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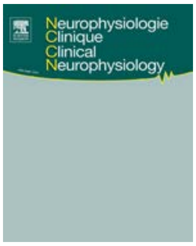

PERSONAL VIEW

Music and movement: Towards a translational approach

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Summary Rhythmic abilities are highly widespread in the general population. Most people can extract the regular beat of music, and align their movements with it. The aim of a translational approach for music and movement is to build on current fundamental research and theories of beat perception and synchronization to devise music-based interventions, which are informed by theory. To illustrate this approach, Parkinson's disease is taken as a model, with a focus on the positive effects of rhythmic auditory cueing on walking. In Parkinson's disease, a relation is found between the success of this music-based intervention and individual differences in rhythmic abilities. Patients with relatively spared rhythmic abilities are the most likely to benefit from cueing. Moreover, rhythmic auditory cueing can be optimized by using mobile technologies (tablets and smartphones), in the form of dedicated apps or serious games. A similar translational approach to the study of music, rhythm, and movement can be extended to remediation of cognitive, speech and language functions in other patient populations, such as children and adults with neurodevelopemental disorders.

Introduction

Human beings have a natural proclivity to react to music, to produce it and enjoy it. Across groups and cultures, and from childhood to older age, we engage in music activities, and are moved by music. Most of us experience music on a daily basis by passive or active listening, playing an instrument, singing and dancing. Given its characteristics and diversity music recruits a variety of brain structures, involved in sensory, motor, cognitive and emotional responses. Thus, music appears as a means, which is ideally suited to stimulate and induce brain plasticity in a wide array of brain networks underpinning these more general functions [31,60,107]. This idea is particularly relevant for devising targeted music-based interventions, for the purpose of rehabilitation in

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various neurological diseases, such as stroke, dementia, and Parkinson's disease (PD) [104,107]. The effectiveness of music-based interventions has been assessed during the last decade via a growing number of controlled studies trying to pinpoint the neuronal networks underlying beneficial effects (reward, plasticity of sensorimotor systems, arousal, affect regulation). Converging evidence shows that music, apart from being an enjoyable activity, is a highly powerful stimulus capable of activating multiple brain networks and showing high potential for supporting or recovering brain functioning, thus enhancing well-being throughout the life span.

Thanks to the current advances in our understanding of the neuronal underpinnings of music perception and performance, the time is ripe to capitalize on the existing knowledge provided by the neurosciences of music to devise theory-driven interventions to be tested in clinical settings (translational approach). In this article, I will show that this approach can be adopted for music-based interventions, which build on our compelling tendency to move to musical beat. I will provide an example of a rhythm-based intervention for PD, and I will show that this intervention can be efficiently implemented by benefitting from low-cost technology.

Moving to music, a widespread ability

Listening to music often urges us to move. An increasing body of evidence from experimental psychology and cognitive neuroscience indicates that rhythm and movement are profoundly linked and that music, due to its temporal regularity and predictability, is ideally suited to engage our body. When we spontaneously or deliberately 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 [71], 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) [65,71]. According to DAT, attention is a dynamic process, which can be successfully modeled by internal neurocognitive self-sustained oscillations [49,87]. Such internal oscillations, corresponding to attentional pulses, synchronize to the most prominent aspects of the sound signal (e.g., tones in an isochronous sequence, beats in music). Attention is thus dynamically shifted to the most salient events in the sound, by a process called ''entrainment'', generating temporal expectations (see Fig. 1).

This propensity to coordinate movement with rhythm is widespread. Humans can naturally and effortlessly move along with a rhythmic auditory stimulus. This ability, not requiring musical training, is common in the general population [98,108]; there are only few people who have difficulties when asked to move to the beat (poor synchronizers; [32,91,94,108]). Synchronization of movement to the beat has mostly been examined with the finger tapping paradigm. In this relatively simple task, participants tap their index finger in synchrony with a pacing stimulus, like a sequence of isochronously presented tones, or music (for reviews, see [97,99]). Beat perception can also be tested in purely perceptual tasks (e.g., the Beat Alignment Test - BAT - in which a listener has to detect whether or not tones are aligned with the musical beat) [64]. More recently, batteries including a vast array of tests capable of assessing rhythmic skills, including sensorimotor synchronization to the beat have been devised. Examples are the Battery for the Assessment of Auditory Sensorimotor and Timing Abilities (BAASTA) [34], developed in our lab, and the Harvard Beat Alignment Test (H-BAT) [48]. The added value of having multiple tests (perceptual and sensorimotor) providing a profile of rhythmic skills, as opposed to single tasks, is that they multiple measures are capable of characterizing the timing capacities of distinct populations and are sensitive to individual differences [10,14,26,34—36,44,95]. Testing rhythmic abilities with a number of tasks is capable of revealing multiple facets of human timing abilities, thereby differentiating individual profiles in both healthy and patient populations. As will be seen below, this is particularly valuable when devising music-based interventions targeting rhythmic skills, which are tailored to individual patients (e.g., personalized rhythmic training).

Beat perception and synchronization abilities are underpinned by complex neuronal networks. Beat tracking, even without a motor response, engages auditory regions of the brain, e.g., the superior temporal gyrus [24,105,112], but also motor regions, including the basal ganglia, premotor cortex, pre-SMA, and the cerebellum [25,28,55,57]. The coupling of a motor response to the beat requires additionally sensorimotor integration areas, e.g., the dorsal premotor cortex [23,28,119]. These

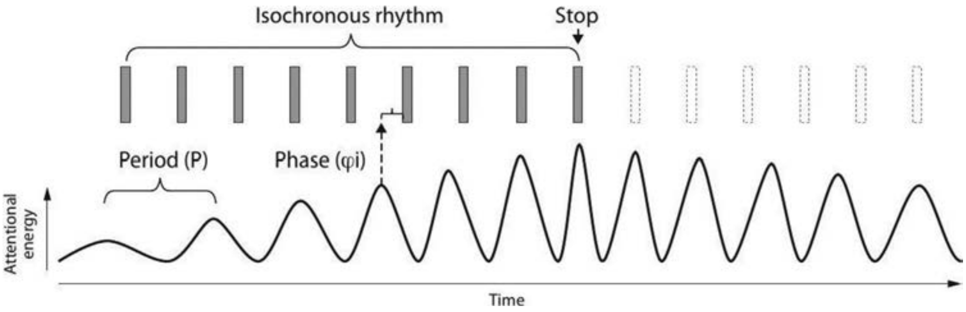

Figure 1 Entrainment in Dynamic Attending Theory.

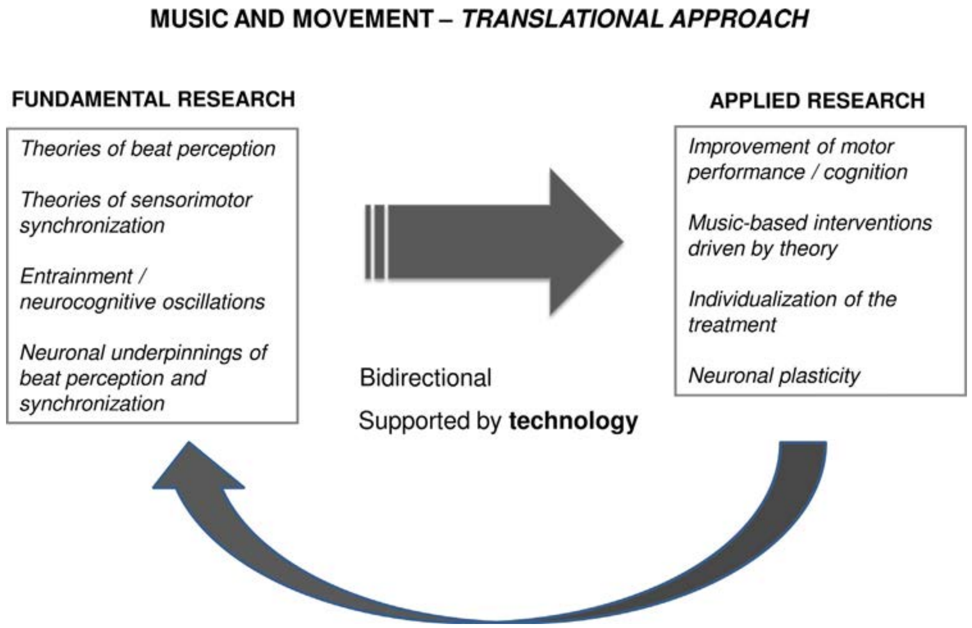

Figure 2 Translational approach in the study of music and movement.

networks can be disrupted, leading to the ensuing rhythmic disorders, in neurodegenerative diseases, e.g., PD [14,56,66,92,110], or neurodevelopmental disorders, e.g., attention-deficit/hyperactivity disorder [86,95], stuttering [44], autism spectrum disorder [2], or speech and language impairments [29,30,53,63].

This knowledge about the behavioral and neuronal mechanisms underlying beat perception and motor synchronization to the beat can play a significant role in guiding music-based interventions. For example, knowing which components of the rhythm system are spared in spite of a brain lesion or congenital anomalies may guide individualized rehabilitation strategies. As we will see later, for example, spared synchronization to the beat in patients with movement disorders can be used as a predictor of the success of a music-based intervention, probably driven by compensatory brain mechanisms. The ultimate goal of this approach is to capitalize on current theories of rhythm perception and production and on their neuronal foundations to build theory-informed rehabilitation strategies with the goal of individualizing the treatment of patient populations. In return, this translational approach, from fundamental to clinical research, can provide highly valuable information about the functioning of rhythm perception and production mechanisms, thus eventually fostering further theory development. This virtuous cycle is illustrated in Fig. 2. As indicated in the figure, translation from fundamental to applied research can nowadays be facilitated by technology, which provides cost-efficient, highly available, and highly motivating means to implement music interventions. An example of translational research building on the relation between musical rhythm and movement is provided below by focusing on movement rehabilitation in PD.

Rhythm for motor rehabilitation

Presentation of rhythmic stimuli as a tool for rehabilitation is used with some success in patients with movement disorders [51,109] but also in the elderly [50]. In particular, gait disorders have been targeted in a number of studies. Gait disorders, common in older adults, represent a major challenge for the Health Care System, and a growing economic burden for society given the steady increase in the ageing population. Dysfunctional gait (i.e., a slow, broad-based, shuffling, and cautious walking pattern; ''senile gait disorder'') [103] is observed in about 1/3 of the population above 70 years of age among community-residing older adults [115], a proportion increasing with age [41]. Gait speed, a hallmark of health and functional status [21], declines with age and is a strong predictor of disability, healthcare utilization, nursing home admission, and mortality [22,88]. Moreover, reduced gait speed is treated as a warning sign anticipating cognitive decline and allowing to predict its onset [20]. Gait dysfunctions are a major cause of falls in older adults (WHO Global Report on Falls Prevention in Older Age, 2007). Among community-dwelling older adults over 64 years of age, approximately 28—35% of people experience falls [15].

Troubles with locomotion assume dramatic proportions in patients suffering from PD [54]. PD is the second most common neurodegenerative disorder (after Alzheimer's disease), and the most common serious movement disorder [61]. Worldwide, about 4 million people suffer from PD, with more than 1.2 million only in Europe [4]. These numbers will tend to increase as a result of the ageing 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 [38,40].

Typical motor impairments observed in PD, such as slowness of movement, limb rigidity, and postural instability cause gait disorders, more visible at late stages of the illness [79]. 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) [52,54,78,79]. Gait disorders in PD are utterly debilitating, by limiting functional independence, increasing the likelihood of falls [16,79], and eventually leading to institutionalization. Falls are a major source of morbidity and disability in PD. From 38 to 87% of PD patients experience falls [27], typically a recurrent phenomenon in the disease.

In both healthy older adults and patients with PD, falling entails severe consequences, including head injuries, fractures (hip in particular), and in some instances leads to death [117]. Falls also produce fear of new falls [1] which results in loss of independence, reduced mobility, increased osteoporosis, reduced social activity and depression [16]. It is noteworthy that Europe displays the highest mortality rate worldwide due to falls, accounting for 6.6—11.3 deaths per 100,000 inhabitants (WHO, Noncommunicable Disease and Mental Health Cluster, 2002). In sum, because of the prevalence of walking disorders in older adults and their devastating consequences, there is urgent need for flexible and cost-efficient rehabilitation strategies aimed at limiting or delaying the gait decline in the elderly, thus ultimately fostering healthy aging [93].

The example of PD

There is clinical evidence that gait can be improved by asking patients with motor dysfunctions to walk along with rhythmic sounds, such as a metronome or music [109,113]. PD is a prototypical example showing promising effects of rhythmic auditory cueing (RAC) on gait kinematics [51,70]. RAC is a cost-efficient method complementary to medication, for coping with motor symptoms in PD. The patient matches her/his walking speed to a rhythmical stimulation such as a repeated isochronous sound (i.e., metronome) or music with a salient beat structure [75,113]. Patients typically benefit from auditory cues presented at rates ranging from 80% to 125% of their preferred stepping frequency [19], which is usually around 100 steps/min [84]. In the presence of a rhythmic stimulus PD patients typically walk faster, increase their step length [75], and tend to walk without showing freezing episodes [6]. Notably, long-term positive effects on walking in everyday life (even in the absence of stimulation) are reported following RAC-based rehabilitation programs [73]. PD patients exhibit faster walking speed [100], and show significant reduction of freezing phenomena [82]. Similar motor improvements can be achieved when rehabilitation via RAC is carried out at home with a dedicated cueing device (see the RESCUE project — Rehabilitation in Parkinson's Disease: Strategies for Cueing) [84]. Whether these beneficial effects of the therapy persist long-term is still under debate. Considerable performance deterioration is observed within 12 weeks after the therapy [83]; yet, others report rather negligible decline in gait performance, if at all, after 4—6 weeks [14,74].

A possible framework for interpreting the benefits of RAC builds on an existing model of temporal prediction and timing, developed in the context of auditory processing at different levels of stimulus complexity such as speech and tones [33,68,69,105,106]. The framework includes two networks (see Fig. 3). The basal ganglia-thalamo-cortical network (BGTC, in violet) is engaged in the attention-dependent evaluation of temporal intervals, and self-generation of movements. The network is involved in action initiation and explicit timing (i.e., overt estimates of stimulus duration). The cerebello-thalamo-cortical network (CTC, in cyan), is involved in the pre-attentive encoding of event-based temporal structure, and matching movements to exogenous cues [28,69]. When functional, the BGTC and CTC networks afford the extraction of the rhythmic features of a predictable auditory sequence (e.g., the musical beat), the development of temporal expectations via entrainment, and the coupling of action to the salient events in the temporal structure.

The functionality of the BGTC network breaks down in PD, due to a progressive loss of neurons in the substantia nigra [43]. This deficit, beyond the motor symptoms characteristic of PD, affects perception and production of temporal intervals [2], hindering the planning of the temporal structure of a sequence of actions. Yet, the CTC network is spared by the disease, thus allowing unimpaired coding of prominent discrete events in the temporal structure (e.g., musical beats). Such event-based representation of temporal structure paves the ground for dynamic attending (i.e., providing attractors for attentional oscillations), generating an expectancy scheme via entrainment [69].

One possibility 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 [33,85]. There is evidence of enhanced cerebellar activity after gait training via rhythmic stimulation [39]. Another possibility is that even if the BGTC network is deregulated in PD, its residual activity might still afford some degree of beat processing [35,56] thus providing sufficient temporal pacing of movement initiation and execution. Residual beat processing may provide sufficient resources for some of the patients to benefit from rhythmic cues. To date, it is still unclear which of the aforementioned networks, BGTC or CTC, underpins the beneficial effects of RAC. However, in both cases, it is apparent that the response to rhythmic cueing should be mediated by mechanisms involved in beat perception and synchronization. Thus, individual differences in these abilities are expected to be good predictors of the response to RAC.

Individual differences and success of the treatment

There are indications from studies with healthy 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 [72]. Until very recently, it was unclear

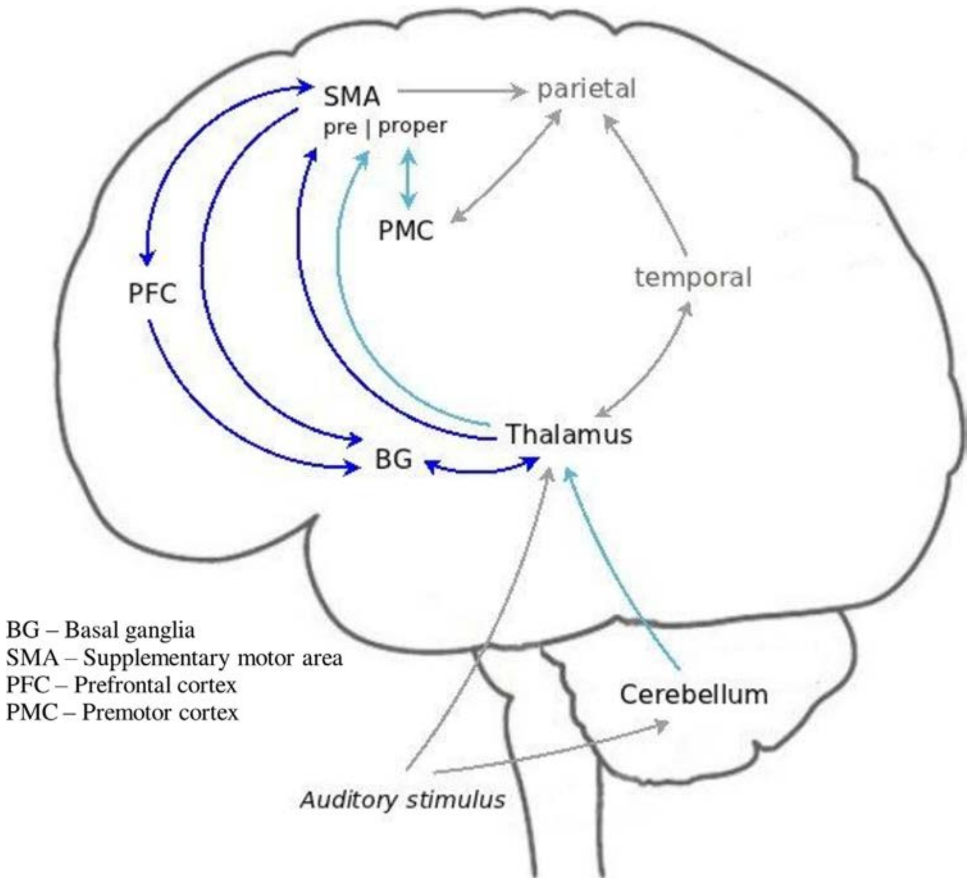

Figure 3 Basal ganglia-thalamo-cortical (BGTC) and cerebello-thalamo-cortical (CTC) networks in Parkinson's disease during RAS (from Dalla Bella et al., 2015).

whether individual differences in beat perception and synchronization affect the response to rhythmic cueing in PD. We addressed this question in our laboratory [26,36], by asking a group of 39 patients with PD and matched controls to walk together with rhythmic stimuli (e.g., highly familiar march music). The rate of the rhythmic stimuli was individualized, namely it was 10% faster relative to each participant's preferred cadence. To quantify patients' synchronization ability, the alignment between the footfalls and the stimulus beat times was computed. Moreover, beat perception was tested with the Beat Alignment Test (BAT) [64], taken from BAASTA [34]. The tasks consisted in detecting whether a metronome was aligned or not with the beat of musical excerpts. Even though at the group level, patients, like controls, positively responded to RAC, by increasing speed and stride length, not all patients showed the effect. The criterion we used to compare patients' response to the cueing was the smallest clinically significant difference in gait speed (0.06 m/s) [59]. With that criterion in mind, out of 39 patients, 22 showed a positive response while the other 17 had a non-positive response. Even more importantly, cueing was detrimental for 6 patients, who significantly decreased their gait speed with RAC (−0.18 m/s, on average) compared to no stimulation. What distinguished patients with positive and non-positive response to RAC? 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 (tested with the BAT). Moreover, patients with positive response to cueing rated their perceptual abilities and musical training higher than the others on the Gold-MSI (Goldsmiths Musical Sophistication Index) scales [80]. Finally, patients with positive response to RAC obtained lower scores than other patients in a test of cognitive flexibility (Wisconsin Card Sorting Task). Thus, a good response of patients with PD to the stimulation is related to spared rhythmic abilities. In contrast, patients with impaired synchronization to the beat or poor beat perception tend not to benefit from RAC. This information can be used quite successfully to predict the immediate outcome of RAC on individual patients' response. For example, we showed recently that beat perception, gait velocity at baseline, and cognitive flexibility taken together can predict quite successfully (Nagelkerke $R^2 = 0.77$) whether a patient will respond positively or not to RAC [26].

The link between individual differences in rhythmic abilities and the effect of RAC in patients with PD is not confined to the immediate effect of the stimulation. In a previous study we focussed on the relation between individual differences in rhythmic abilities and the effect of a RAC-based training in a small group of patients with PD [35]. Patients were submitted to a RAC-based training in which they had to walk with rhythmic music (a familiar excerpt with a superimposed metronome) for 30 min, three times per week, for a month. Gait and synchronization to the beat (tested with BAASTA) were assessed before and after the training program. As with the immediate effects of RAC, patients' response to the training program was highly variable. Some patients showed a positive response; others, a non-positive response qualified by the same criterion as above (i.e., smallest clinically significant difference in gait speed). Interestingly, synchronization of movement to the beat (in both tapping and gait) was successful in predicting the response to RAC-based training. Patients showing low synchronization variability and capable to adapt their movement to a stimulation change are highly likely to positively respond to the intervention.

In sum, a rhythm-based intervention for gait rehabilitation in PD is well-motivated given that beat perception and synchronization engage networks, which are either impaired by the disease (BGTC) or spared (CTC). A rhythm-intervention can thus either help recover the functioning of some of these networks or capitalize on spared networks. Owing to the variability typical of the disease, patients with PD are also highly variable in their ability to perceive and synchronize to the beat. This variability has an effect on the success of rhythm-based interventions. Our recent findings indicate that beat perception and synchronization should be taken into account to screen patients who are the most likely to benefit from RAC. In addition, even more importantly, they will serve to detect those patients who may significantly worsen their performance. Note, however, that even if for some patients the effect of the stimulation on gait is null (but not deleterious), walking with music may still increase a patient's mobility and motivation to walk, due to other effects of music. Music is a highly motivating stimulus acting on dopaminergic mechanisms and known for its ability to engage emotions and stimulate the reward system [17,102]. Thus, walking with music, a rewarding activity in itself, may have beneficial effects like increasing mobility and the patient's quality of life. This possibility will need to be assessed on a case-by-case basis by the clinician.

A bridge towards technology

On average, RAC was shown to have positive effects on gait in PD, with fluctuations in effect size depending on the specific study [51]. However, the observed variability in patient response to RAC-based interventions should raise a red flag, especially due to the potentially deleterious effects of the treatment in some patients. 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 tasking in the elderly [8,9,42], and even more in PD [13,101].

This example of variable response to a music-based intervention is particularly instructive as it shows the need for treatment individualization, as a way to optimize rehabilitation. An individualized RAC should first capitalize on patients' spared rhythmic abilities, e.g., fostering spontaneous synchronization to the beat, and also assist the patient when these abilities are impaired [36]. This idea can be implemented efficiently via mobile technologies affording monitoring of motor behavior via dedicated sensors, e.g., accelerometers or inertial measurement units (IMUs) while tailoring rhythmic stimulation to patients' performance in real time. The goal of this technology is to compensate for patients' rhythmic deficits, by assisting them in synchronizing footsteps to the beat. By aiming to achieve step-to-beat synchronization via mobile technologies we plan to selectively target audio-motor coupling mechanisms, e.g., engaging CTC networks, thus increasing the effectiveness of music-based interventions. A step-to-beat mapping strategy can implement bidirectional coupling, e.g., WalkMate [62,81] or DJogger [77], or mutual coordination, making predictions about the conditions in which spontaneous synchronization of gait is more likely [36]. The latter solution is particularly desirable as it is expected to foster spontaneous step-to-beat synchronization. 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. Mutual synchronization is currently implemented in mobile technology and being tested with patients with PD (BeatHealth project, http://www.euromov.eu/beathealth/).

Mobile technology can also pave the way to implementing rhythm-based training programs, such as RAC, in an entertaining and motivating setting. An interesting possibility is to exploit the power of serious games for rehabilitation. A serious game is a game specifically targeted for training and education purposes, for example for motor or cognitive rehabilitation; it is usually entertaining and motivating, widely accessible to the public, and cost-efficient [5,67]. Serious games have been extensively used in therapy (for a review, see [96]), stroke [47,116], PD [7,58,76], and healthy older adults [111]. Encouraging results of training cognitive functions, i.e. working memory and executive functions, were obtained, but with some limitations [89]. With regard to rhythm-based games out in the market, there are a few limitations, e.g., reduced temporal precision and poor selectivity for rhythmic skills, which make them not satisfactory for training rhythmic abilities [11]. For this purpose we recently introduced a new serious game (Rhythm Workers) [12] on a tablet device for training rhythm abilities, via auditory-motor synchronization (finger tapping) and beat perception. In a pilot study, we used Rhythm Workers as part of an at-home self-rehabilitation program for training of rhythmic abilities in patients with PD [37]. Excellent suitability of the serious game for this purpose was shown, as well as an improvement of beat perception in patients. These preliminary findings suggest that rhythm-based serious games may be a promising avenue for successful rehabilitation of rhythmic abilities in patients with PD, and, more generally, for patients with rhythm disorders.

Conclusions

The goal of this article was to show that a translational approach building on the widespread and robust relation between musical rhythm and movement is highly desirable. To illustrate this point, I took PD as a model. Movement rehabilitation in PD with RAC served to demonstrate that music-basic interventions can be theory-driven, and can capitalize on individual differences in rhythmic abilities among patients. A standardized assessment of these abilities is a critical step for devising invidualized RAC programs to limit potential deleterious effects of RAC while maximizing its benefits. Finally, this example served to illustrate that recent technological advances in mobile technologies can be instrumental to implementing and disseminating rhythm-based music interventions. This can take the form of an app in a smartphone, or of a serious game implemented on a tablet device. Assistive rehabilitation strategies implemented via these technological solutions have the advantage of being typically entertaining and motivating, cost-effective, and usable in home-rehabilitation programs. They should be devoted further studies in the future.

Apart from PD, timing and rhythm disorders are found in neurodevelopmental disorders such as attention-deficit/hyperactivity disorder [86,95], developmental stuttering [44], autism spectrum disorder [3], and speech and language impairments [29,30,53,63]. Moreover, beat perception and synchronization are associated with other cognitive abilities such as working memory, sustained attention or language and reading skills in children [45,90,114,118]. There are indications that rhythmic information may play a critical role for example in improving reading skills in dyslexia [18,46]. A translational approach akin to the one adopted for motor rehabilitation in PD could be extended to remediation of cognitive, speech and language functions in these patient populations. Devising individualized rhythm-based musical interventions for these populations, while exploiting mobile technologies, may become part of the research agenda for the years to come.

Disclosure of interest

The author declares that he has no competing interest.

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