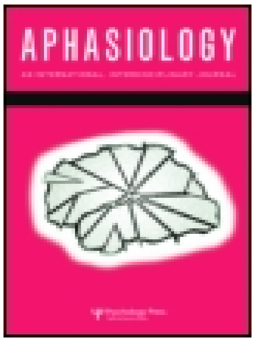

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Music-based interventions for aphasia could act through a motor-speech mechanism: a systematic review and case–control analysis of published individual participant data

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REVIEW

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Music-based interventions for aphasia could act through a motor-speech mechanism: a systematic review and case–control analysis of published individual participant data

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ABSTRACT

Background: Melodic Intonation Therapy, a music-based intervention for the recovery of oral language production in aphasia, has been shown to be particularly effective in patients with Broca's aphasia compared to other aphasia subtypes. It has been suggested that this therapy might improve language output by acting on motor-speech deficits often associated with Broca's aphasia. In this article, we examine the relevance of a motor-speech mechanism for music-based interventions designed to improve verbal expression in patients with any type of aphasia.
Aim: To test the association between the presence of motor-speech disorders (MSDs) and improvement with music-based protocols targeting verbal expression in participants with aphasia.
Methods and procedures: We conducted a systematic review of publications reporting language production outcomes following a music-based intervention in participants with aphasia and performed a case–control analysis on extracted individual participant data (IPD). The databases PubMed, MEDLINE (1800 to 9 March 2018), and PsycINFO (1806 to March 2018) were screened, followed with cross-referencing. We recorded data at the level of study and, when possible, at the IPD level. When not explicitly reported, we applied a series of heuristics to infer the presence/absence of an MSD in participants. Binomial logistic regressions were performed to ascertain the effects of the presence of an MSD, aphasia severity, treatment duration (in weeks), and treatment intensity (hours/week) on the likelihood that participants would show a speech or a language improvement following intervention.
Outcomes & Results: Forty original articles were included in this review. Twenty-two reported sufficient details to be included in our IPD analysis, for a total sample of 105 participants. Most interventions included some sort of singing as their primary music-based facilitation technique for language production. For speech improvement, statistically significant predictor variables were the presence of an MSD and treatment intensity. For language improvement, statistically significant predictor variables were the presence of an MSD, treatment intensity, and duration. Severity of aphasia was not associated with the likelihood of speech or language improvement.

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Supplementary data for this article can be accessed here.

Conclusion: Music-based interventions for language production in aphasia may act via a motor-speech mechanism. We suggest that music and singing-based therapies might be further investigated as treatment options for patients with MSDs, whether associated with aphasia or not.

Music-based interventions for aphasia have long interested clinicians and scientists. These therapeutic approaches are based on the observation that people with aphasia often have relatively preserved musical abilities (Bouillaud, 1865; Hébert, Racette, Gagnon, & Peretz, 2003; Peretz, Gagnon, Hébert, & Macoir, 2004; Schlaug, Marchina, & Norton, 2008; Stahl, Henseler, Turner, Geyer, & Kotz, 2013; Stahl, Kotz, Henseler, Turner, & Geyer, 2011; Wilson, Pearsons, & Reutens, 2006). In non-fluent aphasia, words can be better produced when patients sing familiar songs or novel lyrics in synchrony with an auditory model compared to when speaking (Racette, Bard, & Peretz, 2006; Straube, Schulz, Geipel, Mentzel, & Miltner, 2008; Yamadori, Osumi, Masuhar, & Okubo, 1977). Music-based interventions have leveraged these abilities for improving speech and language in aphasic patients. These protocols are usually administered by speech-language therapists, as in Melodic Intonation Therapy (MIT, Albert, Sparks, & Helm, 1973; Sparks, Helm, & Albert, 1974), by music therapists, as in the SIPARI protocol (Jungblut, 2009), or by both, as in Speech Music Therapy for Aphasia (SMTA, De Bruijn, Zielman, & Hurkmans, 2005). Some group interventions, such as participating in a choir, have also been proposed (e.g., Tamplin, Baker, Jones, Way, & Lee, 2013).

The most cited music-based intervention for aphasia (Hurkmans et al., 2012) is MIT (Albert & Bear, 1974; Albert et al., 1973). MIT is a formalised singing-based approach in which the speech-language therapist asks the patient to repeat with him/her a series of sentences embedded in a melody that exaggerates and simplifies the prosody of speech. This facilitation technique—referred to as intoned speech—is gradually replaced by normal speech by progressing through treatment levels. The efficacy of MIT on language production outcomes such as sentence repetition and informativeness of connected speech (efficacy of conveying accurate information) has been demonstrated in several studies (see Zumbansen, Peretz, & Hébert, 2014b for a review) and, more recently, in a randomised control trial (RCT), making this therapy one of the best-supported speech-language therapy approaches for aphasia recovery (Van Der Meulen, Van De Sandt, Heijenbrok-Kal, Visch-Brink, & Ribbers, 2014). However, the efficacy of MIT seems to be influenced by the clinical profile of aphasic patients. In 1994, the American Academy of Neurology published criteria for selecting patients most likely to respond well to MIT: unilateral brain lesions, relatively preserved auditory comprehension, non-fluent verbal production with diminished articulatory agility and effortful initiation of speech, poor repetition (even for single words), motivation and emotional stability, and good auditory span. It was concluded that patients with Broca's aphasia or variants of this syndrome are good candidates for MIT (Benson et al., 1994). In Broca's aphasia, verbal comprehension is relatively preserved compared to expression. Oral language is non-fluent and characterised by anomia (i.e., word-retrieval difficulty), agrammatism (i.e., grammar and syntax deficit), and often also by apraxia of speech

(AOS), a motor-speech disorder affecting the planning or programming of speech movements (Ballard, Granier, & Robin, 2000; McNeil, Robin, & Schmidt, 1997).

It has been suggested that MIT might be especially beneficial in Broca's aphasia (as compared to other aphasic syndromes) primarily through its effect on AOS (e.g., Mauszycki, Nessler, & Wambaugh, 2016; Tonkovich & Marquardt, 1977; Wan, Zheng, Marchina, Norton, & Schlaug, 2014; Zumbansen et al., 2014b). Support for this motor-speech hypothesis for the MIT mechanism includes the following factors: (a) AOS commonly co-occurs with Broca's aphasia compared to other aphasic syndromes (Basso, 2003; McNeil & Kent, 1990) and (b) agrammatism, a clinical marker of Broca's aphasia, does not greatly improve with MIT (Helm-Estabrooks & Albert, 2004). In early publications on MIT, authors asked whether the primary effect of the treatment would be to improve articulation (Helm-Estabrooks, 1983; Naeser & Helm-Estabrooks, 1985). Indeed, it is possible that improved language production in standard oral language tests following MIT might be due to motor-speech improvement because a reduction in AOS would allow language competence to be better expressed orally. However, over the years, longitudinal studies have predominantly tested MIT for its effect on language (Mauszycki et al., 2016; Zumbansen et al., 2014b).

Numerous clues suggest that the motor-speech deficits frequently associated with aphasia could be improved by the musical aspect of MIT. In participants with non-fluent aphasia, cross-sectional analyses have reported better intelligibility while singing and have related this facilitation effect to rhythmicity (Boucher, Garcia, Fleurant, & Paradis, 2001; Laughlin, Naeser, & Gordon, 1979; Racette et al., 2006; Stahl et al., 2011). It has been observed that sung words are articulated at a slower rate than spoken words, allowing more time for planning and articulation (Stahl & Kotz, 2014; Stahl et al., 2011). In line with this idea, Laughlin et al. (1979) have shown that syllable lengthening during MIT sessions helps participants with non-fluent aphasia to produce more phrases. Moreover, singing promotes regularity between syllable onsets due to musical beat structure, allowing for better timing predictability compared to normal speech (Gordon, Magne, & Large, 2011). According to the predictive coding and dynamic attending theories, word articulation might be facilitated by pacing via neural mechanisms of enhanced anticipation and better coupling of perception and production (Kotz & Schwartze, 2015; Schön & Tillmann, 2015). Finally, singing or rate/rhythm strategies have long been used for the facilitation of speech in various MSDs, whether or not co-occurring with aphasia. For example, singing facilitates fluency in people who stutter (Andrews, Howie, Dozsa, & Guitar, 1982; Colcord & Adams, 1979; Davidow, Bothe, Andreatta, & Ye, 2009; Glover, Kalinowski, Rastatter, & Stuart, 1996; Healey, Mallard, & Adams, 1976). Rate/rhythm strategies have been used in dysarthria, a disorder affecting the execution of speech movements (e.g., Hustad, Jones, & Dailey, 2003; Pilon, McIntosh, & Thaut, 1998; Yorkston, Hammen, Beukelman, & Traynor, 1990), and are one of the most common treatment approaches for AOS (Brendel & Ziegler, 2008; Dworkin, Abkarian, & Johns, 1988; Wambaugh & Martinez, 2000; Wertz, Lapointe, & Rosenbeck, 1984). The fact that rhythm-based strategies, and, potentially, singing, are effective techniques for the treatment of MSDs suggests that MIT and, more generally, music-based interventions, could target the speech disorders often associated with aphasia, i.e., AOS and dysarthria.

Manifestations of motor-speech and language symptoms are intertwined in verbal expression of patients with concomitant aphasia and an MSD. For example, errors when naming objects can be interpreted as the result of anomia (the core symptom of aphasia) or difficulty planning or producing speech movements (MSD). In order to test the hypothesis of a motor-speech mechanism in music-based intervention for aphasia, one could measure the treatment-related changes in motor speech separately from treatment-related changes in language symptoms. Better progression in speech compared to language outcomes would validate the hypothesis. In a longitudinal study showing the role of singing on the effect of MIT on language improvement (Zumbansen, Peretz, & Hébert, 2014a), we included a measure of motor-speech agility as a secondary outcome. We chose the Diadochokinetic rate (DDK) subtest of the Apraxia Battery for Adults-2 (ABA2, Dabul, 2000). This task consists of rapid repetitions of simple or complex syllables (e.g., *pa, pla*) to assess motor-speech agility. No significant variation was apparent in any participant based on severity norms provided in this battery, although they all improved on the repetition score of non-trained sentences and informativeness of connected speech. This is in contrast with previous studies showing that the DDK task is sensitive to normal ageing in terms of rate (Bilodeau-Mercure & Tremblay, 2016) and intelligibility (Parnell & Amerman, 1987). It is possible that more extensive analyses of the outcomes would have revealed post-treatment improvements in this measure, but additional evidence is needed.

Hurkmans et al. (2015) led a single-subject study with five participants with aphasia and AOS to test the efficacy of another music-based intervention for aphasia, SMTA. In this intervention, repetitive speech production exercises were guided and supported by musical instruments and singing. The authors found mixed results on scores of the Diagnostic Instrument of AOS (Feiken & Jonkers, 2012) despite significant improvement in intelligibility in verbal functional communication (their primary outcome measure) and repetition of non-trained words and sentences. In sum, the assessment methods for AOS are primarily diagnostic tools and may not be appropriate for testing the motor-speech mechanism of music-based intervention for aphasia in experimental and quasi-experimental studies.

As an alternative, in this article, we examine the literature systematically and analyse published data using a case–control approach. We address the following question: are MSDs a common denominator among patients successfully treated with music-based protocols for language production in aphasia? Our hypothesis is that patients with an MSD are more likely to benefit from a music-based intervention, supporting the notion of a motor-based mechanism for music interventions. A secondary objective is to determine if other factors affect the likelihood of benefiting from a music-based intervention, including aphasia severity and treatment duration and intensity. We expect that aphasia severity will not affect the likelihood of benefiting from a music-based intervention, but that treatment duration/intensity will, with longer and more intense treatments associated with higher likelihood of improvement.

Methods

A systematic literature search was conducted to identify studies reporting quantitative changes in oral language production in people with aphasia following a music-based intervention. We considered the Preferred Reporting Items for a Systematic review and Meta-Analysis of Individual Participant Data (PRISMA-IPD, Stewart et al., 2015). Where applicable, PRISMA-IPD steps were applied.

Inclusion and exclusion criteria

Types of studies

Study types were classified according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins, 2011). We included longitudinal studies of various types: RCTs, single-case, and case series studies, cohort studies, and (controlled) before and after studies. Systematic reviews were also included, but only for cross-referencing.

Types of participants

We included adults of any gender diagnosed with aphasia following brain damage of a non-degenerative nature. Thus, participants with dementia or Parkinson's disease were excluded. We also excluded any developmental motor-speech problems such as developmental stuttering. Original studies in which aphasia was not consistently present in participants were excluded. This last criterion was not applied to systematic reviews, which were only retained for cross-referencing during the data collection process.

Types of intervention

We included studies in which an intervention was based on musical elements such as melody or rhythm, whether listened to, sung, or played. Group (such as a choir) as well as individual interventions (such as MIT) were included.

Types of outcome measures

We included studies reporting changes in quantitative measures of speech and language production. Studies reporting only functional verbal communication outcomes (which combine both expressive and receptive language components) were excluded.

Search methods for identification of studies

Peer-reviewed journal articles in English or French were considered because we could read efficiently in these languages. Electronic literature databases screened included PubMed, MEDLINE (1800 to 2018/03/09), and PsycINFO (1806 to March 2018) with the following keywords in these specific Boolean combinations: (aphasia OR dysphasia OR aphasic OR motor-speech disorder OR apraxia OR dyspraxia OR dysarthria OR speech OR language) AND (rehabilitation OR therapy OR treatment) AND (music OR melodic OR intonation OR sing OR choir OR choral OR rhythm). An example of the full electronic search strategy is provided for PsycINFO in supplemental material 1.

After applying selection criteria to the electronic results, one review author (AZ) checked reference lists of the retained articles for cross-referencing.

Data collection and analysis

Selection of studies

All titles and abstracts for each record retrieved from the electronic search were independently assessed by the two authors. Obviously irrelevant references were discarded. For all other references full articles were obtained. All articles were then read independently by the authors, and all articles that did not meet the inclusion criteria were discarded. Any disagreement after these independent reviews was resolved by consensus. For each new relevant record found via cross-referencing, the full-text article was also obtained and assessed. We kept a record of both the article and the reason for the exclusion for all excluded studies.

Study designs and risk of bias assessment

Using Cochrane's classification of quantitative studies (Higgins, 2011), one review author (PT) determined the types of study design. The same author used the Cochrane Collaboration's tool for assessing risk of bias in included studies. No study was excluded based on the risk of bias.

Data extraction and management at the study level

We extracted the following data from the selected articles:

- Intervention name and dosage (total number of sessions, duration of sessions, frequency, and total length of treatment period).
- Oral production tasks used for the assessment of the dependent variable. These tasks were classified as measuring speech (e.g., DDK, repetition), language (e.g., naming), or both (e.g., connected speech) depending on the dependent variable considered (see Table 1).
- Dependent variables. Dependent variables were classified as measuring speech (e.g., per cent correct syllables, correct repetition, rating of articulation or intelligibility in connected speech), or language (e.g., correct naming, correct information units in connected speech). The presence of improvement was considered positive if one or more of these outcomes were reported as improved by authors as compared to the baseline measurements.
- Total sample size.

Table 1. Speech and language tasks and variables reported in the studies reviewed.

Tasks	Speech variables	Language variables
Repetition of trained or non-trained words or sentences	Correct items Correct consonants Production duration First syllable production duration Response latency	–
Rapid repetition of similar or alternating syllables (i.e., Diadochokinesis test)	Correct syllables/time	–
Production of trained or non-trained words or sentences in response to objects or picture prompts (i.e., naming), in situation (i.e., responsive) or in sentence completion	Correct syllables	Correct items Correct words
Connected speech obtained in spontaneous speech, conversation, role-playing, semi-structured interview, picture description, description of common procedures, or story retelling	Articulatory agility rating (in BDAE) Intelligibility rating (in ANELT) Articulation and prosody rating (in AAT) Syllables/phrases	Global rating (e.g., AAT; BDAE; WAB; SLTA; ADP; ANELT) Words/phrases CIUs CIUs/time Comprehensibility rating (ANELT)
Verbal fluency test	–	Words/time
Automatised series	–	Correct items

Note. AAT = Aachener Aphasie Test; BDAE = Boston Diagnostic Aphasia Examination; WAB = Western Aphasia Battery; SLTA = Standard Language Test for Aphasia; ADP = Aphasia Diagnostic Profiles; ANELT = The Amsterdam—Nijmegen Everyday Language Test; CIU = Correct Information Unit.

- Number of participants treated with a music-based intervention.

We only considered participants treated with a music-based intervention, omitting those allocated to other treatments. The following clinical characteristics were gleaned from each of the original studies: aphasia aetiology, aphasia severity type, severity and stage post-onset, absence, or presence of MSDs. When not explicitly reported, presence (p) of an MSD was presumed based on one or more of the following rules:

(p1) mention of verbal apraxia, or dyspraxia, or all synonyms with AOS (American Speech-Language-Hearing Association, 2017);
(p2) description of poor articulatory agility, poorly articulated, effortful, or slurred speech;
(p3) diagnosis of Broca's aphasia by authors considering AOS as a necessary clinical marker for the diagnosis of this aphasia type.

The absence (a) of MSDs was suspected in case of

(a1) fluent aphasia;
(a2) descriptions of good articulatory agility or relative preservation in some tasks of non-automatised oral production, such as repetition or naming.

The presence/absence of improvement and presence/absence of MSDs were extracted by the authors. Any disagreements were resolved by consensus. Notably, it was decided not to presume the presence of an MSD if only bucco-facial, bucco-lingual, or limb apraxia was mentioned because these terms are usually not considered synonymous with AOS or dysarthria. The other data were extracted by one of the review authors (AZ).

Data extraction and management at the IPD level

For each participant, one review author (AZ) recorded the above-mentioned clinical characteristics from studies where sufficient individual data were provided. Based on information available (severity rating or Aphasia Quotient), an ordinal variable for aphasia severity was computed (1 = mild; 2 = mild to moderate; 3 = moderate; 4 = moderate to severe; 5 = severe). The total number of hours of intervention and the duration of treatment in weeks were computed or estimated from available dosage data. Moreover, a treatment intensity variable was computed by dividing the number of treatment hours by treatment duration in weeks. Criteria used to consider that a change was significant at the individual level were recorded (e.g., statistical test, progression criterion included in standardised tests, clinical significance). The second review author independently retrieved data related to the improvement and MSD status for each participant. Disagreements were resolved by consensus.

Data analyses

Two series of binomial logistic regressions were performed on the IPD detailed in the previous paragraph to determine variables predicting the dichotomous dependent variables speech improvement (yes/no) and language improvement (yes/no).

The first set of analyses was conducted to test our main hypothesis, namely that aphasic patients with an associated MSD are more likely to benefit from a music-based intervention than patients without MSDs, supporting the notion of a motor-based mechanism in music interventions. We also included treatment duration (in weeks) and intensity (hours/week) in the models, expecting that increasing treatment dosage would increase the likelihood of an improvement. Linearity of the continuous independent variables (treatment duration and intensity) with respect to the logit of the dependent variables (speech improvement and language improvements) was assessed separately via the Box and Tidwell (1962) procedure. A Bonferroni correction was applied using all six terms in each model resulting in statistical significance being accepted when $p < .008$ (Tabachnick & Fidell, 2014). Based on this assessment, all continuous independent variables were found to be linearly related to the logit of the speech improvement variable. For the language improvement variable, the intensity variable was log 10 transformed to respect the linearity condition. The Omnibus Tests of Model Coefficients is reported for each analysis as well as the Wald coefficient for each term in the model.

The second set of analyses was conducted to test our second hypothesis, namely that aphasia severity would not affect the likelihood of benefiting from a music-based intervention, but that treatment duration/intensity would. Because aphasia severity ratings were only available for 65 patients (62% of all cases), we chose not to include the ordinal aphasia severity rating variable in the previous analysis in order to not reduce the power of the analysis that assessed our main hypothesis. In this second analysis, we included MSD status as an independent variable to ensure that any potential effect of aphasia severity is independent from the presence of an MSD.

Results

Study selection and IPD obtained

The flow chart in Figure 1 illustrates the article sampling process. Electronic searches in databases identified a total of 1,452 records, 928 of which were peer-reviewed journal articles in English or French. Excluding duplicates, this first search produced 778 records. After independent screening of title and abstracts by the two authors, 709 records were discarded because they did not meet selection criteria (16 disagreements were resolved by consensus). Full-text articles were obtained for the remaining 69 records and read independently. Twenty-seven articles considered ineligible according to selection criteria were discarded (eight disagreements were resolved by consensus). The reference lists of the retained articles (38 original studies and 4 systematic reviews) were checked for additional articles. Two additional articles were included, for a final inclusion list of 40 original studies. Systematic reviews were discarded at this point.

IPD with regard to improvement (one of our main variables of interest) were available in 32 out of the 40 articles. Of these, 22 also reported sufficient information to determine presence or absence of MSDs in participants (the other main variable of interest in this review). These 22 studies represented a total of 137 participants. Discarding 27 of them who were not exposed to a music-based intervention and 5 for whom presence of MSD could not be stated, we were able to include 105 participants for IPD analyses. Aphasia severity was available for 65 out of these 105 participants (61.9%).

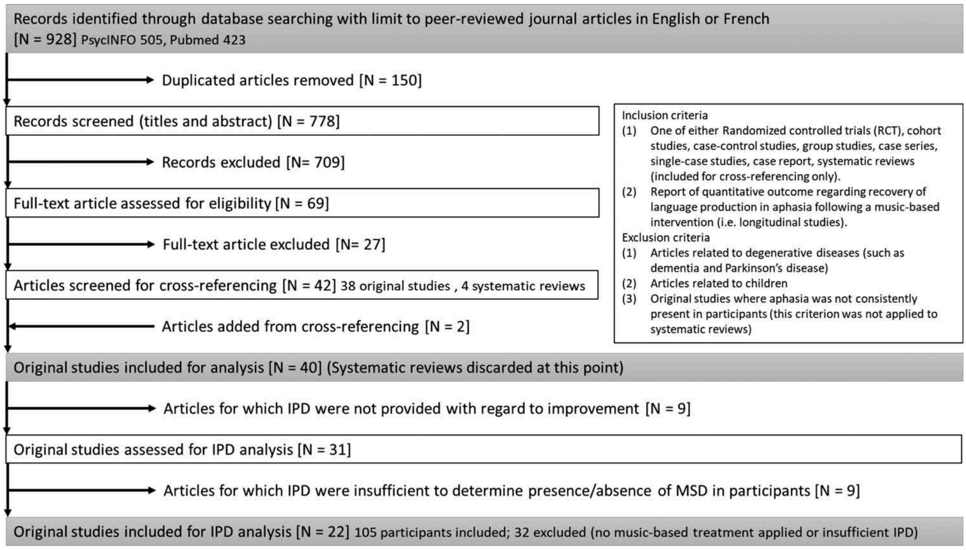

Figure 1. Flow diagram of article and individual patient data (IPD) collection.

Study characteristics

The 40 original studies selected are listed in Table 2 along with their research design, intervention type, outcomes, and participant characteristics. Most studies were case series (16/40; 40%) and single-case studies (10/40; 25%). Most group studies were controlled (six controlled before and after designs, five RCTs, and one crossover trial), with only two uncontrolled before and after studies. The risk of bias was assessed for each study based on Cochrane's method. As reported in Figure 2 (for details, see supplementary material 2), about 75% of all studies were evaluated as presenting a high risk of bias related to randomisation and allocation concealment. Most studies used no control participant and no randomisation methods. In terms of blinding, approximately 60% of all studies did not provide enough information to assess the risk. Most studies, however, did not report attrition and appear to be at low risk of bias resulting from incomplete data. Overall, we estimate the risk of bias to be relatively high in these studies.

A range of music-based interventions are represented. All but one intervention (recreational choir practice, Zumbansen et al., 2017) were individual interventions. The interventions included active music therapy protocols using a variety of singing-related exercises (Jungblut, Huber, Mais, & Schnitker, 2014; Jungblut, Suchanek, & Gerhard, 2009; Kim & Tomaino, 2008), sometimes associated with MIT (Lim et al., 2013) or more traditional speech-language therapy (Raglio et al., 2016). In one study, a combination of music and speech therapy was reported, which utilised speech drills that were supported by adapted music accompaniment, i.e., STMA (Hurkmans et al., 2015). Purely rhythmic interventions were presented as the main treatment of interest in four studies (Brendel & Ziegler, 2008; Mauszycki & Wambaugh, 2008; Wambaugh & Martinez, 2000; Wambaugh, Nessler, Cameron, & Mauszycki, 2012) or as a control treatment in two (Stahl et al., 2013; Wilson et al., 2006). In three studies proposing singing therapies,

Table 2. Characteristics of the original studies included in this review.

Reference	Study type	N in music-based intervention (total *N*)	Music-based intervention (dosage)	Aetiology	Lesion location	Stage [a]	Aphasia type (severity)	Oral production task assessed	Speech improvement	Language improvement	MSD[b]
Akanuma et al., 2016	Case series	10 (10)	Singing therapy (30 min once a week for 10 weeks)	Stroke	Mixed LH and RH	Chronic	Various types (mild to severe)	Naming; verbal fluency test; connected speech	n/a	Variable (3/10 participants improved)	Undetermined
Al-Janabi et al., 2014	Case series	2(2)	MIT (6 sessions of 40 min, twice a week, for 3 weeks)	Stroke	LH (F, T)	Chronic	Broca (moderate to severe)	Repetition of trained and non-trained sentences; naming; verbal fluency test; automatised series	Variable (1/2 participants improved)	Variable (1/2 participants improved)	Undetermined
Baker, 2000	Case series	2 (2)	MMIT (30 min 3–8 times a week for 4–27 months)	TBI	Mixed LH and RH	Subacute to chronic	nr	Production of trained words and sentences	n/a	1	p_1
Belin et al., 1996	Case series	7 (7)	TMR (over 1 month to 9 years)	Stroke	LH (MCA territory)	Subacute to chronic	Broca (severe, $N = 2$) or global (severe, $N = 5$)	Repetition; naming	1	1	Undetermined
Bonakdarpour et al., 2003	Uncontrolled before and after study	7 (7)	MIT (3–4 times a week for 1 month)	Stroke	LH (Broca's region or subcortical)	Chronic	Non-fluent with relatively preserved comprehension	Repetition; naming; connected speech	1	1	Undetermined
Breier et al., 2010	Case series	2 (2)	MIT (2 blocks of treatment with 3 weeks break. One block = 30 min twice a day, 2 days a week for 3 weeks)	Stroke	LH (F, P, ± extention to T)	Chronic	Mixed (moderate)	Production of trained sentences	n/a	Variable (1/2 participant improved)	Undetermined
Brendel & Ziegler, 2008	Cross-over trial	10 (10)	Metrical Pacing Therapy (8 sessions of 50 min, 4 times a week, for 2 weeks)	Stroke	LH (MCA ±- BG)	Subacute to chronic	1 Broca; 8 not classified (mild to severe; No aphasia in 1 participant)	DDK; repetition of non-trained sentences; repetition; connected speech	1	1	p
Conklyn et al., 2012	RCT	16 (30)	MMIT (10–15-min daily over 2 days)	Stroke	LH (MCA territory)	Acute to chronic	Broca (severe)	Repetition and production of trained sentences in situation	0	1	Undetermined
Cortese et al., 2015	Uncontrolled before and after study	6 (6)	TMR adapted to Italian (30–40 min 4 times a week for 16 weeks)	Stroke	LH	Chronic	Broca (severe)	Repetition; naming; connected speech	1	1	p_3
Goldfarb & Bader, 1979	Single-case study	1 (1)	pMIT (60 min each day for 23 days)	Stroke	LH (F)	Chronic	Global (severe)	Repetition of trained sentences	1	n/a	Undetermined
Haro-Martinez et al., 2017	Case series	4 (4)	MIT adapted to Spanish (18 sessions of 30 min, 3 times a week, for 6 weeks	Stroke	LH (MCA)	Chronic	Non-fluent (moderate to severe)	Repetition	Variable (3/4 participants improved)	n/a	p_2
Hough, 2010	Single-case study	1 (1)	pMIT (1 h 3 times a week for 8 weeks)	Stroke	LH	Chronic	Broca (moderate)	Repetition of trained and non-trained sentences; repetition; naming; connected speech	1	1	p

(*Continued*)

Table 2. (Continued).

Reference	Study type	N in music-based intervention (total *N*)	Music-based intervention (dosage)	Aetiology	Lesion location	Stage [a]	Aphasia type (severity)	Oral production task assessed	Speech improvement	Language improvement	MSD[b]
Hurkmans et al., 2015	Case series	5 (5)	SMTA (24 sessions of 30 min twice a week with pauses, over 12–20 weeks)	Stroke	Mixed LH and RH	Subacute to chronic	Various types (moderate to severe)	DDK; repetition; connected speech	1	1	p
Jungblut et al., 2009	Single-case study	1 (1)	Music therapy—SIPARI (360 sessions over 4 years)	Stroke	LH (thalamus reaching up to the radiate crown)	Chronic	Global (severe)	Repetition; naming; connected speech	1	1	Undetermined
Jungblut et al., 2014	Case series	3 (3)	Music therapy—SIPARI (50 sessions of 60 min, twice a week, over 25 weeks)	Stroke	LH	Chronic	Non-fluent (severe)	Repetition; naming; connected speech	1	1	p
Keith & Aronson, 1975	Single-case study	1 (1)	Singing therapy (60 min or more once a week for 2 months)	Stroke	LH	Subacute	Non-fluent (severe)	Repetition; naming; sentence completion; connected speech	n/a	1	p
Kim & Tomaino, 2008	Case series	7 (7)	Music therapy (8–12 sessions of 30 min, 3 times a week, for 4 weeks)	Stroke	LH	Chronic	Various types (mild to severe)	Verbal productions during treatment sessions	1	1	Variable (4 p; 3 a)
Lim et al., 2013	Controlled before and after study	9 (9)	Music therapy and MIT (60 min/day twice a week for 1 month)	Stroke	Mixed LH and RH	Subacute to chronic	Non-fluent	Repetition; naming; connected speech	1	1	Undetermined
Mauszycki & Wambaugh, 2008	Single-case study	1 (1)	Rate control treatment (total of 39 sessions of 30–45 min, twice a week)	Stroke	nr	Chronic	Anomic (mild)	Repetition of trained and non-trained sentences	1	n/a	p
Mauszycki et al., 2016	Case series	2 (2)	pMIT applied to wh-questions (total of 40 sessions of 45–60 min, 3 times a week)	Stroke	LH	Chronic	Broca (moderate)	Production of wh-questions in situation	1	1	p
Morrow-Odom & Swann, 2013	Single-case study	1 (1)	MIT (30 sessions of 90 min, 5 days a week, for 7 weeks)	Stroke	RH	Chronic	Global (severe)	Repetition of trained sentences; repetition; connected speech	1	1	Undetermined
Naeser & Helm-Estabrooks, 1985	Case series	8 (8)	MIT (nr)	Stroke or TBI	Mixed LH and RH	Acute to chronic	Various types (moderate to severe)	Connected speech	Variable (4/8 participant improved)	Variable (4/8 participant improved)	Variable (6 p_2; 3 a_2)
Popovici & Mihailescu, 1992	Controlled before and after study	80 (160)	Variation of MIT (60–120 min daily for 2–4 weeks)	Stroke or TBI	nr	Subacute to chronic	Broca	Repetition; naming	1	1	Undetermined
Popovici, 1995	Controlled before and after study	240 (480)	Variation of MIT (unclear)	Stroke, TBI or tumour	nr	Subacute	Broca, Wernicke or anomic (mild to severe)	Repetition; naming	1	1	Undetermined

(*Continued*)

Table 2. (Continued).

Reference	Study type	N in music-based intervention (total *N*)	Music-based intervention (dosage)	Aetiology	Lesion location	Stage [a]	Aphasia type (severity)	Oral production task assessed	Speech improvement	Language improvement	MSD[b]
Raglio et al., 2016	RCT	10 (10)	Music therapy and SLT (30 min twice a week for 15 weeks)	Stroke	LH (F and/or T and/or O)	Chronic	Non-fluent (mild to severe, $N = 8$) or fluent (mild or severe, $N = 2$)	Naming; connected speech	n/a	1	Variable (7 p; 3 a)
Schlaug et al., 2008	Case series	2 (2)	MIT (40 sessions of 90 min 5 times a week for 8 weeks)	Stroke	LH (Broca's region and anterior part of the STG)	Chronic	Broca (severe)	Naming; connected speech	1	1	Undetermined
Schlaug et al., 2009	Case series	6 (6)	MIT (75 sessions)	Stroke	LH	Chronic	Non-fluent (moderate to severe)	Naming; connected speech	n/a	1	Undetermined
Sparks et al., 1974	Case series	8 (8)	MIT (nr)	Stroke	LH	Chronic	Non-fluent	Naming; connected speech	n/a	Variable (6/8 participants improved)	Variable (6 p; 2 a)
Springer et al., 1993	Controlled before and after study	12 (12)	Stimulation approach (6 sessions of 60 min over 2 weeks)	Stroke	nr	Subacute to chronic	Broca or Wernicke (moderate)	Production of trained and non-trained words in situation	n/a	1	Variable (2 p; 10 a)
Stahl et al., 2013	Controlled before and after study	5 (15)	Singing or rhythmic therapy (60 min 3 times a week for 6 weeks)	Stroke	LH (MCA territory or BG)	Chronic	Non-fluent	Repetition of trained and non-trained sentences	1	n/a	p
Tabei et al., 2016	Single-case study	1 (1)	MIT adapted to Japanese (9 sessions of 45 min once a day for 9 days)	Stroke	LH (putamen)	Chronic	Non-fluent (severe)	Repetition; naming; connected speech	1	1	p_2
van der Meulen et al., 2012	Single-case study	2 (2)	MIT (3–5 h per week for 6 weeks)	Stroke	LH	Acute or chronic	Non-fluent (severe)	Repetition of trained; repetition; naming; connected speech	Variable (1/2 participants improved)	Variable (1/2 participants improved)	p_2
Van Der Meulen et al., 2014	RCT	16 (27)	MIT (5 h per week for 6 weeks)	Stroke	LH	Subacute	Broca (severe)	Repetition of trained and non-trained sentences; repetition; naming; connected speech	1	1	p_2
van Der Meulen et al., 2016	RCT	16 (17)	MIT (3–5 h per week for 6 weeks)	Stroke	LH	Chronic	Non-fluent	Repetition of trained and non-trained sentences; repetition; naming; connected speech	1	0	p_2
Wambaugh & Martinez, 2000	Single-case study	1 (1)	Rate/rhythm control treatment (total of 21 sessions of approx. 60 min, 3 times a week)	Stroke	LH (MCA territory)	Chronic	Broca (nr)	Repetition of trained and non-trained words	1	n/a	p

(*Continued*)

Table 2. (Continued).

Reference	Study type	N in music-based intervention (total *N*)	Music-based intervention (dosage)	Aetiology	Lesion location	Stage [a]	Aphasia type (severity)	Oral production task assessed	Speech improvement	Language improvement	MSD[b]
Wambaugh et al., 2012	Case series	7 (10)	Rate/rhythm control treatment (minimum 10 sessions of approx. 60 min, 3 times a week until plateau or 90% success)	Stroke	LH or RH	Chronic	Broca (severe to moderate)	Repetition of trained and non-trained words	Variable (5/7 participants improved)	n/a	p
Wan et al., 2014	Controlled before and after study	11 (20)	MIT (75 sessions of 90 min, five times a week for 15 weeks)	Stroke	LH	Chronic	Non-fluent (moderate to severe)	Connected speech	n/a	1	6 p_2; 5 undetermined
Wilson et al., 2006	Single-case study	1 (1)	pMIT or rhythmic therapy (twice a week, for 4 weeks + home training)	Stroke	LH (MCA territory)	Chronic	Broca (severe)	Production of trained and non-trained sentences	n/a	1	p
Zumbansen et al., 2014a	Case series	3 (3)	Variation of MIT (18 sessions of 60 min 3 times a week for 6 weeks)	Stroke	LH	Chronic	Broca (moderate to severe)	DDK; repetition of trained and non-trained sentences; connected speech	1	1	p
Zumbansen et al., 2017	RCT	7 (22)	Choir (2 h once a week for 26 weeks)	Stroke or tumour	nr	Chronic	Various types (mild to moderate)	DDK; repetition; naming; automatised series; connected speech	Variable (1/7 participants improved)	Variable (2/7 participants improved)	Variable (2 p; 5 a)

Note. MIT = Melodic Intonation Therapy; MMIT = modified MIT; pMIT, palliative MIT; SLT = speech-language therapy; SMTA = Speech Music Therapy for Aphasia; TMR = Thérapie Mélodique et Rhythmée; SIPARI = Singing-Intonation-Prosody-Breathing-Rhythm-Improvisation; TBI = traumatic brain injury; LH = left hemisphere; RH = right hemisphere; F = frontal lobe; T = temporal lobe; P = parietal lobe; O = occipital lobe; BG = basal ganglia; STG = superior temporal gyrus; MCA = middle cerebral artery; DDK = Diadochokinesis test; 1 = improvement; 0 = no improvement; n/a = not available; nr = not reported.

[a] Aphasia was classified as acute up to 2 weeks post-onset and as chronic from 4 months post-onset.

[b] Reasons for suspecting the presence (p) or absence (a) of motor speech deficit (MSD) are indicated as p = explicit mention of presence of MSD (AOS or dysarthria); p_1 = mention of verbal apraxia or dyspraxia, any synonym of AOS, p_2 = descriptions of poor articulation, effortful or slurred speech; p_3 = diagnosis of Broca's aphasia for authors considering AOS as a necessary clinical marker for the diagnostic of this aphasia type; a = explicit mention of absence of MSD; a_1 = fluent aphasia; a_2 = descriptions of good articulation or relative preservation of non-automatic oral production tasks, such as repetition or naming.

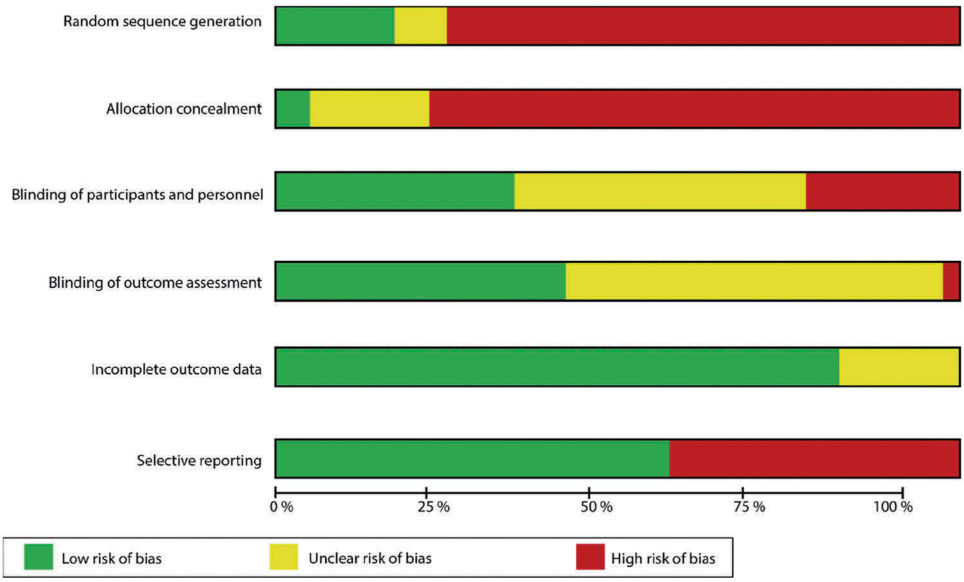

Figure 2. Evaluation of the risk of bias in the 40 articles reviewed.

participants were trained to produce new lyrics based on new (Keith & Aronson, 1975) or familiar melodies (Akanuma, Meguro, Satoh, Tashiro, & Itoh, 2016; Stahl et al., 2013). The majority of studies (25 studies; 62.5%) used MIT (13 studies) or a variation of it (12 studies). Modified MIT (MMIT) interventions use more complex melodies than the original MIT and resemble singing therapies with non-familiar melodies. These interventions focus on individualising the selected melodies and lyrics to adapt to the patient's needs and abilities (Baker, 2000; Conklyn, Novak, Boissy, Bethoux, & Chemali, 2012). Palliative versions of MIT apply the typical intonation technique to a limited set of phrases repetitively trained to allow their memorisation (Wilson et al., 2006; Goldfarb & Bader, 1979; Hough, 2010; Mauszycki et al., 2016), which is usually avoided in original MIT by varying large number of sentences during sessions (Sparks, 2008; Zumbansen et al., 2014b). One study used a mixed approach by using repetitively presented and new sentences during each session (Zumbansen et al., 2014a). The French version of MIT, named TMR ("Thérapie Mélodique et Rhythmée") appears in one study with French participants (Belin et al., 1996) and was adapted to Italian in another (Cortese, Riganello, Arcuri, Pignataro, & Buglione, 2015). In Romania, variations of MIT were adapted to target either verbal expression or comprehension and were tested with a large number of participants (Popovici, 1995; Popovici & Mihailescu, 1992). Finally, the stimulation approach used by Springer et al. to train Wh-questions (Springer, Willmes, & Haag, 1993) also included the intonation technique of MIT. In sum, all but six (purely rhythmic) interventions (85%) were based on singing. Of note is the extreme heterogeneity of intervention dosages, with periods of intervention ranging from 2 days (Conklyn et al., 2012) to 9 years (Belin et al., 1996).

All but one study included participants with aphasia following stroke (Baker, 2000). Chronic patients were more often included (37 studies) than subacute (10 studies) or acute patients (3 studies). There was a variety of aphasia diagnoses but non-fluent types were more common than fluent types. A few participants with fluent aphasia types (e.g., anomic, transcortical sensorial, or Wernicke's aphasia) were included in six studies (Akanuma et al., 2016; Hurkmans et al., 2015; Kim & Tomaino, 2008; Mauszycki & Wambaugh, 2008; Springer et al., 1993; Zumbansen et al., 2017). With the exception of one study (Mauszycki & Wambaugh, 2008), no study included participants with fluent aphasia diagnoses exclusively. In that study, the participant had mild anomia with concomitant mild AOS such that his fluency may have been problematic.

The presence or absence of MSDs was explicitly mentioned in only 17 articles (42.5%). After applying a series of heuristic rules to the remaining articles, we were able to infer the presence or absence of MSDs in all participants in eight more studies and in 6 out of 11 participants in the music-intervention group of Wan et al. (2014). In the latter study, our judgement was based on scores at the DDK subtest of the apraxia battery ABA2 (Dabul, 2000) which were reported for these six participants. All scores corresponded to abnormal articulatory agility according to ABA2 norms. In the remaining articles, participants' speech was not sufficiently described such that the MSD status was undetermined. These results were obtained after independent checking by both authors and resolution by consensus of three disagreements out of 40 ratings.

A variety of verbal production tasks and dependent variables was used across studies (see Table 1 for a synthesis) and most studies used more than one outcome measure. Table 2 indicates positive changes in speech or language outcomes if at least one of the dependent variables was reported as improved. In most cases, improvement was supported by statistical tests or criteria from the norms of clinical tests. If a measure was based on a clinical scale, we assumed that improvement corresponded to a clinically perceptible change. For example, the rating of connected speech in the Western Aphasia Battery—Revised (Kertesz, 2006) consists of two sub-scales for the assessment of content (scored on 10 points), fluency, grammatical competence, and paraphasia (scored on 10 points). Each point is justified by detailed and often quantitative observations. The two review authors independently retrieved information on speech and language changes in all studies. Three disagreements were resolved by consensus. Speech outcomes were reported in 30 studies. Twenty-three (76.66%) reported clear improvement in all participants, six (20%) reported variable changes depending on participants, and one (3.33%) found no improvement (Conklyn et al., 2012). The latter study had the lowest intervention dosage among all included studies (10–15 min daily over two days). Language outcomes were reported in 34 studies, of which 26 reported positive changes (76.47%), 7 (20.58%) reported variable changes, and 1 (2.94%) reported no change. In studies where both speech and language outcome were reported (24/40), 18 studies found positive changes in both speech and language in all participants (45%).

IPD characteristics

Table 3 displays the characteristics of 105 participants taken individually. These IPD (from 22 studies) are representative of participants characteristics described previously for the 40 original studies selected in this review. Most had acquired aphasia following stroke, had lesions located exclusively in the left hemisphere, were in the chronic stage post-onset, and had moderate or severe aphasia. With the exception of one study with only two participants (Baker, 2000), the type of aphasia was mentioned and comprised

Table 3. Characteristics of individual patient data (IPD) included in this review.

Authors	Intervention type	Patient ID	Aetiology	Lesion location	Stage [a]	Aphasia type [b]	Total treatment time (hours)	Treatment duration (weeks)	Speech improvement	Language improvement	MSD [b, c]
Baker, 2000	MMIT	Jeff	TBI	LH (carotid artery territory)	Subacute	nr	76	17	n/a	1	p_1
		Tara	TBI	Bilateral (LH more than RH)	Chronic	nr	252	117	n/a	1	p_1
Cortese et al., 2015	TMR (Italian)	1	Stroke	LH.	Chronic	Broca (5)	37	16	1	1	p_3
		2	Stroke	LH.	Chronic	Broca (5)	37	16	1	1	p_3
		3	Stroke	LH.	Chronic	Broca (5)	37	16	1	1	p_3
		4	Stroke	LH.	Chronic	Broca (5)	37	16	1	1	p_3
		5	Stroke	LH.	Chronic	Broca (5)	37	16	1	1	p_3
		6	Stroke	LH.	Chronic	Broca (5)	37	16	1	1	p_3
Haro-Martinez et al., 2017	MIT (Spanish)	1	Stroke	LH. (MCA territory)	Chronic	Non-fluent (3)	9	6	1	n/a	p_2
		2	Stroke	LH. (MCA territory)	Chronic	Non-fluent (3)	9	6	1	n/a	p_2
		3	Stroke	LH. (MCA territory)	Chronic	Non-fluent (5)	9	6	0	n/a	p_2
		4	Stroke	LH. (MCA territory)	Chronic	Non-fluent (5)	9	6	1	n/a	p_2
Hough, 2010	pMIT	BR	Stroke	LH.	Chronic	Broca	24	8	1	1	p (3)
Hurkmans et al., 2015	SMTA (Dutch)	Participant 1	Stroke	LH (MCA territory)	Subacute	Broca (3)	12	20	1	1	p (1)
		Participant 2	Stroke	LH (PCA territory)	Subacute	Broca (3)	12	15	1	1	p (5)
		Participant 3	Stroke	LH (MCA territory)	Chronic	Global (5)	12	12	1	1	p (1)
		Participant 4	Stroke	RH (MCA territory)	Subacute	Broca (3)	12	15	1	1	p (1)
		Participant 5	Stroke	LH (MCA territory)	Subacute	Wernicke (5)	12	15	1	1	p (5)
Jungblut et al., 2014	SIPARI (German)	Mr. U.	Stroke	LH (Sylvian)	Chronic	Broca (5)	50	25	1	1	p (3)
		Mrs. A.	Stroke	LH (T, F, caudate nucleus, BG, internal capsule)	Chronic	Global (5)	50	25	1	1	p (5)
		Mr. H.	Stroke	LH (Sylvian)	Chronic	Global (5)	50	25	1	1	p (5)
Keith & Aronson, 1975	Singing therapy	KA75 (nr)	Stroke	LH	Subacute	Non-fluent (5)	9	9	n/a	1	p (5)
Kim & Tomaino, 2008	Music therapy	#1	Stroke	LH	Chronic	Non-fluent (5)	6	4	1	1	p
		#2	Stroke	LH	Chronic	Non-fluent (5)	6	4	1	1	p
		#3	Stroke	LH	Chronic	Non-fluent (3)	6	4	1	1	p
		#4	Stroke	LH	Chronic	Mixed (5)	6	4	1	1	a
		#5	Stroke	LH	Chronic	Mixed (2)	6	4	1	1	a
		#6	Stroke	LH	Chronic	Non-fluent (5)	6	4	1	1	p
		#7	Stroke	LH	Chronic	Mixed (5)	6	4	1	1	a
Mauszycki & Wambaugh, 2008	Rate control treatment	MW08 (nr)	Stroke	nr	Chronic	Anomic (1)	24	20	1	n/a	p (1)
Mauszycki et al., 2016	pMIT applied to wh-questions	P1	Stroke	LH (MCA territory)	Chronic	Broca (3)	35	13	1	1	p (3)
		P2	Stroke	LH (F, BG)	Chronic	Broca (3)	35	13	1	1	p (3)

(*Continued*)

Table 3. (Continued).

Authors	Intervention type	Patient ID	Aetiology	Lesion location	Stage [a]	Aphasia type [b]	Total treatment time (hours)	Treatment duration (weeks)	Speech improvement	Language improvement	MSD [b, c]
Naeser & Helm-Estabrooks, 1985	MIT	GR1	Stroke	LH (F including Broca, PVWM, ant. I)	Acute	Broca	nr	nr	1	1	p_2
		GR2	Stroke	LH (F including Broca, PVWM)	Subacute	Broca	nr	nr	0	1	p_2
		GR3	Stroke	LH (internal capsule, BG, PVWM)	Subacute	Non-fluent	nr	nr	1	1	p_2
		GR4	Stroke	LH (T, F including Broca, PVWM) + RH (supramarginal and angular)	Chronic	Broca	nr	nr	1	1	p_2
		PR5	TBI + stroke	LH (T, F including Broca, supramarginal and angular, PVWM) + RH (small, superior to supramarginal)	Chronic	Global	nr	nr	1	0	p_2
		PR6	Stroke	LH (Internal capsule, BG, T isthmus, PVWM)	Chronic	Non-fluent	nr	nr	0	0	a_2
		PR7	Stroke	LH (F including Broca, PVWM) + RH (small, F)	Chronic	Broca	nr	nr	0	0	p_2
		PR8	Stroke	LH (incomplete Broca)	Chronic	Non-fluent	nr	nr	0	0	a_2
Sparks et al., 1974	MIT	BR1	Stroke	LH	Chronic	Non-fluent	nr	nr	n/a	1	p_2
		BR2	Stroke	LH	Chronic	Non-fluent	nr	nr	n/a	1	p_2
		BR3	Stroke	LH	Chronic	Non-fluent	nr	nr	n/a	1	p_2
		BR4	Stroke	LH	Chronic	Non-fluent	nr	nr	n/a	1	p_2
		MR1	Stroke	LH	Chronic	Non-fluent	nr	nr	n/a	1	p_2
		MR2	Stroke	LH	Chronic	Non-fluent	nr	nr	n/a	1	p_2
		NSR1	Stroke	LH	Chronic	Non-fluent	nr	nr	n/a	0	a_2
		NSR2	Stroke	LH	Chronic	Non-fluent	nr	nr	n/a	0	a_2
Springer et al., 1993	Stimulation approach (German)	Patient 1	Stroke	nr	Chronic	Broca (3)	6	2	n/a	0	a
		Patient 2	Stroke	nr	Chronic	Broca (3)	6	2	n/a	0	a
		Patient 3	Stroke	nr	Subacute	Wernicke (3)	6	2	n/a	1	a
		Patient 4	Stroke	nr	Chronic	Wernicke (3)	6	2	n/a	0	a
		Patient 5	Stroke	nr	Chronic	Broca (3)	6	2	n/a	1	p
		Patient 6	Stroke	nr	Chronic	Broca (3)	6	2	n/a	1	p
		Patient 7	Stroke	nr	Chronic	Broca (3)	6	2	n/a	1	a
		Patient 8	Stroke	nr	Chronic	Broca (3)	6	2	n/a	1	a
		Patient 9	Stroke	nr	Chronic	Wernicke (3)	6	2	n/a	1	a
		Patient 10	Stroke	nr	Chronic	Broca (3)	6	2	n/a	1	a
		Patient 11	Stroke	nr	Chronic	Broca (3)	6	2	n/a	0	a
		Patient 12	Stroke	nr	Chronic	Broca (3)	6	2	n/a	1	a
Tabei et al., 2016	MIT (Japanese)	TM16 (nr)	Stroke	LH (putamen)	Chronic	Non-fluent (5)	7	2	1	1	p_2

(*Continued*)

Table 3. (Continued).

Authors	Intervention type	Patient ID	Aetiology	Lesion location	Stage [a]	Aphasia type [b]	Total treatment time (hours)	Treatment duration (weeks)	Speech improvement	Language improvement	MSD [b, c]
van der Meulen et al., 2012	MIT (Dutch)	DS	Stroke	LH	Chronic	Non-fluent (5)	24	6	0	0	p_2
		VD	Stroke	LH (MCA territory)	Acute	Non-fluent (5)	24	6	1	1	p_2
van der Meulen et al., 2016	MIT (Dutch)	Patient 1	Stroke	LH	Chronic	Non-fluent	24	6	1	1	p_2
		Patient 2	Stroke	LH	Chronic	Non-fluent	24	6	1	1	p_2
		Patient 3	Stroke	LH	Chronic	Non-fluent	24	6	1	0	p_2
		Patient 4	Stroke	LH	Chronic	Non-fluent	24	6	0	0	p_2
		Patient 5	Stroke	LH	Chronic	Non-fluent	24	6	1	1	p_2
		Patient 6	Stroke	LH	Chronic	Non-fluent	24	6	0	0	p_2
		Patient 7	Stroke	LH	Chronic	Non-fluent	24	6	1	0	p_2
		Patient 8	Stroke	LH	Chronic	Non-fluent	24	6	0	0	p_2
		Patient 9	Stroke	LH	Chronic	Non-fluent	24	6	1	1	p_2
		Patient 10	Stroke	LH	Chronic	Non-fluent	24	6	0	0	p_2
		Patient 11	Stroke	LH	Chronic	Non-fluent	24	6	1	0	p_2
		Patient 12	Stroke	LH	Chronic	Non-fluent	24	6	0	0	p_2
		Patient 13	Stroke	LH	Chronic	Non-fluent	24	6	1	0	p_2
		Patient 14	Stroke	LH	Chronic	Non-fluent	24	6	1	0	p_2
		Patient 15	Stroke	LH	Chronic	Non-fluent	24	6	0	0	p_2
		Patient 16	Stroke	LH	Chronic	Non-fluent	24	6	0	1	p_2
Wambaugh & Martinez, 2000	Rate/rhythm control	WM00 (nr)	Stroke	LH (MCA territory)	Chronic	Broca	21	7	1	n/a	p (2)
Wambaugh et al., 2012	Rate/rhythm control	P1	Stroke	LH (MCA territory)	Chronic	Broca	28	10	1	n/a	p
		P2	Stroke	LH (ACA territory)	Chronic	Broca	6	2	1	n/a	p
		P4	Stroke	LH (MCA territory)	Chronic	Broca	22	8	1	n/a	p
		P5	Stroke	LH (MCA territory)	Chronic	Broca	10	4	1	n/a	p
		P6	Stroke	RH (MCA territory)	Chronic	Broca	10	4	0	n/a	p
		P7	Stroke	LH (MCA territory)	Chronic	Broca	21	7	1	n/a	p
		P9	Stroke	LH (MCA territory)	Chronic	Broca	18	6	1	n/a	p
		P10	Stroke	LH (BG)	Chronic	Broca	20	7	0	n/a	p
Wan et al., 2014	MIT	P1	Stroke	LH (MCA territory)	Chronic	Non-fluent	113	15	n/a	1	p_2
		P3	Stroke	LH (MCA territory)	Chronic	Non-fluent	113	15	n/a	1	p_2
		P4	Stroke	LH (MCA territory)	Chronic	Non-fluent	113	15	n/a	1	p_2
		P5	Stroke	LH (MCA territory)	Chronic	Non-fluent	113	15	n/a	1	p_2
		P9	Stroke	LH (MCA territory)	Chronic	Non-fluent	113	15	n/a	1	p_2
		P10	Stroke	LH (MCA territory)	Chronic	Non-fluent	113	15	n/a	1	p_2
Wilson et al., 2006	pMIT	KL	Stroke	LH (MCA territory)	Chronic	Broca (5)	8	4	n/a	1	p

(Continued)

Table 3. (Continued).

Authors	Intervention type	Patient ID	Aetiology	Lesion location	Stage [a]	Aphasia type [b]	Total treatment time (hours)	Treatment duration (weeks)	Speech improvement	Language improvement	MSD [b, c]
Zumbansen et al., 2014a	MIT (French)	FL	Stroke	LH	Chronic	Broca (3)	18	6	1	1	p (3)
		FS	Stroke	LH	Chronic	Broca (5)	18	6	1	1	p (5)
		JPL	Stroke	LH	Chronic	Broca (3)	18	6	1	1	p (3)
Zumbansen et al., 2017	Choir (French)	P03	Stroke	nr	Chronic	Tr. S. (3)	52	26	0	1	a
		P04	Stroke	nr	Chronic	Tr. S. (3)	52	26	0	0	a
		P06	Stroke	nr	Chronic	Tr. S. (2)	52	26	0	0	a
		P08	Stroke	nr	Chronic	Tr. M. (5)	52	26	0	0	p (5)
		P10	Stroke	nr	Chronic	Mixed (5)	52	26	1	1	p (3)
		P12	Stroke	nr	Chronic	Mixed (3)	52	26	0	0	a
		P13	Stroke	nr	Chronic	Mixed (3)	52	26	0	0	a

Note. MIT = Melodic Intonation Therapy; MMIT = modified MIT; pMIT, palliative MIT; SMTA = Speech Music Therapy for Aphasia; TMR = Thérapie Mélodique et Rhythmée; SIPARI = Singing-Intonation-Prosody-Breathing-Rhythm-Improvisation; TBI = traumatic brain injury; LH = left hemisphere; RH = right hemisphere; F = frontal lobe; T = temporal lobe; P = parietal lobe; O = occipital lobe; BG = basal ganglia; STG = superior temporal gyrus; MCA = middle cerebral artery; PVWM = periventricular white matter; Tr. S = transcortical sensorial; Tr. M = transcortical motor; 1 = improvement; 0 = no improvement; n/a = not available; nr = not reported.

[a] Aphasia was classified as acute up to 2 weeks post-onset and as chronic from 4 months post-onset.

[b] Aphasia or MSD severity, if reported, is indicated as follows: (1) = mild; (2) = mild to moderate; (3) = moderate; (4) = moderate to severe; (5) = severe.

[c] Reasons for suspecting the presence (p) or absence (a) of motor speech deficit (MSD) are indicated as p = explicit mention of presence of MSD (AOS or dysarthria); p_1 = mention of verbal apraxia or dyspraxia, any synonym of AOS, p_2 = descriptions of poor articulation, effortful or slurred speech; p_3 = diagnosis of Broca's aphasia for authors considering AOS as a necessary clinical marker for the diagnostic of this aphasia type; a = explicit mention of absence of MSD; a_1 = fluent aphasia; a_2 = descriptions of good articulation or relative preservation of non-automatic oral production tasks, such as repetition or naming.

mostly non-fluent variants (95 cases, either with Broca's [39], transcortical motor [1], mixed [6], global [4], or undetermined non-fluent type [45]). Fluent variants included Wernicke's (four cases), transcortical sensorial (three cases), and one anomic aphasia.

Treatment dosage varied across participants, ranging from 2 to 117 weeks, with an average of 11 ± 13.63 weeks. A measure of treatment intensity (number of hours of treatment/number of weeks of treatment) revealed that intensity was also heterogeneous, ranging from 0.6 hr/week to 7.5 hr/week with an average of 2.97 ± 1.55 hr/week.

We independently retrieved information on the presence/absence of MSDs in all participants, with no disagreements. The presence/absence of MSDs was explicitly reported in half of the cases (52/105) and was otherwise presumed based on our predefined rules (see "Methods" section). A fifth of the sample did not present any MSD (22/105), such that 83 participants had an associated MSD. MSD severity was rarely reported (19/105 cases) and ranged from mild to severe.

We independently retrieved information on speech and language changes in all participants, with no disagreement. Speech outcomes were reported in 75 participants. Improvement was found in 54 of them (72%; Table 4). Language outcomes were reported in 91 participants, of which 64 improved (70.32%; Table 6). Out of 61 participants for whom both speech and language outcome were available, 15 (24.59%) did not improve in any measure, 6 (9.84%) improved only in speech, 3 (4.92%) only in language, and 37 (60.66%) improved in speech and language.

IPD analyses: effect of MSDs

Speech outcomes

Out of 75 cases in which speech was measured, 51 (68%) had an MSD and exhibited a speech improvement, 7 (9.33%) had no MSD and did not improve, 14 (18.67%) had an MSD but did not improve, and 3 (4%) had no MSD but improved (Table 4). A binomial logistic regression was performed to ascertain the effects of the MSD status, treatment duration in weeks and treatment intensity on the likelihood that participants have a speech improvement. The logistic regression model was statistically significant, $\chi^2(3) = 18.62$, $p < .0005$. The model explained 35.8% (Nagelkerke R^2) of the variance in the speech outcome and correctly classified 82.1% of cases. Of the three predictor variables, only two were statistically significant: MSD and treatment intensity (as shown in Table 5). The likelihood of a music-based intervention improving speech outcomes is about 21 times higher in aphasic patients with an MSD than in those without. Increasing treatment intensity was associated with a relatively decreased likelihood of exhibiting a speech improvement.

Table 4. Contingency table of speech improvement and presence of motor-speech disorders (MSD) in IPD.

		Improved on speech measures		
		Yes	No	Total
MSD	Yes	51 (68%)	14 (18.67%)	65 (86.67%)
	No	3 (4%)	7 (9.33%)	10 (13.33%)
	Total	54 (72%)	21 (28%)	75 (100%)

Table 5. Logistic regression predicting likelihood of speech improvement based on MSD, treatment duration (weeks), and intensity (hours/weeks).

	β	*SE*	Wald	*df*	*p*	OR	95% CI for OR
MSD	3.023	1.187	6.487	1	.011	20.56	[2.008, 210.6]
Treatment duration	−.103	.056	3.418	1	.065	.902	[.809, 1.0]
Treatment intensity	−1.473	.504	8.547	1	.003	.229	[.085,.615]

Note. β = unstandardised beta coefficients; OR = odds ratio; CI = confidence interval.

Language outcomes

Out of 91 cases in which language was measured, 54 (59.34%) had an MSD and improved, 12 (13.19%) had no MSD and did not improve, 15 (16.48%) had an MSD but did not improve, and 10 (10.99%) had no MSD but improved (Table 6). The logistic regression model was statistically significant, $\chi^2(3) = 7.89$, $p = .048$. The model explained 14.4% (Nagelkerke R^2) of the variance in the language outcome and correctly classified 69.3% of cases. Of the three predictor variables, only two were statistically significant: MSD status and treatment intensity (as shown in Table 7). The odds of a music-based intervention improving language outcomes is about four times higher in aphasic patients with an MSD than in those without. Increasing treatment intensity was associated with a relatively decreased likelihood of exhibiting a language improvement.

IPD analyses: effect of aphasia severity

Speech outcomes

Out of the 75 cases in which speech was measured, aphasia severity ratings were available for 59 (69.4%). A binomial logistic regression was performed to ascertain the effects of MSD status, aphasia severity, treatment duration in weeks, and treatment intensity on the likelihood that participants show speech improvement. The logistic regression model was statistically significant, $\chi^2(4) = 15.36$, $p = .004$. The model explained 41.4% (Nagelkerke R^2) of the variance in the speech outcome and correctly classified 90.2% of all cases. Of the four predictor variables, only one was statistically significant: MSD (as shown in Table 8). The odds of a music-based intervention improving speech outcomes was about 18 times higher in aphasic patients with an MSD than in those without.

Table 6. Contingency table of language improvement and presence of MSD in IPD.

		Improved on language measures		
		Yes	No	Total
MSD	Yes	54 (59.34%)	15 (16.48%)	69 (75.82%)
	No	10 (10.99%)	12 (13.19%)	22 (24.18%)
	Total	64 (70.33%)	27 (29.67%)	91 (100%)

Table 7. Logistic regression predicting likelihood of language improvement based on presence of an MSD, treatment duration (weeks), and intensity (hours/weeks).

	β	*SE*	Wald	*df*	*p*	OR	95% CI for OR
MSD	1.325	.631	4.408	1	.036	3.762	[1.092, 12.96]
Treatment duration	.002	.022	0.008	1	.927	1.002	[.959, 1.046]
Treatment intensity (log 10 transformed)	−2.897	1.463	3.921	1	.048	.055	[.003, .971]

Note. β = unstandardised beta coefficients; OR = odds ratio; CI = confidence interval.

Table 8. Logistic regression predicting likelihood of speech improvement based on aphasia severity, presence of an MSD, treatment duration (weeks), and intensity (hours/weeks).

	β	*SE*	Wald	*df*	*p*	OR	95% CI for OR
MSD	2.88	1.21	5.57	1	.018	17.87	[1.63, 195.79]
Aphasia severity	.097	.275	.124	1	.724	1.10	[.642, 1.89]
Treatment duration	−.106	.057	3.42	1	.065	.9	[.804, 1.01]
Treatment intensity	−1.28	.746	2.949	1	.086	.278	[.064, 1.19]

Note. β = unstandardised beta coefficients; OR = odds ratio; CI = confidence interval.

Language outcomes

Out of the 91 cases in which language was measured, aphasia severity ratings were available for 69 (75.8%). A binomial logistic regression was performed to evaluate the effects of MSD status, aphasia severity, treatment duration in weeks, and treatment intensity on the likelihood that participants show a language improvement. The logistic regression model was statistically significant, $\chi^2(4) = 22.87$, $p \leq .005$. The model explained 57.5% (Nagelkerke R^2) of the variance in the language outcome and correctly classified 86.3% of all cases. Of the four predictor variables, two were statistically significant: treatment duration and treatment intensity (as shown in Table 9). Increasing treatment dosage (duration or intensity) was associated with a decreased likelihood of exhibiting a language improvement.

Discussion

This systematic review was undertaken to examine the relevance of a motor-speech mechanism to explain the effect of music-based intervention on aphasia rehabilitation. Using a case–control analysis of published IPD, we found that participants with aphasia and a concomitant MSD were significantly more likely to exhibit speech and language improvements after a music-based intervention than aphasic participants without MSDs. Aphasia severity, in contrast, did not predict improvement in speech or language. Thus, it is possible that music-based interventions act on the motor system, resulting in improvement of motor-speech deficits that are often associated with aphasia.

Impact of music-based interventions on speech and/or language functions

The motor-speech hypothesis of music-based interventions for aphasia adds to current understanding of the mechanisms through which music and singing may promote aphasia recovery. Merrett, Peretz, and Wilson (2014) propose an organisational

Table 9. Logistic regression predicting likelihood of language improvement based on aphasia severity, presence of MSD, treatment duration (weeks), and intensity (hours/weeks).

	β	*SE*	Wald	*df*	*p*	OR	95% CI for OR
MSD	4.745	2.661	3.179	1	.075	115	[.624, 211194]
Aphasia severity	−.46	1.163	.156	1	.693	.631	[.065, 6.17]
Treatment duration	−.286	.124	5.288	1	.021	.751	[.589, .959]
Treatment intensity (log 10 transformed)	−25.29	12.35	4.194	1	.041	.000	[.00, .338]

Note. β = unstandardised beta coefficients; OR = odds ratio; CI = confidence interval.

framework for these mechanisms according to four non-mutually exclusive levels of explanation: (a) neuroplastic reorganisation of language function, (b) activation of the mirror neuron system and multimodal integration, (c) utilisation of shared or specific features of music and language, and (d) motivation and mood. Because the motor-speech hypothesis simply changes the focus of the effect of the intervention from language to the motor component of oral language production, we suggest that it is compatible with all these levels.

Importantly, our results do not suggest that music-based interventions would help the motor-speech function exclusively since a number of participants with (54) and without MSDs (10) did improve on language outcomes. Moreover, most participants for whom both speech and language outcome were available improved in both measures. Speech and language are connected by tight links. Language is mostly received and produced via speech, inner-speech is engaged for maintaining linguistic material in working memory (Baddeley, 2003; Buchsbaum & D'Esposito, 2008; Camos & Barrouillet, 2014), and neural networks for speech and language are partly overlapping, especially when it comes to superordinate control mechanisms (Hertrich, Dietrich, & Ackermann, 2016). Thus, at least at some levels, interventions affecting speech might have an impact on language and vice versa.

We found MSDs associated with higher probabilities of exhibiting speech improvement (OR = 21; Table 5) than oral language production improvement (OR = 4; Table 7) in patients with aphasia treated with music-based interventions. Because speech is an inherent component of oral language production, this result might appear unexpected. However, we minimised the impact of speech on language outcomes by applying a systematic distinction between speech and language measures, even when they were collected from a unique language expression task (e.g., in connected speech, see Table 1). This distinction was not always made in the articles themselves. It was sometimes concluded that participants improved in language skills although, in our opinion, the measure evaluated speech (e.g., syllable accuracy when repeating trained sentences), but see the limits section later.

Rhythm- or singing-based interventions for MSD

Most of the interventions we reviewed relied primarily on singing, even though we did not restrict our literature search to therapies using this form of musical expression. This is not surprising given that (a) voice is the most natural, immediately available musical instrument, (b) songs with lyrics associate music and speech production, and (c) patients with non-fluent aphasia have been found to better produce words in singing conditions than when speaking naturally. In contrast, singing therapies are less common in the AOS literature (Ballard et al., 2015; Wambaugh, Duffy, McNeil, Robin, & Rogers, 2006). MIT, a well-known singing-based therapy for aphasia, has been explored in case studies with developmental AOS (Helfrich-Miller, 1994; Krauss & Galloway, 1982; Lagasse, 2012; Martikainen & Korpilahti, 2011) but not with the intention to treat acquired AOS, although we found that many aphasic patients treated with MIT also had an MSD. This treatment intention is probably the reason why MIT has been overlooked as a possible treatment for acquired AOS in systematic reviews (Ballard et al., 2000, 2015; West, Hesketh, Vail & Bowen, 2005). We found that most studies targeting aphasia with music-based interventions also included participants with concomitant MSDs, and AOS was more often explicitly reported than dysarthria. Thus, future systematic reviews on AOS may want to include aphasia literature in which patients are diagnosed with concomitant AOS.

Some of the studies included in this review had the primary intention to treat AOS even if the participants also had aphasia (Brendel & Ziegler, 2008; Hurkmans et al., 2015; Mauszycki & Wambaugh, 2008; Wambaugh & Martinez, 2000; Wambaugh et al., 2012). In most of these studies, a purely rhythmic-based intervention was used (Table 2). Rhythm is omnipresent in a category of treatments recommended for AOS (Ballard et al., 2015). Rate/rhythm strategies include hand-tapping paired with word or sentence production (Wambaugh & Martinez, 2000; Wertz et al., 1984) and control of speech rate by encouraging prolonged speech production in synchrony with rhythmic sequences (Brendel & Ziegler, 2008; Dworkin et al., 1988; Wambaugh & Martinez, 2000). Improvement has been reported with these purely rhythmic-based treatments, but they have not demonstrated a beneficial effect over and above articulatory-kinematic approaches, the most recommended approach for treating AOS to date (Wambaugh et al., 2012).

It is not yet known if singing (with its inherent rhythmic aspect) could enhance the effect of purely rhythmic strategies. For now, findings comparing these approaches in participants with aphasia and AOS are equivocal (Stahl et al., 2013; Zumbansen et al., 2014a). However, combining singing with typical articulatory-kinematic strategies for the treatment of AOS had a superior effect than articulatory-kinematic strategies alone in a single-subject study with two participants (Aitken Dunham, 2010). As pointed out by others (Merrett et al., 2014; Racette et al., 2006), the pleasure associated with music and singing could help participants adhere to intensive treatment programmes. Moreover, music might encourage maintenance of an appropriate pace during motor-speech drills, which are deemed necessary to treat MSDs. In patients with progressive dysarthria due to Parkinson's disease, several protocols have been developed such as the Music Therapy Voice Protocol and the Voice and Choral Singing Treatment to improve communicative functions. A positive effect of these therapies on vocal intensity was found (Di Benedetto et al., 2009; Evans, Canavan, Foy, Langford, & Ruth, 2012; Haneishi, 2001; Yinger & Lapointe, 2012). In contrast, relatively few studies measured the effect of singing-based therapies on speech intelligibility in this population. Thus, for now, there is only limited evidence that such interventions can improve speech in Parkinson's disease (Haneishi, 2001) as well as post-stroke dysarthria (Mitchell, Bowen, Tyson, Butterfint, & Conroy, 2017; Tamplin, 2008). In sum, the manner in which singing can be successfully used in a therapy needs to be further explored. Integrating language-independent speech measures and manipulating rhythmic and melodic cues during music-based interventions may contribute to advancing current understanding of the relative contribution of the different components of singing to speech and language improvements.

Impact of intervention duration and intensity

Intervention duration and intensity were significant predictors of speech and language improvements. The general idea is that sufficient amounts and intensity of treatment are necessary to obtain significant gains in aphasia therapy (Bhogal, Teasell, Foley, & Speechley, 2003; Bhogal, Teasell, & Speechley, 2003). However, in our analyses, increased treatment dosage was associated with less likelihood of exhibiting improvement. Treatment duration and intensity were highly heterogeneous in our data, which could affect the validity of the results. Nevertheless, our results should encourage future research to refine the understanding of the association between treatment dosage and efficacy in aphasia therapy. One possibility is that this association might not be linear. A clinician usually looks for a different strategy when there is no improvement or when a plateau is reached. Continuing the same approach at the same dosage despite a lack of therapeutic effect might be deleterious. In RCTs on aphasia therapy post-stroke, where protocols are usually not as individualised as in clinical practice, there is significantly more discontinuation among participants allocated to high- versus low-intensity treatment groups (Brady, Kelly, Godwin, Enderby, & Campbell, 2016). Thus, sufficient dosage is most probably necessary for treatment efficacy, but beyond this threshold the simple statement "more is better" may not be accurate.

Limitations

There are several important limitations to this literature-based analysis. The first pertains to the lack of explicit mention of presence/absence of MSDs in participants' characteristics in half of the reviewed papers (23/40) and participants included in our IPD analysis (53/105). The lack of reporting MSDs is probably related to the historical complexity and evolution of the terminology related to aphasia, AOS, and dysarthria (Buttet-Sovilla, Overton-Venet, & Laganaro, 2010; Duffy, 2012; McNeil et al., 1997). Dysarthria is now defined as a neurological motor-speech disorder affecting the strength, range of motion, speed, and precision of the speech musculature, whereas AOS is regarded as a disorder of motor planning of speech movements in the absence of impaired muscle control (American Speech-Language-Hearing Association, 2018). In practice, dysarthria is relatively easy to differentiate from aphasia. In contrast, motor speech, or phonetic errors in AOS can be difficult to disentangle from phonological errors in aphasia. According to a recent systematic review, widely agreed-upon differential features of speech in AOS include slow speech rate due to protracted segments and intersegment durations, phoneme distortions or distorted phoneme substitutions, and dysprosody (Ballard et al., 2015). These features were usually not reported in the articles we reviewed, except for studies focussing on AOS rather than aphasia. Thus, confusion between aphasic- and apraxic-type expression disorders was the primary risk in assuming presence of MSDs in the studies we collected. Notably, some aspects of expression may appear similar to AOS in conduction aphasia (McNeil et al., 1997). Because conduction aphasia is part of the fluent aphasia category, we assumed absence of MSDs in all types of fluent aphasia. This was done to reduce the risk of type 1 error (false alarms). In MSDs, expression is impaired in all voluntary oral production tasks. Thus, the absence of MSDs was also presumed in all cases of non-fluent aphasia where expression was relatively preserved in some of these tasks, such as repetition compared to naming, or when this dissociation was implicit in the reported type of aphasia (i.e., transcortical motor aphasia).

The distinction we made between speech and language measures is another limitation to this study because there is still no consensus in this matter. In AOS literature, where speech is the primary target, the most frequently used outcome measures are perceptually judged accuracy of phoneme or word production, word or utterance duration, speech rate, and/or dysfluency (Ballard et al., 2015). Most clinical studies on AOS include aphasic participants, probably because AOS without aphasia is rare. One could argue that measures taken from speech segments other than phonemes or meaningless syllables could be influenced by language skills such as word finding difficulty or agrammatism that also disrupt the fluency of verbal output in aphasia. As Ballard et al. noted, there are ongoing efforts to solve this issue (e.g., Ballard et al., 2014; Haley, Jacks, de Riesthal, Abou-Khalil & Roth, 2012; Vergis et al., 2014; Whitwell et al., 2013). One interesting option consists of measuring purely phonetic aspects of connected speech because this task can be used to observe generalisation of improvements to untrained and ecologically valid material. Recently, den Ouden et al. (2017) found that the presence and severity of AOS could be predicted in connected speech by different phonetic-acoustic measures (dispersion of F1, F2, and voiced-stop VOT) and that these measures did not correlate with aphasia severity. We encourage further examination of these measures, especially their test–retest reliability and sensitivity to change for their use in longitudinal experimental studies of music-based interventions.

Finally, an important limitation to this literature-based analysis is a high risk of bias of the studies, especially in terms of the lack of randomisation and concealment (high risk in nearly 75% of all studies), and a generalised lack of information about blinding of participants and blinding of outcome assessment in about 50% of all studies. Future studies on music-based interventions should report aphasic and MSD diagnoses in participants. Moreover, the integration of control participants with a random allocation of treatment as well as some level of blinding for the analysis of data would go a long way in reducing the risk of bias in this field of research.

Conclusion

The present literature review suggests that music-based interventions have a stronger impact on speech than on language-related symptoms, and that their impact on the recovery in patients with aphasia is stronger in patients with an associated MSD. Most interventions included some sort of singing as their primary music-based facilitation technique. If music- and singing-based interventions improve MSDs associated with aphasia, then these treatments should be considered for MSDs, whether they are associated with aphasia or not.

Disclosure statement

No potential conflict of interest was reported by the authors.

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