Rhythmic auditory stimulation as a treatment in Parkinson's disease: an integrative review

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Abstract

Parkinson's disease (PD) is characterized by classic motor symptoms resulting from changes in the basal ganglia. The external auditory cues called rhythmic auditory stimulation (RAS) have been used to synchronize the internal rhythm maladjusted in patients with PD. The objective of this work was to analyze the types of auditory stimuli, the sound sources, and the outcomes of the RAS interventions used in patients with PD. In order to do so, an integrative review in the scientific bases PubMed, ScienceDirect, Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs) and Biblioteca Virtual em Saúde (BVS) was carried out. The search strategy Parkinson's disease or Parkinson's disorder and acoustic stimulation was

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used. After crossing the descriptors and obtaining the articles in the scientific databases, the selection started. First, the titles and abstracts were read, followed by the full articles. Finally, data were extracted from selected articles, analyzed, and critically discussed. Eleven articles were eligible for this review. Among these, nine were classified in level 1B of evidence according to the criteria of the Oxford scale. Two articles used melodic stimuli and only one article used prosodic stimuli. The majority of the articles used headphones as a sound source, and eight articles showed promising results in the motor component of patients with PD when submitted to intervention protocols with RAS. In conclusion, RAS improves the motor performance of patients with PD and the association of melodic, prosodic, or ecological stimuli with artificial sounds (metronome, tones, and binaural beats) provided through headphones has shown to be the most promising way for RAS intervention in PD patients.

Keywords

Audiology. Parkinson's disease. Music. Speech. Language and hearing science.

Estimulações auditivas rítmicas como tratamento na doença de Parkinson: uma revisão integrativa

Resumo

A doença de Parkinson (DP) é caracterizada pelos sintomas motores clássicos decorrentes das alterações nos gânglios da base. As pistas auditivas externas, denominadas estimulações auditivas rítmicas (*rythmic auditory simulation* [RAS]), têm sido utilizadas como sincronizadoras do ritmo interno desajustado nos pacientes com DP. Este trabalho objetivou analisar os tipos de estímulos auditivos, as fontes sonoras e os desfechos das intervenções de RAS utilizadas nos pacientes com DP. Para tal, realizou-se uma revisão integrativa em que as bases científicas PubMed, ScienceDirect, Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs) e Biblioteca Virtual em Saúde (BVS) foram contempladas, utilizando-se a estratégia de busca *Parkinson's disease* ou *Parkinson's disorder* e *acoustic stimulation*. Após o cruzamento dos descritores e a obtenção dos artigos nas bases científicas de dados, os crivos foram iniciados; primeiramente, títulos e resumos foram lidos e, em seguida, os artigos completos. Após essa etapa, os dados foram extraídos dos artigos selecionados, analisados e discutidos criticamente, considerando-se, enfim, 11 artigos elegíveis para esta revisão. Dentre esses, nove foram enquadrados no nível 1B de evidência de acordo

com os critérios da escala Oxford, dois artigos utilizaram estímulos melódicos e apenas um artigo utilizou estímulo prosódico. A maioria dos artigos utilizou fones de ouvidos como fonte sonora. Ainda, oito artigos apresentam resultados promissores no componente motor dos pacientes com DP quando submetidos a protocolos de intervenções com RAS. Concluiu-se, então, que as RAS melhoram o desempenho motor dos pacientes com DP e a associação dos estímulos melódicos, prosódicos ou ecológicos com os sons artificiais (metrônomo, tons e batidas binaurais) fornecidos através de fones de ouvidos demonstrou ser a forma mais promissora para intervenção de RAS nos pacientes com DP.

Palavras-chave

Audiologia. Doença de Parkinson. Música. Fala. Fonoaudiologia.

Estimulación auditiva rítmica como tratamiento en la enfermedad de Parkinson: una revisión integradora

Resumen

La enfermedad de Parkinson (EP) se caracteriza por síntomas motores clásicos resultantes de cambios en los ganglios basales. Las señales auditivas externas denominadas estimulación auditiva rítmica (*rythmic auditory stimulation* [RAS]) se han utilizado para sincronizar el ritmo interno desadaptativo en pacientes con EP. El objetivo de este trabajo fue analizar los tipos de estímulos auditivos, las fuentes sonoras y los resultados de las intervenciones RAS utilizadas en pacientes con EP. Com ese fin, se hice una revisión integradora en la que se consideraron las bases científicas PubMed, ScienceDirect, Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs) y Biblioteca Virtual em Saúde (BVS). Se utilizó la estrategia de búsqueda *Parkinson's disease* o *Parkinson's disorder* y *acoustic stimulation*. Luego de cruzar los descriptores y obtener los artículos en las bases científicas, comenzó la selección. En primer lugar, se leyeron los títulos y los resúmenes, seguido de la lectura de los artículos completos. Finalmente, los datos fueron extraídos de artículos seleccionados, analizados y discutidos críticamente. Once artículos fueron elegibles para esta revisión. Entre estos, nueve fueron clasificados en el nivel 1B de evidencia según los criterios de la escala de Oxford, dos artículos utilizaron estímulos melódicos y solo un artículo utilizó estímulos prosódicos. La mayoría de los artículos utilizaron auriculares como fuente de sonido y ocho artículos mostraron resultados

prometedores en el componente motor de pacientes con EP cuando se sometieron a protocolos de intervención con RAS. En conclusión, RAS mejora el rendimiento motor de los pacientes con EP y la asociación de estímulos melódicos, prosódicos o ecológicos con sonidos artificiales (metrónomo, tonos y pulsaciones binaurales) proporcionados a través de auriculares ha demostrado ser la forma más prometedora de intervención RAS en pacientes con EP.

Palabras clave

Audiología. Enfermedad de Parkinson. Música. Discurso. Fonoaudiología.

INTRODUCTION

Auditory rhythms are sequences of sounds repeated at regular intervals, and their wide sound spectrum is currently being applied in several areas of health to prevent, diagnose (e.g., ultrasound), and relieve disease symptoms, such as using the human audible sound spectrum through rhythmic auditory stimulation (RAS) in neonatology (ZHU *et al*., 2015), pediatrics (KENNELLY, 2000), palliative care (GUTGSELL *et al*., 2013), neurological (BRANCATISANO; BAIRD; THOMPSON, 2020), and psychiatric disorders (SHARDA *et al*., 2018).

Neurological disorders are, specially, significant beneficiaries of this resource. This fact is observed when the physical and melodic nature of music are combined with the RAS strategy, for example, to stimulate and maintain the movement of individuals with Parkinson's disease (PD) (DE BARTOLO *et al*., 2020), when rhythms are used through the sound pulses of the metronome to synchronize the PD patients' walk (GALLO MCISAAC; GARBER, 2014), or when ecological sounds (YOUNG *et al*., 2016) are launched as RAS approaches. In addition, metronome beats simultaneously to music are being investigated by the scientific community as movement synchronizers in PD patients (THAUT *et al*., 2019).

Time and space are two sound components and are intrinsically related to rhythm, a connection that is lost in PD patients (FAHN, 2003), once they lose automaticity and motor rhythmicity. Although non-motor symptoms are strongly associated with PD (SCHAPIRA; CHAUDHURI; JENNER, 2017), the dominant dysfunctions are the motor ones, such as rigidity, postural instability,

rest tremor, and bradykinesia, due to the progressive reduction of dopamine in the *substantia nigra*, which is also responsible for changes in the connectivity of neural circuits in the basal *nuclei* (FAHN, 2003). The walk only develops in a cadenced, automatic, balanced, and harmonic way when there is the integrity of the locomotor brain circuits responsible for automatism, in such a way that the lack of regularity in the walk and the difficulty in performing movements are evident in patients with PD, due to the impairment of this neuronal network (YIN, 2014).

Humans can synchronize their internal rhythm through external auditory clues once the temporal predictability of auditory clues should contribute to the realignment in neural networks of dysfunctional connectivity (CALABRÒ *et al*., 2019). This phenomenon occurs through the frontoparietal circuits (SHINE *et al*., 2013) of the auditory (BRAUNLICH *et al*., 2019), motor, and premotor areas (CHEN; PENHUNE; ZATORRE, 2008), cortico-basal ganglia-thalamocortical connectivity network (SZEWCZYK-KROLIKOWSKI *et al*., 2014), and the cerebellum-thalamocortical network (PELZER *et al*., 2013). Thus, the main objective of this review is to analyze the types of auditory stimuli, sound sources, and outcomes of RAS interventions in PD patients.

METHODS

This research carried out an integrative review, in which the searches of the data in the literature were conducted in August 2021. The scientific databases PubMed, ScienceDirect, Latin American and Caribbean Literature on Health Sciences (Literatura Latino-Americana e do Caribe em Ciências da Saúde [Lilacs]), and Virtual Health Library (VHL) were included.

Search strategies were adapted to the PICO method (patient, intervention, comparison, and outcome) (Chart 1), and the Medical Subject Headings (MeSH) descriptors were used. In addition, the boolean operators “and” and “or” were combined with the keywords, ensuring methodological accuracy. Thus, the following strategy resulted: Parkinson’s disease or Parkinson’s disorder and acoustic stimulation.

Chart 1 Descriptors used according to the PICO method

Patient	Parkinson's disease or Parkinson's disorder
Intervention	Acoustic stimulation
Comparison	-
Outcome	Intervention outcome
Study type	Clinical trial Case-control Cross-sectional

Source: Elaborated by the authors.

The articles were selected following the eligibility criteria: reports that studied Parkinson and analyzed interventions exclusively based on auditory stimulation, from the last ten years (2011-2021), in English, Spanish, and Portuguese. Articles that used dance as an intervention and requested cognitive instructions from participants beyond movement synchronization with the RAS were excluded.

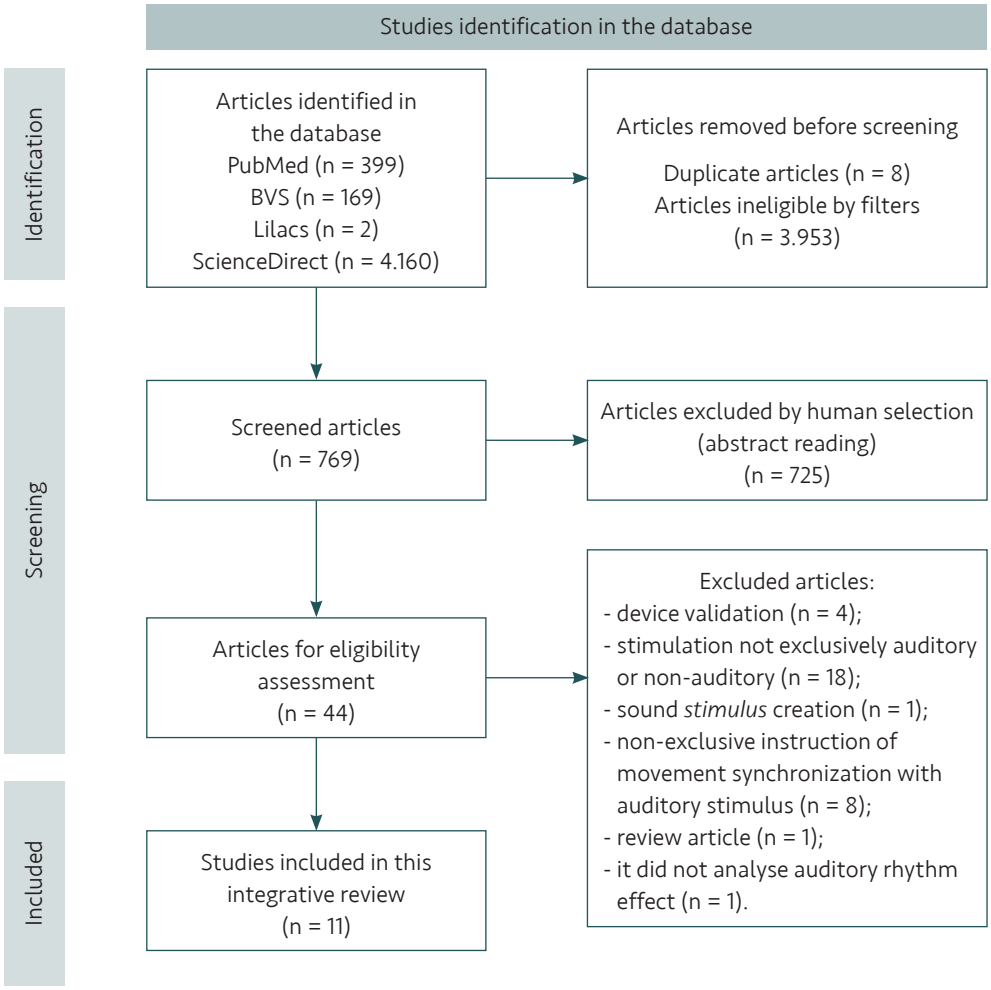
The sieves were initiated after crossing the descriptors and obtaining the articles in the scientific databases. First, the titles and abstracts were read, followed by the full papers.

The main information was abstracted and tabulated during the entire reading of the articles selected for this review: country of execution of the research, participants, objectives, sound rhythm, sound source, and outcomes. Thus, the manuscripts were classified according to the Oxford scale of evidence level (1 to 5 and from "A" to "D"). Finally, the data were analyzed and critically discussed.

RESULTS

The literature search resulted in 4,730 articles. After applying filters in the databases and removing duplicates, 769 manuscripts were screened. Then, the titles and abstracts were read, and 725 papers were excluded, resulting in 44 for a full reading. Finally, 11 articles were eligible for this review (Figure 1).

Figure 1 Flow diagram adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 for new systematic reviews that included database and registry searches only



Source: Elaborated by the authors.

Among the 11 articles with RAS intervention protocols selected, nine were classified as level 1B of evidence according to the Oxford scale criteria. Two papers used melodic stimuli, and only one used prosodic stimuli. Most of the articles used headphones as a sound source, and eight of them showed promising results in the motor component of patients with PD when submitted to intervention protocols with RAS (Table 1).

Table 1 Articles with sound rhythm-based intervention protocol in PD patients between 2011 and 2021

Autor/year	Country/sample No.	Level of evidence	Study type/ objective(s)	Rhythmic auditory stimulation (RAS) and sound source characteristics	Results
Baram *et al.* (2016).	• Israel • 16 Parkinson's disease (PD) patients.	1B	• Uncontrolled clinical trial. • To compare the effects of closed and open circuit feedback on the gait of patients with PD.	• Closed-circuit: a click-like sound that provides feedback through headphones. • Open circuit: pulses from an external metronome that does not provide feedback.	• Closed-circuit auditory feedback improves walking speed and stride length in PD patients. • Closed-circuit auditory feedback training has residual effects.
Belluscio *et al.* (2021).	• Italy • 20 PD patients.	1B	• Uncontrolled clinical trial. • To verify whether stride-adjusted RAS in the PD patient improves gait patterns.	• RAS based on the golden ratio (φ – rhythm). • Circumaural headphones.	• Results show improvements in stride length, walking speed and foot clearance. • RAS based on φ-rhythm is correlated with compensation of defective internal rhythm in PD.
Chang *et al.* (2019).	• China • 21 PD patients: 11 with freezing of gait (FOG) and ten with no freezing of gait (nFOG).	1B	• Randomized crossover clinical trial. • To investigate and compare the effects of the "walking on the spot" training session with RAS between groups.	• The RAS was the beats of a metronome set at 110% of the participant's usual cadence.	• "Walking on the spot" training with RAS improved lower limb movement variability. • PD patients with FOG may benefit more from this training than those with nFOG.

(*continua*)

Tabela 1 Articles with sound rhythm-based intervention protocol in PD patients between 2011 and 2021 (*continuation*)

Autor/year	Country/sample No.	Level of evidence	Study type/ objective(s)	Rhythmic auditory stimulation (RAS) and sound source characteristics	Results
Dotov *et al.* (2019).	• France • 20 PD patients. • 20 matched case-control.	3B	• Case-control. • To compare the "drag" effect on gait cadence by two interactive and two non-interactive auditory stimuli between PD patients and matched controls.	• The auditory *stimulus* consisted of metronome beats with triangular timbre or four musical excerpts, such as Mozart's Turkish march adapted for the piano. The metronome beats corresponded to the music tracks' beats. • Wireless headphones.	• The mutual interactive *stimulus* produced the most potent "entrainment" in PD patients and controls, with no differences between the groups. • The *stimulus* adapted to the gait of each participant.
Gallo, McIsaac, and Garber (2014).	• United States of America • 22 PD patients.	1B	• Randomized crossover clinical trial. • To determine the effect of auditory clues on the economy of treadmill walking. • To determine the effect of auditory clues on the perception of effort in PD patients.	• The RAS consisted of the metronome beats.	• Poorer walking economy and higher energy expenditure occurred during walking in self-selected mode and at the fastest walking speed, but there was no apparent difference at the slower speed. • Potential gains from auditory clues may come at a poorer energy cost and walking.

(*continua*)

Tabela 1 Articles with sound rhythm-based intervention protocol in PD patients between 2011 and 2021 (*continuation*)

Autor/year	Country/sample No.	Level of evidence	Study type/ objective(s)	Rhythmic auditory stimulation (RAS) and sound source characteristics	Results
Gálvez *et al.* (2018).	• Spain • 14 PD patients.	1B	• Controlled, randomized, double-blind clinical trial. • To investigate the binaural beats influence on PD patients.	• A ten-minute binaural beat presented rhythmically and masked by pink noise. • The *stimulus* resembles the sea sound at a low volume. • Headphones.	• No significant changes in gait performance, heart rate, or anxiety level were identified in the patients. • In the control stimulation, no significant changes were identified in the variables analyzed.
Hove *et al.* (2012).	• China • 20 PD patients. • 18 controls (young adults).	3B	• Case-control. • To compare the effects of walking with fixed-time rhythmic auditory stimulation and interactive rhythmic auditory stimulation.	• RAS (100 ms sinusoidal tones at 523 and 700 Hz were played). • In the fixed-time RAS: the *stimulus* is presented in constant time. • In the interactive condition, the *stimulus* time changed in response to the participant's gait. • Circumaural headphones.	• Patients and controls rarely synchronized to fixed-time RAS, and when they did, their fractal scale decreased from levels 1/f healthy. • Five minutes after the removal of interactive rhythmic stimulation, PD patients' gait retained a large fractal scale, suggesting that the interaction stabilized the internal rhythm-generating system and reintegrated timing networks.

(*continua*)

Tabela 1 Articles with sound rhythm-based intervention protocol in PD patients between 2011 and 2021 (*continuation*)

Autor/year	Country/sample No.	Level of evidence	Study type/ objective(s)	Rhythmic auditory stimulation (RAS) and sound source characteristics	Results
Janzen, Haase, and Thaut (2019).	• United States of America • 41 PD patients; (three groups: no intervention; stimulation + finger movements and stimulation + arm movements).	1B	• Controlled clinical trial. • To investigate whether the immediate effects of RAS training of arm or finger movements modulate gait speed.	• Metronome was used for the auditory stimuli (1 kHz sine wave, 85 dB sound pressure level). • Free field: speaker placed one meter in front of the subject.	• Patients who completed the auditory-motor training consisting of finger tapping associated with the metronome sound obtained significant increases in gait speed and cadence. • Waving the arms in alternate movements in synchrony with the metronome did not change gait speed or cadence.
Stegemöller *et al*. (2016).	• United States of America • 41 PD patients (three groups: 18 PD patients performing rapid movements; ten PD patients with slow movements; 13 controls).	1B	• Clinical trial. • To determine whether the repetitive finger movement performance by acoustic clues above 2Hz differs between the less and more affected side in PD patients. • To analyze whether the clinical motor scores differ between groups.	• A series of acoustic tones were presented at a rate of 1 Hz for 15 intervals and then increased by 0.25 Hz every 15 intervals until it reached 3 Hz (50ms, 500 Hz, 80dB).	• No significant differences between the more and less affected sides. • Comparison of disease severity, tremor, and stiffness between the groups' performance revealed no significant differences. • The participants who rushed had worse posture and postural instability scores.

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Tabela 1 Articles with sound rhythm-based intervention protocol in PD patients between 2011 and 2021 (*continuation*)

Autor/year	Country/sample No.	Level of evidence	Study type/ objective(s)	Rhythmic auditory stimulation (RAS) and sound source characteristics	Results
Thaut *et al.* (2019).	• Canada • 60 patients with PD (30 allocated in experimental group 1 [24 weeks] and 30 in control group 2 [eight to 16 weeks]).	1B	• Randomized controlled clinical trial. • To evaluate whether RAS training reduces the number of falls in PD patients with a history of frequent falls.	• Music coupled to the beats of the metronome: folk and classical instrumental music with 2/4 stronger sounds, recorded digitally using the keyboards to modulate beat cadence rates. • Free field or headphones.	• RAS training significantly reduced the number of falls in PD and modified key gait parameters such as speed and stride length.
Young *et al.* (2016).	• United States of America • 19 PD patients (two groups: ten patients with nFOG and nine patients with FOG).	1B	• Clinical trial. • To examine interactively the two specific suggestion parameters of action relevance and of continuity to observe which of these improved temporal regulations. • To compare the effects between the nFOG and FOG groups.	• Auditory clues: sounds of footsteps in a hallway, the sound of the metronome, sounds of footsteps on gravel, bursts of white noise. • Headphones.	• Action-relevant sensory clues (footsteps) induced more significant reductions in temporal variability during an on-site walking task in the FOG group compared to clues that do not represent an action. • The combination of both stimuli (gravel + noise bursts) led to a significant increase in the walk-in-place duration before the first freeze compared to the metronome and footstep clues in the hallway.

Source: Elaborated by the authors.

DISCUSSION

The Oxford scale of level of evidence is widely used in the scientific community. Thus, nine of the included articles have a level of evidence 1B, and two, 3B, denoting articles designed as clinical trials and case controls.

The RAS interventions present interesting characteristics: while some only present rhythm, such as the metronome beats (GALLO; MCISAAC; GARBER, 2014; CHANG *et al*., 2019), others present rhythm and melody, such as instrumental music (DOTOV *et al*., 2019). There is also the one that combines rhythm, melody, and prosody when the music is sung (DOTOV *et al*., 2019), and the auditory clues, called "ecological", for example, when the sound of footsteps is recorded and transmitted to the patients (YOUNG *et al*., 2016). Clearly, all the mentioned auditory stimuli are rhythmic. Only two studies in this review used melodic stimuli: the first used melodic (instrumental music) and prosodic (sung music) stimuli associated with metronome beats (DOTOV et al., 2019), and the other used only melodic stimuli with metronome beats (THAUT et al., 2019); one article used the ecological sound (recording footsteps in the corridor or on the gravel) associated with metronome pulses or white noise bursts (YOUNG *et al*., 2016), respectively. Eight manuscripts used only artificial stimuli (metronome sound, tones, and binaural beats (GALLO; MCISAAC; GARBER, 2014; CHANG *et al*., 2019; BARAM *et al.*, 2016; BELLUSCIO *et al*., 2021; GÁLVEZ *et al*., 2018; HOVE *et al*., 2012; JANZEN; HAASE; THAUT, 2019; STEGE-MÖLLER *et al*., 2016). The association of the musical or ecological *stimulus* with artificial *stimulus* seems to be a positive strategy once it strongly emphasizes the auditory rhythm to be synchronized to the movement, providing an external auditory clue to the PD patient more robustly.

Research conducted by Young *et al*. (2016) used recorded footstep sounds as RAS. Characterized as a biological and natural sound that reproduces the effect of action and contrasts it with the non-continuous and mechanical sound of the metronome or the tones, this study demonstrated that PD patients with freezing of gait (FOG) had better results when the strategy used was ecological auditory stimulation. The results are even more advantageous when associating the sound of footsteps on gravel with white noise bursts (YOUNG *et al*., 2016). The three studies that did not observe positive changes when associating RAS with motor activity in PD patients used artificial sounds

(metronome, tones, and binaural beat) (GALLO; HAASE; THAUT, 2014; GÁLVEZ *et al*., 2018; STEGEMÖLLER *et al*., 2016), suggesting that they can be used as reinforcers of musical and ecological sound, or even with adjustments that resemble the physiological rhythm, when used alone.

In the *spectrum* of audible sounds for humans, speech occupies a prominent place. The psychoacoustic properties in the human voice, added to the harmonic and melodic characteristics, which result in sung music, seem to be a promising approach compared to the artificial sound of the metronome used in several articles. However, recited poetry, intrinsically characterized by strong prosodic content, was not found in any study. Finally, both sung music and poetry have emotional components of literary content and prosody, directly related to the limbic system, responsible for modulating motor output in the basal ganglia (AOKI *et al*., 2019), misaligned in PD patients. Thus, sung music and recited poems as RAS strategies in PD patients seem to be a strategy for synchronizing movement and organizing the internal rhythm by using the limbic-ganglia basal connection (AOKI *et al*., 2019) as a potentiating pathway.

Most of the studies used headphones (GALLO; MCISAAC; GARBER, 2014; YOUNG *et al*., 2016; THAUT *et al*., 2019; CHANG *et al*., 2019; DOTOV *et al*., 2019; BARAM *et al*., 2016; BELLUSCIO *et al*., 2021; GÁLVEZ *et al*., 2018; HOVE *et al*., 2012; STEGEMÖLLER *et al*., 2016) as a sound source for intervention with RAS, and only two used free field (THAUT *et al*., 2019; JANZEN; HAASE; THAUT, 2019). No article used pure musical instruments or the human voice as a resource during the intervention. The use of headphones is a reasonable option since the sound is conducted directly to the patient's external acoustic *meatus*, and it also excludes the interference of ambient sounds.

Among the 11 articles selected, two used upper limb movements (JANZEN, *et al*., 2019; STEGEMÖLLER *et al*., 2016), and nine used lower limb movements (GALLO; HAASE; THAUT, 2014; YOUNG *et al*., 2016; THAUT *et al*., 2019; CHANG *et al*., 2019; DOTOV *et al*., 2019; BELLUSCIO *et al*., 2021; BARAM *et al*., 2016; GÁLVEZ *et al*., 2018; HOVE *et al*., 2012; JANZEN; HAASE; THAUT, 2019), associated with RAS in PD patients. When analyzing whether the auditory-motor training of finger or arm movements caused generalization to gait movements, Janzen, Haase, and Thaut (2019) observed that the metronome beats associated with finger movements improved the speed and cadence of the gait. In contrast, the arm movements did not change the gait patterns in PD patients. Examining the performance between finger

movements associated with RAS on the more and less affected side of PD patients, Stegemöller's group of scientists found no significant differences (STEGEMÖLLER *et al*., 2016).

In the research conducted by Baram *et al*. (2016), it was found that auditory feedback correlated to gait with RAS has more favorable and residual effects when compared to open circuit stimulation in PD patients. In turn, a study conducted by the research group of Gallo, McIsaac, and Garber (2014) concluded that treadmill walking associated with RAS could result in worse walking and increased energy cost at self-selected and slightly faster speeds. Similarly, a group of scientists created a laboratory *stimulus* similar to the sound of the sea by conducting a binaural beat on PD patients and observed no significant changes in gait performance, heart rate, or anxiety level (GÁLVEZ *et al*., 2018).

Although most studies investigate gait patterns associated with RAS, the reduction of falls were also identified in PD patients when performing auditory-motor training in a study conducted by Thaut *et al*. (2019). Chang *et al*. (2019) identified an improvement in PD patients' FOG when defending the audio-motor training and using auditory clues to synchronize the gait without moving out of place.

Human gait has a harmonic cadence determined by an internal physiological rhythm supported by an underlying organic substrate, the base *nuclei* (CALABRÒ *et al*., 2019). Belluscio *et al*. (2021) used the golden ratio to develop a RAS adjusted to each patient's walk. It showed a positive outcome in stride length, walking speed, and foot clearance, demonstrating that auditory stimulation based on the internal fractal of the individualized gait is an adjunct to improve impaired movement flow in PD patients (BELLUSCIO *et al*., 2021).

Most of the studies analyzed present in the intervention protocol the need for patients to consciously synchronize (cognitive function) the auditory track with the motor activity, denoting an audio-motor training that demands attention, concentration, and significant energy expenditure. Besides the intrinsic difficulty of the motor act found in these patients and the high energy cost caused by the rest tremor, due to the base pathophysiology, they also need to use extra energy, as they must try to control their movements adjusting to the synchronicity of the auditory rhythmic activity. Dotov *et al*. (2019) proposed that PD patients only listened to the RAS without needing to synchronize with

gait consciously, and a spontaneous neuronal "entrainment" occurred primarily in the PD patients and the group with mutual interactive *stimulus*. Corroborating this finding, the interactive RAS, i.e., adjusted to the patient's stride, retained a high fractal scale (physiological rhythm), suggesting that the interaction between the steps and the auditory clue can stabilize the dysregulated internal rhythm of PD patients, in agreement with Hove *et al*. (2012).

A curious fact observed in the research is the lack of standardization of intervention protocols with RAS, hindering a careful analysis and indicating the need for a reproducibility science, in which the studies that showed effective responses would be reproduced with new groups of PD patients to validate the intervention protocols.

The reduced number of articles that use prosodic and melodic stimuli probably is because the descriptor used for the selection was acoustic stimulation. Thus, the compositions that specifically used acoustic characteristics (e.g., metronome sound) were mainly contemplated. Thus, it is suggested to expand the descriptors for future reviews. Additionally, the implications of RAS on the non-motor components strongly associated with PD also deserve investigation.

FINAL CONSIDERATIONS

The RAS improves the motor performance of PD patients and can be used as an adjuvant, complementary, and low-cost treatment to synchronize the maladjusted motor rhythmicity. The association of melodic, prosodic, or ecological stimuli with artificial sounds (metronome, tones, and binaural beats) provided through headphones proved to be the most promising way for RAS intervention in PD patients. Finally, there is a need for the standardization of RAS intervention protocols for PD patients by the scientific community.

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