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Simone Dalla Bella
Université de Montréal

Chapter 15

The use of rhythm in rehabilitation for patients with movement disorders

Simone Dalla Bella[1,2,3]
[1]International Laboratory for Brain, Music, and Sound Research (BRAMS), Montreal, QC, Canada, [2]Department of Psychology, University of Montreal, Montreal, QC, Canada, [3]Centre for Research on Brain, Language and Music (CRBLM), Montreal, QC, Canada

Introduction

Humans, across groups and cultures, and from childhood to older age, engage in music activities, and are moved by music. We experience music very often in our everyday environment, by passive or active listening. Some of us deliberately engage in music activities such as playing an instrument, singing, and dancing. These activities involving music are typically multisensory and, owing to their complexity, recruit various neuronal networks mediating sensory, motor, cognitive, and emotional responses. These functions are not devoted to music per se. Some of them are general functions spanning across domains and which can be modified via musical training or activities, as a privileged vehicle for inducing brain plastic changes (Dalla Bella, 2016; Herholz & Zatorre, 2012; Sihvonen et al., 2017). The possibility that music can change the brain is particularly appealing in the context of devising targeted music-based interventions, for rehabilitation in various neurological diseases, such as stroke, dementia, and Parkinson's disease (PD) (Särkämö, 2018; Sihvonen et al., 2017). Indeed, music has a very high potential as a tool for rehabilitation. Music is capable of engaging parallel brain circuitries underpinning reward, sensory and motor processes, arousal, and affective regulation. In addition, music activities are particularly enjoyable, thus making adherence to treatment more likely, and enhancing well-being throughout the life span. Current advances in our understanding of the brain structure and functioning underlying music can add to this endeavor, by fostering theory-driven interventions to be tested in clinical settings (translational approach; Dalla Bella, 2018; Sihvonen et al., 2017). In this chapter I will focus in

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particular on interventions driven by the rhythmic properties of music, and by their tendency to recruit the motor system. A model of the success of these interventions is PD, to which I will devote particular attention.

Moving to musical beat: a widespread and pleasurable activity

A widespread response to music, deliberate and spontaneous, is to move to its beat. Listening to music with a very salient beat structure (e.g., a march or a waltz) often compels us to move. Human proclivity to move to music and to experience this activity as very pleasurable is linked to what is called musical “groove.” This is associated to properties of musical structure such as rhythmic complexity, syncopation, and harmonic complexity (Matthews, Witek, Heggli, Penhune, & Vuust, 2019; Vuust & Witek, 2014; Witek, Clarke, Wallentin, Kringelbach, & Vuust, 2014), as well as individual differences in listeners’ attitudes (Senn, Kilchenmann, Bechtold, & Hoesl, 2018). An increasing body of evidence from experimental psychology and cognitive neuroscience indicates that the rhythm conveyed by an auditory stimulus and movement are tightly linked. Music, owing to its temporal regularity and predictability, is ideally suited to engage our body. When we tap our feet or sway our body along with our preferred song, while synchronizing our steps to the beats delivered by our MP3 player during jogging, dancing, or while performing synchronized sports (e.g., swimming), we entrain to the regular pulse of music.

Matching movements to a beat is possible because the temporal dynamics of rhythmic sound (e.g., its periodicity) drives our attention (Large & Jones, 1999), and thereby allows predicting when an upcoming event is going to occur (e.g., the next musical beat). Allocation of attention to the temporal dynamics of a rhythmic stimulus is described by the dynamic attending theory (DAT) (Jones & Boltz, 1989; Large & Jones, 1999). According to DAT, attending is a dynamic process, which can be successfully modeled by internal neurocognitive self-sustained oscillations (Fujioka, Trainor, Large, & Ross, 2012; Nozaradan, Peretz, Missal, & Mouraux, 2011). Internal oscillations, which have been associated to attentional pulses, synchronize to the most prominent aspects of the sound signal (e.g., tones in an isochronous sequences, beats in music). Attention is dynamically shifted to the most salient events in the sound, through a process called “entrainment,” thus generating temporal expectations. The mechanisms leading to couple movement to the perceived beat play a critical role in understanding how rhythm can be harnessed to stimulate or reactivate the motor system in patients with motor disorders. These mechanisms are reviewed below.

Moving to musical beat: cognitive and neuronal underpinnings

The majority in the general healthy population are well equipped to move to the beat of music. Apart from some exceptions, namely individuals who poorly synchronize to the beat (Palmer, Lidji, & Peretz, 2014; Sowiński & Dalla Bella, 2013), this ability is very common and relatively independent from musical training (Repp, 2010; Sowiński & Dalla Bella, 2013). The proclivity to move spontaneously to the beat is visible very early during development (within the first 2 years of life; Zentner & Eerola, 2010), while precise audiomotor synchronization appears a bit later, particularly in a social setting (Kirschner & Tomasello, 2009). Motor synchronization to the beat involves both the perception of the main periodicity underlying a temporal pattern, simple or complex, and the motor processes needed to couple motor events to the beat. Beat perception can be tested with tasks such as the Beat Alignment Test (BAT) in which a listener has to detect whether tones are aligned or not with the musical beat (Iversen & Patel, 2008). Motor synchronization to the beat is often assessed by asking participants to tap their finger in synchrony with a pacing stimulus, like a metronome or music (finger tapping paradigm; Repp, 2005; Repp & Su, 2013). More recently, more complex batteries of tests have been devised to assess a full array of rhythmic abilities, perceptual and sensorimotor. Examples are the Battery for the Assessment of Auditory Sensorimotor and Timing Abilities (BAASTA, Dalla Bella, Farrugia, et al., 2017), developed in our lab, and the Harvard BAT (Fujii & Schlaug, 2013). The advantage of these batteries over single tests is their ability to characterize profiles of rhythmic abilities and their sensitivity to individual differences in various populations (for BAASTA, see Bégel et al., 2017, submitted; Benoit et al., 2014; Cochen De Cock et al., 2018; Dalla Bella, Benoit, et al., 2017; Dalla Bella, Dotov, Bardy, & Cochen de Cock, 2018; Dalla Bella, Farrugia, et al., 2017; Falk, Müller, & Dalla Bella, 2015; Puyjarinet, Bégel, Lopez, Dellacherie, & Dalla Bella, 2017). As will be shown below, detecting individual profiles of rhythmic abilities in patient populations may play a pivotal role in devising personalized rhythm-based interventions.

The ability to move to the beat requires the coordinated action of various neuronal networks (Damm et al., 2020). Perceiving the beat of an auditory sequence engages auditory regions of the brain (the superior temporal gyrus; Chen, Penhune, & Zatorre, 2008a; Schwartze & Kotz, 2013; Thaut, 2003). In addition, classical motor regions including the basal ganglia, premotor cortex, presupplementary motor area, and the cerebellum light up during beat perception, notwithstanding the lack of an overt motor response (Chen, Penhune, & Zatorre, 2008b; Coull, Cheng, & Meck, 2011; Grahn & Brett, 2007; Grahn & Rowe, 2009; Paquette, Fujii, Li, & Schlaug, 2017). The coupling of a motor response to the beat is afforded by sensorimotor integration regions (dorsal premotor cortex; Chen, Zatorre, & Penhune, 2006; Coull et al., 2011; Zatorre, Chen, & Penhune, 2007). Malfunctioning of these networks is associated with rhythmic deficits found in neurodegenerative disorders such as PD (Benoit et al., 2014; Grahn & Brett, 2009; Jones & Jahanshahi, 2014; Pastor, Artieda, Jahanshahi, & Obeso, 1992; Spencer & Ivry, 2005), as well as in neurodevelopmental disorders including attention-deficit hyperactivity disorder (Noreika, Falter, & Rubia, 2013; Puyjarinet et al., 2017), developmental coordination disorder (Trainor, Chang, Cairney, & Yao-Chuen, 2018), stuttering (Falk et al., 2015), autism spectrum disorder (Allman, Pelphrey, & Meck, 2012), and speech and language impairments (Bégel et al., submitted; Corriveau & Goswami, 2009; Corriveau, Pasquini, & Goswami, 2007; Goswami, 2011; Huss, Verney, Fosker, Mead, & Goswami, 2011).

In a nutshell, current knowledge of the behavioral and brain mechanisms underpinning rhythmic abilities reveals that rhythmic musical stimuli can engage motor areas in the brain. Interestingly, temporal predictions driven by rhythmic auditory stimuli and their oscillatory neuronal counterpart are reinforced by overt motor production, which in turn improves perception (Morillon & Baillet, 2017; Morillon, Schroeder, & Wyart, 2014). Hence, moving to the beat of a rhythmic stimulus provides ideal conditions to enhance temporal prediction and attending, while improving both perceptual and motor performance at the expected times. This has particular relevance for the aforementioned patient populations showing impaired temporal prediction and rhythmic processes. Moving to an auditory beat can be exploited to pave the way to effective and individualized rhythm-based interventions. Indeed, identifying the components of the rhythm system spared by brain lesion or congenital anomalies may guide individualized rehabilitation strategies. In this chapter I will show how this approach can be used successfully for predicting the success of a music-based rhythm intervention in PD.

Rhythm, a successful tool for motor rehabilitation

The presentation of rhythmic stimuli has shown beneficial effects on motor behavior in patients with movement disorders (e.g., Ghai, Ghai, Schmitz, & Effenberg, 2018; Spaulding et al., 2013), but also in older healthy adults (Ghai, Ghai, & Effenberg, 2018). The vast majority of studies focused on gait disorders, given their functional relevance for patient populations, their deleterious impact on quality of life, and the associated economic burden. Dysfunctional gait, namely a slow, broad-based, shuffling, and cautious walking pattern ("senile gait disorder"; Salzman, 2010) is not uncommon in older adults. It is observed in about one-third of adults above 70 years of age among community-residing older adults (Verghese et al., 2006), a proportion increasing with age (Downton & Andrews, 1991). Particular attention is paid to gait speed, as it is a hallmark of health and functional status (Cesari, 2011), it declines with age and is a strong predictor of disability, healthcare utilization, nursing home admission, and mortality (Blain, Carriere, & Sourial, 2010; Cesari et al., 2005; Ostir, Kuo, Berges, Markides, & Ottenbacher, 2007; Shumway-Cook, Guralnik, & Phillips, 2007; Studenski, Perera, & Patel, 2011). Reduced gait speed in older adults is also treated as a warning sign of cognitive decline and a good predictor of its onset (Aggarwal, Wilson, & Beck, 2006; Buracchio, Dodge, Howieson, Wasserman, & Kaye, 2010; Inzitari, Newman, & Yaffe, 2007). Importantly, gait dysfunctions are a major cause of falls in older adults. Among community-dwelling older adults over 64 years of age, approximately 28%–35% of people experience falls (Blake et al., 1988).

Gait disorders are exacerbated by neurodegenerative disorders and are a hallmark of PD (Grabli et al., 2012). PD is the second most common neurodegenerative disorder (after Alzheimer's disease), and the most common serious movement disorder (Hirtz et al., 2007). Worldwide, about 4 million people suffer from PD, with more than 1.2 million just in Europe (Andlin-Sobocki, Jönsson, Wittchen, & Olesen, 2005). These numbers will tend to increase as a result of the aging population. For example, the prevalence in Europe is estimated at 160 PD patients per 100,000 among people aged 65 and older; this number is forecasted to double by 2030 (de Rijk et al., 1997; Dorsey et al., 2007).

PD results from the progressive loss of neurons in the substantia nigra, disrupting dopaminergic projections to the basal ganglia (caudate nucleus and putamen) and leading to a deregulation of basal ganglia–thalamocortical (BGTC) circuitries. Three cardinal symptoms characterize PD, namely resting tremor, limb rigidity, and bradykinesia (or akinesia) (Jankovic, 2008; Kalia & Lang, 2015; Samii, Nutt, & Ransom, 2004). The first symptom to appear is resting tremor, an involuntary low-frequency repetitive movement caused by contracting muscles. Tremor usually occurs unilaterally, worsens over time, and sometimes extends bilaterally. Rigidity refers to abnormal muscle stiffness or lack of flexibility in the limbs or other body parts, preventing muscles from stretching and relaxing; it similarly affects agonist and antagonist muscles. Bradykinesia indicates a general slowness of voluntary movement (akinesia, when voluntary movement is practically absent). It is one of the most disabling deficits in PD, has deleterious effects on fine motor control, and is visible in tasks such as writing or finger tapping. Postural instability and gait disorders, albeit they are not treated as cardinal symptoms per se, are also important motor signs in PD, gaining importance as the disease progresses (Bloem, 1992; Grabli et al., 2012; Koller & Montgomery, 1997). At the initial stages of the disease, gait dysfunctions can be detected in conditions of dual-task, for example, when patients walk while performing a concurrent task (e.g., speech or simple arithmetic calculation) tapping into limited attentional resources and executive functions (see Al-Yahya et al., 2011; Kelly, Eusterbrock, & Shumway-Cook, 2012). Parkinsonian gait is characterized by small steps (i.e., reduced stride length), unchanged or slightly increased cadence (steps/min) compensating for the reduced stride length, reduced gait velocity, together with festination and freezing (i.e., difficulty in gait initiation or stopping when turning or approaching an object) (Giladi, 2001; Grabli et al., 2012; Morris, Huxham, McGinley, Dodd, & Iansek, 2001; Morris, Iansek, Matyas, & Summers, 1994).

Gait and balance disorders are major therapeutic challenges in PD as they negatively impact the activities of daily living, and represent a growing economic burden for the healthcare system (Grabli et al., 2012). Gait deteriorates over time, impairing mobility, limiting independence, and reducing quality of life (Elbaz et al., 2002). The increased likelihood of falls (Morris et al., 2001; Samii et al., 2004) is a major reason for morbidity and disability in PD (Contreras & Grandas, 2012), leading to fractures and head injuries that may be fatal (de Lau, Verbaan, van Rooden, Marinus, & van Hilten, 2014). From 38% to 87% of PD patients experience falls (Contreras & Grandas, 2012). Falls are a quite common outcome of motor disorders such as PD. An interesting meta-analysis has reported that the recurrent falling rate for PD patients was 57% among those patients who had reported previous falls (Pickering et al., 2007). Recurrent falls are highly disabling. Falling often leads to severe consequences, including head injuries, fractures (hip in particular), and, in some instances, death (Wenning et al., 1999). Falls are also typically associated to the fear of new falls (Adkin, Frank, & Jog, 2003), which result in loss of independence, reduced mobility, increased osteoporosis, reduced social activity, and depression (Bloem, Hausdorff, Visser, & Giladi, 2004). Falls in PD also increase institutionalization rates. Overall the direct economic burden of falls in PD has been estimated to be twice as big as for of nonfallers (Spottke et al., 2005). Unfortunately, gait and balance disorders respond quite poorly to long-term dopamine-replacement therapy (Grabli et al., 2012; Sethi, 2008). This situation motivates the search for complementary nonpharmacological interventions to improve gait in PD (Tomlinson et al., 2012).

Beneficial effects of music and rhythm in Parkinson's disease

There are several options for alleviating motor symptoms in PD, including pharmacotherapy, surgery, neuromodulation, and nonpharmacological treatments (e.g., physical therapy). A common treatment is to prescribe patients a dopamine-replacement therapy (with levodopa and dopamine agonists), to compensate for the decay of the basal-ganglia dopaminergic track (for a review, Connolly & Lang, 2014). Other methods, some of them invasive, aim at reducing the deregulation of BGTC circuitries via the removal of deep-brain structures (e.g., pallidotomy or thalamotomy; see Lozano, Tam, & Lozano, 2018, for a critical review), surgery combined with deep-brain stimulation (e.g., of the subthalamic nucleus; Benabid, Pollak, Louveau, Henry, & de Rougemont, 1987; Kalia, Sankar, & Lozano, 2013), and, more recently, neuromodulation using transcranial magnetic stimulation or transcranial direct current stimulation (Benninger & Hallett, 2015).

Complementary to pharmacotherapy and the other aforementioned interventions, nonpharmacological treatments are considered as a way to improve quality of life and reduce or control the motor symptoms of PD (Rubinstein, Giladi, & Hausdorff, 2002). These methods are based on physical and exercise therapies (Kwakkel, de Goede, & van Wegen, 2007), and span from sitting and standing, body resistance training, articulation for posture and balance, to endurance and strengthening exercises for improving general physical conditions. Physical therapy in general has shown some beneficial effects in improving patients' physical functioning, quality of life, leg strength, balance, and gait (Goodwin, Richards, Taylor, Taylor, & Campbell, 2008). Here I will focus on the methods making use of external rhythmic cues, with a particular attention to musical stimulation.

Music is perfectly suited to convey rhythmic stimulation. Moving to a musical beat is not only activating neuronal structures underlying rhythm and motor control, some of which are impaired in PD (see below), but also, being a highly participatory and motivating activity, is known to engage the reward system (Salimpoor, Zald, Zatorre, Dagher, & McIntosh, 2015). Thus therapies using music and rhythm as tools for motor rehabilitation in PD can have positive effects on patients' exercise capacity and motivation, fostering social participation, increase adherence, and ultimately enhance quality of life on top of improving motor symptoms (Pacchetti et al., 2000; Pohl, Dizdar, & Hallert, 2013; Ziv & Lidor, 2011). Along this line, there is growing evidence of positive effects of dance-based interventions, such as tango, on motor symptoms, quality of life, and social participation in PD (Duncan & Earhart, 2012; Earhart, 2009; Foster, Golden, Duncan, & Earhart, 2013; Hackney & Earhart, 2009; for beneficial effects of music and dance in healthy older adults, see Chapter 11: Toward music-based auditory rehabilitation for older adults).

Positive effects of presenting rhythmic cues (rhythmic auditory cueing—RAC) on gait in patients with PD have been reported since 1942 (Von Wilzenben, 1942). PD is a prototypical example showing promising effects of RAC on gait kinematics (Ghai et al., 2018; Kwakkel et al., 2007). The intervention is relatively simple and consists of instructing the patient to walk together with a regular stimulation in the form of a repeated sound (a metronome; e.g., Elston, Honan, Powell, Gormley, & Stein, 2010; Enzensberger, Oberlander, & Stecker, 1997; Howe, Lovgreen, Cody, Ashton, & Oldham, 2003) or a piece of music with a salient beat, sometimes with an embedded metronome (e.g., Benoit et al., 2014; McIntosh, Brown, Rice, & Thaut, 1997; Thaut, Rice, Braun Janzen, Hurt-Thaut, & McIntosh, 1996). The stimulation rate is typically individualized relative to patients' preferred cadence (number of steps/min). Patients typically benefit from auditory cues presented at rates ranging from 80% to 125% of their preferred cadence (Bryant, Rintala, Lai, & Protas, 2009), which usually hovers around 100 steps/min (Nieuwboer et al., 2007). When a rhythmic stimulus is presented, PD patients typically walk faster, increase their step length (McIntosh et al., 1997), and reduce the frequency of freezing episodes (Arias & Cudeiro, 2010). This effect of RAC is immediate but usually disappears once the stimulation is stopped. Interestingly, longer term positive effects on walking in everyday life even in the absence of stimulation are found following RAC-based interventions (Lim et al., 2005). In these protocols patients are submitted to programs in which they are asked to walk with RAC a few times a week for several weeks; gait is tested in the absence of rhythmic stimuli before and after the rehabilitation program. After the intervention, PD patients show faster walking speed (Rochester, Burn, Woods, Godwin, & Nieuwboer, 2009), and a significant reduction of freezing phenomena (Nieuwboer, 2008). Comparable motor benefits can be achieved when rehabilitation via RAC is carried out in a home environment with a stimulating device (e.g., see the RESCUE project—Rehabilitation in Parkinson's Disease: Strategies for Cueing) (Nieuwboer et al., 2007). A critical question is to what extent these beneficial effects of RAC persist over time, considering the inevitable decline linked to neurodegeneration. To date, evidence is not conclusive in this respect. In some cases performance deterioration is observed within 12 weeks after the therapy (Nieuwboer et al., 2001); yet, others report rather negligible decline in gait performance, if at all, after 4–6 weeks (Benoit et al., 2014; Marchese, Diverio, Zucchi, Lentino, & Abbruzzese, 2000).

Which are the mechanisms and brain circuitries supporting the beneficial effects of RAC on walking in PD? A possibility, which has been put forward recently, is that the effect of RAC is mediated by a general purpose system responsible for beat perception and motor synchronization to a beat (Dalla Bella, Benoit, Farrugia, Schwartze, & Kotz, 2015; Dalla Bella, 2018; Nombela, Hughes, Owen, & Grahn, 2013; see also Damm et al., 2020). This is the same system affording tracking the beat of simple and complex rhythmic sequences, and coupling of movement to the beat across various behaviors, such as finger tapping, walking, and speaking (Puyjarinet et al., 2019). This idea builds on processes underlying temporal prediction and timing, identified in the context of auditory processing at different levels of stimulus complexity such as speech and tones (Kotz & Schwartze, 2010; Schwartze & Kotz, 2013; Schwartze, Rothermich, Schmidt-Kassow, & Kotz, 2011). The model, illustrated in Fig. 15.1, involves two parallel networks. The BGTC network (in violet) supports the attention-dependent evaluation of temporal intervals, and self-generation of movements. The network is involved in action initiation and in overt estimate of stimulus duration. The cerebellum–thalamocortical (CTC) network (in cyan) supports the preattentive encoding of the temporal structure of event sequences, and matching movements to external cues (Coull et al., 2011; Kotz & Schwartze, 2011). Functional BGTC and CTC networks are essential for extracting the beat structure of a predictable auditory sequence, developing temporal expectations of the upcoming events (i.e., the following beats), and aligning movements to the beat.

As a result of the progressive loss of neurons in the substantia nigra (Factor & Weiner, 2008) the BGTC is deregulated in PD. This is associated with deficits in the perception and production of temporal intervals

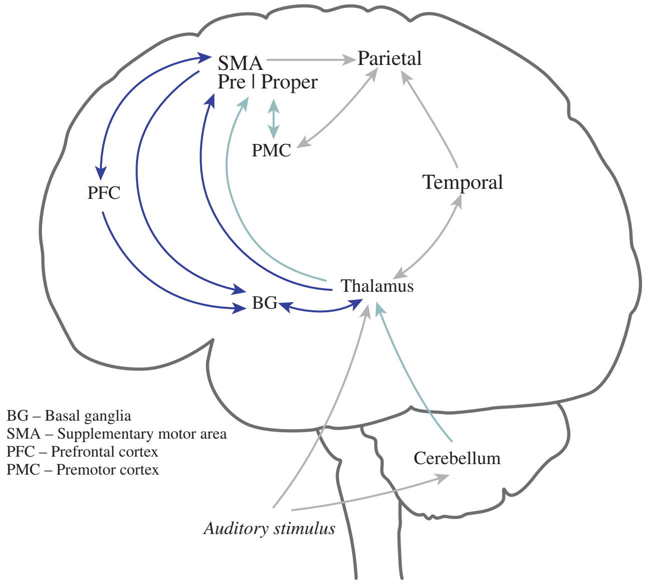

FIGURE 15.1 Networks underlying rhythmic auditory cueing in Parkinson's disease. *From Dalla Bella, S., Benoit, C. E., Farrugia, N., Schwartze, M., & Kotz, S. A. (2015). Effects of musically cued gait training in Parkinson's disease: Beyond a motor benefit.* Annals of the New York Academy of Sciences, 1337*, 77–85.*

(Allman & Meck, 2011), as well as in beat perception (Benoit et al., 2014; Grahn & Brett, 2009). Yet, the CTC network is spared by the disease, thus allowing for unimpaired coding of prominent discrete events in the temporal structure (e.g., musical beats). This representation of temporal structure paves the way to dynamic attending (i.e., providing attractors for attentional oscillations), generating an expectancy scheme via entrainment (Kotz & Schwartze, 2011) and providing a temporal scaffolding for synchronized action.

Within this framework, two possibilities can be envisioned to explain the effects of RAC. One is that the malfunctioning of the BGTC network in PD is compensated by the recruitment of the CTC network, affected later during the progression of the disease (Dalla Bella et al., 2015; Nombela et al., 2013). In keeping with this hypothesis, enhanced cerebellar activity after gait training with RAC was found in one study (del Olmo, Arias, Furio, Pozo, & Cudeiro, 2006). Another possibility is that the deregulated BGTC network still affords some degree of beat processing (Dalla Bella, Benoit, et al., 2017; Dalla Bella et al., 2018). Residual beat processing may provide sufficient information for temporal pacing of movement initiation and execution so that some of the patients can benefit from rhythmic cues. To date it is still unclear which of the networks support the beneficial effects of RAC. However, in both cases, it is hypothesized that the response to RAC is mediated by beat perception and synchronization mechanisms. Thus individual differences in these abilities are expected to be good predictors of the response to RAC.

Individual differences in rhythmic abilities predict the success of rhythmic auditory cueing

There is a paucity of research on the link between individual rhythmic skills and the widespread ability to walk to the rhythm of an external stimulus. Gait is often treated as mostly an autonomous spinally controlled process with limited adaptability (Dietz, 2003; Dimitrijevic, Gerasimenko, & Pinter, 1998; Pearson & Gordon, 2000), dominated by body dynamics which imposes a preferential rate of stepping. However, top-down cortical contributions to gait control are seen in situations of dual-task. The dual-task paradigm consists of providing the individual a secondary cognitive task (e.g., counting backward) together with a primary task, such as walking (Al-Yahya et al., 2011; Woollacott & Shumway-Cook, 2002). Walking in a dual-task situation is typically more challenging than walking alone, by requiring more cognitive resources such as selective attention and flexibility. This is particularly important in older adults, which are typically more affected by a dual-task due to a reduced cognitive reserve (Yogev-Seligmann et al., 2010). With regard to rhythmic skills, there is recent evidence in healthy young adults that beat perception affects gait when participants synchronize with rhythmic stimuli. Walking to music with a less-salient beat (low-groove) is detrimental to gait (i.e., reducing cadence and step length) in particular for participants with poor beat perception (Leow, Parrott, & Grahn, 2014; Ready, McGarry, Rinchon, Holmes, & Grahn, 2019).

Until very recently, it was unclear whether individual differences in rhythmic abilities in PD patients can act as predictors of their response to RAC. To test this hypothesis we asked patients with PD and matched controls to walk together with highly familiar march music (Cochen de Cock et al., 2018; Dalla Bella et al., 2018). No explicit instruction to synchronize heel strikes to the beat was given, as this is known to hinder gait kinematics (Leow, Waclawik, & Grahn, 2018). The rate of the rhythmic stimuli was 10% faster relative to each participant's preferred cadence. We measured the alignment between the footfalls and the stimulus beat times, reflecting patients' synchronization ability. Moreover, we assessed beat perception with the BAT (Iversen & Patel, 2008), taken from BAASTA (Dalla Bella, Farrugia, et al., 2017), in which participants detected whether a metronome was aligned or not with the beat of musical excerpts. Patients, like controls, positively responded to RAC, by increasing speed and stride length. Yet, patients varied significantly in their response to the stimulation. Out of 39 patients, 22 increased their walking speed above the smallest clinically significant difference (>6 cm/s) (Hass et al., 2014). The other 17 did not exhibit a positive response to RAC. With our surprise, cueing was detrimental for six patients, who significantly decreased their gait speed (−18 cm/s, on average, compared to no stimulation) and the length of their strides (−11 cm). These different responses to RAC were linked to patients' rhythmic abilities. Patients with a positive response to RAC were more apt to align the footfalls to the beat (good synchronizers) and had relatively spared beat perception relative to controls (see Fig. 15.2). Moreover, patients with positive response to cueing rated their perceptual abilities and musical training higher than the others (Goldsmiths Musical Sophistication Index; Müllensiefen, Gingras, Musil, & Stewart, 2014). In sum, a good response to RAC is related to spared rhythmic abilities, while impaired synchronization to the beat or poor beat perception make the stimulation either useless or, in the worst of the cases, deleterious. This finding is consistent with the view that general rhythm processes may mediate the gait response to RAC. In addition, it provides guidelines to predict a positive effect of RAC based on the performance in simple rhythmic tasks. Along this line, we showed recently that beat perception, gait velocity at baseline, and cognitive flexibility taken together can predict quite successfully whether a patient will respond positively or not to RAC (Cochen de Cock et al., 2018). Interestingly, the link between individual rhythmic abilities and the effects of RAC is not likely to be confined to the immediate effects of the stimulation. Rhythmic abilities can predict the success of a RAC-based intervention. In a recent study in which PD patients were

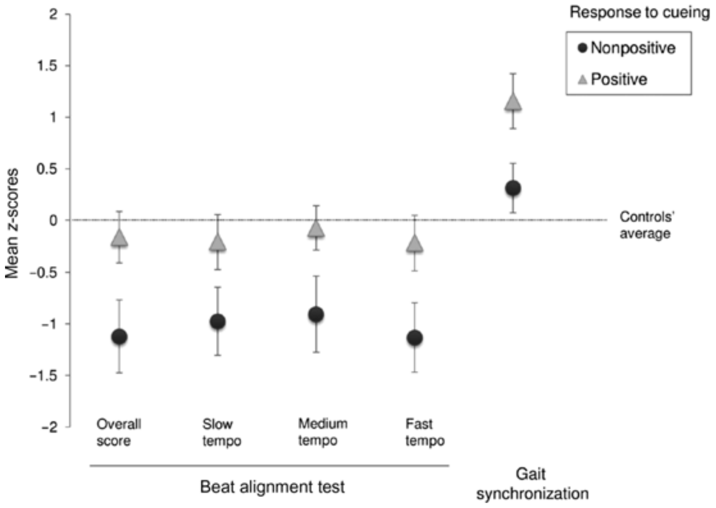

FIGURE 15.2 Performance of patients with positive response (*light-gray triangles*) and nonpositive response to rhythmic auditory cueing (*dark-gray circles*) in beat perception (BAT), and synchronization of footfalls to the beat. Error bars are SE of the mean. *BAT*, Beat Alignment Test. *From Dalla Bella, S., Dotov, D. G., Bardy, B., & Cochen de Cock, V. (2018). Individualization of music-based rhythmic auditory cueing in Parkinson's disease.* Annals of the New York Academy of Sciences, 1423, 308−317.

submitted to a RAC-based intervention (walking with rhythmic music, three times per week, for a month), we found that low synchronization variability and the ability to adapt movement to a stimulation change in a tapping task are good predictors of success for the intervention (Dalla Bella, Benoit, et al., 2017).

In sum, a rhythm-based intervention for gait rehabilitation in PD is well-motivated as it taps into mechanisms either impaired by the disease (BGTC), by partly helping in recovering their functioning, or spared (CTC). Critically, variability in beat perception and synchronization typical of the disease plays an important role in predicting the success of the intervention. An assessment of rhythmic abilities before the intervention may serve to identify the patients who are likely to benefit most from the intervention, and those who may significantly worsen their performance. However, even if for some patients the stimulation brings no effect on their gait, walking with music may still increase a patient's motivation to walk and general mobility. Music is a highly motivating stimulus acting on dopaminergic mechanisms and known for its ability to engage emotions and stimulate the reward system (Blood & Zatorre, 2001; Salimpoor et al., 2015). Thus walking with music, a rewarding activity in itself, may have beneficial effects like increasing mobility and the patient's quality of life.

Harnessing technology for improving rhythm-based rehabilitation

In spite of RAC positive effects on gait in general (Ghai et al., 2018), the possibility of deleterious effects of RAC and in general the variability in patient response mitigate the initial optimism. Patients unable to build on relatively spared rhythmic processing, and generally with reduced cognitive resources, may be confronted with a dual-task situation when asked to walk with music. Walking is particularly affected by dual tasks in older adults (Beauchet, Dubost, Aminian, Gonthier, & Kressig, 2005; Beauchet, Dubost, Gonthier, & Kressig, 2005; Dubost et al., 2006), and even more in PD (Belghali, Chastan, Cignetti, Davenne, & Decker, 2017; Rochester, Galna, Lord, & Burn, 2014).

Variable response to a rhythm-based intervention suggests that treatment individualization is in order to select the appropriate parameters for the intervention. Individualized RAC should (1) capitalize on patients' spared rhythmic abilities, and (2) assist the patient whenever these abilities are impaired (Dalla Bella, 2018; Dalla Bella et al., 2018). This idea has been recently implemented in our lab by harnessing mobile technologies for monitoring motor behavior via dedicated sensors (accelerometers), and for tailoring rhythmic stimulation to patients' performance in real time (Dotov et al., 2019). This technology intervenes to compensate for patients' rhythmic deficits, by assisting them in synchronizing footsteps to the beat. By fostering step-to-beat synchronization via mobile technologies, we expect to increase the effectiveness of music-based interventions, and increase the engagement of spared compensatory mechanisms (i.e., CTC networks). Step-to-beat mapping strategies were adopted in the past to implement bidirectional coupling (WalkMate—Miyake, 2009; Hove, Suzuki, Uchitomi, Orimo, & Miyake, 2012; DJogger—Moens et al., 2014). Another possibility is mutual coordination, in which technology is used to make predictions about the conditions in which spontaneous synchronization of gait is more likely (Dalla Bella, 2018; Dalla Bella et al., 2018; Dotov et al., 2019). The latter solution is particularly desirable as it is expected to foster spontaneous step-to-beat synchronization by mimicking natural interpersonal coordination. We proposed an implementation of this solution by modeling rhythmic (periodic) properties of gait and of the stimulus with a Kuramoto system of coupled phase oscillators. This individualized solution tailors the stimulation to the patient's cadence, thus keeping step-to-beat synchronization, while driving the patient towards an optimal value (i.e., higher cadence). An illustration of this interactive system is provided in Fig. 15.3. We compared gait in the presence of mutually interactive RAC to standard RAC (non-interactive), and to a purely mirroring strategy (i.e., musical rhythm shadowing the patient's gait timing). We found that mutually interactive RAC is the one affording the most improvement in cadence, while fostering the alignment of patients' footfalls to the beat (Dotov et al., 2019). This solution will be implemented in further studies on

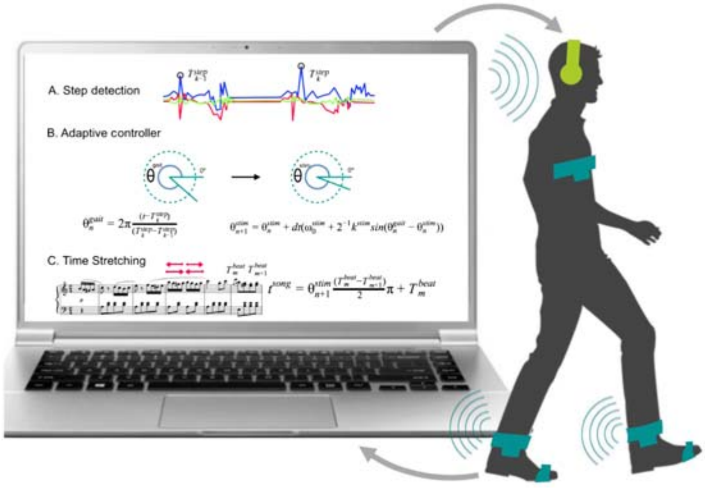

FIGURE 15.3 Interactive rhythmic auditory cueing using mutual synchronization modeled via a Kuramoto system of coupled oscillators. *From Dotov, D. G., Cochen de Cock, V., Geny, C., Ihalainen, P., Moens, B., Leman M., … Dalla Bella, S. (2019). The role of mutual synchronization and predictability in entraining walking to an auditory beat.* Journal of Experimental Psychology: General, 148*(6), 1041–1057.*

PD with the goal of further testing its efficacy in a large cohort of patients and to examine the underlying neuronal underpinnings.

Another possibility to implement rhythmic training is to exploit the power of serious games for rehabilitation. A serious game is a game specifically targeted to motor or cognitive rehabilitation, and education purposes. By definition, it is meant to be entertaining, motivating, widely accessible to the public, and cost-efficient (Annetta, 2010; Kato, 2012). Serious games have been extensively used in therapy (for a review, see Rego, Moreira, & Reis, 2010), in stroke (Friedman et al., 2014; Webster & Celik, 2014), PD (Barry, Galna, & Rochester, 2014; Harris, Rantalainen, Muthalib, Johnson, & Teo, 2015; Mendes et al., 2012), and in healthy older adults (Sun & Lee, 2013). Encouraging results in training cognitive functions (working memory, executive functions) were obtained, but with some limitations (Owen et al., 2010). We recently adopted a serious game approach to rhythmic training. Although nowadays there are a few off-the-shelf rhythm-based games, they present limitations, such as reduced temporal precision, and poor selectivity for rhythmic skills, which make them poor candidates for training rhythmic abilities in a clinical setting (Bégel, Di Loreto, Seilles, & Dalla Bella, 2017). For this purpose we devised a new serious game for training rhythm abilities (Rhythm Workers, Bégel, Seilles, & Dalla Bella, 2018), implemented on a tablet device. The game trains rhythmic abilities by asking the player to tap on a tablet device to the beat of musical excerpts of increasing complexity, or to detect whether a metronome is aligned or not to the beat. This protocol was tested recently in a proof-of-concept study, as part of an at-home self-rehabilitation program for training rhythmic abilities in patients with PD (Dauvergne et al., 2018). In this pilot study the serious game showed excellent suitability, as well as an improvement of beat perception in patients. These first results are promising, motivating further research on rhythm-based serious games as a tool for the rehabilitation of rhythmic and motor abilities in patients with PD, and, more generally for patients with rhythm disorders.

Conclusion

In this chapter I reviewed evidence that musical rhythm can act as a powerful tool in rehabilitation for patients with movement disorders. To do so, I adopted a genuinely translational approach building on the widespread and robust relation between musical rhythm and movement (Dalla Bella, 2018). PD was chosen as a model given the peculiar response of patients with the disease to external rhythmic stimuli, and the rich literature on the beneficial effects of rhythm on walking. That gait features can be improved in PD via rhythmic stimulation depending on patients' spared rhythmic abilities is a nice demonstration that rhythm-based interventions can be theory-driven. By capitalizing on current knowledge of normal rhythmic processes, predictions can be made about the success of an intervention knowing patients' individual performance. A standardized assessment of rhythmic abilities thus appears as a critical step to devise individualized RAC programs to limit potential deleterious effects of RAC while maximizing its benefits. Finally, I showed that recent advances in mobile technologies (interactive applications, serious games) can be instrumental to implementing and disseminating rhythm-based music interventions. In particular, assistive rehabilitation strategies implemented via mobile technologies hold particular promise, as they are typically entertaining, motivating, cost-effective, and usable in home-rehabilitation programs. Notably, gait dysfunctions are not uncommon in healthy older adults and deterioration in the neuronal control of movement is also associated with cognitive impairment (in Alzheimer's disease and mild cognitive impairment; Franssen, Souren, & Torossian, 1999; Nadkarni, Mawji, McIlroy, & Black, 2009; Pettersson, Olsson, & Wahlund, 2005; Wittwer, Andrews, & Webster, 2008; Wittwer, Webster, & Menz, 2010). An approach akin to the one adopted for motor rehabilitation in PD can be extended to these populations. Devising individualized rhythm-based musical interventions for older adults, exploiting mobile technologies, may soon become part of the research agenda.

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