

MUSIC THERAPY FOR STROKE PATIENTS: A SYSTEMATIC REVIEW WITH META-ANALYSIS

Sanita Šuriņa

Rīga Stradiņš University, Latvia

Jana Duhovska

Rīga Stradiņš University, Latvia

Kristīne Mārtinsone

Rīga Stradiņš University, Latvia

Abstract. *There are numerous trials, showing positive results for using the music therapy for stroke patient rehabilitation. Therefore, summarizing the data from these trials is an actual topic. The objective, of this research, was to summarize the data from trials about the use of music therapy methods and techniques, especially the rhythmic auditory stimulation, for improving of the motor functions for stroke patients, by creating a systematic review of randomized controlled trials, with meta-analysis. The trials were searched in MEDLINE, Cochrane Trial Register and EBSO databases. The trial quality was evaluated by the PEDro scale. 20 randomized controlled trials were included in the systematic review. The meta-analysis for 5 gait outcomes, including gait speed, steps per minute, step length, gait symmetry, Time up and go test, and 7 arm function outcomes, including Fugl-Meyer test, ARAT test, Box and blocks test, Wolf motor function test, Nine hole peg test, shoulder flexion, elbow extension, was conducted. According to the results of the meta-analysis, gait exercises, combined with rhythmic auditory stimulation, provide statistically significant improvement, compared with gait exercises alone. Concerning the use of rhythmic auditory stimulation and other music therapy interventions for arm function rehabilitation, a statistically significant improvement was not detected.*

Keywords: *hemiparesis, music therapy, rehabilitation, rhythmic auditory stimulation, stroke.*

Introduction

According to data from the World Health Organization, each year there are 15 million people who are diagnosed with stroke (World Health Organization, 2018). According to U.S. statistics, 45% of stroke patients after being discharged from hospital return home, 24% go to rehabilitation facilities, while 31% go to social-care institutions (American Heart Association, 2015). Such statistics show the importance of rehabilitation in the treatment of stroke patients. Recovering motor functions, after suffering a stroke, is one of the most important rehabilitation tasks. Increasing number of studies indicate that the music therapy

contributes to the recovery of arm and leg motor functions for stroke patients. However, not all of these studies are considered to be methodologically qualitative, and not all methodologically high-quality studies are compiled in systematic reviews.

Aim of this study was to develop a systematic review with meta-analysis including trials assessing effectiveness of music therapy in alleviating the stroke patient motion disorders. Whereas tasks of the study were to select randomized controlled trials; to evaluate the methodological quality of the trials; to create a systematic review of trials with meta-analysis, comparing the effectiveness of music therapy and standard therapy in reducing stroke effects. The methodological quality and relevance of the trials for inclusion in the systematic review was determined using the PEDro trial quality scale. Randomized controlled trials, with parallel groups, or crossover trials, with sufficient methodological quality, without a restriction on the language of the publication, if the trial had an abstract in English and the trial was published by October 18, 2018, were considered as eligible for inclusion in the systematic review.

The systematic review includes studies about stroke patients with hemiparesis, without age and sex restrictions. The site of brain damage, or time after stroke, were not used as criteria for inclusion.

The systematic review includes trials in which music therapy or music therapy in combination with standard therapy is compared with standard therapy. Intervention could be one of the following music therapy interventions:

- playing a music instrument, under the supervision of a therapist, with an aim to improve fine and gross motor skills;
- gait exercises with rhythmic auditory stimulation;
- arm exercises with rhythmic auditory stimulation.

Literature review

There are several studies that have been carried out to assess the usage of sensor-motor systems (Bradt, Magee, Dileo, Wheeler, & McGilloway, 2010) in a motor function rehabilitation programmes. One of these models - rhythmic auditory stimulation (RAS) for motor function training for stroke patients, has shown significant improvements (Thaut et al., 2007; Schauer & Mauritz, 2003). In this model, rhythm acts as a sensor incentive to induce stability and encourage the organisation of motor control in the nervous system. During the gait exercises, with RAS (using metronome symmetric pulse patterns and incorporating them into music), with certain cycle frequencies, gait improvement (steps per minute, gait symmetry, balance) was observed. The benefits were significantly larger,

compared to other physiotherapy approaches, used in rehabilitation, such as the Bobata approach (Thaut et al., 2007; Schauer & Mauritz, 2003).

Unlike gait patterns, which, are biologically rhythmic and are considered to be controlled by psychological model generators (Whitall et al., 2011), most arm movement functions are performed according to human will and are biologically unrhythmic. To acquire arm and hand function skills, for example, in sports or music, rhythmic stimuli are successfully used to promote the development of motor skills. As well, approaches to motor rehabilitation in neurology, highlighting the need for re-training, have shown good results and are confirmed by neuropsychological studies regarding the long-term potential (Whitall et al., 2011). The usage of rhythmic stimuli is based on direct coordination of motor responses to sensory irritation. The inclusion of periodicity implies that the brain, in addition to making movement during the stimulus phase, also synchronises the duration of the movement with the incentive interval through a period of adaptation, such as the rhythm interval and duration. Rhythm is a potent neurological stimulus, that humans can automatically associate with certain physical movements. The rhythm provides a clear form, with stable time information, that allows the brain to plan and evaluate paretic arm movement and position changes throughout the entire cycle of motion, which in turn provides sense of time and space for movement (Thaut, Kenyon, Hurt, McIntosh, & Hoemberg, 2002). For example, patients with limited volume of joint movement, who have been practicing certain physical rehabilitation exercises at a certain rhythm, often associate rhythm with muscle memory, resulting in a significant increase in patients' ability to perform movement exercises (Thaut et al., 2002; Paul & Ramsey, 1998). Rhythmic auditory stimulation can be used to stimulate hand grip force, fine motor skills, finger agility and hand coordination (Friedman et al., 2014).

Methodology

The trials included in this study were derived from the MEDLINE, Cochrane Trial Register, EBSO (Academic Search Complete and Health Source – Nursing Academic Edition) electronic databases. In addition, the reference lists of the trials, found in the databases, were also checked. The terms music therapy, rhythmic auditory stimulation, rhythmic cueing, auditory cueing, rehabilitation, stroke, cerebral infarction, and their combinations, were used as search keywords. The publications were searched in English. Publications in other languages were evaluated, if an abstract in English was available. The last comprehensive search was conducted on October 18, 2018.

Number of publications found in databases = 449. Number of publications found in reference lists of the trials = 1. Number of publications, after excluding

duplicates = 217. Number of publications checked by abstracts = 217. Number of checked full text publications = 29. Number of included full text publications = 20.

The following outcomes were included in the systematic review and the meta-analyses:

- Gait outcomes (gait speed (GS), steps per minute (SPM), step length (SL), gait symmetry (GSM), Time up and go test (TUPGT));
- Arm function outcomes (Fugl-Meyer motor assessment of the arm (FMA), Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), Box and Block Test (BBT), Nine Hole Peg Test (NHPT)).
- Amplitude of joint movements (shoulder flexion (SF), elbow flexion (EF)).

The trials were processed by recording the collected data in special forms, and Physiotherapy Evidence Database (PEDro) scale form (The George Institute for Global Health, 2014) was used to assess the methodological quality of the trial and, consequently, the risk of systematic error, as well as the adequacy of statistical data. An Excel table, with data processing formulas, was used to collect other data.

The following data were collected from the selected trials:

- General information: author; name; source (name, year, number, pages).
- Information on the methodological quality of the trial and the availability of statistical data (according to the PEDro scale): criteria and sources for the inclusion of participants; random allocation of participants to groups; blinding of participants, therapists and assessors; data on participant dropout; statistical comparison of groups and variability of primary outcomes.
- Information about trial participants: diagnosis; number of participants in the experimental/control group; age; sex; stroke type; stroke-affected side; time after stroke.
- information on intervention for the experimental and control group: method; intensity.

The evaluation of the quality of the studies, based on the PEDro scale, was carried out in parallel by two researchers, followed by comparison of results and resolving of differences. Studies included in the systematic review yielded an average of 5.85 ± 0.93 points out of 10 possible. Given that the fifth and sixth criterion of the PEDro scale implies that the participants of the trial and therapists are not informed about allocation of the participants to the groups - a criterion that is difficult to provide, the average trial quality can be assessed as good.

Research results

The systematic review includes 20 randomized controlled trials, 3 of which are crossover trials. The included trials investigate the use of rhythmic auditory stimulation (12 studies) and playing of music instruments (8 studies) to reduce motion disorders in stroke patients with hemiparesis. The total number of participants was 701, while the number of participants in one trial ranged from 11 to 92. The average age of participants was 61.2 years. 58.8% of participants were male, 41.2% female (approximate data, as 1 trial did not provide the data). The average time after stroke at the beginning of the trial was 23.8 months (approximate data, as in 1 trial the data were given approximately).

Table 1 contains the trial characteristics. Data about trial participants (number, average age, etc.) are provided first for the experimental group (EG), then, after comma, for the control group (CG). If it is a crossover trial, then the data are equal for both groups, and are provided once. If separate data are not available for EG and CG, the data are common for both groups and are provided once.

Table 1 Trial Characteristics

Trial	Design	Participants	Interventions	Outcomes
Bunketorp-Käll et al., 2017	RCT	D: hemiparesis; N: 40, 41; Age: 62.7±6.7, 63.7±6.7; Sex (M/F): 23/18, 22/19; Stroke type (I/H/U): 32/9/0, 28/13/0; Paretic side (L/R): 20/21, 18/23; TAS: 32.3±14.1, 36.53±14.63	Rhythm-and-music therapy, Standard therapy	TUGT
Cha, Kim, & Chung, 2014	RCCT	D: hemiparesis; N: 41; Age: 60.8±19.8; Sex (M/F): 24/17; Stroke type (I/H/U): 41/0/0; Paretic side (L/R): 22/19; TAS: 8.68±2.35	Gait test with RAS, Gait test without RAS	GS, SPM, SL
Chouhan & Kumar, 2012	RCT	D: hemiparesis; N: 15, 15; Age: 56.73±5.99, 57.33±5.51; Sex (M/F): 12/3, 12/3; Stroke type (I/H/U): 0/0/15, 0/0/15; Paretic side (L/R): no data; TAS: <3, <3	Gait and arm exercises with RAS, Gait and arm exercises without RAS	FMA
Delden et al., 2013	RCT	D: hemiparesis; N: 19,19; Age: 62.6±9.8, 56.9±12.7; Sex (M/F): 11/8, 16/3; Stroke type (I/H/U): no data; Paretic side (L/R): 11/8, 11/8; TAS: 1.8±1.1, 2.6±1.6	Modified bilateral arm training with rhythmic auditory cueing, Standard exercises	FMA, ARAT
Friedman et al., 2014	RCCT	D: hemiparesis; N: 12; Age: 57.0±30.5; Sex (M/F): 7/5; Stroke type (I/H/U): 41/0/0; Paretic side (L/R): 6/4/2; TAS: 34.6±32.5	Exercises with MusicGlove, Standard exercises	FMA, ARAT, BBT, WMFT

Trial	Design	Participants	Interventions	Outcomes
Grau-Sanchez et al., 2018	RCT	D: hemiparesis; N: 19, 20; Age: 60.1, 62.5; Sex (M/F): 11/8, 12/8; Stroke type (I/H/U): 18/1/0, 14/6/0; Paretic side (L/R): no data; TAS: 65.8, 64.9	Playing keyboard and electronic drums, Standard exercises	FMA, ARAT, BBT, NHPT
Jeong & Kim, 2007	RCT	D: hemiparesis; N: 16, 17; Age: 58.0±7.2, 62.2±8.2; Sex (M/F): 11/5, 12/5; Stroke type (I/H/U): 9/7/0, 11/6/0; Paretic side (L/R): 7/9, 9/8; TAS: 65.2±54.4, 87.5±63.6	Exercises with RAS, No therapy	SF
Luft et al., 2004	RCT	D: arm paresis; N: 9, 12; Age: 63.3±15.3, 59.6±10.5; Sex (M/F): 7/2, 5/7; Stroke type (I/H/U): 9/0/0, 12/0/0; Paretic side (L/R): 6/3, 8/4; TAS: 75.0 (IQR: 37.9-84.5), 45.5 (IQR:22.6-66.3)	Bilateral arm training with rhythmic auditory cueing, Standard exercises	FMA, WMFT
Paul & Ramsey, 1998	RCT	D: hemiplegia; N: 10, 10; Age: 61.8±5.1; Sex (M/F): 11/9; Stroke type (I/H/U): no data; Paretic side (L/R): 8/12; TAS: 3.1±1.7	Playing of electronic drums, No therapy	SF, EF
Raglio et al., 2017	RCT	D: hemiparesis; N: 19, 19; Age: 70.4 ± 8.9, 75.4 ± 7.6; Sex (M/F): 8/11, 8/11; Stroke type (I/H/U): 17/2/0, 18/1/0; Paretic side (L/R): 8/5/6, 5/6/8; TAS: 1.5, 2	Playing of musical instruments, Standard exercises	TUGT
Schauer & Mauritz, 2003	RCT	D: hemiparesis; N: 11, 12; Age: 59.0±12.0, 61.0±12.0; Sex (M/F): no data; Stroke type (I/H/U): 32/9/0, 28/13/0; Paretic side (L/R): 7/4, 5/7; TAS: 1.8, 2.2	Gait exercises with musical motor feedback, Standard gait exercises	GS, SPM, SL
Schneider, Schönle, Altenmüller, & Münte, 2007	RCT	D: arm paresis; N: 20, 20; Age: 58.1±9.9, 54.5±10.2; Sex (M/F): 12/8, 15/5; Stroke type (I/H/U): 16/4/0, 18/2/0; Paretic side (L/R): 10/10, 10/10; TAS: 2.1, 1.9	Playing of electronic drums and piano, Standard exercises	ARAT, BBT
Street et al., 2018	RCT	D: hemiparesis; N: 6, 5; Age: 53.2 ± 21.86, 67.6 ± 18.3; Sex (M/F): 2/4, 2/3; Stroke type (I/H/U): 5/1/0, 3/2/0 Paretic side (L/R): no data; TAS: 19, 13.8	Playing of musical instruments, Standard exercises	ARAT, NHPT
Suh et al., 2014	RCT	D: hemiplegia; N: 8, 8; Age: 61.0±14.5, 70.6±12.4; Sex (M/F): 3/5, 3/5; Stroke type (I/H/U): 5/3/0, 6/2/0; Paretic side (L/R): 5/3, 5/3; TAS: 12.9±9.4, 7.5±7.1	Gait exercises with RAS, Gait exercises without RAS	GS, SPM, SL

Trial	Design	Participants	Interventions	Outcomes
Thaut, McIntosh, & Rice, 1997	RCT	D: hemiparesis; N: 10, 10; Age: 73.0±7.0, 72.0±8.0; Sex (M/F): 5/5, 5/5; Stroke type (I/H/U): 6/4/0, 5/5/0; Paretic side (L/R): 5/5, 5/5; TAS: 0.5±0.1, 0.5±0.1	Gait exercises with RAS, Gait exercises without RAS	GS, SPM, SL, GSM
Thaut, Kenyon, Hurt, McIntosh, & Hoemberg, 2002	RCCT	D: hemiparesis; N: 21; Age: 52.7±13.7; Sex (M/F): 13/8; Stroke type (I/H/U): 19/2/0; Paretic side (L/R): 0/21; TAS: 11.4±52.0	Arm function test with RAS, Arm function test without RAS	EF
Thaut et al., 2007	RCT	D: hemiparesis; N: 43, 35; Age: 69.2±11.5, 69.7±11.2; Sex (M/F): 22/21, 19/16; Stroke type (I/H/U): no data; Paretic side (L/R): 23/20, 19/16; TAS: 0.7±0.4, 0.7±0.4	Gait exercises with RAS, Gait exercises according to Neurodevelopmental therapy /Bobath method	GS, SPM, SL, GSM
Tong et al., 2015	RCT	D: hemiparesis; N: 15, 15; Age: 50.1± 14.8 48.6±14.6; Sex (M/F): 13/2, 13/2; Stroke type (I/H/U): 8/7/0, 7/8/0; Paretic side (L/R): 8/7, 6/9; TAS: 5.4±4.8, 5.3±4.1	Playing music instruments, Playing music instruments without sound	FMA
Whitall et al., 2011	RCT	D: arm paresis; N: 42, 50; Age: 59.8±9.9, 57.7±12.5; Sex (M/F): 26/16, 24/26; Stroke type (I/H/U): no data; Paretic side (L/R): 23/18, 25/25; TAS: 54±49.2, 49.2±62.4	Bilateral arm exercises with RAS, Standard arm exercises	FMA, WMFT
Zondervan et al., 2016	RCT	D: hemiparesis; N: 9, 8; Age: 60, 59; Sex (M/F): 5/4, 5/3; Stroke type (I/H/U): no data; Paretic side (L/R): no data; TAS: 5.33 ± 4.14, 3.17±1.66	Exercises with MusicGlove, Standard exercises	ARAT, BBT, NHPT

Abbreviations. *D* – diagnosis; *F* – female; *H* – hemorrhagic; *I* – ischemic; *L* – left; *M* – male; *N* – number of participants; *R* – right; *RCT* – randomized controlled trial; *RCCT* – randomized controlled crossover trial; *U* – unknown; *TAS* – time after stroke (months).

A meta-analysis was conducted for the outcomes measured in at least 2 trials, 12 outcomes in total.

The meta-analysis was performed with Cochrane Collaboration's Review Manager (RevMan) software, version 5.3. All outcomes, included in the meta-analysis, are continuous. The RevMan settings were: inverse variance method, fixed effect analysis model, and the difference in average values as a parameter for the intervention effect. In case of high heterogeneity ($I^2 > 75\%$) for the outcome, the meta-analysis was also performed using a random effect analysis model.

Gait speed. A meta-analysis revealed that for the EG, compared to the CG, gait speed increased on average by 10.22 metres per minute (95% CI: 7.46 to 12.98, overall effect $Z = 7.26$ ($P < 0.00001$)). Statistically significant improvement was found in 2 out of 5 trials (Thaut et al., 1997; Thaut et al., 2007), including the trial with the largest number of participants (Thaut et al., 2007), which largely determined the overall result. Since the statistical heterogeneity of the trials was high ($I^2 = 81\%$), a meta-analysis was also conducted using a random-effect analysis model, where the overall effect $Z = 1.67$ ($P = 0.09$) was not statistically significant.

Steps per minute. A meta-analysis revealed that for the EG, compared to the CG, the number of steps per minute increased on average by 12.75 steps per minute (95% CI: 9.25 to 16.25, overall effect $Z = 7.14$ ($P < 0.00001$)). Statistically significant improvement was found in 2 out of 5 trials (Cha et al., 2014; Thaut et al., 2007), which also had the highest number of participants. Since the statistical heterogeneity of the trials was high ($I^2 = 87\%$), a meta-analysis was also conducted using a random-effect analysis model where the overall effect $Z = 1.78$ ($P = 0.08$) was not statistically significant.

Step length. A meta-analysis revealed that for the EG, compared to the CG, the step length increased on average by 0.07 metres (95% CI: 0.02 to 0.12, overall effect $Z = 2.52$ ($P = 0.01$)). Statistically significant improvement was found in 2 out of 5 trials (Thaut et al., 1997; Thaut et al., 2007). Since the statistical heterogeneity of the trials was high ($I^2 = 81\%$), a meta-analysis was also conducted using a random-effect analysis model where the overall effect $Z = 1.41$ ($P = 0.16$) was not statistically significant.

Gait symmetry. The effects of music therapy on gait symmetry compared to the standard therapy were discussed in 4 trials. 3 trials used RAS in combination with gait exercises. One trial (Schauer & Mauritz, 2003) used auditory feedback, allowing a patient to hear the rhythm of his steps in the audio headphones during gait exercises. Standard care included gait exercises, without rhythm. It should be noted that all 4 studies showed a statistically significant improvement for the gait symmetry, but due to the different definitions of the “gait symmetry”, only two trials could be included in the meta-analysis. In these studies, the gait symmetry is defined as the time ratio of two consecutive steps, using the longest time as a divider. In the event of a completely symmetric gait, this ratio will be 1. In a meta-analysis, this ratio was found to have improved on average by 0.12 (95% CI: 0.09 to 0.15, total effect $Z = 8.68$ ($P < 0.00001$)) for the EG compared to the CG. Statistically significant improvement for gait symmetry was found in 1 out of 2 trials (Thaut et al., 2007). The trials were statistically homogenous ($I^2 = 0\%$).

Time Up and Go test. The impact of music therapy on the time needed to start and complete walking, compared to the standard therapy, was covered by 2 trials (Bunketorp-Käll et al., 2017; Raglio et al., 2017). A meta-analysis revealed

that the EG performed the test on average 1.45 seconds faster than the CG (95% CI: -1.04 to 3.94, total effect $Z = 1.14$ ($P = 0.25$)). Statistically significant improvement was not found in any of the trials. The statistical heterogeneity of the trials was low ($I^2 = 11\%$).

Fugl-Meyer motor assessment of the arm. The effects of music therapy on the functional capabilities of the paretic arm, compared to the standard therapy and measured using the FMA test, are discussed in 7 trials. 4 of them used RAS in combination with arm exercises. In one trial (Friedman et al., 2014), a special device for arm exercises used MusicGlove, which allows a patient to play music using a computer. Standard care included arm exercises, no use of rhythm and special devices. A meta-analysis revealed that the test results were on average 0.76 points worse for the EG compared to the CG (95% CI: -0.95 to -0.57, total effect $Z = 8.00$ ($P < 0.00001$)). Statistically significant improvement in arm function was identified in 1 out of 5 trials (Chouhan & Kumar, 2012). It should be noted that the overall result was almost entirely (98.5% weight) determined by one trial (Whitall et al., 2011). Since the statistical heterogeneity of the trials was high ($I^2 = 78\%$), a meta-analysis was also conducted using a random-effect analysis model, where the overall effect $Z = 1.55$ ($P = 0.12$) was not statistically significant.

Action Research Arm Test. The effects of music therapy on the functional capabilities of the paretic arm, compared to the standard therapy, and measured using the ARAT test, are discussed in 6 trials. One trial (Delden et al., 2013) used rhythmic auditory stimulation in combination with arm exercises. In two trials (Friedman et al., 2014; Zondervan et al., 2016), a special device MusicGlove for arm exercises was used, allowing a patient to play music using a computer. In two trials (Schneider et al., 2007; Grau-Sanchez et al., 2018,) playing of electronic drums and electronic piano was used, in order to train the gross and fine motor skills, respectively. Standard care included arm exercises, with no use of rhythm, special devices and musical instruments. A meta-analysis revealed that the test results were better on average by 1.29 points, for the EG compared to the CG (95% CI: -0.40 to 2.99, total effect $Z = 1.49$ ($P = 0.14$)), but statistically not significant. Statistically significant improvement was not found in any trial. The statistical heterogeneity of the trials was low ($I^2 = 11\%$).

Box and blocks test. The effects of music therapy on the functional capabilities of the paretic arm, compared to the standard therapy, and measured using the BBT test, are discussed in 4 trials. In two studies (Friedman et al., 2014; Zondervan et al., 2016), a special device MusicGlove for arm exercises was used, allowing a patient to play music using a computer. In two studies (Schneider et al., 2007; Grau-Sanchez et al., 2018,) playing of electronic drums and electronic piano was used as arm exercises. Standard care included arm exercises, no use of rhythm, special devices and musical instruments. A meta-analysis revealed that

the EG moved on average 2.44 blocks per minute more than the CG (95% CI: 0.26 to 4.61, total effect $Z = 2.20$ ($P = 0.03$)). Statistically significant improvement in arm function were found in 1 out of 4 studies (Friedman et al., 2014), which largely (74.9% weight) determined the overall result. The statistical heterogeneity of the studies was mean ($I^2 = 56\%$).

Nine Hole Peg Test. The effects of music therapy on the functional capabilities of the paretic arm, compared to the standard therapy, and measured using the NHPT test, are discussed in 3 trials. Two studies used rhythmic auditory stimulation in combination with arm exercises. In one trial (Zondervan et al., 2016), a special device MusicGlove was used for arm exercises, allowing a patient to play music using a computer. A meta-analysis revealed that the EG performed the test on average 1.65 seconds faster than the CG (95% CI: -2.43 to 5.72, overall effect $Z = 0.79$ ($P = 0.43$)). Statistically significant improvement was not found in any of the trials. The trials were statistically homogenous ($I^2 = 0\%$).

Wolf Motor Function Test. The effects of music therapy on the functional capabilities of the paretic arm, compared to the standard therapy, and measured using the WMFT test, are discussed in 3 trials. Two studies used rhythmic auditory stimulation in combination with arm exercises. In one trial (Friedman et al., 2014), a special device MusicGlove was used for arm exercises. Standard care included arm exercises, with no use of rhythm and special devices. A meta-analysis revealed that the EG performed the test on average 0.99 seconds faster than the CG (95% CI: 0.68 to 1.29, total effect $Z = 6.28$ ($P < 0.00001$)). Statistically significant improvement in arm function was identified in 1 out of 3 studies (Whitall et al., 2011), which also almost completely determined the overall result (98.4% weight). The trials were statistically homogenous ($I^2 = 0\%$).

Shoulder flexion. The effects of musical therapy on the amplitude of paretic arm motion in the shoulder joint, compared to the standard therapy, are discussed in 2 trials. One trial (Jeong & Kim, 2007) used rhythmic auditory stimulation in combination with arm exercises. In one trial (Paul & Ramsey, 1998), arm exercises were done playing electronic drums. Standard care included arm exercises, with no use of rhythm and musical instruments. A meta-analysis revealed that for the EG, the shoulder bending angle (shoulder flexion) increased on average by 20.69 degrees (95% CI: -1.85 to 43.24, overall effect $Z = 1.80$ ($P < 0.07$)), but the improvement was not statistically significant due to the high distribution of the results. No statistically significant improvement was found in any trial. The trials were statistically homogenous ($I^2 = 0\%$).

Elbow flexion. The effects of musical therapy on the amplitude of paretic arm motion in the elbow joint, compared to the standard therapy, are discussed in 2 trials. One trial (Thaut et al., 2002) used rhythmic auditory stimulation in combination with an arm function test. In one trial (Paul & Ramsey, 1998), arm exercises were done playing electronic drums. CG performed the arm function

test without rhythmic auditory stimulation and performed arm exercises without using musical instruments. In a meta-analysis, it was found that, for the EG, compared to the CG, the elbow flexion angle increased on average by 3.53 degrees (95% CI: -2.29 to 9.34, overall effect $Z = 1.19$ ($P = 0.23$)), but the improvement was not statistically significant. No statistically significant improvement was found in any trial. The trials were statistically homogenous ($I^2 = 0\%$).

Conclusions and recommendations

In the trials included in this systematic review, the most commonly used music therapy intervention for experimental group was RAS, in combination with gait and/or arm exercises, and was used in 11 out of 20 studies. In one trial (Schauer & Mauritz, 2003), the intervention used can be regarded as a modification of RAS. The intervention used for the control group was usually a gait and/or arm exercises without the use of rhythm.

RAS is the main intervention that has been used to improve the gait outcomes, and it has been used in 6 out of 7 studies.

When performing a meta-analysis and using a fixed-effect analysis model, for all primary gait outcomes (gait speed, steps per minute, step length, gait symmetry) statistically significant improvement was found, compared to the control group. In cases where high heterogeneity ($I^2 > 75\%$) was observed, the meta-analysis of the outcomes was also performed using a random-effect analysis model. In these cases, the positive trend remained, but with a significant increase in confidence interval, no statistically significant improvement was identified for any of the outcomes.

The RAS was also the main intervention, used to improve the arm function outcomes. RAS was used in 6 out of 13 trials. Other interventions playing electronic drums and pianos, to train the gross and fine motor skills, as well as a special device for finger training - MusicGlove, by which the computer can be used as a music instrument.

A meta-analysis was performed for 7 arm function outcomes. Two outcomes (BBT, WMFT) showed statistically significant improvements for EG, compared to the CG. It should be noted, that the overall result in both cases was almost entirely determined by one trial. In the case of a BBT outcome, it was a trial (Friedman et al., 2014), with 74.9% weight. The MusicGlove device was used in this trial. In the case of the WMFT, it was a trial (Whitall et al., 2011) with 98.4% weight. RAS was used in this trial, in combination with arm exercises.

Four other outcomes (ARAT, NHPT, shoulder flexion, elbow flexion) showed improvement for EG, compared to the CG, but improvement was not statistically significant. In the case of elbow flexion outcome, the overall result

was almost entirely determined by one trial (Thaut et al., 2002), with 96.2% weight. In this trial, RAS was used when testing the arm functions.

For the FMA outcome EG showed worse results compared to the CG. For 4 out of the 7 trials, included in the meta-analysis, RAS was used as a music therapy intervention. The overall result was almost entirely determined by one trial (Whitall et al., 2011), with 98.5% of the weight. This trial used RAS as a music therapy intervention.

From the analysis of the results of the systematic review, we can conclude that gait exercises, combined with rhythmic auditory stimulation, produce better results than exercises without rhythm. It should be underlined that there were statistically significant improvements in the meta-analysis of the outcomes using a fixed-effect analysis model for 4 out of 5 gait outcomes. At the same time, it should be noted that despite the increased number of trials in recent years, dedicated to the use of RAS, both the number of trials and the number of participants are still considered relatively small. Further trials, with a larger number of participants, can contribute significantly to the wider use of this method for the rehabilitation of stroke patients.

Regarding the use of rhythmic auditory stimulation and other music therapy interventions to reduce disturbances in arm functions, this systematic review does not provide unequivocal conclusions. For the majority of outcomes, the use of music therapy interventions contributed to greater improvement than standard care, but these improvements were statistically significant for only a few outcomes. Therefore, in view of both the observed positive trends and the limited number of trials carried out so far, further trials with a higher number of participants could provide a more determined reply about the use of music therapy to reduce arm function disorders in stroke patients.

References

- American Heart Association. (2015). *Heart Disease and Stroke Statistics - 2015 Update*. DOI:10.1161/CIR.0000000000000152
- Bradt, J., Magee, W.L., Dileo, C., Wheeler, B.L., & McGilloway, E. (2010). Music therapy for acquired brain injury. *Cochrane Database of Systematic Reviews*, 7.
- Bunketorp-Käll, L., Lundgren-Nilsson, Å., Samuelsson, H., Pekny, T., Blomvé, K., Pekna M., Pekny, M., Blomstrand, C., & Nilsson, M. (2017). Long-Term Improvements After Multimodal Rehabilitation in Late Phase After Stroke: A Randomized Controlled Trial. *Stroke*, 48(7), 1916-1924. DOI:10.1161/STROKEAHA.116.016433
- Cha, Y., Kim, Y., & Chung, Y. (2014). Immediate Effects of Rhythmic Auditory Stimulation with Tempo Changes on Gait in Stroke Patients. *Journal of Physical Therapy Science*, 26(4), 479-482. DOI:10.1589/jpts.26.479
- Chouhan, S., & Kumar, S. (2012). Comparing the effects of rhythmic auditory cueing and visual cueing in acute hemiparetic stroke. *International Journal of Therapy and Rehabilitation*, 19(6), 344-351. DOI:10.12968/ijtr.2012.19.6.344

- Delden, A.L., Peper, C.E., Nienhuys, K.N., Zijp, N.I., Beek, P.J., & Kwakkel, G. (2013). Unilateral Versus Bilateral Upper Limb Training After Stroke. *Stroke*, *44*(9), 2613-2616. DOI:10.1161/strokeaha.113.001969
- Friedman, N., Chan, V., Reinkensmeyer, A.N., Beroukhim, A., Zambrano, G.J., Bachman, M., & Reinkensmeyer, D.J. (2014). Retraining and assessing hand movement after stroke using the MusicGlove: comparison with conventional hand therapy and isometric grip training. *Journal of NeuroEngineering and Rehabilitation*, *11*(1), 76. DOI: 10.1186/1743-0003-11-76
- Grau-Sánchez, J., Duarte, E., Ramos-Escobar, N., Sierpowska, J., Rueda, N., Redón, S., Veciana de las Heras, M., Pedro, J., Särkämö, T., & Rodríguez-Fornells, A. (2018). Music-supported therapy in the rehabilitation of subacute stroke patients: a randomized controlled trial. *Annals of the New York Academy of Sciences*, *1423*(1), 318-328. DOI:10.1111/nyas.13590
- Jeong, S., & Kim, M.T. (2007). Effects of a theory-driven music and movement program for stroke survivors in a community setting. *Applied Nursing Research*, *20*(3), 125-131. DOI:10.1016/j.apnr.2007.04.005
- Luft, A.R., McCombe-Waller, S., Whittall, J., Forrester, L.W., Macko, R., Sorkin, J.D., Schulz, J.B., Goldberg, A.P., & Hanley, D.F. (2004). Repetitive bilateral arm training and motor cortex activation in chronic stroke: a randomized controlled trial. *JAMA*. *292*(15), 1853-1861. DOI: 10.1001/jama.292.15.1853
- Paul, S., & Ramsey, D. (1998). The effects of electronic music-making as a therapeutic activity for improving upper extremity active range of motion. *Occupational Therapy International*, *5*(3), 223-237. DOI:10.1002/oti.77
- Raglio, A., Zaliani, A., Baiardi, P., Bossi, D., Sguazzin, C., Capodaglio, E., Imbriani, C., Gontero, G., & Imbriani, M. (2017). Active music therapy approach for stroke patients in the post-acute rehabilitation. *Neurological Sciences*, *38*(5), 893-897. DOI: 10.1007/s10072-017-2827-7
- Schauer, M., & Mauritz, K.H. (2003). Musical motor feedback (MMF) in walking hemiparetic stroke patients: randomized trials of gait improvement. *Clinical Rehabilitation*, *17*(7), 713-722. DOI: 10.1191/0269215503cr668oa
- Schneider, S., Schönle, P.W., Altenmüller, E., & Münte, T.F. (2007). Using musical instruments to improve motor skill recovery following a stroke. *Journal of Neurology*, *254*(10), 1339-1346. DOI: 10.1007/s00415-006-0523-2
- Street, A.J., Magee, W.L., Bateman, A., Parker, M., Odell-Miller, H., & Fachner, J. (2018). Home-based neurologic music therapy for arm hemiparesis following stroke: results from a pilot, feasibility randomized controlled trial. *Clinical Rehabilitation*, *32*(1), 18-28. DOI: 10.1177/0269215517717060
- Suh, J.H., Han, S.J., Jeon, S.Y., Kim, H.J., Lee, J.E., Yoon, T.S., & Chong, H.J. (2014). Effect of rhythmic auditory stimulation on gait and balance in hemiplegic stroke patients. *NeuroRehabilitation*, *34*(1), 193-199. DOI: 10.3233/NRE-131008.
- Thaut, M.H., Leins, A.K., Rice, R.R., Argstatter, H., Kenyon, G.P., McIntosh, G.C., et al. (2007). Rhythmic auditory stimulation improves gait more than NDT/Bobath training in nearambulatory patients early poststroke: a single-blind, randomized trial. *Neurorehabilitation and Neural Repair*, *21*(5), 455-459. DOI: 10.1177/1545968307300523
- Thaut, M.H., McIntosh, G.C., & Rice, R.R. (1997). Rhythmic facilitation of gait training in hemiparetic stroke rehabilitation. *Journal of the Neurological Sciences*, *151*(2), 207-212. DOI: 10.1016/s0022-510x(97)00146-9

- Thaut, M.H., Kenyon, G.P., Hurt, C.P., McIntosh, G.C., & Hoemberg, V. (2002). Kinematic optimization of spatiotemporal patterns in paretic arm training with stroke patients. *Neuropsychologia*, 40(7), 1073-1081. DOI: 10.1016/s0028-3932(01)00141-5
- The George Institute for Global Health. (2014). *PEDro scale*. Retrieved from: <http://www.pedro.org.au/english/downloads/pedro-scale/>
- Tong, Y., Forreider, B., Sun, X., Geng, X., Zhang, W., Du, H., Zhang, T., & Ding, Y. (2015). Music-supported therapy (MST) in improving post-stroke patients' upper-limb motor function: a randomised controlled pilot study. *Neurological Research*, 37(5), 434-440. DOI:10.1179/1743132815y.0000000034
- Whitall, J., Waller, S.M., Sorkin, J.D., Forrester, L.W., Macko, R.F., Hanley, D.F., Goldberg, A.P., & Luft, A. (2011). Bilateral and unilateral arm training improve motor function through differing neuroplastic mechanisms: a single-blinded randomized controlled trial. *Neurorehabilitation and Neural Repair*, 25(2), 118-129. DOI: 10.1177/1545968310380685
- World Health Organization. (2018). *The Atlas of Heart Disease and Stroke*. Retrieved from https://www.who.int/cardiovascular_diseases/en/cvd_atlas_15_burden_stroke.pdf?ua=1
- Zondervan, D.K., Friedman, N., Chang, E., Zhao, X., Augsburger, R., Reinkensmeyer, D.J., & Cramer, S.C. (2016). Home-based hand rehabilitation after chronic stroke: Randomized, controlled single-blind trial comparing the MusicGlove with a conventional exercise program. *Journal of Rehabilitation Research and Development*, 53(4), 457-472. DOI:10.1682/jrrd.2015.04.0057