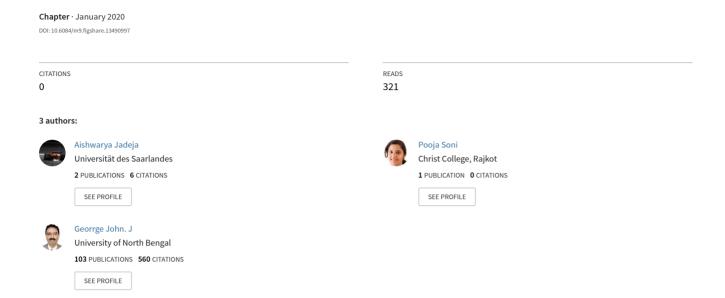
Music and Games: Future Rhythmic Simulation, Implementations and Considerations



MUSIC AND GAMES: FUTURE RHYTHMIC SIMULATION, IMPLEMENTATIONS, AND CONSIDERATIONS

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ABSTRACT

Rhythmic abilities are highly widespread in the general population. The majority can extract the regular beat of the music and align their movements with it. These abilities are eloquent from a cognitive function such as language and memory. When rhythmic skills are challenged by brain damage or neurodevelopmental disorders, remediation strategies based on rhythm can be considered. For example, rhythmic training can be used to enhance motor performance and cognitive and language skills. For rhythmic training, games are also considered as a dynamic factor, and numerous are readily available in the market. Games that train rhythm skills may serve as useful tools for retraining motor and cognitive function in patients with motor or neurodevelopment disorders (e.g., Parkinson's disease, dyslexia, ADHD). Additionally, regular rhythmic patterns facilitate memory encoding and decoding of nonmusical information; hence music is an efficient mnemonic tool. The music as a hierarchical, compound language of the time, with its unique ability to access affective/motivational systems in the brain, provides time structures enhancing perception processes, mainly in the range of cognition, language, and motor learning. It allows for emotional expression and improvement of the motivation for rehabilitation activities. The new technologies of rhythmic sensory stimulation (i.e., Binaural Beat Stimulation) or rhythmic music in combination with rhythmic light therapy appear. These multimodal forms of stimulation are used to treat stroke, brain injury, dementia, and other cognitive deficits.

1. INTRODUCTION

Developmental Dyslexia (DD) is a neurodevelopmental disorder that impairs reading acquisition despite conventional instruction and sociocultural opportunities, normal intelligence, and motivation (Barrouillet *et al.*, 2007; Démonet *et al.*, 2004). This disorder affects ~5% of children in primary school (Habib, 2000; Norton *et al.*, 2015). While recent computational models provide evidence that the cause of the DD is likely to be multifactorial, phonological processing deficits have long been considered as a significant factor in the large majority of dyslexia children (Perry *et al.*, 2019). Phonological activity may impact reading, writing, and other phonological forms. Specifically, the poor development of reading skills in children is a risk for dyslexia. Moreover, the reading difficulty acquitted based on the brain's several regions and cognitive deficits contributes to DD's etiology. Alternatively, the reading procedure requires serial processing of stimuli, which can be achieved by the rapid orientation of visual attention (Näätänen *et al.*, 1978). Besides, this visual attention is hypothesized with two intentional studies about the game's role in dyslexic patients. Also, two types of players play these games: active players and non- active players (Mura *et al.*, 2017). Besides, both show the different enhancement in therapy. In this analysis, this has to be addressed further.

Another training tool is music; humans have a natural tendency to move, spontaneously, to the beat of the music, for example, in Dance, synchronized sport, and in group activities (e.g., waving together at a rock concert). Synchronization of a musical beat is sustained by a complex neuronal network, including perceptual regions, motor regions, and sensorimotor integration areas (Chen *et al.*, 2008; M. H. Thaut, 2003). Disruption in these networks affects the auditory-motor synchronization to a musical beat and other functions such as speech. Consequently, music therapy has evolved from a social science model to a neuroscience model of clinical practice and research. This paradigm shift has formed a new theory known as Neurologic Music Therapy (NMT) (M. Thaut, 2013). A various group of researchers published their computational studies on neurological diseases in recent years (Chirag *et al.*, 2017; Farida & Georrge, 2016; Janvi & Georrge, 2017; Joseph *et al.*, 2015; Kinnari & Georrge, 2017; Patel *et al.*, 2018; Vakhariya Sakina & Georrge, 2016).

The number of brain researches, especially on neuroplasticity and cortical reorganization, has increased concerning the development of new neuroscience technologies (PET and fMRI), which allow

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observing the brain activity during different mental tasks (Linden, 2011). As a result, cognitive neuroscience, also in the clinical range, has developed significantly. The fMRI technique allows for a more detailed localization of areas implicated in psychological symptoms. It might be used to identify areas that support coping strategies, resilience, and treatment effects.

2. BRAIN BASES OF DYSLEXIA

Reading is the linguistic skill and brain structures used in oral language processing and some additional structures associated with visual-object processing and the establishment of visual-linguistic mappings. (see Figure 1).

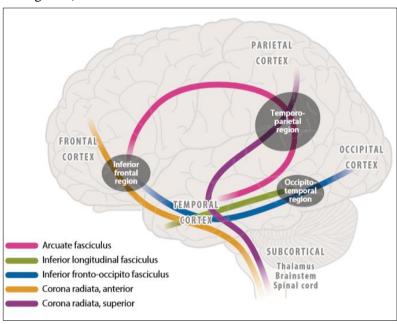


Figure 1: Schematic representation of grey matter regions (*dark grey ovals*) and white matter tracts (coloured lines) that might be relevant for reading. Given the sagittal view of the figure, the corpus is not depicted. Figure adapted with permission from Vandermosten M, Boets B, Wouters J, Ghequiere P. 2012.A qualitative review of diffusion tensor imaging studies in reading and dyslexia. *Neurosci. Biobehav. Rev.* 36:1532-52.

Indeed, functional studies imaging have unswervingly revealed that individuals with dyslexia show abnormal activations of a distributed left hemisphere language network (Démonet et al., 2004; Richlan et al., 2009). Under activations have been reported in two posterior left hemisphere regions: temporoparietal region believed to be crucial for phonological processing and phoneme-grapheme conversion, and an occipitotemporal region, including the so-called visual word form area, that is thought to participate in whole-word recognition. Under activations have been testified in two left hemisphere posterior regions: a temporoparietal region held to be crucial for phonological processing and

phoneme-grapheme conversion occipitotemporal region, including the so-called visual word form area, that is thought to participate in whole-word recognition. Abnormal activation of the left inferior frontal gyrus is also frequently reported. Structural imaging studies have revealed grey matter decreases in this same network. A recent family risk study confirmed that these grey matter decreases predate literacy instruction and are thus not only a consequence of reading failure (Richlan *et al.*, 2011).

Albeit individuals with dyslexia show functional abnormalities in both posterior and anterior language networks, dyslexia have been believed to be a disconnection disorder. Accordingly, much research has used diffusion tensor imaging to explore white matter correlates of dyslexia. The most consistent findings have included local white matter changes (as indexed by fractional anisotropy) in children and adults with dyslexia in left temporoparietal regions and the left inferior frontal gyrus (Darki et al., 2012; Rimrodt et al., 2010). Studies have consistently reported correlations between white matter integrity and phonological skills. This work is beginning to be integrated into neuropsychological theories of dyslexia, and this area should be a continued focus of future research. For example, as discussed above, a disconnection between posterior auditory processing areas and anterior motor planning areas is potentially consistent with disrupted development of phonological representations. Because of its emphasis on letter-sound binding, the orthographic learning hypothesis also aligns with a disconnection account.

3. MUSIC AS A TRAINING TOOL Literacy Skills Language Skills Temporal Spelling Skills Processing **Phonological** Musical **Abilities** Segmentation **Training** Rhythm Copying & **Rapid Auditory** Rhythm Games & **Processing Singing Games**

Figure 2: Music as a training tool

3.1 Mechanism of neurologic music theory

The discovery of entrainment for therapeutic purposes in the early 1990s has led to a healthy body of research evidence that periodicity of auditory rhythmic patterns could improve movement patterns in patients with a movement disorder (Figure 2). "Entrainment" describes a process whereby two rhythmic processes interact with each other in such a way that they adjust towards and eventually 'lock-in' to a common phase. Entrainment also plays a vital role in physiological and behavioral functions. Rhythmic stimulation has influenced sensory material's temporal coordination and organization, especially in motor control and speech (Galińska, 2015). Moreover, auditory entrainment also concerns the listener's mood, which adjusts immediately according to music's emotionality.

Music is a complex temporal stimulus structured in various types of pattern- from spectral pattern to the hierarchical rhythmic structure of a layer of musical pattern. Timing is a crucial component of neural information processing. Musical rhythm pattern helps create temporal structure in neural network activation (Galarreta & Hestrin, 2001). Researchers suggest that music can uniquely engage the brain as a language of the time. Physical exercise accompanied by music can enhance strength and endurance, muscle tone, flexibility, agility, body control, vital capacity, and cardiovascular efficiency. Music becomes not the only motivator for movement and provides a rhythmic structure for movement patterns; for instance, in Parkinson's disease (Naghizadeh, 2017). This technique is defined as a patterned sensory enhancement. It uses the musical pattern to create a functional movement of arms and hands.

Differential neurological processing of musical components using different not only auditory, brain structures. This property allows for access to deficient regions and compensatory takeover of their function through alternative transmission routes and connections (Galińska, 2015). It is possible because neural processing systems for some musical and non-musical functions are standard, and in the case of others, are distinctive (Schlaug, 2009). This switching happens due to the brain's plasticity, and neural cells positively connect as musical training.

In affective-aesthetic response (motivation, emotions), music is a powerful tool that communicates emotions and meaning through its intrinsic symbolic structure of musical elements and emotional responses connected to it through the associative learning process (Berlyne, 1971). The music can organize human behavior and learning procedure. Attention, perception, memory, learning, executive function, and physical responses can influence appropriate affective states. It is considered a central mechanism of music therapy's therapeutic effectiveness (Juslin & Sloboda, 2011).

3.2 The critical pitch and notes

Research has indicated associations between reading and music because music includes pitch and rhythm; the processing of pitch and beats can be evaluated when discussing musical ability. In musical notation, pitch refers to the height of note heads on control, while the vertical distance between notes is the interval. Rhythm is represented via the shape of note and the horizontal distance between notes. There is a high correlation (r= .36-.45) between pitch processing and phonemic awareness in children ages 4-5 years (r= .59-.74) as well as pitch processing and reading skills (Anvari *et al.*, 2002). Such

correlations are also observed between music, tonal memory, chord analysis, and reading abilities in children ages 7-11 years (r=.53-.66). They found a high correlation (r=.64) between rhythm discrimination and reading spelling in 7- and 8- year-old children. Moreover, an integrated analysis showed a somewhat significant relationship (r=.17) between music learning and reading (Lamb & Gregory, 1993). For adults, pitch contour's observation ability was positively correlated (r=.45-.50) with voice and reading skills when speaking out loud. More importantly, high correlations (r=.54) between music learning and language skills were also discovered in children with dyslexia (Foxton *et al.*, 2003). Three studies indicated poor rhythm perception in children with dyslexia or patient with significant symptoms of reading disabilities.

Dyslexic children had difficulties in segmenting the phonemes of characters (such as segmenting sun into /s/. /u/, and /n/), syllables (such as segmenting toothbrush into tooth and brush) and discriminating similar voice articulation (like /p/ and /b/) (Hulme & Snowling, 1992). Some evidence has suggested segmental deficits of phonological processing may result from difficulties. Moreover, studies have been the basis for auditory processing theory, in which difficulties have been mentioned for a dyslexic child. However, gap detection and temporal order judgment are not explained in the processing but are considered the primary feature for rhythmic pattern and core deficit in developmental dyslexia (Ho *et al.*, 2002). For instance, dyslexic children had difficulties in the reproduction of manual motor rhythms.

As per the studies, it is identified that music and reading are positively correlated significantly; the dyslexic child has impaired ability to process with rhythms. Nevertheless, some studies have suggested that the Chinese language is not having issues with the musical rhythm. Chinese dyslexic children have weaker phonological processing, and it's reported that they are doing worst than their chronological age control (Ho *et al.*, 2002).

4. NEUROPSYCHOLOGICAL MEASURES

Children were administered the tests in different studies to evaluate the linguistic, musical, reading, and general cognitive abilities (Figures 2 and 3).

General cognitive abilities: General cognitive abilities and working memory were evaluated through the Intelligence Scale. Auditory attention is one factor: Auditory Attention was assessed using a test from the BIA Battery (Flaugnacco *et al.*, 2015).

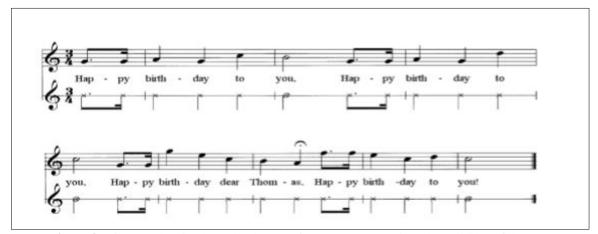


Figure 3. Diagram showing how the rhythm of a song corresponds to the syllables of the text.

Phonological awareness: Phonological awareness was measured using the pseudo-words repetition test of the Promega Battery (Vicari, 2007).

Reading abilities: Reading about a text was assessed using an Italian standardized test for reading abilities MT Reading Test (Cornoldi *et al.*, 2011).

Phonological awareness-Phonemic blending: The phonemic blending task comprised words (nouns) of increasing difficulty, selected from the VARLESS Italian database (Burani C, 2011). Children had to blend sounds into words (e.g. hearing [c]-[a]-[n]-[e] and producing [canel], (dog)).

Phonological awareness: The phonemic segmentation task words were selected from the blending task and just divided the word.

Maximum likelihood Procedure- MLP rise time: Here, the patient has a sequence of three identical pure tones (1 kHz with the onset and offset ramp of 10ms). Each tone lasted 800ms, and the rise time of one of the three tones was varied adaptively. The first trial was set to a 25% difference. Then, a Maximum Likelihood Procedure was used to find the subject threshold. Children had to detect the most extended tone (Grassi & Soranzo, 2009).

Maximum likelihood Procedure- MLP temporal anisochrony: Each tone lasted 100ms and was followed by a 150ms gap. The gap separating the fourth tone from the previous and following tones was lengthened adaptively to find the subject threshold using MLP. Children had to detect whether there was an irregular 'jump' or not.

Tapping: The patient had to tap along a 90 pulse/minute metronome for 40 seconds. Each sound lasted 50 ms, was built using a sinusoidal sound, and ramped with a 1ms ramp at the onset and offset. Patiently listened to the metronome using an open headphone at approximately 75 db and Performed the task holding a pencil in their dominant hand and tapping it on a wooden box containing a microphone (Flaugnacco *et al.*, 2015). They were instructed to do daily. Stimulation and acquisition were run using Audacity 1.3. Tap onsets were calculated using a custom Matlab program and a semi-automatic procedure. Analyses were run on the coefficient of variation.

Rhythm reproduction: The patient had to listen and reproduce ten different rhythms. Each sound of the sequence lasted 65 ms and was built using a MIDI woodblock sound. The same apparatus and settings described for the tapping task were used a deliver stimuli and record behavior. Every item performance was scored by two independent judges from 1 to 9 depending on its similarity to the template stimulus (1 no reproduction, 2 random order and a random number of taps, 3 less number of beats, 4 correct number of taps but wrong temporal order, 5 rhythmic pattern contains one or two interbeat interval errors, 6 rhythmic pattern contains one small error on a single inter-beat interval, 7 good patterns but "unstable" performance, 8 excellent performance containing minor rhythmic deviations, 9 perfect performance) (Flaugnacco *et al.*, 2015). Each child's final mark was the average of the twenty scores (inter judge correlation was 0.89).

Perception of musical meter: The musical meter task same-different judgment. In the "different" trials (= 9), the change in metrical structure (beat =500ms) was caused by adding 100 ms to the accented notes (also altering the beat interval; this seems to be the acritical duration for children with developmental dyslexia (Goswami *et al.*, 2013).

5. MUSIC INTERVENTION

Music is an essential training tool and highly focuses on the rhythm and temporal processing using percussive instruments, use of rhythm syllables [ta, ti-ti,....], rhythmic body movements are accompanying music, sensorimotor synchronization games. No difficulties were found with musical pitch skills, further indicating that timing may be a particular area for dyslexic children. However, casual relationship supports temporal processing for the potential transfer of musical abilities to language abilities. To exemplify, singing might help with learning to read the text. Further research will be required to expand and refine the general model outlined here, preferably with different kinds of musical training and different test of musical skills, perceptual and cognitive skills, and language and literacy skills.

In summary, music lessons have the potential to provide a valuable multisensory learning environment. A particular advantage of music lessons as a language support tool is that they can provide the stage of literacy. There is also a wealth of musical material available for such a remediation approach, from nursery rhymes and folk music to popular music and art music, along with an established tradition of classroom music education. Besides, the potential enjoyment and skill development gained from music lessons offer valuable opportunities for lifelong learning.

6. SERIOUS GAMES

Gamers are everywhere; the importance of games in this era cant be circumvented. A great deal of work over the last two decades has been devoted to devise and promote games for training patients. This stream of research has been encouraged by low-cost and widespread new technologies offering unprecedented opportunities to implement training protocols. An increasing number of technologies are designed to improve health, from smartphone applications to control dietetics (Withings Wi-Fi scales) to movement-based therapy tools using motion capture (Chang *et al.*, 2011). Among them, video games provided entertainment while targeting serious goals, such as the rehabilitation of impaired movement

skills. (e.g., Hammer and Planks, Nintendo Wii games,) or cognitive re-entrainment (e.g., RehaCom) in neurological disease (Saposnik *et al.*, 2010). In particular, games of rehabilitation based on movement that exploits motion capture devices such as the Wii or the Kinect are a promising way to use technology in the context of re-education. This method referred to an "Exergaming". Note that video games can also be used in a severe way for entertainment. For example, video games off-the-shelf are often used for therapeutic purposes by doctors, such as games like Nintendo WiiorKinect (Karahan *et al.*, 2015).

The last several years of studies indicate that cognitive and neuronal underpinning of the benefits linked to health- targeted serious games. In addition to the physical and physiological advantages of serious sports, the outcomes of this kind of training related to perception (e.g., by specialized physiotherapy exercises) (Connolly *et al.*, 2012). Moreover, Cognitive functions such as language can be enhanced by serious games because of the brain's plasticity. For instance, structural changes are happened in the brain due to learning. Also, the considerate changes happen by playing challenging games like *Astro Invader*, *Berzerk*. These promising results indicate that implementing training protocol via serious games may be incredibly valuable for enhancing brain function and therapy and rehabilitation (Anguera *et al.*, 2013).

In swift, games and rhythmic stimulation are promising tools that can be exploited to improve or retrain movement and cognition. It proposed that teaching rhythm skills applied in a serious game would help develop training protocols that could be used to humanize different populations of patients.

6.1 Games that involve music for therapy

Through, experimental evidence concluded that musical games are highly successful in stroke patients. Also, existing games involve rhythm conveyed by auditory stimuli used as training tools. The rhythmic skills are considered the center point for players; based on synchronized movement with stimuli, the temporal structure can be predicted. Besides, most of the cognitive studies in cognitive psychology of rhythm use finger tapping since this is a simple and objective way to study rhythmic skills, but other responses are possible. Finally, games provide feedback on the performance's precision, reflecting the participant's rhythmic skills and has therapeutic potential. For example, a game requiring finger tapping is likely to have a different effect on behavior than a game requiring full-body motion, such as dance (Repp & Su, 2013). Variety of devices fulfilling the criteria above for the analysis like; *Wii, PlayStation*, *PC, Tablet/Smartphone, Xbox, Gameboy*.

6.2 Games that involve full body movements via the external interface

These games have an interesting application in physiotherapy for patients with spinal cord injury, traumatic brain injury, and stroke. *Just Dance* is the most famous dance game among researchers for studies. They focus more on physical exercise and activity than on rhythm. Indeed, the ability of these games to record and score the rhythmic precision of the player is relatively poor because these games focus on discrete movements/actions instead of repeated movements they can not be used for delivering specific training of rhythmic skills. For example, Just Dance is a representation of moves represented by pictures displayed on the screen. The player's score depends on the precision of the movements as compared to a model action sequence. The player has to execute the movements in a given temporal window. Yet, the task is not purely rhythmic, and synchronization to the musical beat is not recorded. Even though these games do not measure rhythmic skill, they provide a motivating setting to dance while monitoring the player's movements and adding a rhythm component to some of these games, as in the case of Dance, maybe a valuable strategy to translate them into a training program (Lange *et al.*, 2009).

6.3 Rhythmic finger taping games on a tablet

An example of these games is *Beat Sneak Bandit*. The player has to tap precisely to the beat to make the character progress, avoid the enemies, and so forth. This feature is used in serious games dedicated to learning, such as *Rhythm Cat*, designed to learn music rhythm notation. One major drawback of these games is that the software's timing precision is inferior to train rhythmic skills. The time window in which a response is considered excellent and extensive (i.e., up to several hundreds of milliseconds) and the recording's temporal variability is high. Also, no feedback on the player's rhythmic performance is provided (Hyde *et al.*, 2009).

Table 1: List of the reviewed rhythm-based games.

Games	Peripheral	Types of response	Output
Dance revolution/dancing	Dance pad (PS2,	Impacts of feet (PS2)/fingers (PC)	Incrementing score
stage	PC)	1	J
Donkey Konga	Bongos	Impacts of hands	Incrementing score
Dancing with the star	Wiimote, Nunchuk (Wii), keyboard (PC)	Hands movement (Wiimote), Key tapping (PC)	Incrementing score
DJ Hero	Turntable replica (Wii, PS 2 and 3, Xbox 360)	Hands and fingers movement on the Turntable	Incrementing score
Everyone sing	Microphone (Wii, PS 3, Xbox 360)	Voice	Incrementing score
Guitar hero	Guitar replica, joystick (Wii, PS 3, Xbox 360), keyboard (PC), screen (tablet, Androîd	Left-hand key tapping, right-hand key moving up and down (Wii, PS3, Xbox 360), screen tapping (tablet), joystick button pressing (Wiimote, pS3, Xbox 360)	Incrementing score
Just Dance	Wiimote (Wii), PS camera, PS move (PS4, PS3), Kinect (Xbox 360, Xbox one)	Hand movement (Wiimote), all- body movement (PS move, PS camera, Kinect	Incrementing score
Rhythm Paradise (USA: Rhythm Heaven Fever	Nintendo DS, Wiimote	Finger tapping on the screen, hand movement (stylus; DS), key tapping (Wii)	Incrementing score
Rockband	Guitar, Drum's replica, Microphone (Wii, Xbox 360, PS3), Tactile screen (iPhone, iPod Touch), Nintendo DS, PSP	Left-hand key tapping, right-hand key moving up and down (mediator-like), feet impact (bass drum), drumsticks impact (Wii, PS3, Xbox 360, Nintendo DS, PSP), screen tapping (iPhone, iPod), joystick button pressing (Wiimote, pS3, Xbox 360), voice (microphone)	Incrementing score
140	Keyboard (PC)	Key pressing	Progression in a level
Osu	Mouse (PC)	Key pressing	Incrementing score
Beatmania	Turntable replica (Arcade, PS1, PS2), Nintendo Gameboy	Hands and fingers movement on the Turntable (Arcade, PS1, PS2), key pressing (Gameboy colour)	Incrementing score
Patapon	PSP	Key tapping	Progression in a level
Rhythm cat	Tablet, Smartphone	Screen tapping, holding, swiping	Incrementing score
Groove coaster zero	Tablet, Smartphone	Screen tapping, holding, swiping	Incrementing score
Igobeat	Tablet, Smartphone	Screen tapping, holding, swiping	Incrementing score
Beat Brite Online PC games	Tablet, Smartphone Keyboard	Screen tapping, holding, swiping Screen tapping	Incrementing score Progression in a level/Incrementing score

6.4 Mobile or computer games with finger key taping

These games can be played on a keyword, using a joystick, or on special devices. One of the most famous is *Guitar Hero*. In this game, the player plays on a guitar replica with five keys and has to push the keys in correspondence with images presented on a screen. The rhythm precision of the response is recorded and used to compute a performance score. The response must appear in a specific temporal window to be considered as good. The same concept is used in many PC games, but keyboards key (e.g., arrows) are used instead of guitar replica. As in tablet games, these games' main weakness is their low temporal precision in recording rhythmic performance (around 100 ms in *Guitar Hero*). Nevertheless, these games are interesting as they represent a good starting point to develop seriousgame applications aimed at training rhythmic skills.

6.5 Console Games Involving Singing

In these games, the player is asked to sing in synchrony with the music. This is not a rhythmic task per se, but the performance involves a rhythmic component. As in classical karaoke, lyrics are presented on the screen. In this case, feedback (score) is provided to the player. At the same time, she/he sings, and a final global score is given at the end of the performance, including temporal precision (the response must appear in a given temporal window to be considered reasonable) and pitch precision.

Even though some of the games above present good ground for training rhythmic skills, their main drawback is that their temporal precision when recording movement relative to the beat is relatively poor. Thus, these games' output measures are insufficient to isolate rhythmic features of the performance (e.g., the variability of the motor performance, the precision of the synchronization with the beat, etc.). Moreover, in none of these games, the rhythmic complexity of musical stimuli has been manipulated. The difficulty is manipulated only through the number of responses required during the game (e.g., number of visual tags which the player has to react to), which is not a rhythmical feature. For example, using music with various beat saliency degrees would allow introducing rhythm-based difficulty levels in the game. This has the advantage that rhythms with increased complexity could be presented progressively throughout the game, potentially leading to improved beat-tracking skills.

7. CONCLUSION

The results of this meta-analysis confirm prior literature highlight the potential role of music and games in enhancing cognitive skills in older adults, school children, and persons affected by developmental disorders. Music is an essential part of our life, and musical training provides an ideal tool for such a new perspective. Whatever the exact mechanism serving provides practical application as well as improvement in the status. Gamers share the most significant part of the market, and portable devices have made training more comfortable. They are low-cost while offering a motivating and user-friendly environment to train rhythmic skills. In neurodegenerative disease training, both the tools have higher importance. It is expected that future advanced tools will be developed for a better curing procedure.

ETHICS DECLARATIONS

Financial interests

The authors declare they have no financial interests

Conflicts of interest

The authors have no conflicts of interest to declare that they are relevant to the content of this article.

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