was approved by the internal review boards of the Colorado State University (reference number: 10-1752H), and written informed consent was obtained from all study participants.

Subjects were randomly assigned based on block randomization to one of three groups: finger tapping training, arm swing training, and a control group. Two patients in the arm swing group and two patients in the finger tapping group were excluded from the final analysis due to difficulties performing the tasks, resulting in a total sample of 37 subjects, with 11 participants in the finger tapping group, 14 participants in the arm swing group, and 12 participants in the control group.

Patient clinical and demographic characterization was completed at baseline. The general severity of the disease was rated according to the Hoehn and Yahr (H&Y) scale (Hoehn & Yahr, 1967) and motor symptoms severity was assessed with the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS Sections III and IV) (Goetz et al., 2008). Part III of the MDS-UPDRS assesses the motor aspects of the disability and includes 33 items evaluating symptoms such as tremor, slowness (bradykinesia), stiffness (rigidity), and balance. Each item is rated on a five-point Likert scale ranging from 0 to 4, with higher scores indicating more severe impairment. Part IV of the scale is comprised of 6 items (also rated on a five-point Likert scale with higher scores indicating more severe symptoms) evaluating motor complications and includes ratings of involuntary movements (dyskinesias), dystonia, and irregular medication responses. The clinical assessment also included the Berg's Balance Scale (BBS) (Berg, Wood-Dauphinee, & Williams, 1995) and the Nine-Hole Peg Test (NHPT) (Mathiowetz, Weber, Kashman, & Volland, 1985). The BBS is a 14-item clinical test administered by a trained therapist assessing impairment in balance function during a series of predetermined functional tasks, with each item consisting of a five-point ordinal scale ranging from 0 to 4, with 0 indicating the lowest level of function and 4 the highest level of function. The NHPT is a manual dexterity test that requires participants to repeatedly place and then remove nine pegs into nine holes, one at a time, as quickly as possible, while the time needed to complete the test is recorded. All participants included in the study were right-handed, except for one participant in the arm swing group.

Clinical and demographic sample characterization at baseline is summarized in Table 1. An analysis comparing baseline clinical and demographic measures between groups was conducted. For continuous variables, an ANOVA with Bonferroni corrections for multiple comparisons was performed, whereas an independent sample Kruskal-Wallis test was performed for nonparametric variables. The results indicated that there were no statistically significant differences between groups at baseline for all clinical and

Table 1
Clinical and demographic characterization of patients in each group at baseline.

	Finger Tapping Group (n = 11)	Arm Swing Group (n = 14)	Control Group (n = 12)
Age (years)	68.4 (5.31)	64.2 (6.32)	67.28 (3.14)
Sex (male/female)	7/4	6/8	4/8
Disease Duration (years)	4.8 (1.4)	7.7 (5.5)	11.71 (12.65)
H&Y	1.16 (0.4)	1.14 (0.5)	1.14 (0.4)
MDS-UPDRS Section III	11 (7)	16 (19)	14 (6)
MDS-UPDRS Section IV	3 (3)	3 (3)	4 (4)
BBS Scores	54 (2.4)	53 (5.1)	54 (1.6)
NHPT Dominant Hand (Sec)	36.74 (20)	37.24 (15)	30.26 (5)
NHPT Non-Dominant Hand (Sec)	34.83 (9)	39.78 (17)	32.58 (6)

Values are Mean (Standard Deviation). H&Y: Hoehn & Yahr Parkinson's scale; MDS-UPDRS: Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale; BBS: Berg's Balance Scale; NHPT: Nine-Hole Peg Test.

demographic measures.

2.2. Materials and procedures

Baseline gait assessment consisted of participants walking on a 14-meter flat walkway at his/her preferred walking cadence while gait parameters (i.e., velocity, stride length, and cadence) were recorded. Gait parameters were recorded with a stride analyzer system (B & L Engineering) consisting of a portable microprocessor worn on a gait belt during the assessments, as well as four sensors worn embedded in the insoles of the subject's shoes placed at the heel, first metatarsal, fifth metatarsal, and the big toe, plus a coupler system to download data from the microprocessor to the computer, and a data analysis software. Data were recorded at the sampling rate of 500 Hz, and the initial and final 2 m of the gait assessment was not included in the data analysis due to variability generated by walking acceleration/deceleration.

Rhythmic Auditory Stimulation training consisted of three blocks of 1-minute training with 30 seconds of rest in between blocks. Participants allocated to the finger tapping group sat on an armless chair in front of a table containing the recording device. Instructions were to tap with the index finger of the least affected hand in synchrony with a metronome. The metronome tempo was set 20% faster than pre-training walking cadence of each participant. The auditory stimuli (1 kHz sinusoidal wave, 85 dB sound pressure level) were delivered with a speaker placed 1 meter in front of the subject, and the tapping data were collected with a circuit system consisting of a contact plate and a metallic probe attached to the subject's index finger with medical tape. Metronome and tapping data were recorded simultaneously using E-Prime software, with tapping onset recorded when the metallic probe contacted the contact plate, and the inter-response interval was defined as the time elapsed between sequential taps (in milliseconds).

In the arm swing group, participants were instructed to swing both arms in an alternating motion in synchrony with a metronome set 20% faster than pre-training walking cadence while seated on an armless chair. Arm kinematics was recorded using an optoelectronic two-dimensional video-based motion analysis system (SELSPOT) at a sampling rate of 60 frames per second. One reflective marker was placed on the dorsal part of the wrist of the least affected arm with the subject seated sideways with respect to the camera. The maximum Y-coordinate (lateral plane of motion) reached by the target during the forward arm swing was compared to the onset of the metronome click. Participants assigned to the control group did not undergo any form of training and rested for 4 minutes.

After the training phase, all participants were instructed to once again walk the 14-meter walkway at his/her preferred walking cadence while gait parameters were recorded. All participants were taking dopaminergic medication and completed the testing during the "ON" phase of medication. The test took approximately one hour to be completed, including assessments, equipment setup, pre-test, training condition, and post-test.

2.3. Data analysis

The primary outcome measures of interest were changes in gait parameters: velocity (m/min), cadence (steps/min), and stride length (meters). An exploratory mixed-design analysis of variance (3 × 2 factors) was conducted to analyze whether there were differences between groups (finger tapping, arm swing, control) when comparing changes in the outcome measures from baseline to post-training testing. Post hoc analyses with Bonferroni corrections to adjust for multiple comparisons were conducted to examine changes in the outcome measures pre- and post-training for each group.

3. Results

An initial analysis of the timing data during the finger tapping and arm swing tasks was conducted to determine whether participants were able to complete the synchronization tasks appropriately. For that, period and synchronization errors of the second experimental block were analyzed. An analysis of the timing data indicated that the average inter-response interval between successive responses for the finger tapping group was 458 ms (range: 417–500 ms) and 476 ms (range: 411–800 ms) for the arm swing group. Results of an independent sample *t*-test revealed that participants in the arm swing group had more difficulties maintaining the tempo set by the metronome (Period Error $\text{Mean}_{\text{arm swing}}$: $M = 77$ ms, $SD = 79$) than those in the finger tapping group (Period Error $\text{Mean}_{\text{tapping}}$: $M = 15$ ms, $SD = 6.8$; $t(13) = 2.891$, $p = .012$). Response variability was also significantly higher in the arm swing (Synchronization Error: $M = 127.92$ ms, $SD = 167.59$) than in the finger tapping group (Synchronization Error: $M = 14.90$ ms, $SD = 8.10$; $t(13) = 2.519$, $p = .026$). Degrees of freedom reported for the *t*-tests were adjusted as the Levene's test for equality of variances suggested a significant difference in the variances between groups.

The analysis of variance considered the effects of time (pre- and post-training) and group (finger tapping, arm swing, control) for each of the primary outcome measures (velocity, cadence, and stride length). Regarding gait velocity, results indicated that there was a significant main effect of time ($F_{1,34} = 4.060$, $p = .05$) and a significant interaction between group and time ($F_{2,34} = 7.334$, $p = .002$), but a non-significant main effect of group ($F_{1,34} = 1.426$, $p = .254$) suggesting that the means for gait velocity for at least two of the groups did not differ significantly. A simple main effect analysis with Bonferroni corrections to adjust for multiple comparisons was conducted to examine changes pre- and post-training in gait velocity for each group (Table 2). Results indicated that there was a significant change from pre- to post-training in gait velocity in the finger tapping group, which increased from an average pre-training gait velocity of 69.75 m/min ($SD = 10.33$) to an average of 76.03 m/min ($SD = 9.20$) after the training ($p = \ < 0.005$). No significant differences in gait velocity pre- and post-training were observed in the arm swing group ($p = .806$) and in the control group ($p = .525$), as displayed in Fig. 1. Further analysis considering the mean difference between pre- and post-training

Table 2
Gait parameters pre- and post-training for each group.

	Finger Tapping Group (n = 11)		Arm Swing Group (n = 14)		Control Group (n = 12)	
	Pre-training	Post-training	Pre-training	Post-training	Pre-training	Post-training
Velocity *(m/min)*	69.95 (10.33)	76.03 (9.20)**	67.12 (14.70)	66.79 (14.93)	65.10 (12.29)	64.20 (10.51)
Cadence *(steps/min)*	109.25 (7.18)	117.50(5.20)**	105.51(13.94)	105.35(15.45)	108.52 (8.64)	108.86 (7.56)
Stride Length *(meters)*	1.27 (0.147)	1.29 (0.135)	1.26 (0.185)	1.25 (0.179)	1.19 (0.178)	1.17 (0.159)

Mean (Standard Deviation). Significant post hoc comparisons with Bonferroni corrections are represented with asterisks (**$p < .005$).

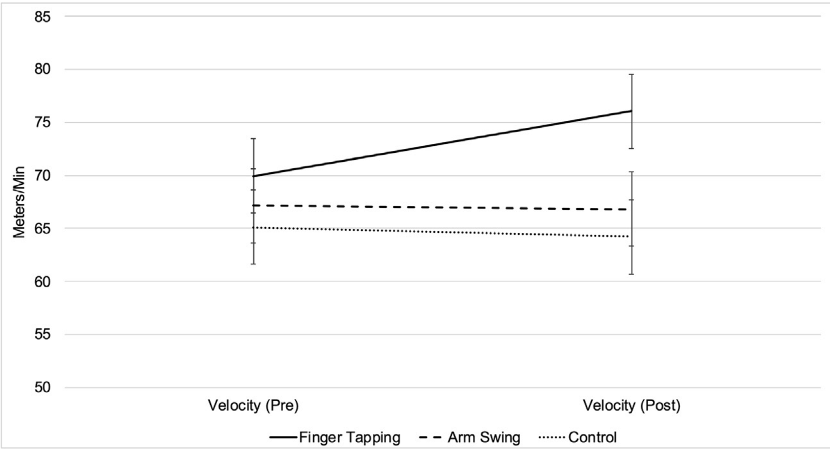

Fig. 1. Changes in gait velocity (meters/min) pre- and post-training in the finger tapping (solid line), arm swing (dashed line), and control (dotted line) groups. Standard error bars are shown. Statistically significant changes pre- and post-training were observed only in the finger tapping group ($p < .005$).

demonstrated that gait velocity increased an average of 9.5% ($SD = 9.2$) after finger tapping training, whereas arm swing training did not significantly impact gait velocity (< 1%). There were no significant differences between training groups in gait velocity at baseline.

In relation to gait cadence, results indicated that there was a significant main effect of time ($F_{1,34} = 19.739$, $p < .005$) and a significant interaction between time and group ($F_{2,34} = 17.669$; $p < .005$), but a non-significant main effect of group ($F_{1,34} = 1.734$, $p = .192$). A post-hoc analysis with Bonferroni corrections examining changes pre- and post-training in gait cadence for each group showed that there was a significant change from pre- ($M = 109.25$ steps/min; $SD = 7.18$) to post-training ($M = 117.50$ steps/min;

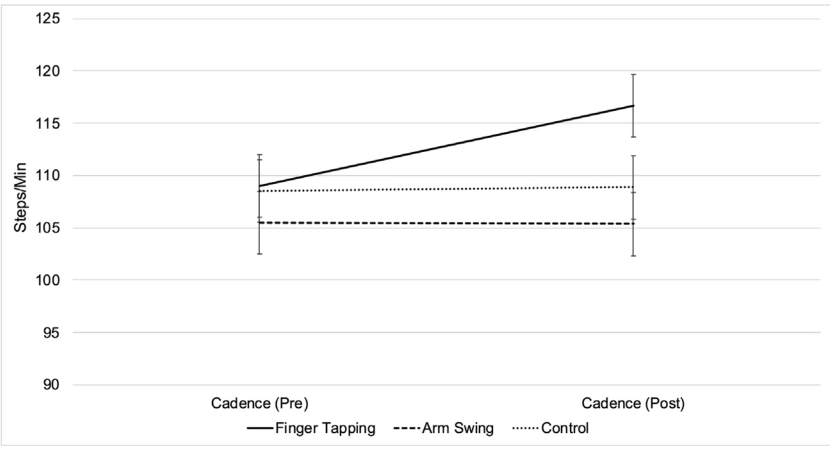

Fig. 2. Changes in gait cadence (steps/min) pre- and post-training in the finger tapping (solid line), arm swing (dashed line), and control (dotted line) groups. Standard error bars are shown. Statistically significant changes pre- and post-training were observed only in the finger tapping group ($p < .005$).

SD = 5.20) in the finger tapping group ($p < .005$), an improvement of 8% (SD = 5.6) (Table 2). There were no significant changes in gait cadence pre- and post-training for arm swing training (p = .879) and in the control group (p = .759) (Fig. 2). No statistical differences between groups in gait cadence were observed at baseline.

The analysis indicated that there were no significant changes in stride length from pre- to post-training in none of the groups (Table 2). The main effect of time ($F_{1,34}$ = 0.062, p = .805), the main effect of group ($F_{1,34}$ = 1.195, p = .315), and time and group interaction ($F_{2,34}$ = 1.048, p = .362) did not reach statistical significance.

4. Discussion

The purpose of the present study was to investigate rhythmic priming across effector systems. For that, we examined the immediate effects of Rhythmic Auditory Stimulation training of finger or arm movements on gait parameters of patients with Parkinson's Disease. The results indicate that patients who undertook 4-minute auditory-motor training consisting of finger tapping to a metronome set to 20% faster than the pre-training walking cadence showed significant increases in gait velocity and cadence in the post-training assessment. However, swinging the arms in an alternating motion in synchrony with the metronome did not change gait speed in the post-training assessment. These findings suggest that auditory-motor entrainment in one effector system may prime a second effector system. Interestingly, however, the priming effect on gait was only observed in the finger tapping condition and not with synchronized arm swing movements.

It is possible that finger tapping primed a common central timekeeping mechanism that persisted across effector systems. This hypothesis is supported by the notion that discretely produced movements, such as finger tapping, rely primarily on an internal clock-like mechanism (Zelaznik et al., 2005). An important aspect of this timing mechanism also referred to as event timing, is that the temporal control of discrete movements requires an explicit temporal representation of the time interval to be produced. Conversely, smooth and continuous movements would rely on a distinct timing mechanism called emergent timing, whereby timing regularities emerge from the dynamics of the movement (i.e., movement trajectory and velocity) in the absence of an explicit internal temporal representation. Previous research found that these timing mechanisms are not mutually exclusive and that priming of a common central timekeeping mechanism can have significant effects across time and tasks. It has been shown, for instance, that task order (Jantzen et al., 2004, 2007, 2002; Zelaznik & Rosenbaum, 2010), music training (Baer, Thibodeau, Gralnick, Li, & Penhune, 2013; Braun Janzen, Thompson, Ammirante, & Ranvaud, 2014), and the presentation of auditory feedback (Grahn et al., 2011; Lorås, Sigmundsson, Talcott, Öhberg, & Stensdotter, 2012; Studenka et al., 2012; Zelaznik & Rosenbaum, 2010), can prime an internal temporal representation that directly affects the performance and the timing strategy adopted on subsequent tasks. More specifically, studies have demonstrated that the timing processes adopted to perform a finger-tapping task can persist and interfere with the timing mechanism engaged during the execution of subsequent circle-drawing tasks – considered a typical emergent timing task (Studenka et al., 2012; Zelaznik & Rosenbaum, 2010; but see Pope & Studenka, 2018). Based on these findings, it is possible to suggest that finger tapping may have successfully primed a common central timekeeping mechanism that persisted over tasks and effector systems, directly affecting gait speed on the post-training assessment.

On the other hand, pendular movements, such as arm swing during locomotion, have a tendency to oscillate at their characteristic resonant frequency (Holt, Jeng, Ratcliffe, & Hamill, 1995). The system's preferred or resonant frequency is determined by biomechanical constraints such as length and mass distribution of the limbs (e.g., Dahl, Huron, Brod, & Altenmüller, 2014), and is associated with efficient oxygen consumption and muscle activity (Russell & Apatoczky, 2016). Despite a clear ability to adapt to external timing demands and override the system's intrinsic oscillatory frequency, studies using the continuation paradigm have demonstrated that, after an external pacemaker is turned off, rhythmic smooth movements have a tendency to drift toward their resonant frequency due to the intrinsic mechanical properties of the effector in relation to the target frequency (Peckel, Pozzo, & Bigand, 2014; Yu, Russell, & Sternad, 2003). Moreover, there is evidence that moving a limb at a frequency much faster or slower than its resonant frequency incurs significant costs, as seen by a significant decrease in accuracy and stability (Fujiyama, Hinder, Garry, & Summers, 2013; Peternel, Sigaud, & Babič, 2017; Van Der Wel, Sternad, & Rosenbaum, 2009). Therefore, it possible that arm movements drifted back to their respective resonant frequency once the external temporal cues were removed in the post-training assessment, which would explain why there were no significant differences between gait kinematics at baseline and post-training in the present study. This hypothesis could be tested in future studies by analyzing changes in walking speed over the course of the trials. Additionally, considering the emergent timing concept that smooth movements rely less on a clock-like timing mechanism, one could argue that – unlike finger tapping - arm swing training would not prime a common central timekeeping mechanism. Thus, once the metronome was removed, the emergent properties of the interaction between the neuromuscular system with the environment would have dictated the timing regularities of these movements in the post-training assessment.

Alternatively, it is possible that performing the arm swing training in a seated position reduced the coupling between arms and legs, thus inhibiting rhythmic priming. It has been suggested that the passive pendular motions of arm swing movements during human walking are stabilized by rhythmic muscular activation that originates from neural pathways that connect cervical and lumbar spinal circuits (Dietz, 2002; Meyns et al., 2013; Zehr & Duysens, 2004). Indeed, studies have demonstrated that moving the arms in locomotor-like motion (i.e., alternating or anti-phase arm swing) activates spinal networks underlying interlimb coordination during gait (Hiraoka et al., 2011; Huang & Ferris, 2004; de Kam et al., 2013; Knikou, 2007; Massaad et al., 2014; Selionov et al., 2016; Sylos-Labini et al., 2014; for review, see Zehr et al., 2016). However, recent findings suggest that the priming effect of synchronized arm movements on the lower limb circuitry may be influenced by several factors, including the number of limbs engaged during interlimb locomotor activity and the type of muscles engaged (e.g., flexors vs. extensors) (Balter & Zehr, 2006; de Ruiter, Hundza, & Zehr, 2010; Dragert & Zehr, 2009; Nakajima, Mezzarane, Hundza, Komiyama, & Zehr, 2014; for review, see Zehr et al., 2016). For instance, Balter and Zehr (2006) found that the effect of rhythmic arm movement on leg muscles reflexes was minor when the legs were not moving, corroborating earlier findings that the size of the soleus H-reflex was reduced during bilateral arm cycling when subjects were seated (Frigon, 2004). These studies thus indicate that task constraints may interfere with the coupling strength between arm and legs during locomotor-like movements. It is, therefore, possible that arm swing movements may be less susceptible to rhythmic priming because more biomechanical constraints need to be overcome.

Finally, one can also raise the possibility that rhythmic priming across effector systems, as seen in the finger tapping condition, is associated with a widespread modulation of cortical auditory-motor interconnectivity with distributed effects. It is known that the firing rates of auditory neurons, triggered by auditory rhythms, entrain the firing patterns of motor neurons, and that the auditory system has richly distributed fiber connections to cortical and subcortical motor-related regions of the brain (Crasta, Thaut, Anderson, Davies, & Gavin, 2018; Ermolaeva & Borgest, 1980; Felix, Fridberger, Leijon, Berrebi, & Magnusson, 2011; Molinari, Leggio, De Martin, Cerasa, & Thaut, 2003; Nozaradan, Zerouali, Peretz, & Mouraux, 2015; Paltsev & Elner, 1967; Rossignol & Melvill Jones, 1976). Evidence at multiple levels of inquiry demonstrates that there is a strong functional and anatomical link between auditory and motor-related areas (Chen, Penhune, & Zatorre, 2008; Chen, Zatorre, & Penhune, 2006; Fernández-Miranda et al., 2015; Fujioka, Trainor, Large, & Ross, 2012; Grahn & Brett, 2007; Ross, Iversen, & Balasubramaniam, 2016). Moreover, brain areas involved in sensorimotor synchronization and timing, such as premotor cortices, supplementary motor areas, the cerebellum, the basal ganglia, respond to multiple effectors (for review: Chauvigné, Gitau, & Brown, 2014; Iversen & Balasubramaniam, 2016; Leow & Grahn, 2014; Merchant, Grahn, Trainor, Rohrmeier & Fitch, 2015; Teki, Grube, & Griffiths, 2012). Therefore, one can speculate that auditory-motor entrainment induced during the finger tapping could have generated a residual resonance or secondary entrainment that affected adjacent interconnected neurons. Nozaradan and colleagues (2015) found that there is a dynamic coupling between distant brain areas during rhythmic sensorimotor synchronization corresponding to the interaction of 2 distinct neural entrainment processes. The beat-related entrainment refers to the neural entrainment of neural populations resonating at the frequency of the auditory rhythms (Large & Kolen, 1994; Large, 2008; Nozaradan, Peretz, & Mouraux, 2012a, 2012b), and a distinct motor-related neural entrainment that occurs at the frequency of the movement underlying the production of synchronized movements (Bourguignon et al., 2011; Daffertshofer, Peper, & Beek, 2005; Hickok, Farahbod, & Saberi, 2015; Kourtis, Seiss, & Praamstra, 2008). This study also found evidence of movement-induced enhancement of beat-related neural responses over the hemisphere contralateral to the moving hand (Nozaradan et al., 2015), revealing a widespread modulation of neural activity at homologous brain regions. Therefore, one cannot exclude the possibility that the neural entrainment within neuronal populations involved in finger tapping would also generate activity within associated or adjacent neuronal populations. Extending the current findings using neuroimaging methods with a greater spatial resolution such as magnetoencephalography or invasive recording of local field potentials would be an interesting avenue for future research to confirm this interpretation.

The present findings have direct implications for motor rehabilitation and extend the current application of rhythmic-based interventions. To date, therapeutic interventions such as Rhythmic Auditory Stimulation have successfully used auditory cues (metronome or rhythmically accentuated music with embedded metronome clicks) to prime the motor system by providing a continuous time reference and generating expectations for when a movement needs to be performed, thus increasing the quality and precision of motor responses (Thaut et al., 2015). The results here presented open the possibility of using rhythmic auditory-motor training of other movements, such as finger tapping, as pre-gait exercises to prime the motor system. Further investigation is needed to investigate whether rhythmically cued pre-gait finger tapping exercises may help improve bradykinesia in Parkinson's Disease, and to better understand whether performing the arm swing auditory stimulation training in a seated position engages the leg muscles reflexes differently than with simultaneous leg and arm movements or with arm movements alone but not seated. Recent studies have found evidence that enhancing the amplitude and synchronization of arm swinging improved interlimb coordination and gait patterns in patients with traumatic brain injury (Ustinova et al., 2017), incomplete spinal cord injury (Zhou et al., 2018), and stroke (Stephenson, De Serres, & Lamontagne, 2010). However, these clinical protocols included arm activity simultaneous to leg movements (for review, Zehr et al., 2016), warranting further research on the effectiveness of simultaneous versus isolated arm or leg training in gait rehabilitation.

5. Conclusion

The present study supports the hypothesis that rhythmic priming is possible across effector systems by demonstrating that Rhythmic Auditory Stimulation training of finger movements had immediate effects on gait velocity and cadence of patients with Parkinson's Disease. Results also revealed that swinging the arms in an alternating motion in synchrony with the metronome did not change gait speed in the post-training assessment. These findings, therefore, suggest that finger tapping may prime a common central timekeeping mechanism that persists across effector systems, whereas arm swing movements may be a biomechanically constrained pendular function, possibly better reflecting emergent timing mechanisms, that might not be useful for rhythmic priming for gait. These findings have significant implications for motor rehabilitation and the use of rhythmic auditory cues to prime the motor system and open new avenues for further investigation of the mechanisms underlying cross-effector coupling.

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Declaration of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.humov.2019.03.001.

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