Music therapy for acquired brain injury (Review)

Bradt J, Magee WL, Dileo C, Wheeler BL, McGilloway E

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[**Intervention Review**]

Music therapy for acquired brain injury

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ABSTRACT

Background

Acquired brain injury (ABI) can result in impairments in motor function, language, cognition, sensory processing and emotional disturbances. This may severely reduce a survivor's quality of life. Music therapy has been used in rehabilitation to stimulate brain functions involved in movement, cognition, speech, emotions and sensory perceptions. A systematic review is needed to gauge the efficacy of music therapy as a rehabilitation intervention for people with ABI.

Objectives

To examine the effects of music therapy with standard care versus standard care alone or standard care combined with other therapies on gait, upper extremity function, communication, mood and emotions, social skills, pain, behavioral outcomes, activities of daily living and adverse events.

Search strategy

We searched the Cochrane Stroke Group Trials Register (February 2010), the Cochrane Central Register of Controlled Trials (*The Cochrane Library* Issue 2, 2009), MEDLINE (July 2009), EMBASE (August 2009), CINAHL (March 2010), PsycINFO (July 2009), LILACS (August 2009), AMED (August 2009) and Science Citation Index (August 2009). We handsearched music therapy journals and conference proceedings, searched dissertation and specialist music databases, trials and research registers, reference lists, and contacted experts and music therapy associations. There was no language restriction.

Selection criteria

Randomized and quasi-randomized controlled trials that compared music therapy interventions and standard care with standard care alone or combined with other therapies for people older than 16 years of age who had acquired brain damage of a non-degenerative nature and were participating in treatment programs offered in hospital, outpatient or community settings.

Data collection and analysis

Two review authors independently assessed methodological quality and extracted data. We present results using mean differences (using post-test scores) as all outcomes were measured with the same scale.

Main results

We included seven studies (184 participants). The results suggest that rhythmic auditory stimulation (RAS) may be beneficial for improving gait parameters in stroke patients, including gait velocity, cadence, stride length and gait symmetry. These results were based on two studies that received a low risk of bias score. There were insufficient data to examine the effect of music therapy on other outcomes.

Authors' conclusions

RAS may be beneficial for gait improvement in people with stroke. These results are encouraging, but more RCTs are needed before recommendations can be made for clinical practice. More research is needed to examine the effects of music therapy on other outcomes in people with ABI.

PLAIN LANGUAGE SUMMARY

Music therapy for acquired brain injury

Acquired brain injury can result in problems with movement, language, sensation, thinking or emotion. Any of these may severely reduce a survivor's quality of life. Many innovative therapy techniques have been developed to help recover lost functions and to prevent depression. Music therapy involves using music to aid rehabilitation. Specific treatments may include the use of rhythmic stimulation to aid movement and walking, singing to address speaking and voice quality, listening to music to reduce pain and the use of music improvisations to address emotional needs and enhance a sense of wellbeing. We identified and included seven studies (involving 184 participants) in this review, all of which were carried out by a trained music therapist. The results suggest that rhythmic auditory stimulation may be beneficial for improving measures of walking, but there was insufficient information to examine the effect of music therapy on other outcomes. Further clinical trials are needed.

BACKGROUND

Acquired brain damage embraces a range of conditions involving rapid onset of brain injury, including trauma due to head injury or postsurgical damage, vascular accident such as stroke or subarachnoid hemorrhage, cerebral anoxia, toxic or metabolic insult such as hypoglycemia, and infection or inflammation (RCP 2004). Acquired brain injury (ABI) can result in impairments in motor function, language, cognition, sensory processing as well as emotional disturbances. Hemiplegia and hemiparesis are common and may severely reduce a survivor's quality of life. Consequently, a primary concern in rehabilitation for acquired brain injury is the restoration of motor function. The improvement of ambulation and upper extremity function directly affects the level of independence of the patient related to activities of daily living. The affected individual is likely to be left with communication impairments, such as a severely reduced ability to understand, speak, and use spoken and written language, which can result in isolation. Furthermore, brain damage often leads to disturbances in memory, learning, and awareness. Sensory disturbances and neuropathic pain may result from damage to the nervous system. Finally, there may be behavioral implications resulting in disinhibition, apathy and motivation. Recovery of lost functions and skills after acquired brain damage is typically incomplete, putting survivors at increased risk for depression. Effective treatment of depression may bring substantial benefits by improving medical status, enhancing quality of life, and reducing pain and disability (van de Port 2007; Whyte 2006).

Acquired brain injury causes significant levels of disabilities which tend to result in long-term problems. It is estimated that in 2003 there were 135,000 people living with long-term problems following brain injury in the UK and a further 300,000 people living with disabilities stemming from stroke (NA 2003). Figures from the US exceed those in the UK with an estimated 1.5 million people who sustain a traumatic brain injury each year, of whom 80,000 to 90,000 will be left with long-term disability (NCIPC 2001). Approximately 5.3 million Americans or 2% of the population of all ages have long-term or lifelong needs for help to perform personal activities of daily living following traumatic brain injury (Thurman 1999). Finally, the World Health Organization estimated that, in 2001, there were over 20.5 million strokes worldwide. With the population ageing, even if the stroke incidence stagnates, the number of stroke patients requiring medical and rehabilitation care will rise dramatically over the next two decades (WHO 2002). Further work needs to be done to identify the direct and indirect financial costs of acquired brain injury to society within the UK (Turner-Stokes 2003). However, within the US, the costs associated with traumatic brain injury alone were estimated to be around USD 60 billion for 2000 (Finkelstein 2006). Acquired brain injury therefore has significant effects on society in terms of human and economic costs.

Many innovative therapy techniques have been developed to help the restoration of lost functions and to aid in prevention and treatment of depression in acquired brain injury survivors. Music therapy has been used in rehabilitation settings to stimulate brain functions involved in movement, cognition, speech, emotions, and sensory perceptions. Interventions range from the use of rhythmic auditory stimulation to aid in the execution of movement and normalization of gait parameters (Thaut 1993), to music listening and singing to reduce pain (Kim 2005), to the use of music listening, music improvisations, composition and song discussions to address emotional needs and enhance the sense of wellbeing (Nayak 2000). Music listening has also been used by non-music therapists in rehabilitation settings to enhance relaxation, provide distraction, and reduce pain. It is important to distinguish music therapy interventions from the administration of music to patients by medical personnel. Music therapists have specific clinical training in assessing individual patients' needs. Clinical practice is underpinned by music therapy theory. Treatment involves selecting from a range of music-based interventions, using both music and the therapist-patient relationship as agents of change. In many countries, music therapists are board-certified, registered and/or licensed as professionals. Therefore, interventions are classified as music therapy if the following components are present: (1) implementation of goal-directed music interventions by a trained music therapist, and (2) the use of music experiences individualized to patient need. In rehabilitation settings, these interventions may include (1) listening and moving to live, improvised or pre-recorded music as well as rhythmic auditory stimulation, (2) performing music on an instrument, (3) improvising music spontaneously using voice or instruments or both, (4) singing or vocal activities to music, (5) music-based speech and language activities, (6) composing music, and (7) music combined with other modalities (e.g. imagery, art) (Dileo 2007; Magee 2006; Magee 2009).

Many research studies on the use of music in rehabilitation of acquired brain injury have suffered from small sample size, making it difficult to achieve statistically significant results. In addition, differences in factors such as study designs, methods of interventions, and intensity of treatment have led to varying results. A systematic review is needed to more accurately gauge the efficacy of music therapy as a rehabilitation intervention for people with acquired brain injury as well as to identify variables that may moderate its effects.

OBJECTIVES

1. To identify randomized controlled trials (RCTs) examining the efficacy of music therapy in addressing recovery in patients with acquired brain injuries.

2. To compare the efficacy of music therapy and standard care with (a) standard care alone, (b) standard care and placebo treatments, or (c) standard care and other therapies.

3. To compare the efficacy of different types of music therapy interventions.

METHODS

Criteria for considering studies for this review

Types of studies

All prospective RCTs, parallel group designs as well as cross-over trials, of any language, published and unpublished, were eligible for entry. We included controlled clinical trials (CCTs) with quasi-randomized or systematic methods of treatment allocation (e.g. alternate allocation of treatments) because only a limited number of RCTs were identified.

Types of participants

We included patients of any gender and older than 16 years of age who had acquired brain damage of a non-degenerative nature and were participating in treatment programs offered in hospital, outpatient or community settings at the time that they received music therapy. This includes traumatic brain injury, stroke, anoxia, infection and any mixed cause. We excluded any condition of a progressive nature. We did not use the site of lesion and stage of rehabilitation as inclusion or exclusion criteria.

Types of interventions

We included all studies in which standard treatment combined with music therapy was compared with: (1) standard care alone, (2) standard care with placebo, or (3) standard care combined with other therapies. In addition, we considered studies only if (1) music therapy was delivered by a formally trained music therapist or by trainees in a formal music therapy program, and (2) one of the following music therapy interventions was used (Magee 2006):

- clinical improvisation in which participants are involved in active music making in dialogue with the therapist using musical instruments or voice;
- voice and singing techniques including song-singing programs, melodic intonation therapy or modified melodic

intonation therapy, vocal intonation therapy, rhythmic speech cueing, and therapeutic singing;

- rhythmic auditory stimulation or rhythmic auditory cueing;
- receptive techniques in which participants listen to music;
- song-writing;
- any combination of the above.

Types of outcome measures

Primary outcomes

Rehabilitation of mobility is crucial in acquired brain injury rehabilitation to enhance personal independence. Therefore, we selected the following primary outcomes for this review.

1. Improvement in gait, measured by changes in gait velocity, cadence, stride length, stride symmetry, stride timing.
2. Improvement in upper extremity function, measured by hand grasp strength, frequency and duration of identified hand function, spatiotemporal arm control.

Secondary outcomes

1. Communication (e.g. language production, parameters of voice production, speaking fundamental frequency)
2. Mood and emotions (e.g. depression, anger, anxiety)
3. Social skills and interactions (e.g. eye contact, non-verbal interactions)
4. Pain
5. Behavioral outcomes (e.g. participation in treatment, motivation, self-esteem)
6. Activities of daily living
7. Adverse events (e.g. death, fatigue, falls)

Search methods for identification of studies

See the 'Specialized register' section in the Cochrane Stroke Group module.

We searched the Cochrane Stroke Group Trials Register, which was last searched by the Managing Editor on 25 February 2010. In addition, we searched the following electronic bibliographic databases and trials registers:

- Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 2, 2009) (Appendix 1);
- MEDLINE (1950 to July 2009) (Appendix 2);
- EMBASE (1980 to August 2009) (Appendix 3);
- CINAHL (1982 to March 2010) (Appendix 4);
- PsycINFO (1967 to July 2009) (Appendix 5);
- LILACS (Latin American and Caribbean Health Sciences Literature) (1982 to August 2009) (Appendix 6);
- AMED (Allied and Complementary Medicine) (1985 to August 2009) (Appendix 7);
- Science Citation Index (1974 to August 2009) (Appendix 8);
- CAIRSS for Music (Computer-Assisted Information Retrieval Service System) (August 2009) (Appendix 9);
- Proquest Digital Dissertations (1861 to August 2009) (Appendix 10);
- ClinicalTrials.gov (http://www.clinicaltrials.gov/) (August 2009) (Appendix 11);
- Current Controlled Trials (http://www.controlled-trials.com/) (August 2009) (Appendix 12);
- The National Research Register (NRR) Archive (https://portal.nihr.ac.uk/Pages/NRRArchiveSearch.aspx) (August 2009) (Appendix 13);
- Rehab Trials.org (http://www.kesslerfoundation.org/) (August 11 2009) (Appendix 14);
- Indexes to Theses in Great Britain and Ireland (http://www.theses.com/) (August 2009) (Appendix 15);
- Music Therapy World (www.musictherapyworld.net) (November 2007): this specialist music therapy research database is no longer functional, however we handsearched archives of dissertations and conference proceedings (Appendix 16).

We handsearched the following music therapy journals and conference proceedings:

- *Arts in Psychotherapy* (1974 to 2009; 39(4));
- *Australian Journal of Music Therapy* (1990 to 2009;20);
- *Australian Music Therapy Association Bulletin* (1977 to 2005; final issue);
- *British Journal of Music Therapy* (1987 to 2009;23(1));
- *Canadian Journal of Music Therapy* (1976 to 2009;15(1));
- *International Journal of the Arts in Medicine* (1993 to 1999;6(2), final issue);
- *Journal of Music Therapy* (1964 to 2009;46(2));
- *Japanese Journal of Music Therapy* (2005 to 2006;2; latest issue available online);
- *Musik-, Tanz-, und Kunsttherapie (Journal for Art Therapies in Education, Welfare and Health Care)* (1999 to 2009;20(1));
- *Musiktherapeutische Umschau* (1980 to 2009;30(3));
- *Music Therapy* (1981 to 1996;14(1), final issue);
- *Music Therapy Yearbook* (1951 to 1962; final issue);
- *Music Therapy Perspectives* (1982 to 2009;27(1));
- *Nordic Journal of Music Therapy* (1992 to 2009;18(1));
- *Music Therapy Today* (online journal of music therapy) (2000 to 2007;3, final issue);
- *New Zealand Journal of Music Therapy* (1987 to 2006;20, latest issue with available online abstracts);
- *Voices* (online international journal of music therapy) (2001 to 2009;9(2));
- Canadian Conference Proceedings (2004 to 2006);
- The World Music Therapy Congress Proceedings (1993 to 1999);
- The European Music Therapy Congress Proceedings (1992 to 2007).

In an effort to identify further published, unpublished and ongoing trials, we searched the bibliographies of relevant studies and reviews and contacted experts in the field. We consulted music therapy association web sites to help identify music therapy practitioners and conference information (e.g. American Music Therapy Association (http://www.musictherapy.org), the British Society for Music Therapy (http://www.bsmt.org/), the Association of Professional Music Therapists (APMT) (http://www.apmt.org/), Music Therapy World (http://musictherapyworld.net)). We also consulted a global network of professional music therapists working in neurology (Music Therapy Neurology Network http://www.rhn.org.uk/institute/mtnn).

We did not apply any language restrictions for either searching or trial inclusion.

Data collection and analysis

Selection of studies

Four review authors (JB, BW, WM, and EM) conducted the searches as outlined in the Search methods for identification of studies. One review author (JB) and a graduate research assistant scanned titles and abstracts of each record retrieved from the search and deleted obviously irrelevant references. When a title or abstract could not be rejected with certainty, a graduate assistant obtained the full article, which was then inspected by two review authors (BW and WM) independently. Both review authors used an inclusion criteria form to assess the trial's eligibility for inclusion. One review author (JB) checked the inter-rater reliability for trial selection, and in case of disagreement or uncertainty, consulted a third review author (CD). We kept a record of both the article and the reason for exclusion for all excluded studies.

Data extraction and management

One author (JB) and a trained research assistant independently extracted data from the selected trials using a standardized coding form. They discussed any differences in data extraction and sought the input of a third review author (CD) when needed. We extracted the following data:

General information

- Author
- Year of publication
- Title
- Journal (title, volume, pages)
- If unpublished, source
- Duplicate publications
- Country
- Language of publication

Trial information

- Study design (parallel group, cross-over)
- Randomization
- Randomization method
- Allocation concealment
- Allocation concealment method
- Level of blinding

Intervention information

- Type of intervention (e.g. clinical improvisation, voice or singing technique, rhythmic auditory stimulation or rhythmic auditory cueing, music listening, song writing, combination)
- Music selection (detailed information on music selection in cases of music listening, beat selection in cases of rhythmic auditory stimulation)
- Music preference (patient preferred versus researcher selected in cases of music listening)
- Professional level of music therapist (professional or student in training)
- Length of intervention
- Intensity of intervention
- Comparison intervention

Participant information

- Total sample size
- Number of experimental group
- Number of control group
- Gender
- Age
- Ethnicity
- Diagnosis
- Site of lesion
- Degree of neurological damage
- Rehabilitation stage
- Setting
- Inclusion criteria

Outcomes

We planned to extract statistical information for the following outcomes (if applicable):

1. parameters of gait (e.g. velocity, cadence, stride length, stride symmetry, stride timing);
2. parameters of upper extremity function (e.g. hand grasp strength, frequency and duration of identified hand function, spatiotemporal arm control);
3. communication outcomes (e.g. language production; parameters of voice production, speaking fundamental frequency);
4. mood and emotion outcomes (e.g. depression, anger, anxiety);

5. social interactions outcomes (e.g. eye contact, non-verbal interactions);
6. pain;
7. behavioral outcomes (e.g. participation in treatment, motivation);
8. activities of daily living;
9. adverse events (e.g. death, fatigue, falls).

Assessment of risk of bias in included studies

Two review authors (JB and CD) independently assessed all included trials for trial quality. We used the following four criteria for quality assessment.

1. Method of randomization

- Was the trial reported as randomized? Yes/No
- Was the method of randomization appropriate? Yes/No/ Unclear

We rated randomization as appropriate if every participant had an equal chance to be selected for either condition and if the investigator was unable to predict to which treatment the participant would be assigned. We rated date of birth, date of admission, or alternation as inappropriate.

2. Allocation concealment

We used the ratings of A - adequate, B - unclear and C - inadequate in accordance with section 6.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008).
A - adequate: methods to conceal allocation include (1) central randomization, (2) serially numbered, opaque, sealed envelopes, or (3) other descriptions with convincing concealment.
B - unclear: authors did not adequately report on method of concealment.
C - inadequate: allocation was not adequately concealed (e.g. alternation methods were used).

3. Blinding

With music therapy studies, it is not possible to blind participants and those providing the music therapy interventions. However, outcome assessors can be blinded. In this review, we marked blinding as 'yes', 'no', or 'unclear' as it pertains to blinding of outcome assessors.

4. Incomplete data addressed

We gave a rating of adequate when numbers of dropouts and reasons for drop out were reported or if we were able to obtain this information from the study author. If there were no withdrawals and this was indicated in the study, we gave the study a rating of adequate.
We used these four criteria to give each article an overall quality rating, based on section 6.7.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008).
A - low risk of bias, all four criteria met.
B - moderate risk of bias, one or more of the criteria only partly met.
C - high risk of bias, one or more criteria not met.
We planned to use the overall quality assessment rating for sensitivity analysis. We did not exclude studies based on a low quality score.

Dealing with missing data

We analyzed data on an endpoint basis, including only participants for whom final data point measurement was obtained (available case analysis). We did not assume that participants who dropped out after randomization had a negative outcome.

Assessment of heterogeneity

We investigated heterogeneity using the I^2 test with $I^2 > 50\%$ indicating significant heterogeneity.

Assessment of reporting biases

We could not examine publication bias because the outcomes included had a maximum of two trials.

Data synthesis

One review author (JB) entered all trials included in the systematic review into Review Manager 5 (RevMan 2008). JB conducted the data analysis and this was reviewed by CD for accuracy. We presented the main outcomes in this review as continuous variables. We calculated standardized mean differences for outcome measures using the results from different scales; we used mean differences for results using the same scales. We calculated pooled estimates using the fixed-effect model unless there was substantial heterogeneity, in which case we used the random-effects model to obtain a more conservative estimate. We determined levels of heterogeneity using the I^2 statistic (Higgins 2002). We calculated 95% confidence intervals (CI) for each effect size estimate. This review did not include any categorical variables.
We made the following treatment comparison:

- music therapy versus standard care alone.

Subgroup analysis and investigation of heterogeneity

We planned the following sub-analyses a priori as described by Deeks 2001 and as recommended in section 8.8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008), but could not perform them because of an insufficient number of studies:

- type of music therapy intervention;
- dosage of music therapy; and
- diagnosis.

Sensitivity analysis

We planned to examine the influence of study quality using a sensitivity analysis where the results of including and excluding lower-quality studies are compared. However, this was not possible because there were only two trials per outcome.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification; Characteristics of ongoing studies.

Results of the search

The database searches and handsearching of conference proceedings and journals identified 3855 citations; we retrieved 94 references for possible inclusion. If necessary we contacted chief investigators to obtain additional information on study details and data. We found many trials on the effects of rhythmic auditory stimulation (RAS) on gait in people with acquired brain injury; however, most of those were one group pre-test/post-test designs. In addition, several trials examined melodic intonation therapy for speech improvement, but we excluded these because the intervention was not implemented by a trained music therapist or the trial was not a RCT or CCT. Fourteen references to seven studies met all the inclusion criteria.

Included studies

We included seven studies with a total of 184 participants. These studies examined the effects of music therapy on gait parameters (Thaut 1997; Thaut 2007), speech outcomes (Jungblut 2004), hemiparetic arm movement (Paul 1998; Thaut 2002), agitation and orientation (Baker 2001) and pain during exercise (Kim 2005) in patients with an acquired brain injury. Fifty-four per cent of the participants were male. The average age of the participants was 59.4 years. The studies were conducted in four different countries: USA (Paul 1998; Thaut 1997; Thaut 2002), South Korea (Kim 2005), Germany (Jungblut 2004), Australia (Baker 2001), and USA and Germany (Thaut 2007) by professional music therapists. Five of the seven studies did not report on the ethnicity of the participants (Jungblut 2004; Paul 1998; Thaut 1997; Thaut 2002; Thaut 2007). Trial sample size ranged from 10 to 78 participants. Three studies used rhythmic auditory stimulation (RAS) as the music therapy intervention (Thaut 1997; Thaut 2002; Thaut 2007). RAS involves the use of rhythmic sensory cuing of the motor system. It engages entrainment principles in which “rhythmic auditory cues synchronize motor responses into stable time relationships. The fast-acting physiological entrainment mechanisms between auditory rhythm and motor response serve as coupling mechanisms to stabilize and regulate gait patterns” (Thaut 2007) or reaching arm movements. Two studies (Thaut 1997; Thaut 2007) examined the effects of RAS versus standard neurodevelopmental therapy (NDT/Bobath) on improvement in gait as measured by changes in gait velocity, cadence, stride length, and stride symmetry. Both studies included stroke patients two to three weeks post-stroke. Patients were eligible if they were able to complete five stride cycles with hand-held assistance. The training duration of Thaut 1997 was six weeks with training held twice daily, 30 minutes each session, five days a week. Thaut 2007 followed the same protocol but the training duration was only three weeks. One study (Thaut 2002) examined the effects of RAS on spatiotemporal control of reaching movements of the paretic arm. In this study, patients were asked to move their affected arm back and forth for 30 seconds as evenly timed as possible between two touch-sensitive sensors (for details about sensor placement please see Thaut 2002). Patients completed one trial with and one trial without RAS in a randomized cross-over trial. During rhythmic trials, patients were asked to move their affected arm in time with the metronome beat.

Other music therapy interventions included electronic music making (Paul 1998), rhythmic-melodic voice training (SIPARI®) (Jungblut 2004) and listening to pre-recorded songs (Kim 2005) or live music (Baker 2001).

Paul 1998 evaluated the effects of music-making activity on elbow extension in participants with hemiplegia. Electronic music devices were used that required active shoulder flexion and elbow extension and that enabled easy sound manipulation by the participants. Electronic paddle drums were individually set to the maximum range of motion of each participant. Participants in the music therapy group participated in music-making activity for 30 minutes twice a week for 10 weeks. The control group participated in a physical exercise group in which they were encouraged to reach their affected extremity as far as they could in different directions.

Only one trial (Jungblut 2004) that examined the effects of music therapy on speech parameters met our inclusion criteria. This study used SIPARI® with participants who suffered from chronic aphasia (Broca's aphasia or global aphasia) due to stroke with a mean aphasia duration of 11.5 years and who were no longer receiving speech therapy. SIPARI® is a music therapy technique that is based on specific use of the voice. It actively works with the remaining speech capabilities in the right hemisphere of aphasic patients, namely singing, intonation, prosody embedded in physiologically appropriate breathing (Atmung). The SIPARI method also employs instrumental and vocal rhythmic exercises and music improvisations to practice communication scenarios. Participants in the experimental group (eight participants) received 20 group music therapy sessions and 10 individual sessions over a period of seven months. Participants in the control group (five participants) did not receive any music therapy.

Listening to pre-recorded music involves methods where the patient is directed to listen to audio recordings of music played on any media device such as compact discs, vinyl recordings, cassettes, or other digital technology, and is not required to be involved actively in making the music him/herself. Listening to live music involves methods where the patient is directed to listen to vocal or instrumental music created by the therapist (or another) within the patient's environment, and is not required to be involved actively in making the music him/herself. One trial (Baker 2001) examined the effects of music therapy on agitation and orientation levels in 22 people with a severe head injury with a diagnosis of post-traumatic amnesia. Participants were exposed to three conditions (listening to live music, listening to taped music, no music), in random order, twice over six consecutive days. The songs in the live and taped music condition were identical and were suggested by family members as the participant's preferred music. We found one RCT that investigated the effects of listening to pre-recorded music on pain in people with acquired brain injury. Kim 2005 exposed 10 stroke patients to music (listening to songs and listening to karaoke instrumental music) and no music conditions during upper extremity joint exercises over an eight-week period.

Frequency and duration of treatment sessions greatly varied among the studies. The total number of sessions ranged from three sessions to 60 sessions. Most sessions lasted 30 minutes, with the exception of one RAS trial that used 30 seconds trial intervals for different treatment conditions (Thaut 2002). Details on frequency and duration of sessions for each trial are included in the Characteristics of included studies table.

Four studies used parallel group designs (Jungblut 2004; Paul 1998; Thaut 1997; Thaut 2007), whereas the other studies used cross-over designs. Not all studies measured all outcomes identified for this review.

Details of the studies included in the review are shown in the Characteristics of included studies table.

Excluded studies

We identified 21 additional experimental research studies that appeared eligible for inclusion. However, we excluded these after closer examination or after receiving additional information from the chief investigators. Reasons for exclusions were: (1) not an RCT or CCT (16 studies), (2) insufficient data reporting (one study), (3) could not be categorized as music therapy (as defined by the authors in the background section) (two studies), (4) comparative study of two music therapy interventions (one study), and (5) control participants did not have ABI (one study).

Details of the excluded trials are listed in the Characteristics of excluded studies table.

Risk of bias in included studies

We included studies that used appropriate methods of randomization (e.g. computer-generated table of random numbers, draw of lots, flip of coins) (Baker 2001; Kim 2005; Thaut 1997; Thaut 2002; Thaut 2007) as well as studies that used alternate group assignment as allocation method (Jungblut 2004; Paul 1998).

Four studies used allocation concealment (Kim 2005; Thaut 1997; Thaut 2002; Thaut 2007). In three trials, blinding of the outcome assessors was not used (Baker 2001; Kim 2005; Thaut 2002), and this inevitably introduced potential for biased assessment. Blinding of intervention allocation is not possible in music therapy interventions, adding another layer of possible bias.The dropout rate was less than 20% for four of the trials (Baker 2001; Paul 1998; Thaut 1997; Thaut 2007). Two studies had a drop out rate between 24% and 29% (Jungblut 2004; Kim 2005), and one study did not report on drop-out rate (Thaut 2002). Most studies reported reasons for dropout. Detailed information on dropout rate is included in the Characteristics of included studies table.

As a result, only two studies (Thaut 1997; Thaut 2007) received a low risk of bias rating. For all other studies there was a high risk of bias. Risk of bias is detailed for each study in the risk of bias tables included with the Characteristics of included studies table.

As all but two trials were rated at the same level (high risk) and because of the limited number of studies per outcome, we did not carry out sensitivity analysis on the basis of overall quality rating.

Effects of interventions

Primary outcomes

Gait

Two studies (Thaut 1997; Thaut 2007) with a total of 98 participants examined the effects of RAS versus standard neurodevelopmental therapy (NDT/Bobath) on improvement in gait as measured by changes in gait velocity, cadence, stride length, and stride symmetry.

The pooled estimate of these two studies indicated that RAS improved gait velocity by an average of 14.32 meters per minute compared to the control group (95% CI 10.98 to 17.67, $P < 0.00001$), and results were consistent between the two studies ($I^2 = 0\%$) (Analysis 1.1). The RAS group also showed significantly greater improvements in stride length (MD = 0.23 meters, 95%

CI 0.14 to 0.32, $P < 0.00001$, $I^2 = 0\%$) (Analysis 1.2) and gait cadence (MD = 16.71 steps/minute, 95% CI 3.40 to 30.01, P = 0.01, $I^2 = 69\%$) (Analysis 1.3) than the standard treatment group. However, the results were inconsistent for gait cadence, with the larger study (Thaut 2007) showing a greater cadence improvement (22.00 steps/minute, 95% CI 16.94 to 27.06, N = 78) than the smaller study (Thaut 1997) (8.00 steps/minute, 95% CI -6.47 to 22.47, N = 20). Finally, the RAS intervention led to greater improvements in gait symmetry (defined as the ratio between the swing time of two consecutive steps using the longer step as the denominator) than standard treatment (MD = 0.12, 95% CI 0.09 to 0.15, $P < 0.00001$) and these results were consistent between the two studies ($I^2 = 0\%$) (Analysis 1.4).

Upper extremity function

Two trials (Paul 1998; Thaut 2002) measured the effects of music therapy on upper extremity function in hemispheric stroke patients. Elbow extension angle was the only common outcome measure in these two studies. However, because of the significant clinical heterogeneity of the studies, their effect sizes were not pooled.
Thaut 2002 examined the effects of RAS on spatiotemporal control of reaching movements of the paretic arm in 21 patients. Results indicated that RAS increased the elbow extension angle by 13.8% compared to the non-rhythmic trial, and this difference was statistically significant (P = 0.007). Results further indicated that variability of timing and reaching trajectories were reduced significantly (35% and 40.5%, respectively, $P < 0.05$).
Paul 1998 evaluated the effects of music-making activity on elbow extension in 20 participants with hemiplegia. The elbow extension (measured from 135 to 0 with negative numbers expressing limitations) post-intervention was -29.4 (SD 29.49) for the experimental group and -39.2 (SD 38.19) for the control group. This difference was not statistically significant. Post-test shoulder flexion data indicated no statistically significant difference (P = 0.44) between the music therapy group (85.6°, SD 26.71) and the control group (71.8°, SD 39).

Secondary outcomes

Communication

Jungblut 2004 examined the effects of a music therapy method, SIPARI®, as described in the Included studies section, on speech parameters in 13 participants with chronic aphasia. Post-treatment speech evaluation found that the use of SIPARI® was effective in improving articulation and prosody (effect size (ES) = 2.12, P = 0.024), speech repetitions (ES = 1.29, P = 0.045), and speech comprehension (ES = 1.36; P = 0.037). The effect on labeling was not statistically significant (ES = 0.74, P = 0.22). The total speech profile of the music therapy participants on the Aachen Aphasia Test was improved significantly compared to the control group (ES = 2.08, P = 0.003).

Behavioral outcomes

One trial (Baker 2001) examined the effects of listening to live music and listening to taped music on agitation and orientation levels in 22 people with a severe head injury with a diagnosis of post-traumatic amnesia. Listening to live music had a significant effect on participant orientation levels (as measured by the Westmead PTA scale) compared to the no music control condition (ES = 0.82, $P < 0.001$), and this effect was slightly larger than the effect of listening to taped music compared to the control condition (ES = 0.72, $P < 0.001$). Listening to live music was also effective in reducing agitation scores (as measured by the Agitation Behavior Scale) (ES = 5.01 ABS units, $P < 0.0001$). Agitation also decreased after listening to taped music (6.25 ABS units, $P < 0.0001$).The difference in effect between live and taped music was not statistically significant (1.2 ABS units, P = 0.8).

Pain

Kim 2005 examined the effects of listening to pre-recorded music on pain in people with acquired brain injury. Pain ratings on a zero-to-10 numeric scale indicated that there was no statistically significant difference in pain ratings between the music and the no-music condition ($P > 0.05$).
We did not identify any studies that addressed the other secondary outcomes listed in the Secondary outcomes section, namely mood and emotions, social skills and interactions, activities of daily living and adverse events.

DISCUSSION

Summary of main results

The results of this review suggest that rhythmic auditory stimulation (RAS) may be beneficial for improving gait velocity, cadence, stride length and stride symmetry in stroke patients. These results were based on two studies that received a low risk of bias score. However, given the limited number of studies and the small total sample size (98 participants), more RCTs are needed to strengthen this evidence.
Two trials investigated the effects of music therapy on upper extremity function in hemispheric stroke patients. Because of clinical heterogeneity, these results could not be pooled. One study (Thaut 2002) found significant improvement in elbow extension, variability of timing and reaching trajectories during rhythmic auditory stimulation. In contrast, one study (Paul 1998) that examined the effects of active music making on elbow extension and

shoulder flexion did not find statistically significant results. More research is needed to investigate which music therapy techniques are most effective for improvement of upper extremity function.

Few trials that examined the effects of music therapy on the secondary outcomes in this review met our inclusion criteria. The results of one trial (Jungblut 2004) indicated that SIPARI®, a music therapy rhythmic-melodic voice training technique, significantly improved the speech profile of people with chronic aphasia. One RCT (Baker 2001) found that music therapy is effective in reducing agitation and improving orientation levels in people with post-traumatic amnesia following a severe head injury. In a trial evaluating the effects of music therapy on pain levels during upper extremity exercise in stroke patients, no support was found for the effectiveness of listening to music for pain management (Kim 2005). More RCTs are needed to investigate the effects of music therapy on these outcomes before any reliable conclusions can be drawn.

Other secondary outcomes listed in the Secondary outcomes section of this review, namely mood and emotions, social skills and interactions, activities of daily living and adverse events were not addressed in any of the trials that met our inclusion criteria.

Overall completeness and applicability of evidence

This review included seven trials. The strength of our review is that we searched all available databases and a large number of music therapy journals, checked reference lists of all relevant trials, contacted relevant experts for identification of unpublished trials and reviewed publications for eligibility without restricting language. In spite of such a comprehensive search, it is still possible we missed some published and unpublished trials. We requested additional data where necessary for all trials we considered for inclusion. This allowed us to get accurate information on the trial quality and data for most trials and helped us make well-informed trial selection decisions.

The results of two studies suggest that RAS may be effective for improving gait velocity, cadence, stride length, and stride symmetry in stroke patients. These findings coincide with data from non-controlled trials about the beneficial effects of RAS on gait in patients with acquired brain injury (Thaut 1993; Thaut 1997b). As pointed out in Thaut 1997, hemispheric stroke patients may benefit from RAS because auditory rhythm is processed bilaterally, and no difference was observed in performance between left and right hemispheric patients. However, more RCTs are needed to further support this evidence.

One trial examined the effects of RAS on hemiparetic arm movements in stroke patients. The positive results of this study are supported by evidence of non-controlled trials (Malcolm 2009; Thaut 1999). Given the fact that rhythmic stimulation appears to induce temporal stability and enhance motor control in walking, it could very well be that rhythmic cueing has a similar effect on upper extremity functioning. Even though functional arm movements, unlike gait, are "discrete, biologically non-rhythmic, and volitional" (Thaut 2002), rhythmic stimuli are successfully used to enhance the execution of motor skills in non-rehabilitation areas such as music performance and sports (Thaut 2002). It is important that additional RCTs are conducted to further examine the potential benefits of RAS on upper extremities functioning.

The RAS trials solely included hemiparetic stroke patients. The majority of the patients had middle cerebral artery strokes (78%). Patients in the gait trials (Thaut 1997; Thaut 2007) entered the studies within four weeks of the stroke incident and were categorized as a stage four or early stage three on the Brunnstrom recovery scale. Patients in the upper extremity trial (Thaut 2002) were, on average, 11.4 (SD 5.2) months post-stroke before admission to the study and were categorized as a stage four to five on the Brunnstrom recovery scale. Site of lesion and length of post-injury recovery period are important factors to consider when selecting music interventions for adults with acquired brain injury. However, because of the limited number of studies in this review and the heterogeneity of neurological injury, recommendations linking specific interventions to specific neurological damage cannot be made at this time.

Single controlled clinical trials have shown promising results for the effects of music therapy on speech, agitation and orientation levels in people with acquired brain injury but no conclusions can be drawn at this time regarding the clinical applicability of this evidence. In addition, several RCTs and CCTs which could not be categorized as music therapy (as defined by the authors in the background section) have reported positive effects of listening to music and music making on cognitive and motor outcomes for ABI populations (Särkämö 2008; Schneider 2007).

Quality of the evidence

The quality of reporting in general was poor with only one study detailing the method of randomization, allocation concealment and level of blinding (Thaut 2007). We needed to contact the chief investigators of all other studies to provide additional methodological and statistical information. As a result, only two studies (Thaut 1997; Thaut 2007) received a low risk of bias rating. Both of these studies contributed evidence on the effects of RAS on gait parameters. However, because of the limited number of trials, the results on gait parameters need to be interpreted with caution.

It is important to consider the potential bias introduced by incomplete outcome data. For the gait studies (Thaut 1997; Thaut 2007) there were no drop-outs in Thaut 1997 (personal communication with author). In Thaut 2007, participant drop-outs were much higher in the control group. Reasons for withdrawal were hospital transfer, early discharge, medical complications, or unspecified personal reasons. Since both studies implemented the same intervention and their results were highly homogenous (I^2 = 0% for three out of four gait parameters), one could assume that

the incomplete data of Thaut 2007 did not bias the results. However, since the raw data could not be accessed and no intention-to-treat analyses were used, we cannot be certain of this.
The quality of evidence of the other trials was poor because of high risk of bias and limited number of studies.

AUTHORS' CONCLUSIONS

Implications for practice

Rehabilitation of mobility is crucial in stroke rehabilitation. The results of two studies included in this review suggest that rhythmic auditory stimulation may help improve gait velocity, cadence, stride length and stride symmetry in stroke patients. These results are encouraging, but more RCTs are needed before recommendations can be made for clinical practice. As most of the included studies successfully improved motor outcomes with rhythm-based methods, we suggest that rhythm may be a primary factor in music therapy methods facilitating functional gains with this population.

At this time, there is not sufficient evidence from RCTs or CCTs to support the use of music therapy for improvement of upper extremity function, speech, agitation and cognitive orientation. Other secondary outcomes listed in this review, namely mood and emotions, social skills and interactions, activities of daily living and adverse events, were not addressed in any of the trials that met our inclusion criteria. In the absence of sufficient evidence, recommendations for clinical practice cannot be made for these outcomes.

Implications for research

This review shows encouraging results for the effects of rhythmic auditory stimulation (RAS) on gait parameters; however, more RCTs are needed to strengthen the current data. Several small non-controlled trials have shown impressive results of RAS for gait improvement. This, combined with the results of the two RCTs included in this review, warrants the progression to much needed large scale studies on the effects of RAS on gait. Likewise, the results of one RCT included in this review on the effects of RAS on upper extremity function in stroke patients combined with the positive results of non-controlled trials, calls for continued research commitment on the efficacy of this specific music therapy intervention for hemiparetic stroke patients. Since four of the studies producing significant results involved rhythm-based methods to address upper limb and gait functioning, we recommend more RCT investigations of rhythmic auditory stimulation across functional domains.

Future studies need to examine the relationship between the frequency and duration of RAS interventions and treatment effects. Thaut 2007 also recommended that future studies (1) compare RAS against other current gait-training methods besides neurodevelopmental treatment/Bobath, (2) investigate the effect of RAS combined with other current gait therapy techniques, and (3) study the effect of RAS in long-term outpatient or community-based settings.

More RCTs are needed to examine the effect of music therapy interventions on speech in people with acquired brain injury. We identified several trials but could not include them in this review because of lack of a control group, lack of randomization, or lack of pseudo-randomization. Given the many clinical reports in the music therapy literature of beneficial effects of music on speech in this population, research efforts need to focus on conducting music therapy trials with high quality designs.

Future studies should consider including the following outcomes: agitation, cognitive orientation, mood and emotions, social skills and interactions, activities of daily living and adverse events.

Finally, several studies in this review used a small sample size (10 to 20 participants). Future studies need to include power analyses so that sufficiently large samples are used.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Baker 2001

Methods	RCT Cross-over trial
Participants	22 adults with a severe head injury with a diagnosis of post-traumatic amnesia, scoring less than or equal to 8 on the Westmead PTA Scale on the day prior to commencement of the experiment. Live music therapy condition: 22 patients Taped music condition: 22 patients Control condition: 22 patients Mean age: 34 years (SD 15.34) Sex: 5 female, 17 male Ethnicity: 72.7% Australian, 9% Croatian, 4.5% Taiwanese, 4.5% Bangladeshi, 9% Italian Setting: rehabilitation hospital Country: Australia
Interventions	Music conditions: listened to 10 to 12 minutes of live or taped music conditions. The music conditions were individualized for each participant and comprised 3 music pieces that were chosen from selections suggested by family members. All styles of music were permitted. The same 3 pieces were played during the live music condition and the taped music condition, and played in the same order. During both the live and taped music conditions, the researcher was present in the room sitting opposite and facing the participant. In the taped music condition, the music selections were played free-field on an audio cassette player. No headphones were used because this could agitate the patient. Control condition: the music therapist was present in the room but no music was played. Participants were free to do whatever they wanted. Like in the music conditions, the verbal interactions were kept to a minimum. Number of sessions: 6 (2 of each condition) Length of session: 10 to 12 minutes each
Outcomes	Agitation (Agitation Behavior Scale): effect size reported Level of orientation (Westmead PTA Scale): effect size reported
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer-generated list of random numbers
Allocation concealment?	No	No allocation concealment used

Baker 2001 (*Continued)*

Blinding? Objective outcomes	No	Blinding of outcome assessors (unit nurses) was attempted but the authors reported that the nurses could still hear the music coming from the rooms at times (personal communication)
Incomplete outcome data addressed? All outcomes	Yes	1 drop-out because of early resolution of PTA

Jungblut 2004

Methods	Pseudo-randomized controlled trial (alternate group allocation) 2-arm parallel group design
Participants	13 stroke patients suffering from chronic aphasia (Broca's aphasia and global aphasia) who were no longer receiving speech therapy. Mean duration of aphasia: 11.5 years Music therapy group: 8 participants Control group: 5 participants Mean age: 63.8 years experimental group; 67.8 years control group Sex: 6 female, 7 male Ethnicity: not reported Setting: outpatient services Country: Germany
Interventions	Music therapy group: rhythmic-melodic voice training (SIPARI®) sessions. SIPARI® is a music therapy technique that is based on specific use of the voice. It actively works with the remaining speech capabilities in the right hemisphere of aphasic patients, namely singing, intonation, prosody embedded in physiologically appropriate breathing (Atmung). The SIPARI method also employs instrumental and vocal rhythmic exercises and music improvisations to practice communication scenarios. Control group: no treatment Number of sessions: 20 group music therapy sessions and 10 individual sessions over a period of 7 months
Outcomes	Articulation and prosody, repetitions, labeling, speech comprehension, total speech profile (Aachener Aphasie Test): effect size reported
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	No	Alternate group allocation
Allocation concealment?	No	No allocation concealment used

Jungblut 2004 (*Continued)*

Blinding? Objective outcomes	Yes	Independent outcome assessors were used
Incomplete outcome data addressed? All outcomes	Yes	1 experimental and 1 control participant were excluded because they could not be clearly classified as having global aphasia or Broca's aphasia. In addition, 2 more control participants had to be excluded because they became gravely ill during the research study time frame.

Kim 2005

Methods	RCT Cross-over trial
Participants	10 adult stroke patients; 8 with severe hemiplegia, 2 with mild hemiplegia Approximately 3 years post-stroke Music therapy conditions: 10 participants Control condition: 10 participants Mean age: not reported, age range: 61 to 73 years Sex: 9 female, 1 male Ethnicity: 100% South Korean Setting: daycare center for seniors Country: South Korea
Interventions	Music therapy conditions: (1) listening to taped songs with lyrics, and (2) listening to karaoke accompaniment (without lyrics) during upper extremities exercises Control condition: no music during upper extremities exercises
Outcomes	Pain: no post-test means or change scores were reported; only F-statistic and significance level
Notes	The author informed us that she no longer had access to the raw data; therefore, no means or SD could be obtained

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer-generated list of random numbers
Allocation concealment?	Yes	All participants underwent the 3 conditions in random order
Blinding? Objective outcomes	No	Blinding not possible as only subjective pain report was used

Kim 2005 (*Continued*)

Incomplete outcome data addressed? All outcomes	Yes	4 patients withdrew due to health condition or frequent absences (personal communication with author)

Paul 1998

Methods	Pseudo-RCT 2-arm parallel group design
Participants	20 adults with unilateral cerebral hemiplegia determined to have reached their maximum capacity of physical function and subsequently discharged from occupational and physical therapies. All participants had at least 10 degrees of limitation in active shoulder flexion and elbow extension. Mean duration post-stroke: 93.4 days (SD 49.5). Music therapy group: 10 participants Control group: 10 participants Mean age: 61.75 years (SD 5.1) Sex: 9 female, 11 male Ethnicity: not reported Setting: nursing/rehabilitation facility Country: USA
Interventions	Music therapy group: participants engaged in active music improvisation sessions with the music therapist using electronic music devices that allowed for easy sound manipulation. Improvisations emphasized steady rhythmic pulses. Control group: physical exercise group conducted by recreational therapist for the same duration as the music therapy group Number of sessions: 2 times per week for 10 weeks Duration of each session: 30 minutes
Outcomes	Active shoulder flexion (JAMAR goniometer): pre-test and post-test values are reported Elbow extension (JAMAR goniometer): pre-test and post-test values are reported
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	No	Alternate group allocation
Allocation concealment?	No	No allocation concealment used
Blinding? Objective outcomes	Yes	Occupational therapist who completed the goniometric measurements was unaware of group assignment
Incomplete outcome data addressed? All outcomes	Yes	There were no withdrawals

Thaut 1997

Methods	RCT 2-arm parallel group design
Participants	20 adults with hemiparetic stroke Average post-stroke:16.1 (SD 4) days for experimental group, 15.7 (SD 4) days for control group Mean age: 73 years (SD 7) experimental group, 72 years (SD 8) control group Sex: 10 female, 10 male Ethnicity: not reported Setting: hospital Country: USA
Interventions	Music therapy group: RAS Control group: standard neurodevelopmental treatment/Bobath Number of sessions: twice daily for 6 weeks Duration of session: 30 minutes
Outcomes	Gait parameters: velocity, stride length, cadence, symmetry: pre-test and post-test values EMG variability: change score
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer-generated list of random numbers (personal communication)
Allocation concealment?	Yes	Recruiters did not know group conditions (personal communication)
Blinding? Objective outcomes	Yes	Outcome assessors (physical therapists) were blinded to the experiment
Incomplete outcome data addressed? All outcomes	Yes	No participant loss (personal communication)

Thaut 2002

Methods	RCT Cross-over trial
Participants	21 adults with left hemispheric stroke Mean post-stroke: 11.4 (SD 5.2) months Music therapy condition: 21 participants Control condition: 21 participants Mean age: 52.7 years (SD 13.7) Sex: 8 female, 13 male

Thaut 2002 (*Continued*)

	Setting: out-patient services Country: USA
Interventions	Music therapy condition: RAS Control condition: non-cued repetitive training Number of sessions: 1 session with RAS and 1 session without external time cueing Length of session: 30 seconds each
Outcomes	Arm timing, variability of movement timing, wrist trajectories, wrist trajectory variability, elbow range of motion: pre-test and post-test values
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer-generated list of random numbers (personal communication)
Allocation concealment?	Yes	Serially numbered opaque sealed envelopes (personal communication)
Blinding? Objective outcomes	No	No blinding used
Incomplete outcome data addressed? All outcomes	Unclear	It is not clear whether there were any participant withdrawals

Thaut 2007

Methods	RCT 2-arm parallel group design
Participants	78 adults with subacute hemiparetic stroke Approximately 21 days post-stroke Music therapy group: 43 participants Control group: 35 participants Mean age: 69.2 years (SD 11.5) experimental group; 69.7 years (SD 11.2) control group Sex: 37 female, 41 male Ethnicity: not reported Setting: 2 research centers Country: USA and Germany
Interventions	Music therapy group: RAS Control group: standard neurodevelopmental therapy/Bobath Number of sessions: daily, 5 days/week for 3 weeks Duration of session: 30 minutes

Thaut 2007 (*Continued)*

Outcomes	Gait parameters: velocity, stride length, cadence, symmetry: post-test values Patient satisfaction with treatment: F-statistic and P value
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer-generated list of random numbers
Allocation concealment?	Yes	Serially-numbered opaque sealed envelopes
Blinding? Objective outcomes	Yes	Outcome assessors were unaware of group assignment
Incomplete outcome data addressed? All outcomes	Yes	23% dropouts in German center, 10% in US center (absolute numbers are not reported) Reasons: hospital transfer, early discharge, medical complications, unspecified personal reasons

PTA: post-traumatic amnesia
RAS: rhythmic auditory stimulation
RCT: randomized controlled trial
SD: standard deviation

Characteristics of excluded studies *[ordered by study ID]*

Baker 2004	Not RCT or CCT
Baker 2005	Not RCT or CCT
Cofrancesco 1985	Not RCT or CCT
Cohen 1992	Unacceptable treatment allocation method
Cohen 1995	Compared rhythmically cued speech, melodically cued speech, and verbal speech of patients who had been receiving music therapy No standard treatment group Insufficient data reporting
Ford 2007	Not RCT or CCT
Goh 2001	Planned to be conducted as RCT, however, only 2 participants enrolled

(*Continued*)

Hitchen 2007	Insufficient data collection (personal communication)
Hurt 1998	Not RCT or CCT
Lin 2007	Not administered by music therapist
Magee 2002	Comparative study of 2 music therapy interventions
Malcolm 2009	Not RCT or CCT
Moon 2008	Not RCT or CCT (personal communication with author's project advisor)
Nayak 2000	Not RCT or CCT People were assigned to music therapy group individually or groups of varying sizes as this was the only way they were available to the researchers, compromising the randomization procedures (personal communication)
Prassas 1997	Not RCT or CCT
Purdie 1997	Not RCT or CCT
Studebaker 2007	Not RCT or CCT
Särkämö 2008	Not music therapy as defined by authors of this review Participants listened to prerecorded music without music therapist present
Thaut 1992	Control participants were normal people
Thaut 1993	Not RCT or CCT
Thaut 1997b	Not RCT or CCT
Thaut 1999	Not RCT or CCT

CCT: controlled clinical trial
RCT: randomized controlled trial

Characteristics of studies awaiting assessment *[ordered by study ID]*

Eslinger 1997

Methods	Randomized controlled trial
Participants	Brain-injured patients

Eslinger 1997 *(Continued)*

Interventions	Music therapy group: 20 active music therapy sessions over 10 weeks Control group: social support group sessions
Outcomes	Self-perceived competency, emotional empathy, cognitive empathy, social-emotional perception, depression and emotional expression
Notes	Study results have not been published We have requested additional study details and data from the authors This information could not be provided at this time but will be provided for the update of this review

Characteristics of ongoing studies *[ordered by study ID]*

Ala-Ruona 2010

Trial name or title	Examining the effects of active music therapy on post-stroke recovery: a randomised controlled cross-over trial
Methods	Randomized controlled cross-over trial; computer generated randomization
Participants	45 stroke patients
Interventions	Music therapy condition: 2 (60-minute) weekly sessions of active music therapy in individual setting over a period of 3 months The music therapy includes a combination of structured musical exercises with different levels of difficulty, interactive clinical improvisation, rhythmic dynamic playing with changing movement sequences, music assisted relaxation and therapeutic discussion Control condition: standard care according to the Finnish Current Care guidelines for stroke
Outcomes	Functional disability and activities of daily living independency (BI), level of impairment (NIHSS), disability grade (mRs), neglect (BIT) and motor function of upper extremity (ARAT)
Starting date	
Contact information	Professor Esa Ala-Ruona Email: esa.ala-ruona@jyu.fi
Notes	

Breitenfeld 2005

Trial name or title	Is there a benefit for aphasic stroke patients treated with music therapy?
Methods	Controlled clinical trial: randomization method unknown at this time
Participants	Aphasic stroke patients

Breitenfeld 2005 *(Continued)*

Interventions	Music therapy
Outcomes	Speech
Starting date	
Contact information	Dr Demarin Vida Email: vida.demarin@zg.t-com.hr
Notes	Preliminary results were presented at the 14th European Stroke Conference (30 patients) Authors will provide data as soon as the study is completed

Magee 2006

Trial name or title	Music therapy for adults with acquired brain injury
Methods	Validation study of measurement tools for music therapy with adults with acquired brain injury in rehabilitation
Participants	Adults with acquired brain injury
Interventions	Music therapy
Outcomes	Functional outcomes across behavioral, visual, auditory, communication and physical domains
Starting date	
Contact information	Email: drwmagee@rhn.org.uk
Notes	Multisite project validating 2 music therapy measures

ARAT: Action Research Arm Test
BI: Barthel index
BIT: Behavioral Inattention Test
mRS: modified Rankin Scale
NIHSS: National Institutes of Health Stroke Scale

DATA AND ANALYSES

Comparison 1. Music therapy versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Gait velocity	2	98	Mean Difference (IV, Fixed, 95% CI)	14.32 [10.98, 17.67]
2 Gait stride length	2	98	Mean Difference (IV, Fixed, 95% CI)	0.23 [0.14, 0.32]
3 Gait cadence	2	98	Mean Difference (IV, Random, 95% CI)	16.71 [3.40, 30.01]
4 Gait symmetry	2	98	Mean Difference (IV, Fixed, 95% CI)	0.12 [0.09, 0.15]

Analysis 1.1. Comparison 1 Music therapy versus control, Outcome 1 Gait velocity.

Review: Music therapy for acquired brain injury

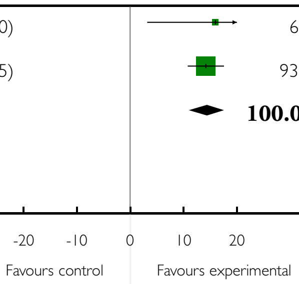
Comparison: 1 Music therapy versus control

Outcome: 1 Gait velocity

Study or subgroup	Experimental N	Experimental Mean(SD)[meters/min]	Control N	Control Mean(SD)[meters/min]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Thaut 1997	10	48 (18)	10	32 (10)		6.9 %	16.00 [3.24, 28.76]
Thaut 2007	43	34.5 (9.1)	35	20.3 (6.5)		93.1 %	14.20 [10.73, 17.67]
Total (95% CI)	**53**		**45**			**100.0 %**	**14.32 [10.98, 17.67]**

Heterogeneity: Chi^2 = 0.07, df = 1 (P = 0.79); I^2 =0.0%

Test for overall effect: Z = 8.39 (P < 0.00001)



Analysis 1.2. Comparison 1 Music therapy versus control, Outcome 2 Gait stride length.

Review: Music therapy for acquired brain injury

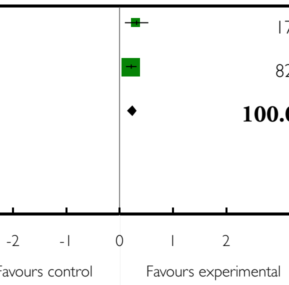
Comparison: 1 Music therapy versus control

Outcome: 2 Gait stride length

Study or subgroup	Experimental N	Experimental Mean(SD)[meters]	Control N	Control Mean(SD)[meters]	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Thaut 1997	10	1 (0.3)	10	0.69 (0.19)		17.5 %	0.31 [0.09, 0.53]
Thaut 2007	43	0.88 (0.21)	35	0.67 (0.24)		82.5 %	0.21 [0.11, 0.31]
Total (95% CI)	**53**		**45**			**100.0 %**	**0.23 [0.14, 0.32]**

Heterogeneity: $Chi^2 = 0.65$, df = 1 (P = 0.42); $I^2 = 0.0\%$

Test for overall effect: Z = 4.85 (P < 0.00001)



Analysis 1.3. Comparison 1 Music therapy versus control, Outcome 3 Gait cadence.

Review: Music therapy for acquired brain injury

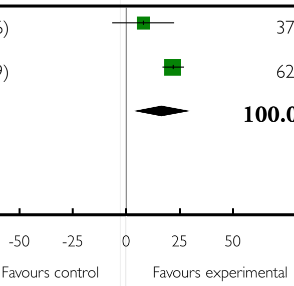
Comparison: 1 Music therapy versus control

Outcome: 3 Gait cadence

Study or subgroup	Experimental N	Experimental Mean(SD)[steps/min]	Control N	Control Mean(SD)[steps/min]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Thaut 1997	10	98 (17)	10	90 (16)		37.8 %	8.00 [-6.47, 22.47]
Thaut 2007	43	82 (12.9)	35	60 (9.9)		62.2 %	22.00 [16.94, 27.06]
Total (95% CI)	**53**		**45**			**100.0 %**	**16.71 [3.40, 30.01]**

Heterogeneity: $Tau^2 = 67.41$; $Chi^2 = 3.20$, df = 1 (P = 0.07); $I^2 = 69\%$

Test for overall effect: Z = 2.46 (P = 0.014)



Analysis 1.4. Comparison 1 Music therapy versus control, Outcome 4 Gait symmetry.

Review: Music therapy for acquired brain injury

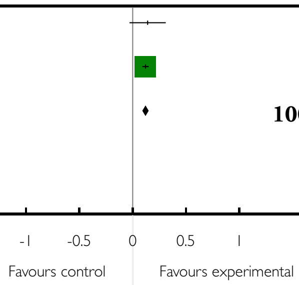
Comparison: 1 Music therapy versus control

Outcome: 4 Gait symmetry

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Thaut 1997	10	0.82 (0.14)	10	0.68 (0.23)		2.7 %	0.14 [-0.03, 0.31]
Thaut 2007	43	0.58 (0.05)	35	0.46 (0.07)		97.3 %	0.12 [0.09, 0.15]
Total (95% CI)	**53**		**45**			**100.0 %**	**0.12 [0.09, 0.15]**

Heterogeneity: Chi^2 = 0.05, df = 1 (P = 0.82); I^2 =0.0%

Test for overall effect: Z = 8.68 (P < 0.00001)



APPENDICES

Appendix 1. CENTRAL search strategy

#1	MeSH descriptor Cerebrovascular Disorders explode all trees
#2	(stroke in All Text or poststroke in All Text or post-stroke in All Text or cerebrovasc* in All Text or (brain in All Text and vasc* in All Text) or (cerebral in All Text and vasc* in All Text) or cva* in All Text or apoplex* in All Text or SAH in All Text)
#3	(brain* in All Text or cerebr* in All Text or cerebell* in All Text or intracran* in All Text or intracerebral in All Text)
#4	(ischemi* in All Text or ischaemi* in All Text or infarct* in All Text or thrombo* in All Text or emboli* in All Text or occlus* in All Text)
#5	(#3 and #4)
#6	(brain* in All Text or cerebr* in All Text or cerebell* in All Text or intracerebral in All Text or intracranial in All Text or subarachnoid in All Text)
#7	(haemorrhage* in All Text or hemorrhage* in All Text or haematoma* in All Text or hematoma* in All Text or bleed* in All Text)

(*Continued*)

#8	(#6 and #7)
#9	MeSH descriptor hemiplegia this term only
#10	MeSH descriptor paresis explode all trees
#11	(hemipleg* in All Text or hemipar* in All Text or paresis in All Text or paretic in All Text)
#12	MeSH descriptor aphasia explode all trees
#13	(aphasi* in All Text or dysphasi* in All Text)
#14	MeSH descriptor craniocerebral trauma this term only
#15	MeSH descriptor brain injuries explode all trees
#16	MeSH descriptor Head Injuries, Closed explode all trees
#17	MeSH descriptor Intracranial Hemorrhage, Traumatic explode all trees
#18	MeSH descriptor skull fractures explode all trees
#19	MeSH descriptor Brain Damage, Chronic this term only
#20	MeSH descriptor Brain Injury, Chronic this term only
#21	MeSH descriptor brain stem explode all trees with qualifiers: IN
#22	MeSH descriptor cerebellum explode all trees with qualifiers: IN
#23	(head in All Text or brain* in All Text or cerebral in All Text or cranial in All Text or craniocerebral in All Text or skull in All Text)
#24	(injur* in All Text or trauma* in All Text or damage* in All Text)
#25	(#23 and #24)
#26	(diffuse in All Text and axonal in All Text and injur* in All Text)
#27	MeSH descriptor anoxia this term only
#28	MeSH descriptor encephalitis explode all trees
#29	MeSH descriptor meningitis explode all trees
#30	MeSH descriptor brain neoplasms explode all trees

(*Continued*)

#31	(anoxi* in All Text or hypoxi* in All Text or encephalit* in All Text or meningit* in All Text)
#32	(brain in All Text or cereb* in All Text)
#33	(neoplasm* in All Text or lesion* in All Text or tumor* in All Text or tumour* in All Text)
#34	(#32 and #33)
#35	MeSH descriptor music this term only
#36	MeSH descriptor music therapy this term only
#37	MeSH descriptor acoustic stimulation this term only
#38	(music* in All Text or rhythmic* in All Text or melod* in All Text)
#39	(auditory in All Text or acoustic in All Text)
#40	(stimulat* in All Text or cue* in All Text)
#41	(#39 and #40)
#42	(sing in All Text or sings in All Text or singing in All Text or song* in All Text or compose in All Text or composing in All Text or improvis* in All Text)
#43	(#35 or #36 or #37 or #38 or #41 or #42)
#44	(#1 or #2 or #5 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #34)
#45	(#43 and #44)

Appendix 2. MEDLINE search strategy

MEDLINE (Ovid)

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or cerebrovascular accident/ or exp brain infarction/ or exp cerebrovascular trauma/ or exp hypoxia-ischemia, brain/ or exp intracranial arterial diseases/ or intracranial arteriovenous malformations/ or exp “Intracranial Embolism and Thrombosis”/ or exp intracranial hemorrhages/ or vasospasm, intracranial/ or vertebral artery dissection/
2. (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw.
3. ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw.
4. ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw.
5. hemiplegia/ or exp paresis/
6. (hemipleg$ or hemipar$ or paresis or paretic).tw.
7. exp aphasia/
8. (aphasi$ or dysphasi$).tw.

9. craniocerebral trauma/ or exp brain injuries/ or exp head injuries, closed/ or exp intracranial hemorrhage, traumatic/ or exp skull fractures/
10. brain damage, chronic/ or brain injury, chronic/
11. exp brain stem/in or exp cerebellum/in
12. ((head or brain$ or cerebral or cranial or craniocerebral or skull) adj5 (injur$ or trauma$ or damage$)).tw.
13. diffuse axonal injur$.tw.
14. anoxia/ or exp encephalitis/ or exp meningitis/ or exp brain neoplasms/
15. (anoxi$ or hypoxi$ or encephalit$ or meningit$).tw.
16. ((brain or cereb$) and (neoplasm$ or lesion$ or tumor$ or tumour$)).tw.
17. or/1-16
18. music/ or music therapy/ or acoustic stimulation/
19. (music$ or rhythmic$ or melod$).tw.
20. ((auditory or acoustic) adj5 (stimulat$ or cue$)).tw.
21. (sing or sings or singing or song$ or compose or composing or improvis$).tw.
22. or/18-21
23. Randomized Controlled Trials/
24. random allocation/
25. Controlled Clinical Trials/
26. control groups/
27. clinical trials/
28. double-blind method/
29. single-blind method/
30. Placebos/
31. placebo effect/
32. cross-over studies/
33. Multicenter Studies/
34. Therapies, Investigational/
35. Research Design/
36. Program Evaluation/
37. evaluation studies/
38. randomized controlled trial.pt.
39. controlled clinical trial.pt.
40. clinical trial.pt.
41. multicenter study.pt.
42. evaluation studies.pt.
43. random$.tw.
44. (controlled adj5 (trial$ or stud$)).tw.
45. (clinical$ adj5 trial$).tw.
46. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
47. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
48. ((multicenter or multicentre or therapeutic) adj5 (trial$ or stud$)).tw.
49. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
50. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
51. (coin adj5 (flip or flipped or toss$)).tw.
52. latin square.tw.
53. versus.tw.
54. (cross-over or cross over or crossover).tw.
55. placebo$.tw.
56. sham.tw.
57. (assign$ or alternate or allocat$ or counterbalance$ or multiple baseline).tw.
58. controls.tw.
59. (treatment$ adj6 order).tw.
60. journal of music therapy.jn.

61. or/23-60
62. 17 and 22 and 61
63. limit 62 to humans

Appendix 3. Embase search strategy

1 CEREBROVASCULAR-DISEASE#.DE. 127204
2 BASAL-GANGLION#.DE. 7146
3 BRAIN-ISCHEMIA#.DE. 27862
4 CAROTID-ARTERY-DISEASE#.DE. 13288
5 CEREBROVASCULAR-ACCIDENT#.DE. 15445
6 BRAIN-HYPOXIA#.DE. 3930
7 BRAIN-ARTERIOVENOUS-MALFORMATION#.DE. 1883
8 BRAIN-EMBOLISM#.DE. 2186
9 THROMBOSIS#.W..DE. 60661
10 8 AND 9 262
11 BRAIN-HEMORRHAGE#.DE. 23280
12 BRAIN-VASOSPASM#.DE. 1756
13 ARTERY-DISSECTION#.DE. 2636
14 BRAIN#.W.DE. 265092
15 13 AND 14 334
16 VERTEBRAL-ARTERY#.DE. 2779
17 ARTERY-DISSECTION#.DE. 2636
18 16 AND 17 419
19 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 10 OR 11 OR 12 OR 15 OR 18 135371
20 (STROKE OR POSTSTROKE OR POST-STROKE).TI,AB. 55444
21 (CEREBROVASC$5 OR BRAIN ADJ VASC$5 OR CEREBRAL ADJ VASC$5 OR CVA$1 OR APOPLEX$2 OR SAH).TI,AB. 18086
22 20 OR 21 69383
23 BRAIN$1 OR CEREB$3 OR CEREBELL$2 OR INTRACRAN$3 OR INTRACERE BRAL 461900
24 23.TI,AB. 311588
25 (ISCH$5 OR CMA OR INFARCT$3 OR THROMBO$3 OR EMBOLIS$1 OR OCCLUS$3).TI,AB. 216016
26 24 NEAR 25 27603
27 (BRAIN$1 OR CEREBR$3 OR CEREBELL$3 OR INTRACEREBRAL OR INTRACRANIAL OR SUBARACHNOID).TI,AB. 314775
28 (HAEMORRHAGE$1 OR HEMORRHAGE$1 OR HAEMATOMA$1 OR HEMATOMA$1 OR BLEED$3).TI,AB. 90167
29 27 NEAR 28 15381
30 HEMIPLEGIA#.W..DE. 3127
31 PARESIS#.W..DE. 1597
32 30 OR 31 4672
33 (HEMIPLEG$2 OR HEMIPAR$4 OR PARESIS OR PARETIC).TI,AB. 8703
34 APHASIA#.W..DE. 5128
35 (APHASI$1 OR DYSPHASI$1).TI,AB. 4272
36 HEAD-INJURY#.DE. 58268
37 BRAIN-INJURY#.DE. 35070
38 BRAIN-HEMORRHAGE#.DE. 23280
39 SKULL-FRACTURE#.DE. OR TRAUMATIC-BRAIN-INJURY#.DE. 5646
40 36 OR 37 OR 38 OR 39 78916
41 BRAIN ADJ DAMAGE ADJ CHRONIC 7
42 BRAIN ADJ STEM 16877
43 BRAIN-STEM#.DE. 43572
44 CEREBELLUM 24297

45 CEREBELLUM#.W..DE. 19781
46 (IN ADJ 43 OR 45).TI,AB. 0
47 (BRAINSTEM OR CEREBELLUM).TI,AB. 26391
48 (43 OR 44 OR 47).TI,AB. 26391
49 (HEAD OR BRAIN$1 OR CEREBRAL OR CRANIAL OR CRAIOCEREBRAL OR SKULL).TI,AB. 364290
50 (INJUR$3 OR TRAUMA$1 OR DAMAGE$1).TI,AB. 317818
51 49 OR 50 625696
52 (DIFFUSE ADJ AXONAL ADJ INJUR$3).TI,AB. 370
53 ANOXIA 2563
54 ANOXIA#.W..DE. 1718
55 ENCEPHALITIS 11397
56 ENCEPHALITIS#.W..DE. 18509
57 MENINGITIS 16834
58 MENINGITIS#.W..DE. 17163
59 BRAIN ADJ NEOPLASMS 157
60 BRAIN-TUMOR#.DE. 29864
61 54 OR 56 OR 58 OR 60 63435
62 (ANOXI$2 OR HYPOX$2 OR ENCEPHALIT$2 OR MENINGIT$2).TI,AB. 50200
63 (BRAIN OR CEREB$5).TI,AB. 296238
64 (NEOPLASM$1 OR LESION$1 OR TUMOR$1 OR TUMOUR$1).TI,AB. 554036
65 63.TI,AB. AND 64.TI,AB. 46422
66 49 NEAR 50 36758
67 19 OR 22 OR 26 OR 29 OR 32 OR 33 OR 34 OR 35 OR 40 OR 48 OR 66 OR 52 OR 61 OR 62 OR 65 336986
68 MUSIC ADJ THERAPY OR MUSIC 3983
69 MUSIC-THERAPY#.DE. OR MUSIC#.W..DE. 3039
70 (MUSIC$2 OR RHYTHMIC$2 OR MELOD$2 OR ACOUSTIC ADJ STIMULATION).TI,AB. 8686
71 (AUDITORY OR ACOUSTIC).TI,AB. 36263
73 (STIMULAT$3 OR CUE$1).TI,AB. 318466
74 71 NEAR 73 2253
75 (SING OR SINGS OR SINGING OR SONG$1 OR COMPOSE OR COMPOSING OR IMPROVIS$3).TI,AB. 4084
76 69 OR 70 OR 74 OR 75 15281
79 RANDOMIZED-CONTROLLED-TRIAL#.DE. 140800
80 RANDOM ADJ ALLOCATION 382
81 RANDOMIZED ADJ ALLOCATION 89
82 CLINICAL-TRIAL#.DE. 432115
83 CONTROL ADJ GROUPS 105179
84 CLINICAL-TRIAL#.DE. 432115
86 (DOUBLE ADJ BLIND ADJ METHOD).TI,AB. 94
90 (RANDOM ADJ ALLOCATION).TI,AB. 382
91 (CONTROL ADJ GROUPS).TI,AB. 104560
92 (DOUBLE ADJ BLIND).TI,AB. 48103
93 (SINGLE ADJ BLIND).TI,AB. 3864
95 PLACEBOS 105823
96 PLACEBO 105823
97 PLACEBO#.W..DE. 75282
98 (PLACEBO ADJ EFFECT).TI,AB. 1233
99 95 OR 96 OR 97 OR 98 105823
100 83 OR 84 OR 90 OR 91 OR 92 OR 93 522209
101 (CROSS ADJ OVER ADJ STUDIES).TI,AB. 2307
103 (MULTICENTER ADJ STUDIES OR MULTICENTER ADJ STUDY).TI,AB. 9887
104 THERAPIES ADJ INVESTIGATIONAL 15
105 (THERAPIES ADJ INVESTIGATIONAL).TI,AB. 15
106 (INVESTIGATIONAL ADJ THERAPIES).TI,AB. 106

107 INVESTIGATIONAL ADJ THERAPY 106
108 (INVESTIGATION ADJ THERAPY).TI,AB. 134
111 (RESEARCH ADJ DESIGN).TI,AB. 6513
114 (PROGRAM ADJ EVALUATION).TI,AB. 848
115 (EVALUATION ADJ STUDIES OR EVALUATION ADJ STUDY).TI,AB. 1440
116 (MULTICENTRE ADJ STUDY).TI,AB. 9887
117 RANDOM$4.TI,AB. 272854
118 (CONTROLLED NEAR TRAIL$1 OR STUD$3).TI,AB. 2227101
119 (CLINICAL NEAR TRIAL$1 OR STUD$3).TI,AB 2264572
120 (CLINICAL NEAR TRIAL$1).TI,AB. 88793
121 (CONTROL OR TREATMENT OR EXPERIMENT$5 OR INTERVENTION).TI,AB 1911277
122 (GROUP$1 OR SUBJECT$1 OR PATIENT$1).TI,AB. 2143855
123 (121 NEAR 122).TI,AB. 452104
124 (QUASI-RANDOM$4 OR QUASI ADJ RAMDOM$4 OR PSEUDO-RANDOM$4 OR PSEUDO ADJ RANDOM$4).TI,AB. 203
125 (MUTICENTER OR MULTICENTRE OR THERAPEUTIC).TI,AB. 252037
126 (TRIAL$1 OR STUD$3).TI,AB. 2321790
127 (MULTICENTER OR MULTICENTRE OR THERAPEUTIC).TI,AB. 252031
128 (127 NEAR 126).TI,AB. 41906
129 (CONTROL OR EXPERIMENT$3 OR CONSERVATIVE).TI,AB. 1033345
130 (TREATMENT OR THERAPY OR PROCEDURE OR MANAGE$4).TI,AB. 1542337
131 (129 NEAR 130).TI,AB. 65544
132 (SINGL$1 OR DOUBL$1 OR TRIPL$1 OR TREBL$1).TI,AB. 465484
133 (BLIND$2 OR MASK$2).TI,AB. 94835
134 (132 NEAR 133).TI,AB. 57683
135 (FLIP OR FLIPPED OR TOSS$2).TI,AB. 2874
136 COIN.TI,AB. 807
137 (136 NEAR 135).TI,AB. 42
138 (LATIN ADJ SQUARE).TI,AB. 536
139 VERSUS.TI,AB. 155325
140 (CROSS-OVER OR CROSS ADJ OVER OR CROSSOVER).TI,AB. 23436
141 PLACEBO$1.TI,AB. 70826
142 SHAM.TI,AB. 21506
143 (ASSIGN$2 OR ALTERNATE OR ALLOCAT$3 OR COUNTERBALANCE$1 OR MULTIPLE ADJ BASELINE).TI,AB. 93768
144 CONTROLS.TI,AB. 702865
145 (TREATMENT$1 NEAR ORDER).TI,AB. 5973
146 (JOURNAL ADJ OF ADJ MUSIC ADJ THERAPY).SO. 0
147 138 OR 139 OR 140 OR 141 OR 142 250805
148 (138 OR 139 OR 140 OR 141 OR 142).TI,AB. 250805
149 (144 OR 146 OR 146).TI,AB. 702865
150 99 OR 100 OR 101 OR 103 OR 108 OR 114 OR 115 OR 116 OR 118 OR 123 OR 128 OR 131 OR 143 OR 137 OR 148 OR 149 2844110
151 150.TI,AB. 2704175
152 67 AND 76 AND 151 990
153 152 AND HUMAN=YES 635

Appendix 4. CINAHL search strategy

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature, 1982 to March 2010; EBSCO
S38 .S28 and S37
S37 .S29 or S30 or S31 or S32 or S35 or S36
S36 .TI (sing or sings or singing or song* or compose or composing or improvis*) or AB (sing or sings or singing or song* or compose or composing or improvis*)
S35 .S33 and S34
S34 .TI (stimulat* or cue*) or AB (stimulat* or cue*)
S33 .TI (auditory or acoustic) or AB (auditory or acoustic)
S32 .TI (music* or rhythmic* or melod*) or AB (music* or rhythmic* or melod*)
S31 .(MH "Singing")
S30 .(MH "Acoustic Stimulation")
S29 .(MH "Music") or (MH "Music Therapy") or (MH "Music Therapy (IowaNIC)") or (MH "Performing Artists") or (MH "Performing Arts")
S28 .S1 or S2 or S5 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S27
S27 .S25 and S26
S26 .TI (neoplasm* or lesion* or tumor* or tumour*) or AB (neoplasm* or lesion* or tumor* or tumour*)
S25 .TI (brain or cereb*) or AB (brain or cereb*)
S24 .TI (anoxi* or hypoxi* or encephalit* or meningit*) or AB (anoxi* or hypoxi* or encephalit* or meningit*)
S23 .(MH "Brain Neoplasms+")
S22 .(MH "Meningitis+")
S21 .(MH "Encephalitis+")
S20 .(MH "Anoxia")
S19 .TI diffuse axonal injur* or AB diffuse axonal injur*
S18 .S16 and S17
S17 .TI (injur* or trauma* or damage*) or AB (injur* or trauma* or damage*)
S16 .TI (head or brain* or cerebral or cranial or craniocerebral or skull) or AB (head or brain* or cerebral or cranial or craniocerebral or skull)
S15 .(MH "Brain Stem/IN") or (MH "Cerebellum/IN")
S14 .(MH "Brain Damage, Chronic")
S13 .(MH "Head Injuries+")
S12 .TI (aphasi* or dysphasi*) or AB (aphasi* or dysphasi*)
S11 .(MH "Aphasia+")
S10 .TI (hemipleg* or hemipar* or paresis or paretic) or AB (hemipleg* or hemipar* or paresis or paretic)
S9 .(MH "Hemiplegia")
S8 .S6 and S7
S7 .TI (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*) or AB (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)
S6 .TI (brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid) or AB (brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid)
S5 .S3 and S4
S4 .TI (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus*) or AB (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus*)
S3 .TI (brain* or cerebr* or cerebell* or intracran* or intracerebral) or AB (brain* or cerebr* or cerebell* or intracran* or intracerebral)
S2 .TI (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc or cva or apoplex or SAH) or AB (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc or cva or apoplex or SAH)
S1 .(MH "Cerebrovascular Disorders+") or (MH "stroke patients") or (MH "stroke units")

Appendix 5. PsycInfo search strategy

Database: PsycINFO; 1806 to July Week 4 2009

1 Music/ (7866)

2 Music Therapy/ (2235)

3 exp Auditory Stimulation/ or acoustic stimulation.mp. (19648)

4 (music$ or rhythmic$ or melod$).tw. (25383)

5 ((auditory or acoustic) adj5 (stimulat$ or cue$)).tw. (4605)

6 (sing or sings or singing or song$ or compose or composing or improvis$).tw. (9531)

7 or/1-6 (52839)

8 cerebrovascular disorders/ or exp cerebral ischemia/ or exp carotid arteries/ or cerebrovascular accident/ or exp brain damage/ or exp embolisms/ or exp cerebral hemorrhage/ or aneurysms/ (29149)

9 (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw. (12629)

10 ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw. (2795)

11 ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw. (1149)

12 hemiplegia/ (592)

13 exp paresis/ (126)

14 (hemipleg$ or hemipar$ or paresis or paretic).tw. (2942)

15 exp aphasia/ (12045)

16 (aphasi$ or dysphasi$).tw. (9512)

17 exp head injuries/ (3939)

18 exp Brain Damage/ (20526)

19 ((head or brain$ or cerebral or cranial or craniocerebral or skull) adj5 (injur$ or trauma$ or damage$)).tw. (25819)

20 diffuse axonal injur$.tw. (99)

21 exp ANOXIA/ (1219)

22 exp encephalitis/ (1000)

23 exp meningitis/ (252)

24 exp brain neoplasms/ (899)

25 (anoxi$ or hypoxi$ or encephalit$ or meningit$).tw. (5125)

26 ((brain or cereb$) and (neoplasm$ or lesion$ or tumor$ or tumour$)).tw. (16302)

27 or/8-26 (72335)

28 empirical study.md. (1177004)

29 followup study.md. (31660)

30 longitudinal study.md. (57905)

31 prospective study.md. (9953)

32 quantitative study.md. (396174)

33 “2000”.md. (Treatment Outcome/Randomized Clinical Trial) (14862)

34 treatment effectiveness evaluation/ (10973)

35 exp hypothesis testing/ (1992)

36 repeated measures/ (449)

37 exp experimental design/ (40424)

38 placebo$.ti,ab. (22661)

39 random$.ti,ab. (82864)

40 (clin$ adj25 trial$).ti,ab. (14727)

41 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab. (13966)

42 or/28-41 (1225715)

43 7 and 27 and 42 (874)

44 limit 43 to human (798)

45 (infant$ or neonat$ or child$).tw. (455254)

46 44 not 45 (635)

Appendix 6. LILACS search strategy

((([MH] (music$)) or (((music and therapy))) or (([MH]"MUSIC THERAPY")) or ((((rhythmic and auditory and stimulation))) or ((([MH] ("auditory stimulation")) AND or (((singing or song$))) AND Group=Humans (313)

Appendix 7. AMED search strategy

Database: AMED (Allied and Complementary Medicine) 1985 to August 2009
1 music/ or music therapy/ or acoustic stimulation/ (540)
2 (music$ or rhythmic$ or melod$).tw. (1145)
3 ((auditory or acoustic) adj5 (stimulat$ or cue$)).tw. (86)
4 (sing or sings or singing or song$ or compose or composing or improvis$).tw. (205)
5 4 or 1 or 3 or 2 (1354)
6 exp Cerebral ischemia/ (102)
7 exp Cerebrovascular disorders/ (5456)
8 carotid artery diseases.mp. (2)
9 exp Cerebrovascular accident/ (1505)
10 brain infarction.mp. (12)
11 exp Brain injuries/ (3171)
12 (stroke or poststroke or post-stroke or cerebrovasc$ or brain vasc$ or cerebral vasc$ or cva$ or apoplex$ or SAH).tw. (6235)
13 ((brain$ or cerebr$ or cerebell$ or intracran$ or intracerebral) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$)).tw. (447)
14 ((brain$ or cerebr$ or cerebell$ or intracerebral or intracranial or subarachnoid) adj5 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).tw. (188)
15 hemiplegia/ or exp paresis/ (956)
16 (hemipleg$ or hemipar$ or paresis or paretic).tw. (1925)
17 (aphasi$ or dysphasi$).tw. (587)
18 exp aphasia/ (408)
19 brain damage.mp. (220)
20 ((head or brain$ or cerebral or cranial or craniocerebral or skull) adj5 (injur$ or trauma$ or damage$)).tw. (4671)
21 diffuse axonal injur$.tw. (21)
22 exp Anoxia/ (109)
23 exp Encephalitis/ (22)
24 exp Meningitis/ (27)
25 exp Brain neoplasms/ (118)
26 (anoxi$ or hypoxi$ or encephalit$ or meningit$).tw. (374)
27 ((brain or cereb$) and (neoplasm$ or lesion$ or tumor$ or tumour$)).tw. (786)
28 or/6-27 (12769)
29 Randomized controlled trials/ (1357)
30 random allocation/ (288)
31 clinical trials/ (1625)
32 Double blind method/ (389)
33 single-blind method/ (1)
34 Placebos/ (504)
35 Research Design/ (1640)
36 Program Evaluation/ (1766)
37 randomized controlled trial.pt. (1384)
38 controlled clinical trial.pt. (69)
39 clinical trial.pt. (1103)
40 multicenter study.pt. (233)
41 evaluation studies.pt. (103)
42 random$.tw. (10474)
43 (controlled adj5 (trial$ or stud$)).tw. (5636)

44 (clinical$ adj5 trial$).tw. (3992)
45 ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw. (16898)
46 (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw. (42)
47 ((multicenter or multicentre or therapeutic) adj5 (trial$ or stud$)).tw. (1096)
48 ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw. (2948)
49 ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw. (1870)
50 (coin adj5 (flip or flipped or toss$)).tw. (3)
51 latin square.tw. (24)
52 versus.tw. (3434)
53 (cross-over or cross over or crossover).tw. (674)
54 placebo$.tw. (2228)
55 sham.tw. (564)
56 (assign$ or alternate or allocat$ or counterbalance$ or multiple baseline).tw. (4709)
57 controls.tw. (3690)
58 (treatment$ adj6 order).tw. (305)
59 or/29-58 (36291)
60 59 and 28 and 5 (26)

Appendix 8. Science Citation Index search strategy

# 59	94	#58 AND #45 AND #11
# 58	>100,000	#57 OR #56 OR #55 OR #54 OR #53 OR #52 OR #51 OR #50 OR #49 OR #48 OR #47 OR #46
# 57	>100,000	TS=((control* or prospectiv* or volunteer*))
# 56	2,536	TS=((prospective stud*))
# 55	6,024	TS=((follow up stud*))
# 54	9,689	TS=((evaluation stud*))
# 53	41,459	TS=((comparative study))
# 52	78,169	TS=((random*))
# 51	15,695	TS=((placebo*))
# 50	25,464	TS=((Clinical trial*))
# 49	548	TS=((single blind method*))
# 48	4,496	TS=((double blind method*))
# 47	16,727	TS=((Randomized controlled trial*))
# 45	24,620	#44 OR #43 OR #42 OR #41 OR #40 OR #39 OR #38 OR #37 OR #36 OR #35 OR #34 OR #33 OR #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR

(*Continued*)

		#19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12
# 44	2,467	TS=((anoxi* or hypoxi* or encephalit* or meningit*))
# 43	1,407	TS=((anoxia or encephalitis or meningitis or brain neoplasm*))
# 42	99	TS=((diffuse axonal injur*))
# 41	466	TS=((chronic brain injury))
# 40	332	TS=((chronic brain damage))
# 39	81	TS=((skull fractures))
# 38	7	TS=((traumatic intracranial haemorrhage))
# 37	19	TS=((traumatic intracranial hemorrhage))
# 36	1,607	TS=((closed head injur*))
# 35	1,337	TS=((brain injuries))
# 34	45	TS=((craniocerebral trauma))
# 33	6,984	TS=((aphasi* or dysphasi*))
# 32	5,368	TS=(Aphasia)
# 31	240	TS=((hemiplegi*or hemipar* or paresis or paretic))
# 30	27	TS=((intracranial haemorrhage))
# 29	12,095	TS=((stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc* or cva* or apoplex* or SAH))
# 28	1	TS=((intracranial artery dissection))
# 27	2	TS=((vertebral artery dissection))
# 26	8	TS=((intracranial vasospasm*))
# 25	150	TS=((intracranial hemorrhage*))
# 24	10	TS=((Intracranial Thrombosis*))
# 23	5	TS=((Intracranial Embolism*))

(*Continued*)

# 22	9	TS=((intracranial arteriovenous malformation*))
# 21	10	TS=((intracranial arterial disease*))
# 20	19	TS=((hypoxia-ischemia))
# 19	27	TS=((cerebrovascular trauma))
# 18	407	TS=((brain infarction))
# 17	373	TS=((cerebrovascular accident))
# 16	211	TS=((carotid artery disease*))
# 15	234	TS=((brain ischemia))
# 14	18	TS=((basal ganglia cerebrovascular disease))
# 13	585	TS=((cerebrovascular disorder*))
# 12	63	TS=((cerebral vascular accident))
# 11	24,182	#10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1
# 10	26	TS=((melodic intonation therapy))
# 9	3,865	TS=((sing OR singing OR song OR sings OR improvis*))
# 8	657	TS=((acoustic cue*))
# 7	1,316	TS=((auditory cue*))
# 6	1,415	TS=((auditory stimulat*))
# 5	490	TS=((acoustic stimulat*))
# 4	463	TS=((acoustic stimulation))
# 3	17,736	TS=((rhythmic* OR melod* OR music*))
# 2	12,135	TS=(music)
# 1	1,089	TS=((music therapy))

Appendix 9. CAIRSS search strategy

1. Brain injur? [as a phrase] OR head injur? [as a phrase] OR skull fracture [as a phrase] (10)
2. Brain damage [as a phrase] OR cerebral trauma [as a phrase] OR brain neoplasm? [as a phrase] (61)
3. Brain tumor? [as a phrase] OR cereb? tumor? [as a phrase] OR brain infarction [as a phrase] (2)
4. cerebrovascular disorder? [as a phrase] OR brain ischemia [as a phrase] OR cerebrovascular accident [as a phrase] (3)
5. intracranial hemorrhage? [as a phrase] OR stroke OR poststroke (17)
6. post-stroke [as a phrase] OR cva OR cereb? Thrombosis [as a phrase] (15)
7. brain thrombosis [as a phrase] OR brain embolism [as a phrase] (0)
8 hemiplegi? OR paresis OR paretic (1)
9. Aphasi? OR dysphasi? (61)

Appendix 10. Proquest Digital Dissertations search strategy

(music) OR ((music therapy)) OR ((rhythmic auditory stimulation)) OR ((acoustic stimulation)) OR ((rhythmic auditory cueing)) OR ((auditory stimulation)) AND (stroke OR head OR brain OR intracranial OR cerebrovascular) (543)

Appendix 11. ClinicalTrials.gov search strategy

music OR (music therapy) OR singing OR song OR songs OR (rhythmic auditory stimulation) OR (rhythmic auditory cueing) OR (acoustic stimulation) OR (acoustic cueing) OR melody OR melodic (247)

Appendix 12. Current Controlled Trials search strategy

music OR (music therapy) (26)

Appendix 13. National Research Register search strategy

(music OR (music therapy) OR (rhythmic auditory stimulation) OR (rhythmic auditory cueing) OR (acoustic stimulation) OR (acoustic cueing) OR melodic) AND (stroke OR poststroke OR cerebrovascular OR (brain ischemia) or (brain infarction) OR (brain injur$) OR intracranial OR aphasi$ OR dysphasi$ OR hemiplegi$ OR paretic OR paresis OR (head injur$) OR (brain trauma) OR (brain damage) OR encephalitis OR meningitis OR (brain tumor) OR (brain neoplasm) OR (brain tumour)) (145)

Appendix 14. Rehab Trials.org

music (0)
music therapy (0)
rhythmic (0)
Auditory stimulation (0)
Acoustic stimulation (0)
Melodic (0)

Appendix 15. Indexes to Theses

(music OR (music therapy) OR (rhythmic auditory stimulation) OR (rhythmic auditory cueing) OR (acoustic stimulation) OR (acoustic cueing) OR melodic) AND (stroke OR poststroke OR cerebrovascular OR (brain ischemia) or (brain infarction) OR (brain injur$) OR intracranial OR aphasi$ OR dysphasi$ OR hemiplegi$ OR paretic OR paresis OR (head injur$) OR (brain trauma) OR (brain damage) OR encephalitis OR meningitis OR (brain tumor) OR (brain neoplasm) OR (brain tumour)) (1)
(music OR (music therapy) OR (rhythmic auditory stimulation) OR (rhythmic auditory cueing) OR (acoustic stimulation) OR (acoustic cueing) OR melodic)AND (stroke OR brain OR head OP cerebrovascular OR intracranial) (14)

Appendix 16. The Specialist Music Therapy Research Database

The database is no longer functional. However, archives of dissertations and conference proceedings were handsearched

HISTORY

Protocol first published: Issue 4, 2007

Review first published: Issue 7, 2010

10 July 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Protocol

- Background, objectives, criteria for considering studies: Bradt, Magee, Dileo, Wheeler (approved by McGilloway)
- Search strategies, methods: Bradt (reviewed and approved by Magee, Dileo, Wheeler, McGilloway).

Review

- Searches: Bradt, Wheeler, Magee, McGilloway
- Trials selection: Wheeler, Magee, Bradt (Dileo, in case of disagreement)
- Interrater reliability (trial selection): Bradt
- Development of coding form: Bradt
- Data extraction: Bradt and trained research assistant
- Quality assessment of trials: Bradt and Dileo
- Data entry: Bradt
- Data analysis: Bradt and Dileo

DECLARATIONS OF INTEREST

Four of the review authors (JB, CD, WM, BW) are music therapists. Wendy Magee is involved in the design, conduct and publication of studies, of which one (Magee 2006) it is currently in the Ongoing studies section. Barbara Wheeler was involved in one study that was considered for this review (Nayak 2000), but it was subsequently excluded.

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Internal sources

- No sources of support supplied

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- State of Pennsylvania Formula Fund, USA.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The following journal was added for the handsearching: *Japanese Journal of Music Therapy.*