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Review

Into the groove: Can rhythm influence Parkinson's disease?☆

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A B S T R A C T

Previous research has noted that music can improve gait in several pathological conditions, including Parkinson's disease, Huntington's disease and stroke. Current research into auditory-motor interactions and the neural bases of musical rhythm perception has provided important insights for developing potential movement therapies. Specifically, neuroimaging studies show that rhythm perception activates structures within key motor networks, such as premotor and supplementary motor areas, basal ganglia and the cerebellum – many of which are compromised to varying degrees in Parkinson's disease. It thus seems likely that automatic engagement of motor areas during rhythm perception may be the connecting link between music and motor improvements in Parkinson's disease. This review seeks to describe the link, address core questions about its underlying mechanisms, and examine whether it can be utilized as a compensatory mechanism.

Contents

> "Every disease is a musical problem; every cure is a musical solution" (Novalis).

In the seventeenth century, the English physician William Harvey described animal movement as "the silent music of the body" (Harvey, 1627–1959). Walking, swimming, crawling, flying, and other complex types of animal movement enable efficient exploration of different habitats, and although each is an inherently distinctive method of locomotion, all share a natural equipoise and fluency enabling swift sensorimotor responses to the environment. This smooth, graceful, "melodic" flow of movement is compromised in patients with Parkinson's disease.

One of the cardinal symptoms of Parkinson's disease (PD) is diminished ability in walking or gait. Patients demonstrate difficulty regulating stride length (Morris et al., 1996), reduced velocity, 'freezing' of gait and increased cadence or step rate (as demonstrated in Fig. 1) (Knutsson, 1972). Despite the success of pharmacological therapies in ameliorating some features of PD, gait deficits can be resistant to medication and over time become one of the most incapacitating symptoms (Blin et al., 1990).

One origin of gait impairment is deficient internal timing, the mechanism that precisely times and coordinates every movement

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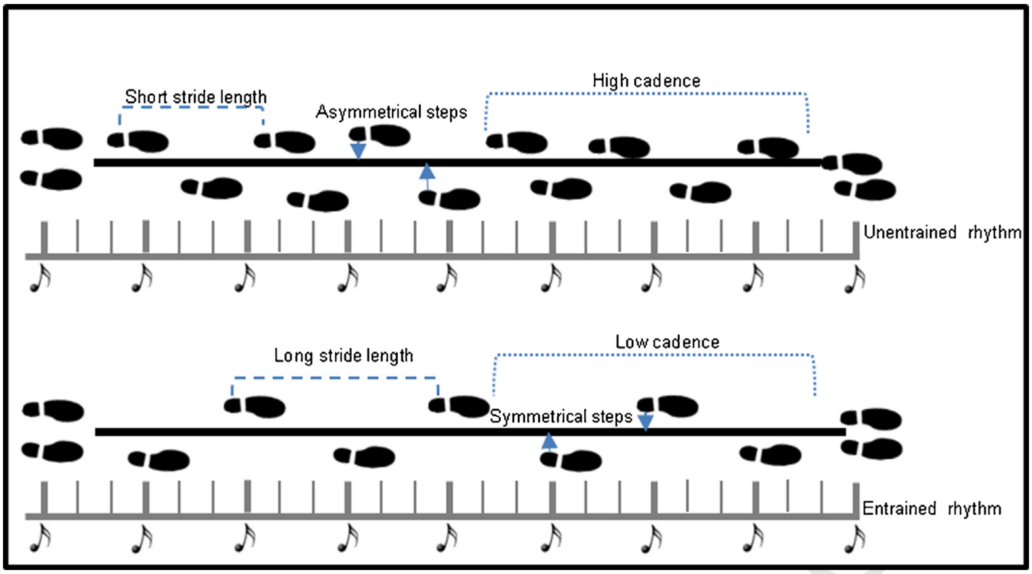

Fig. 1. Schematics of various gait parameters in PD patients with and without rhythm entrainment. The top section depicts a walking pattern before training, characterized by short stride, high cadence, and asymmetry of the steps, which are not synchronized with the music beats. The lower section shows entrainment of gait to the rhythmic beats, with longer stride length, lower cadence, and more symmetrical steps, typical of a more stable gait.

of our body (Jones et al., 2008; Wearden et al., 2008). In PD, the irregular timing of walking pace suggests a disturbance of coordinated rhythmic locomotion (Ebersbach et al., 1999; Skodda et al., 2010; Thaut et al., 2001). Music rehabilitation program make use of acoustic stimuli that enhance the connection between rhythmical auditory perception and motor behaviour (Thaut, 2005), and aim to elicit sustained functional changes to movement in patients, improving quality of life and reducing reliance on medication (Rochester et al., 2010b). Although the beneficial effects of music on gait in PD were initially reported some years ago (Miller et al., 1996; Thaut et al., 1996), more recent work has used music to complement pharmacological therapy. A number of studies have demonstrated that musical rhythm can improve gait and there is general agreement about the promising value of music therapy in PD (Arias and Cudeiro, 2008; Fernandez del Olmo and Cudeiro, 2003; Lim et al., 2005; Rochester et al., 2009; Satoh and Kuzuhara, 2008; Thaut and Abiru, 2010).

However, the scientific basis for the effects of music and rhythm on gait needs reviewing. A precise description of how music influences motor function is essential for designing effective therapeutic programmes in PD. Furthermore, alternative measures, such as neurosurgical treatments, are not suitable for all patients, are expensive and may result in additional complications, which make their application or widespread use challenging. Additionally, pharmacological therapy does not solve gait problems in the long term. After years of examining the effectiveness of rhythm on PD, it is now necessary to discuss: (1) what makes rhythm effective, (2) what other tools, such as neuroimaging, have added to current music-motor knowledge and, (3) which questions remain unanswered regarding motor rehabilitation for PD. In this review we discuss the effects of music on movement, provide an explanatory framework of the neural mechanisms that underlie the processing of musical rhythm, describe how rhythm triggers the motor network, and link this evidence to different Neurological Music Therapies (NMT) assayed to date.

1. Why is rhythmically modulated sound a good therapeutic key for tuning motor function in PD?

The improvement of patients' gait in the presence of external regulatory rhythmical stimuli has been known for over forty years: early studies described functional connections between the auditory and motor system (Rossignol and Jones, 1976). Years later, Thaut and colleagues described how rhythmical auditory stimulation could influence the motor system (through muscle entrainment to auditory stimuli) in PD patients, improving gait parameters such as speed, cadence and stride length (Thaut et al., 1996). These findings were confirmed by other studies (Hurt et al., 1998; McIntosh et al., 1997; Miller et al., 1996; Thaut et al., 2001) that showed that beneficial effects on walking speed persist (albeit briefly) even after stimulus presentation has stopped (McIntosh et al., 1998; Nieuwboer et al., 2009a).

A systematic review (Lim et al., 2005) of the use of rhythmic stimuli in PD supports the effectiveness of auditory stimulation compared to other types of stimulation such as visual, somatosensory (tactile), or combined auditory and visual cues. Studies using auditory cues provided reliable evidence for improved walking speed, stride length and cadence. Although both visual and auditory stimuli may improve gait in PD (Lim et al., 2005), the characteristics of the human auditory system make it a better therapeutic target for two main reasons: (i) reaction times for auditory cues are 20–50 ms shorter than for visual or tactile cues; (ii) the auditory system has a strong bias to detect temporal patterns of periodicity and structure, compared to other sensory systems (Thaut et al., 1999a).

Temporal patterns, or timing mechanisms, are necessary for coordinating precise and structured movements (e.g. handwriting, typing, talking, and walking). In pathological conditions, if faulty timing processes lead to impaired motor performance, musical rhythm could be used to influence the motor system: The temporal sensitivity of the auditory system in combination with the strong temporal characteristics of music (rhythm) can potentially provide a regularizing temporal input to the motor system. Most NMTs have used a strong 'beat' to help initiate movement. A beat is a series of regular, recurring acoustical events. Phenomenologically, beat (or pulse) can be considered a percept; "a response to patterns of timing and (depending on the theorist) stress in the acoustic rhythm" (p. 190) (Large, 2008) which generates a strong temporal expectation of subsequent beats. Although the beat is initially derived from the auditory stimulus, rhythm can also induce an internally generated sense of beat and once the pattern has been established it can continue in the mind of the listener even when the rhythm pauses (Benjamin, 1984; Lerdahl, 1983; Palmer and Krumhansl, 1990). The

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process of synchronizing endogenous sensations of beat with an external rhythm of movement is termed entrainment (Fig. 1).

2. How does music facilitate movement?

Entrainment constitutes the basis of therapeutic music programmes, because a rhythmically structured sound pattern (such as a simple dance tune) creates an anticipatory template of a time sequence marked by beats, which can be used as a continuous reference to map movements. This rhythmical auditory structure may facilitate movement by enabling the timing of muscle activation to synchronize to the temporal structure of beats in the sound pattern. Neural connections between the auditory and motor systems could explain this facilitation. Sounds can exert an influence on the motor pathway, via reticulospinal connections, which prime and alter timing of spinal motor neuron activity (Paltsev and Elner, 1967; Rossignol and Jones, 1976). Connections between the auditory and motor systems have been described along the phylogenetic scale (from fishes to mammals, Mirjany et al., 2011) and are used to explain the 'auditory startle reflex' (Lee et al., 1996), a very rapid behavioural response to sudden sounds. In particular, animal models have been used to examine the neural pathways facilitating this fast response. Double-labelling experiments in rats (Nodal and Lopez, 2003) demonstrate that cochlear root neurons (CRNs) in the auditory nerve project bilaterally to sensorimotor paths, including synapsing on reticulospinal neurons, which could constitute one of the shortest possible circuits for the auditory startle reflex (Lee et al., 1996). In this context, sound can directly increase the excitability of the spinal motor neurons, thereby reducing the time required for the muscle to respond to a given motor command. Additional evidence from other species indicates the consistency of motor-auditory connections: in monkeys direct projections from the auditory cortex to putamen are described (de la Mothe et al., 2006). Empirical testing is still required to further understand how rhythm might facilitate regular motor movements.

In addition to animal models, connections between the auditory and motor systems, in humans have also been described. Neuroimaging studies have examined perceptual and motor synchrony, revealing increased coupling of neural activity between auditory and premotor cortex during rhythm processing (Chen et al., 2006; Grahn and Rowe, 2009), even at a pre-attentive level (Tecchio et al., 2000). Critically, brain areas involved in rhythm processing are closely related to those which subserve movement, such as the premotor cortex, supplementary motor area (SMA), cerebellum and basal ganglia (Bengtsson et al., 2009; Chen et al., 2008; Grahn and Brett, 2007; Lewis et al., 2003; Mayville et al., 2001; Schubotz and von Cramon, 2001; Ullen and Bengtsson, 2003). The basal ganglia, particularly the putamen, is involved with the sequencing of rhythmic events (McIntosh et al., 1997) and may enable 'feeling the beat' (Grahn and Rowe, 2009). The cerebellum, also implicated in sensorimotor associations, may control rhythmic auditory-motor synchronization by monitoring rhythmic patterns and adjusting behaviour to changing tempos (Bijsterbosch et al., 2011; Thaut et al., 2009). This sensory-motor coupling, in which auditory information drives motor action, has been described in healthy volunteers (Chen et al., 2008) and seems to be functional in neurodegenerative diseases such as PD (Miller et al., 1996) and Huntington's disease (Thaut et al., 1999b), as well as in patients with stroke (Thaut et al., 2007, 1997) and traumatic brain injury (Hurt et al., 1998).

3. How are timing mechanisms affected in PD?

Synchronization of movement with rhythm requires continuous entrainment and discrete error correction. This process improves gradually with practice, becoming automatic (Repp, 2010). Parkinson's disease patients experience difficulty in executing automatized movements (Rochester et al., 2010a), such as walking, that are related to dopaminergic function. During healthy motor performance, the basal ganglia and SMA establish a functional loop that maintains adequate preparation for sequential movements. The SMA prepares for predictable forthcoming movement, keeping a "readiness" state. Once the movement starts, the SMA readiness activity stops. This cycle engages with basal ganglia discharges after each sub-movement within an automatized sequence (Mushiake et al., 1990). The loop requires an internal cue to coordinate the cycle. However, in PD this internal cue is impaired, delayed, or missing.

In healthy adults, accurate temporal processing relies on a complex network that includes the putamen, and other structures within the basal ganglia that depend on dopaminergic innervation (which is severely depleted in PD). In addition, other areas are implicated in timing, including the inferior parietal cortex, cerebellar vermis, anterior and posterior cerebellar hemispheres (Thaut, 2003), SMA, pre-SMA, and premotor cortex (Lewis and Miall, 2003; Wiener et al., 2011). During the initial stages of the disease, these areas may provide compensatory assistance to the basal ganglia in response to auditory cues (Eckert et al., 2006; Lewis et al., 2007). In accordance with this idea, a dedicated temporal processing network has been described by Kotz and Schwartze (Kotz and Schwartze, 2010, 2011). This subcortico-thalamo-cortical network includes the cerebellum, basal ganglia, pre-SMA and SMA, which are important for implementing sequential actions. These areas are differentially affected during the neurodegenerative process in PD: at a preclinical stage, hyperactivity in the pre-SMA during action sequencing may be a compensatory mechanism for initial dysfunction, and this compensatory mechanism may be initiated by the cerebellum. In more advanced stages, a selective loss of pyramidal neurons in the pre-SMA may cause under activity in this region, accompanied by poor temporal processing (Kotz and Schwartze, 2011). Neurological motor therapies try to strengthen alternative pathways based on existing connections. The development of compensatory mechanisms for impaired motor loops is the key for PD motor rehabilitation.

4. How does rhythm facilitate timing mechanisms in PD?

The capacity of the auditory system to enhance motor performance is used in neurological therapies (Thaut et al., 1999a) for rehabilitation purposes (de Bruin et al., 2010). Different auditory cues (for example, just a metronome tone, a metronome tone embedded into music or just music), are combined with musical parameters (such as rhythm or metre), to emphasize the regular beats in the auditory rhythm. These well-defined sensory cues help regulate timing and pace in walking (Thaut et al., 2001). These cues may also act as an internal clock that helps to regulate the deficient internal timing and rhythm formation processes in PD (Pastor et al., 1992). Music training programmes can be effective in PD, as patients are able to identify simple rhythms (Skodda et al., 2010), although they may be impaired at discriminating rhythm changes (Grahn, 2009; Grahn and Brett, 2009). In addition, they do not generally report difficulty in sensing a regular beat or enjoying music (Nombela et al., 2013). One issue in determining how NMT helps patients is an apparent paradox between neuroimaging and patient studies. Previous fMRI work has shown that the putamen responds to rhythmic stimuli that induce a sense of beat (Grahn and Brett, 2007; Grahn and Rowe, 2009). However the putamen is thought to be one of the most affected regions in PD (Kish et al., 1998), which invites the question: how can rhythm improve movement in these patients?

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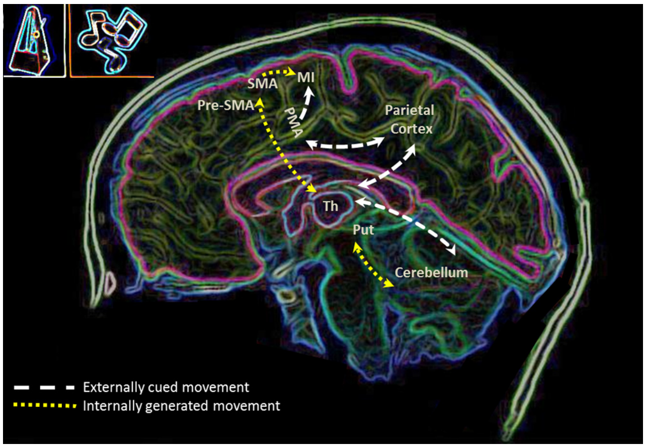

Fig. 2. Auditory-motor action coupling schema. The schema represents how cueing benefits may be associated with the activation of cerebellum-thalamic-cortical circuitry. According to sensorimotor synchronization studies using neuroimaging studies comparing pre and post-therapy, external vs. internal cueing may use different pathways to reach the same key areas. This schema is based on RESCUE Consortium references (Nieuwboer et al., 2009b). Pre-SMA: Pre-supplementary motor area; SMA: Supplementary motor area; MI: Primary motor area; PMA: Premotor area; Th: Thalamus; Put: Putamen.

One potential method to stimulate the putamen could be music as a provider of a strong rhythmical cue. This type of *externally provided* cue may be used as a replacement to the 'internal clock' to facilitate synchrony of movements (Fig. 2). Several imaging studies have demonstrated that self-initiated or self-paced movements are impaired in patients, with concomitant reductions in putamen and related cortical and cortico-striatal activity (Hallett, 2008; Haslinger et al., 2001; Playford et al., 1992; Wu et al., 2010). In contrast, externally paced movements in response to either a tone or a visual cue do not show such severe impairments (Hughes et al., 2010; Jahanshahi et al., 1995). Extrinsic cues are known to facilitate movement (Hallett, 2008), and may provide the input for sequential movements, such as stepping, by reducing the reliance on deficient automatized processes, (Morris et al., 1996). Thus rhythmical music may drive sensorimotor network activity, either by bypassing or facilitating the impaired basal ganglia-SMA loop, enabling improvements in gait.

5. Standardized neurological motor therapy in PD: RAS

Rhythmic Auditory Stimulation (RAS) is one of the earliest and most popular NMTs. It was designed to facilitate rehabilitation of movements that are intrinsically rhythmical (for example, gait). Therefore, the most prominent application of RAS is to gait disorders, for example, in Parkinson's patients (Freedland et al., 2002; Nieuwboer et al., 2007), stroke (Thaut et al., 1997) and traumatically brain injured patients (Hurt et al., 1998). The effectiveness of RAS made it a model for subsequent programmes (Box 1). Typically, RAS utilizes simple metronome beats matched to the patient's baseline gait. Beats can also be emphasized by embedding metronome beats in a musical pattern to encourage rhythmic entrainment. After patients entrain their movement to the beat, the rhythm is then sped up from 5% to 10% over baseline to a pace still comfortable for the patient. Theoretically, as patients practice walking at faster rates, a general coordination of timing and sequencing of movements would take place through the enhancement of motor system function (Thaut, 2005). Alternative versions of RAS have included metronome sounds embedded in expert-selected (McIntosh et al., 1997) or patient-selected music (Thaut et al., 1996). Other programmes have combined auditory stimulation (metronome) with additional motor training, as in the Physical Rehabilitation Program

Box 1: Example of a Rhythmic Auditory Stimulation (RAS) program (Thaut et al., 1996)

One example of a typical Rhythmic Auditory Stimulation (RAS) protocol [59]:
Baseline pre-training measures (without auditory rhythmical stimulation): velocity, stride length, step cadence and electromyography activation pattern for the gastrocnemius and tibialis anterior muscles. Instructions are to walk at usual pace.
1st training week: Patients walk on a flat surface listening to music in which the beat has been emphasized. Three different tempos are used: music is presented at the patients' normal pace ("normal rate"), between 5% and 10% faster than normal ("quick rate") and 15–20%faster than normal ("fast rate"). The music type may be selected from four short instrumental music pieces (e.g. folk, classical, jazz, country). Instructions are to walk in time with the beat.
2nd training week: Each tempo becomes 5–10% faster than previous week.
3rd training week: Each tempo becomes 5–10% faster than previous week.
Pre-training measures are acquired again, without auditory rhythmical stimulation. Instructions are to walk at usual pace.
In a past study, velocity increased by 25%, stride length by 12% and step cadence by 10%. Shape variability and asymmetry decreased in gastrocnemius and tibialis anterior muscles.

(PRP) (del Olmo et al., 2006) which reduced temporal variability of gait. PRP consists of 20 sessions that synchronize gait to the metronome tone, combined with gradually more complex upper limb exercises. Further variations are based on music plus relaxing images and body expression in Active Music Therapy (AMT) (Pacchetti et al., 2000). Finally, external cueing can be substituted by internal generation of the rhythmical signals by internal, covert singing (Satoh and Kuzuhara, 2008).

The positive effects of RAS and its subsequent variations are improvements in gait velocity, cadence and stride length (Thaut et al., 1996). It is more effective in patients 'on' their normal dopaminergic medication than when 'off' medication, and can generate positive short-term carry-over effects on movement after rhythmic cueing has stopped (McIntosh et al., 1998, 1997). Other beneficial outcomes include increases in the symmetry of muscle activation in legs and arms, as well as diminished timing variability (Fernandez del Olmo and Cudeiro, 2003; Miller et al., 1996; Thaut et al., 1998), both of which result in more stable walking (Thaut et al., 1999a). There are very few studies comparing the effectiveness of RAS based on individual variability in UPDRS scores (Lim et al., 2005). Arias and Cudeiro reported benefits in all patients in their study after RAS, but found that the most severe patients benefited the most (Arias and Cudeiro, 2008), suggesting that RAS efficacy is dependent upon individual characteristics.

The effect of auditory stimulation on 'freezing' in PD has also been evaluated. Rhythm appears to positively affects gait: during auditory stimulation, PD patients with more severe symptoms (H&Y stage III) experienced significantly fewer and shorter freezing episodes than before stimulation (Arias and Cudeiro, 2010) and took longer steps than patients with lower UPDRS scores (Arias and Cudeiro, 2008). However, patients with less severe symptoms overall, but who freeze, may not benefit as much from RAS, and may even experience stride length decreases (Willems et al., 2006).

Research in the field does not always support the benefits of music training on gait. Negative effects of RAS were evident when auditory cues were presented at rates of 20% slower than the preferred gait, reducing temporal stability in both PD patients and controls (del Olmo and Cudeiro, 2005; Ebersbach et al., 1999). Plain metronome beats (60–150 beats per minute, bpm) not based on the patient's baseline cadence may even decrease step length

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Table 1
Basic concept for RAS (Lerdahl and Jackendoff, 1983; Palmer and Krumhansl, 1990; London, 2004).

Concept	Definition
Rhythm	A pattern of durations or time intervals, delineated by the sequential onset of events in a stimulus sequence.
Inter-onset-intervals	Time between the beginning of one time interval and the following one. IOI provides the duration of each temporal interval in a rhythm
Beat	Equally spaced recurring saliences that derive from rhythm. Also called 'pulse' or 'tactus'. Is spontaneously perceived when listening to regular rhythm.
Cadence	Number of steps per unit time.
Stride amplitude	Step length. The distance travelled in a single step.
Metre	Repeating patterns of strong and weak beats in rhythm.
Pattern	Temporal structure defined by the time between onsets of stimuli (such as tones, clicks, or other sounds).
Gait	The rhythmic alternation of the trunk and limbs in walking.

and gait cadence when set too low (60 or 90 bpm) or too high (150 bpm) (del Olmo and Cudeiro, 2005; Howe et al., 2003). Similar impairments (decreased walking speed and step length) are observed in the absence of explicit instructions to synchronize walking pace with the beat, listening to freely chosen music that does not control for metre, rhythm or rate (Brown et al., 2009), and combining music with other cues, such as tactile stimulation (Enzensberger et al., 1997). These negative effects may be caused by the diversion of attention to an additional task unrelated to walking, which increases the cognitive load (Brown et al., 2009; Rochester et al., 2009). Directing attention specifically to the movements can be facilitatory, possibly because this reduces the automaticity of actions, which is impaired in PD (Morris et al., 1996). However, even during dual tasks, RAS can have beneficial effects on walking (Rochester et al., 2005). Thus, when the intervention increases demands or divides attention (either synchronizing gait to a non-natural pace or adding cognitive demands to walking), it reduces the therapeutic value of music-motor programmes.

Music interventions in PD alter activity in motor and temporal processing networks. Fernandez del Olmo and Cudeiro (2003) describe the increased glucose uptake in the right anterior lobule of the cerebellum and dentate nucleus as well as the right temporo-parietal junction (involved in temporal encoding/decoding) after musical rhythm therapy. According to the authors, increased activity in the cerebellum might mean access to an alternate pathway to compensate for the damaged basal ganglia-SMA-prefrontal cortex path. This hypothesis is supported by previous studies in which externally driven movements in PD were related to increased activity in the cerebellar-parietal-premotor cortex pathway (Debaere et al., 2003).

Immediate effects of entrainment also have been studied through EMG, measuring the effect of metronome stimulation on the activity of lower-leg muscles (tibialis anterioris and gastrocnemius muscles) in the control of walking movements and positioning of the feet. The variability of measured motor parameters (cadence, stride length and speed) significantly decreased, improving the precise timing of muscle activation (Fernandez del Olmo and Cudeiro, 2003).

In addition to reduced variability of motor parameters, other immediate effects of RAS include longer stride length (Freedland et al., 2002), higher speed (Arias and Cudeiro, 2008) and normalized cadence (Arias and Cudeiro, 2010). Original RAS program report similar improvements (McIntosh et al., 1997; Thaut et al., 1996). Surprisingly, previous studies have not reported significant differences between the effect of a single training session and full programmes (Rubinstein et al., 2002) although no specific comparative studies have been conducted (Table 1).

In summary, the results of RAS and equivalent programmes are dependent on the stage of treated patients, the specific auditory stimuli, and appropriate therapeutic procedures (del Olmo et al., 2006). From a methodological point of view, however, all these studies share the use of a clear and easily discernible beat as the acoustic stimulus. When clear identification of the rhythmic stimulus is not possible, (non-rhythmic cues) RAS may not have any positive effect or it may even have detrimental effects on PD gait (Georgiou et al., 1993; Ma et al., 2009) (Table 2). Q4

In this review we have described several studies on RAS and the effect of different stimuli as cues for movement in PD patients. What is still missing is information about how these improvements can be prolonged. Future research could focus on how to tap into

Table 2
The table shows the benefits associated to RAS variations (Metronome stimulation and Music stimulation). To our knowledge, just one study has evaluated the effect of metronome beats vs. music, which indicated that it is the metronome stimulation by its own that provides better results regarding the time and number of steps needed to walk 40 m (Enzensberger et al., 1997; Lim et al., 2005; Arias and Cudeiro, 2008; Brown et al., 2009; de Bruin et al., 2010; del Olmo and Cudeiro, 2005; Elston et al., 2010; Fernandez del Olmo and Cudeiro, 2003; Freedland et al., 2002; Ito, 2000; Ledger et al., 2008; Lohnes and Earhart, 2011; Rochester et al., 2010b).

Metronome stimulation Authors	Stimulation	Benefits
Freedland et al. (2002)	+10% respect to baseline	Cadence, step length
Del Olmo et al. (2003)	Fixed frequency (100 bpm)	Variability reduction in EMG parameters
Del Olmo et al. (2005)	60, 90, 120 and 150 bmp	Velocity (60, 90) cadence (150)
Willems et al. (2006)	+10%, +20%, −10%, −20% respect to baseline	Step frequency (+10%, +20%) stride length (−10%), speed (+10%)
Arias & Cudeiro (2008)	70–110% respect to baseline	Step amplitude stride time
Ledger et al. (2008)	−10% respect to baseline	Speed, stride length, cadence
Elston et al. (2010)	Baseline	PDQ-39 scpre
Rochester et al. (2010)	Baseline	Speed, step length
Lohnes et al. (2011)	Baseline (+10%, −10%)	No effect
Music stimulation		
Thaut et al. (1996)	Metronome pulse (60–120 bpm) embedded into preferred music	Speed, stride length Cadence
McIntosh et al. (1997)	Metronome pulse (baseline, +10%) embedded into instrumental music	Speed, stride length Cadence
Ito et al. (2000)	Metronome pulse embedded into music	Stride length, gait speed
Brown et al. (2009)	Preferred music	No improvements
de Bruin et al. (2010)	Cadence-matched preferred music	Speed, stride length Cadence

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the circuits underlying non-automatized movements, which can bypass or stimulate the dysfunctional basal ganglia. These compensatory mechanisms may also mediate the improvements during observed musical rhythm training.

6. Conclusions

NMT relies on acoustic stimuli to potentiate the connection between auditory perception and movement, which is possible because rhythm activates the neural circuits involved in motor processing, and these neuroanatomical connections permit music (or rhythm) to act as a cue for movement. In Parkinson's disease, observed improvements in gait are thought to be due to synchronizing movement to the temporal expectation of a regular beat, replacing the impaired internal timing function. The presence of regular beats in auditory stimuli may also increase activity in the putamen and thus compensate for the lack of dopaminergic stimulation. This benefit is not only the improvement of general gait patterns (including postural control), but also the ability to generate complex coordinated movement sequences combining upper and lower limbs (Thaut and Abiru, 2010). However, rhythms should be designed effectively, as they appear to lose therapeutic value when they are not tuned to the individual's pace, or when they become more cognitively demanding. Reticulo-spinal pathways along with cerebellar areas may have a role in mediating the positive effect of music.

Future neurological music therapies for PD should be individually tailored, attending to the specific clinical features and stimulus responding of the individual. In our opinion, the long-term modification of motor patterns may require persistent training under conditions adapted for individual patients.

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