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# Impaired movement timing in neurological disorders: rehabilitation and treatment strategies

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# Abstract

Timing abnormalities have been reported in many neurological disorders, including Parkinson's disease (PD). In PD, motor-timing impairments are especially debilitating in gait. Despite impaired audiomotor synchronization, PD patients' gait improves when they walk with an auditory metronome or with music. Building on that research, we make recommendations for optimizing sensory cues to improve the efficacy of rhythmic cuing in gait rehabilitation. Adaptive rhythmic metronomes (that synchronize with the patient's walking) might be especially effective. In a recent study we showed that adaptive metronomes synchronized consistently with Parkinson patients' footsteps without requiring attention; this improved stability and reinstated healthy gait dynamics. Other strategies could help optimize sensory cues for gait rehabilitation. Groove music strongly engages the motor system and induces movement; bass-frequency tones are associated with movement and provide strong timing cues. Thus, groove and bass-frequency pulses could deliver potent rhythmic cues. These strategies capitalize on the close neural connections between auditory and motor networks; and auditory cues are typically preferred. However, moving visual cues greatly improve visuomotor synchronization and could warrant examination in gait rehabilitation. Together, a treatment approach that employs groove, auditory, bass-frequency, and adaptive (GABA) cues could help optimize rhythmic sensory cues for treating motor and timing deficits.

#### Keywords

gait rehabilitation; Parkinson's disease; rhythmic auditory stimulation; adaptive timing; groove

# Introduction

Motor and perceptual timing abnormalities have been reported in many neurological and developmental disorders, including Parkinson's disease (PD), schizophrenia, autism, and attention deficit/hyperactivity disorder (ADHD).<sup>1</sup> These impairments are likely due to congenital or acquired abnormalities in timing and related brain circuits. Intervention

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strategies often include deep brain stimulation and dopaminergic medication. However, noninvasive and nonpharmacological treatment strategies, including music and rhythm-related interventions (which have no known negative side effects), can be harnessed to target the timing deficits. Based on recent work, we review some treatment strategies that could help optimize the sensory cues used in Parkinson gait rehabilitation.

#### Rhythmic auditory stimulation in Parkinson gait rehabilitation

PD and basal ganglia dysfunction are associated with impaired motor timing.<sup>2–4</sup> Timing deficits in PD commonly occur in gait and can manifest as slow shuffling strides, an accelerating gait, or highly variable and random stride times. Gait impairments in PD have debilitating consequences and can increase the risk of falling and immobility and ensuing problems such as isolation, cognitive decline, and reduced quality of life.<sup>3</sup>

Many studies have demonstrated that rhythmic auditory stimulation (RAS) can improve gait in Parkinson patients.<sup>5,6</sup> For example, walking with an auditory metronome can improve walking speed and stride length<sup>7,8</sup> and reduce timing variability.<sup>9</sup> The stabilizing effect of RAS likely stems from the close neural connections between auditory and motor regions.<sup>5,6</sup> RAS is a promising and effective rehabilitation tool that is noninvasive, low cost, and free from negative side effects.

Despite its proven effectiveness, RAS as typically employed has a few limitations. First, a fixed-tempo metronome requires that the patient synchronize her or his footsteps with the auditory rhythm. Parkinson patients, however, have an impaired ability to synchronize with auditory rhythms.<sup>10</sup> Additionally, synchronizing one's footsteps with a metronome typically requires some attention and volition. Gait rhythms rarely synchronize spontaneously with auditory rhythms when an individual is not explicitly instructed to synchronize.<sup>11</sup> Little empirical evidence supports stable spontaneous synchrony of gait with auditory rhythms, and informal observation of people walking near music corroborates the rarity of spontaneous synchrony. Due to impaired synchronization abilities, spontaneous synchronization is likely even more rare in PD patients.

Another potential limitation of synchronizing with a fixed-tempo metronome is that stride times unfold in a restricted range (around the metronome tempo) rather than the flexible ebbs and flows indicative of healthy gait. In healthy gait, strides unfold in a 1/*f*-like fractal structure and have long-range correlations, whereas in PD, neighboring strides unfold more randomly and have low fractal scaling.<sup>3</sup> Synchronizing with a fixed-tempo metronome lowers fractal scaling of stride times away from healthy levels.<sup>12,13</sup> Fractal structure is associated with adaptability,<sup>3</sup> and overtraining one tempo could decrease gait flexibility, which is required to interact with a dynamically changing environment.

#### Adaptive RAS in PD

Some of the above limitations can be overcome with extensions to the typical RAS paradigm. One method to improve gait stability, reinstate natural gait dynamics, and bypass patients' synchronization impairments is to use an adaptive or interactive rhythmic metronome. An interactive metronome is a system that tracks the human's movement timing

and adapts its timing accordingly. Several interactive systems have been proposed, developed, and tested in various conditions.<sup>14–18</sup> In finger tapping, Keller and colleagues have examined how various parameter settings of a computer-controlled interactive system affect the human's phase and period correction as well as the resulting degree of synchrony.<sup>16,18,19</sup> Behavioral results indicated that synchronization is most stable when the interactive metronome implements a moderate amount of error correction, similar to those that another human might employ. In an fMRI study, when synchronizing with such optimally adaptive metronomes, coordination was judged to be easier, and less activation was observed in cognitive control brain regions; this effortless coordination could be akin to being "in the groove."<sup>18</sup>

For gait applications Miyake and colleagues developed an interactive system termed WalkMate that uses foot-pressure sensors that send step-timing information to a portable computer that uses adaptive nonlinear oscillators (with adjustable entrainment parameters) to control an auditory metronome.<sup>20</sup> We tested whether this interactive metronome system could improve gait dynamics in Parkinson patients.<sup>21</sup> In that study PD participants and healthy controls walked through a long corridor in three cuing conditions: (1) with an interactive metronome that adjusts its phase and period based on the person's step timing; (2) with a fixed-tempo metronome (set to the person's initial gait tempo); and (3) in a silent control condition. Results showed that, in the interactive condition, PD patients' gait was synchronized with the audio rhythm; their fractal scaling of stride times returned to levels of healthy participants; and they felt more stable. In the fixed-tempo condition, neither the PD patients nor controls synchronized with the auditory rhythms, and the patients' fractal scaling remained at impaired levels. The lack of spontaneous synchronization of gait with the fixed-tempo rhythms was noteworthy. Even though passively listening to auditory rhythms consistently activates motor regions,<sup>22-26</sup> the auditory rhythms did not "hijack" or exogenously drive walking rhythms. Auditory rhythms are likely less able to drive step timing (compared to other movements such as finger tapping or head bobbing) because the timing of footsteps is constrained by the need to be positioned at the right time to support the body's (moving) center of mass. Rhythmic movements without such stability constraints, like finger tapping, are more flexible and hence free to adjust timing and integrate sensory cues. In phase-correction experiments, slightly shifted metronome onsets are integrated into the timing of the upcoming movement cycle,<sup>27,28</sup> and this "phase correction" is stronger for finger tapping than step timing.<sup>29,30</sup> When a pacing cue is highly misaligned with movement timing, the misaligned pacing cue is not as readily integrated into movement timing;<sup>27,31</sup> and in walking, highly misaligned cues are less likely integrated due to stability constraints.

In order to integrate auditory cues into movement timing, the cues should be roughly aligned with the movement.<sup>32</sup> The interactive system aligns the auditory cues to step timing, so that the sensory cues can be integrated into the motor output timing. This serves to stabilize gait timing; extreme stride times will be tempered by external cues (which should always be closer to the mean than extreme values), and the system provides a type of "memory" in that its output timing is based on previous beats (to decrease randomness). Computational modeling of the interactive system under various entrainment parameters could be informative for better understanding the exact mechanisms.<sup>33</sup>

Matching auditory and motor rhythms can be achieved through interactive technology (i.e., programming an adaptive system to synchronize with the person) or the human's volition (i.e., intention to synchronize with a metronome rather than ignore it). Volitional alignment is a reliable method to align movements with auditory cues and influence step timing and is clearly effective in experimental and laboratory settings.<sup>11</sup> However, a busy real-world environment presents greater attentional demands, and, because synchronizing gait with auditory rhythms requires some attention, an interactive system could be especially effective in real-world settings to the extent that it reduces the need to attend to the pacing signal.

Other work demonstrates the efficacy of interactive timing systems in gait applications. Parkinson patients who walked with the interactive WalkMate system showed an increase of fractal structure in stride times (but no difference in speed) after training with the system over a few days.<sup>34</sup> Leman and colleagues have developed an interactive system that alters the phase and rate of *music* based on a person's stride times. This interactive music player can improve physiological function during exercise<sup>35</sup> and improve gait in Parkinson patients.<sup>36</sup> Such an interactive music player could be especially effective for gait rehabilitation because of its potential motivational properties as well as the possibility to introduce optimal features into the signal (as described below).

#### Musical groove and motor system engagement

Another way to improve the efficacy of RAS in gait rehabilitation is to optimize auditory signals. RAS most commonly uses an auditory metronome that plays beeps or clicks, and successful RAS applications have also used metronomes embedded in music or simply music.<sup>5,6,37,38</sup> Gait rehabilitation could benefit from using music that is especially powerful at inducing movement.<sup>39</sup>

Some music is highly compelling and potent to engage the motor system and encourage listeners to move. The musical quality associated with movement induction has received substantial research attention and is often termed "groove."<sup>40–42</sup> Songs rated as "high groove" afford more accurate movement synchrony and induce more spontaneous movement.<sup>41</sup> Thus, the phenomenon of groove is largely about stable sensorimotor coupling<sup>41,43</sup> and captures the music's efficiency for entrainment.<sup>42</sup> Many musical qualities are thought to promote groove. Rhythmic qualities that promote the ease of synchrony include an increased number of metrical levels,<sup>44</sup> rhythmically rich reinforcement of the beat<sup>43</sup> as in syncopation,<sup>45,46</sup> and, generally speaking, a repetitive rhythm with a clear pulse.<sup>40,47</sup> Ratings of groove are highly consistent among individuals,<sup>41</sup> suggesting that some features of the audio signal are especially compelling at engaging the human motor system.

In a recent study on the neural underpinnings of groove, we examined participants' motor system activity while they listened to high- versus low-groove music.<sup>48</sup> Musicians and nonmusicians listened to musical clips that were rated by Janata et al.<sup>41</sup> as having high groove or low groove, as well as to control stimuli consisting of spectrally matched noise. Participants received single-pulse (excitatory) transcranial magnetic stimulation (TMS) over the primary motor cortex, and we measured the ensuing motor evoked potential (MEP) in

the contralateral hand and arm muscles as an index of motor system activity. Results showed that, for musicians, the high-groove music yielded larger MEPs than did low-groove music and noise, with this effect being more pronounced on the beat than off. These results suggest that high-groove music engages the motor system more strongly and that corticospinal excitability is modulated in time with the beat of a high-groove song. Results for nonmusicians unexpectedly showed that MEPs were smaller for high-groove music than for low-groove music and noise. This result for the nonmusicians might stem from the need to suppress motor system activity when listening to high-groove music under experimental instructions to remain still. Alternatively, in light of nonmusicians' tendency to feel the beat relatively earlier than musicians (i.e., nonmusicians tend to tap earlier before the beat than musicians<sup>49</sup>), it is possible that our TMS pulses (presented directly on the beat) occurred after the ideal excitatory phase and in a refractory trough for the nonmusicians (compare with other studies investigating auditory-motor coupling that presented TMS pulses 100 ms before the beat 50,51). In sum, high-groove music modulated corticospinal excitability in both groups, whereas low-groove music had no effect compared to a noise-control condition. Thus, groove music's direct and potent effect on the motor system could be harnessed for gait rehabilitation.

This leads to the question of what specific musical or audio features are related to movement induction and groove. In our TMS study, we used music information retrieval (MIR) tools<sup>52</sup> to extract audio features of the high- and low-groove stimuli. Even with a small set of songs (four songs in each category), we observed that the high-groove songs contained greater spectral flux (i.e., a measure of the fluctuation of frequency content) in the low-frequency bands.<sup>48</sup> We corroborated this connection between bass-frequency energy and perceived groove in a much larger corpus of commercially available songs as well as with novel musical stimuli that manipulated the frequency range of the bass.<sup>53</sup>

#### Low-pitched tones and timing cues

In addition to influencing groove ratings, bass frequencies also have a pronounced effect on actual movement. Low-pitched frequencies were associated with more active movement and increased temporal regularity of movement in motion-capture studies of moving to music.<sup>54,55</sup> When participants synchronized tapping movements with chords containing small onset asynchronies, tap timing was more strongly influenced by the lower-pitched tone.<sup>56</sup> Furthermore, when participants performed a challenging off-beat tapping task that required them to avoid tapping in synchrony with pacing tones, it was more difficult to do so with sequences containing low tones than for sequences of high tones.<sup>57</sup> The tendency to move along with the lower-pitched tones is reflected by the musical convention that bass-ranged instruments often lay down the rhythmic foundation and provide the pulse on metrically strong beats.58,59,<sup>a</sup>

We recently used EEG to examine the neural basis of the tendency to carry rhythmic timing information in lower-pitched tones.<sup>60</sup> We presented rhythmic sequences that consisted of

<sup>&</sup>lt;sup>a</sup>Melodic information on the other hand is typically carried by higher-pitched voices; interestingly, pitch information of the higher voice is encoded more robustly by the auditory cortex.  $^{71,72}$ 

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simultaneous high- and low-pitched piano tones and occasionally presented one of the tones 50 ms earlier than expected. Unexpected timing deviants of each tone produced a mismatch negativity (MMN) response in the EEG signal. However, the MMN was larger for timing deviants in the lower- than higher-pitched stream. This indicates a more robust temporal encoding of the lower-pitched stream. We used the same stimuli in a finger-tapping experiment and found that motor timing was also more influenced by the lower-pitched tones. Together these experiments show that the lower-pitched tones have a greater influence on the perception of timing and on auditory-motor synchronization.

Finally, to localize the source of the low-tone timing, we input the stimuli into a biologically plausible model of the auditory periphery<sup>61</sup> and looked at the estimated spike counts on the auditory nerve. The modeling revealed that superior time encoding for the lower-pitched piano tones arises in the cochlea of the inner ear.<sup>b</sup> Thus, we suggest that the musical convention to place timing cues and the rhythmic pulse in the lower-pitched instruments likely arises from basic auditory physiology.<sup>60</sup>

### Visual metronomes in gait rehabilitation

Most sensory cuing studies in PD use auditory rhythms that capitalize on the close neural connections between auditory and motor regions and the high temporal resolution of the auditory system. Indeed, in studies comparing auditory and visual cues, PD patients strongly preferred and showed greater gait improvements with auditory cues compared to flashing visual cues.<sup>9,62,63</sup> Difficulty synchronizing with visual flashes is long established in fingertapping studies.<sup>27</sup> However, synchronization improves dramatically with moving visual targets,<sup>64–66</sup> and compatibly moving stimuli increase activation in the basal ganglia (timingrelated regions that are impaired in PD).<sup>67</sup> Moving stimuli are "modality appropriate" for the visual system, which excels at processing spatial and motion information.<sup>68</sup> In light of improved synchronization with moving visual targets, future work could investigate the efficacy of using moving visual cues in Parkinsonian gait rehabilitation. Previous technical limitations made this difficult, but portable visual displays are now widely available and enable the use of compatibly moving visual cues in glasses. Additionally, a number of studies show that stationary visual stripes taped on the ground can improve Parkinsonian gait.<sup>69</sup> A portable glasses-mounted display that *virtually* superimposes target lines on the path could prove effective in gait and allow mobility of these visual cues. Some individuals are especially successful at synchronizing with moving visual cues,<sup>70</sup> and the use of optimal moving or spatial visual cues could warrant evaluation in gait rehabilitation. Finally, multisensory cuing systems that capitalize on modality appropriateness by including complementary auditory and visual information could promote optimal cue integration and stable synchronization.

<sup>&</sup>lt;sup>b</sup>Nonpitched percussion tones with a broad spectrum and a sharp onset should also produce a clear burst of spikes on the auditory nerve and provide a clear timing cue, although we did not examine this.

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# Conclusion

In sum, timing impairments exist in a number of neurological disorders including PD. Gait impairments can be alleviated with RAS for many PD patients. The efficacy and usability of RAS could be improved further with sensory cues that optimize the ease of entrainment. We suggest a GABA (groove, auditory, bass-frequency, adaptive) approach for rhythmic cues. An adaptive system that tracks and adapts to the human's step timing could decrease attentional needs, stabilize gait, and increase motivation in the patient. One strategy would be to vary the cooperativity of the adaptive system parametrically, starting with settings that make synchronization easy but then progressively challenging the patient to prepare for the uncertainties and perturbations that characterize the real world.<sup>33</sup> Other strategies to improve synchrony include using groove music that strongly engages the motor system and using low-pitched pulses that provide strong timing cues. Treatment strategies rightfully focus on auditory cuing, but visual cues that incorporate spatial or moving cues could also improve synchrony and warrant examination. Applying rhythmic interventions to clinical disorders can alleviate symptoms and improve quality of life as well as help us better understand the underlying temporal processing. Gaining knowledge on this temporal processing and what differentiates responders from nonresponders can provide insight into treatments and eventually cures.

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