Contents

[List of tables 1](#_Toc91676458)

[1. Literature search procedure 1](#_Toc91676459)

[1.1. Electronic searches 1](#_Toc91676460)

[1.2. Search terms 1](#_Toc91676461)

[2. Lists of primary studies considered 1](#_Toc91676462)

[2.1. Included studies 1](#_Toc91676463)

[2.2. Excluded studies 1](#_Toc91676464)

[3. Tests and outcome measures in primary studies 1](#_Toc91676465)

[4. Supplementary meta-analysis methods 1](#_Toc91676466)

[4.1. RCTs 1](#_Toc91676467)

[4.2. Case reports 1](#_Toc91676468)

[5. Results tables 1](#_Toc91676469)

[5.1. Overall RCT meta-analyses 1](#_Toc91676470)

[5.2. RCT meta-analyses of domain categories 1](#_Toc91676471)

[5.3. Overall IPD meta-analyses 1](#_Toc91676472)

[5.4. IPD meta-analyses of domain categories 1](#_Toc91676473)

[5.5. IPD meta-analyses with aphasia stage (MPO) as a moderator 1](#_Toc91676474)

[5.6. IPD meta-analyses with MIT protocol as a moderator 1](#_Toc91676475)

[5.7. Meta-analyses with only the change in control groups (taken from the RCTs). 1](#_Toc91676476)

[5.8. IPD meta-analyses with aphasia stage (months post-onset, MPO) as a moderator for pretest scores only. 1](#_Toc91676477)

[6. Supplementary References 1](#_Toc91676478)

# List of tables

[eTable 1: List of studies included in the present meta-analysis. 1](#_Toc91676479)

[eTable 2: List of initially included but later excluded studies (cf lists of *Eligibility criteria*). a: Substantial variation from MIT protocol; b: Non-validated tests; c: No contrast of trained vs untrained items; d: No pre&post data; e: Other essential data not reported; f: Untrustworthy source, e.g. non-peer-reviewed journal; g: Patient(s) 17 or younger. 1](#_Toc91676480)

[eTable 3: List of all tests considered. 1](#_Toc91676481)

[eTable 4: Categorisation scheme showing how, for each target syndrome, Subtests → Tests → Abilities → Domains. 1](#_Toc91676482)

[eTable 5: Overall RCT meta-analyses. 1](#_Toc91676483)

[eTable 6: RCT meta-analyses of domain categories. 1](#_Toc91676484)

[eTable 7: Overall IPD meta-analyses. 1](#_Toc91676485)

[eTable 8: IPD meta-analyses of domain categories. 1](#_Toc91676486)

[eTable 9: IPD meta-analyses with aphasia stage (months post-onset, MPO) as a moderator. 1](#_Toc91676487)

[eTable 10: IPD meta-analyses with MIT protocol as a moderator. 1](#_Toc91676488)

[eTable 11: Meta-analyses with only the change in control groups (taken from the RCTs). 1](#_Toc91676489)

[eTable 12: IPD meta-analyses with aphasia stage (months post-onset, MPO) as a moderator for pretest scores only. 1](#_Toc91676490)

# Literature search procedure

The systematic literature search in literature databases yielded 606 hits; through searching the trial registers 7 additional trials were found. These 613 items have been subjected to a duplicate check for identical publications found through the different search tools combined. They were checked with the “duplicate detection” feature of the reference management software Zotero (Corporation for Digital Scholarship; https://www.zotero.org/), with the following procedure: When all of the duplicate items had the same publication form and all of the duplicates had an abstract, we kept the first one in the list (by order of importing into Zotero); if not, we kept the first item of the duplicates having an abstract. With different publication entries from the same study, we followed the preference hierarchy: journal article > book chapter > conference proceedings. After this process of eliminating all supplicates 143 items remained. Following this first step we read and checked all abstracts of the remaining articles against the exclusion criteria. Within this step 44 articles were excluded, leaving 99 articles that checked all eligibility criteria. As the final step the full texts of all remaining articles were reviewed. During two rounds, 78 articles were excluded, leaving 22 final articles that fit all our inclusion criteria and could therefore be included in this meta-analysis.

## Electronic searches

We searched the following databases: *Cochrane Library* (last searched 06.08.2021), *CINAHL EBSCOhost* (06.08.2021), *PsycINFO OVID* (1806 to August 2021), *Web of Science* (06.08.2021), *PubMed* (06.08.2021), *Scopus* (06.08.2021), *Medline* *OVID* (1946 to August 2021) *PSYNDEX OVID* (1977 to August 2021), *Music Periodicals Database* (06.08.2021), and *ProQuest Dissertations & Theses Global* (06.08.2021).

We also searched trial registers, including *International Clinical Trials Registry Platform* (ICTRP,<https://www.isrctn.com/>; 06.08.2021), *National Research Register* (UK),<http://www.nihr.ac.uk/>; 06.08.2021), *Clinical Trials.gov* ([www.clinicaltrials.gov](http://www.clinicaltrials.gov); 06.08.2021), *Netherlands Trials Register*[www.trialregister.nl](http://www.trialregister.nl); 06.08.2021), and the *German clinical trials Register*<https://www.drks.de/drks_web/>; 06.08.2021)

Additionally, we performed searches in Google Scholar (06.08.2021) and in the grey literature database OpenGrey.eu (<http://www.opengrey.eu/>; 06.08.2021). Messages soliciting any unpublished data were additionally sent to:

* aphasia associations
  + National Aphasia Association, NAA, https://www.aphasia.org
  + Australian Aphasia Association (AAA), https://aphasia.org.au
  + Fédération Nationale des Aphasiques de France (FNAF), http://aphasie.fr/
* music therapy associations
  + American Music Therapy Association (AMTA), https://www.musictherapy.org/
  + British Association for Music Therapy (BAMT), https://www.bamt.org
* mailing lists
  + AUDITORY
  + Musicology-all
* authors of all included studies

Finally, to ensure no studies were omitted we consulted the list of studies in published systematic reviews and meta-analyses concerning MIT 1–5.

Since no filters relating to methods used or publication type were applied to our searches, we manually separated and kept the empirical studies from the overall results.

## Search terms

*CINAHL:*

((MM "Aphasia+") OR "aphasia" OR (MH "Aphasia, Broca") OR (MH "Aphasia, Transcortical Sensory") OR (MH "Aphasia, Wernicke")) AND (((MH singing or singing ) AND ("speech therapy" or (MH "Speech Therapy+")) OR "melodic intonation therapy")))

ClinicalTrials.gov

"melodic intonation therapy"

*Cochrane Library*

"melodic intonation therapy" AND aphasia

("speech therapy“ in Ti Abstr Key OR MeSH descriptor [speech therapy] explode all trees) AND singing\* in Ti Abstr Key

*Deutsches Register klinischer Studien (DRKS)/German clinical trials register*<https://www.drks.de/drks_web/>

melodic intonation therapy

melodische intonationstherapie

*Google Scholar*

„melodic intonation therapy“

„melodische intonationstherapie“

*ICTRP (International Clinical Trials Registry Platform)*

"melodic intonation therapy"

*Medline OVID*

("melodic intonation therapy".ab. or "melodic intonation therapy".ti. or "melodic intonation therapy".id. or ((singing.ab. or singing.id. or singing.ti. or singing/) AND (speech therapy/ or "speech therapy".ab. or "speech therapy".id. or "speech therapy".ti.))) AND (aphasia.ab. or aphasia.id. or aphasia.ti. or exp aphasia)

*Music Periodicals Database*

"melodic intonation therapy" and aphasia

*National Research Register (UK):* [*http://www.nihr.ac.uk/*](http://www.nihr.ac.uk/)

"melodic intonation therapy"

*Netherlands Trials Register www.trialregister.nl*

Melodic intonation

*OpenGrey.eu http://www.opengrey.eu/*

„melodic intonation therapy“

*ProQuest Dissertations & Theses Global*

„melodic intonation therapy“

*PsycINFO OVID*

("melodic intonation therapy".ab. or "melodic intonation therapy".ti. or "melodic intonation therapy".id. or ((singing.ab. or singing.id. or singing.ti. or singing/) AND (speech therapy/ or "speech therapy".ab. or "speech therapy".id. or "speech therapy".ti.))) AND (aphasia.ab. or aphasia.id. or aphasia.ti. or exp aphasia)

*PSYNDEX OVID*

("melodic intonation therapy".ab. or "melodic intonation therapy".ti. or "melodic intonation therapy".id. or ((singing.ab. or singing.id. or singing.ti. or singing/) AND (speech therapy/ or "speech therapy".ab. or "speech therapy".id. or "speech therapy".ti.))) AND (aphasia.ab. or aphasia.id. or aphasia.ti. or exp aphasia)

*PubMed*

(„melodic intonation therapy“ OR ((singing [MeSH Terms] OR singing) AND ("speech therapy"[MeSH Terms] OR "speech therapy")) AND (aphasia[MeSH Terms] OR aphasia)

*Scopus*

((( TITLE-ABS-KEY ( singing ) AND (TITLE-ABS-KEY ( "speech therapy" OR "language therapy" ))) OR ( TITLE-ABS-KEY ( "melodic intonation therapy" ))) AND ( TITLE-ABS-KEY ( aphasia))

*Web of Science*

TOPIC: (("melodic intonation therapy") OR TOPIC: ("singing" AND ("speech therapy" OR "language therapy")) AND TOPIC: aphasia

# Lists of primary studies considered

## Included studies

eTable 1: List of studies included in the present meta-analysis.

| **Study type** | **1st auth** | **Year** | **Title** | **N (MIT group)** | **N (ctrl group)** | **IPD** | **MIT variant** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| case series | Akanuma | 2016 | Singing can improve speech function in aphasics associated with intact right basal ganglia and preserve right temporal glucose metabolism: Implications for singing therapy indication | 10 | - | 1 | singing therapy |
| case series | Belin | 1996 | Recovery from nonfluent aphasia after melodic intonation therapy: A PET study | 7 | - | 1 | TMR |
| single case | Bitan | 2018 | Changes in Resting-State Connectivity following Melody-Based Therapy in a Patient with Aphasia | 1 | - | 1 | MMIT |
| uncontrolled before and after study | Cortese | 2015 | Rehabilitation of aphasia: application of melodic-rhythmic therapy to Italian language | 6 | - | 1 | MRT |
| case series | Haro-Martínez | 2017 | Adaptation of melodic intonation therapy to Spanish: a feasibility pilot study | 4 | - | 1 | MIT |
| RCT | Haro-Martínez | 2019 | Melodic intonation therapy in post-stroke nonfluent aphasia: a randomized pilot trial | 20 | 20 | 0 | MIT |
| single case | Hatayama | 2021 | Music intonation therapy is effective for speech output in a patient with non‐fluent aphasia in a chronic stage | 1 | - | 1 | MIT |
| single case | Homan | 2015 | A Combination of Therapeutic Techniques: Severe Broca’s Aphasia | 1 | - | 1 | MMIT |
| case series | Hurkmans | 2015 | The effectiveness of Speech–Music Therapy for Aphasia (SMTA) in five speakers with Apraxia of Speech and aphasia | 5 | - | 1 | SMTA |
| case series | Jungblut | 2014 | Paving the Way for Speech: Voice-Training-Induced Plasticity in Chronic Aphasia and Apraxia of Speech—Three Single Cases | 3 | - | 1 | SIPARI |
| case series | Naeser | 1985 | CT Scan Lesion Localization and Response to Melodic Intonation Therapy with Nonfluent Aphasia Cases | 8 | - | 1 | MIT |
| single case | Primassin | 2014 | Melodische Intonationstherapie bei einer aphasischen Patientin in der (Post-) Akutphase | 1 | - | 1 | MIT |
| single case | Slavin | 2018 | A Case Study Using a Multimodal Approach to Melodic Intonation Therapy | 1 | - | 1 | SMTA |
| controlled before and after study | Stahl | 2013 | How to engage the right brain hemisphere in aphasics without even singing: evidence for two paths of speech recovery | 5 | - | 1 | singing therapy |
| single case | Tabei | 2016 | Improved Neural Processing Efficiency in a Chronic Aphasia Patient Following Melodic Intonation Therapy: A Neuropsychological and Functional MRI Study | 1 | - | 1 | MIT |
| single case | van de Sandt-Koenderman | 2010 | A Case Study of Melodic Intonation Therapy (MIT) in the Subacute Stage of Aphasia: Early Re-re activation of Left Hemisphere Structures | 1 | - | 1 | MIT |
| uncontrolled before and after study | van de Sandt-Koenderman | 2018 | Language lateralisation after Melodic Intonation Therapy: an fMRI study in subacute and chronic aphasia | 9 | - | 1 | MIT |
| case series | van der Meulen | 2012 | Melodic Intonation Therapy: Present Controversies and Future Opportunities | 2 | - | 1 | MIT |
| RCT | van der Meulen | 2014 | The Efficacy and Timing of Melodic Intonation Therapy in Subacute Aphasia | 23 | 25 | 0 | MIT |
| RCT | van der Meulen | 2016 | Melodic Intonation Therapy in Chronic Aphasia: Evidence from a Pilot Randomized Controlled Trial | 16 | 17 | 0 | MIT |
| single case | Wilson | 2006 | Preserved singing in aphasia: a case study of the eﬃcacy of the Melodic Intonation Therapy | 1 | - | 1 | palliative MIT (pMIT) |
| case series | Zumbansen | 2014 | The Combination of Rhythm and Pitch Can Account for the Beneficial Effect of Melodic Intonation Therapy on Connected Speech Improvements in Broca’s Aphasia | 3 | - | 1 | MIT |

## Excluded studies

eTable 2: List of initially included but later excluded studies (cf lists of *Eligibility criteria*). a: Substantial variation from MIT protocol; b: Non-validated tests; c: No contrast of trained vs untrained items; d: No pre&post data; e: Other essential data not reported; f: Untrustworthy source, e.g. non-peer-reviewed journal; g: Patient(s) 17 or younger.

| **Study** | | | | **Reason for exclusion** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Type** | **First author** | **Year** | **Title** | a | b | c | d | e | f | g |
| case series | Al-Janabi | 2014 | Augmenting melodic intonation therapy with non-invasive brain stimulation to treat impaired left-hemisphere function: two case studies |  | 1 | 1 | 1 |  |  |  |
| case series | Baker | 2000 | Modifying the Melodic Intonation Therapy Program for Adults With Severe Non-fluent Aphasia |  | 1 |  |  |  |  |  |
| case series | Breier | 2010 | Changes in maps of language activity activation following melodic intonation therapy using magnetoencephalography: Two case studies |  | 1 | 1 |  |  |  |  |
| case series | Kim | 2008 | Protocol Evaluation for Effective Music Therapy for Persons with Nonfluent Aphasia |  | 1 | 1 | 1 |  |  |  |
| case series | Mauszycki | 2016 | Melodic intonation therapy applied to the production of questions in aphasia |  | 1 | 1 |  |  |  |  |
| case series | Schlaug | 2009 | Evidence for plasticity in white-matter tracts of patients with chronic Broca’s aphasia undergoing intense intonation-based speech therapy. |  | 1 |  |  |  |  |  |
| case series | Schlaug | 2008 | From Singing to Speaking: Why Singing May Lead to Recovery of Expressive Language Function in Patients with Broca's Aphasia |  | 1 | 1 |  |  |  |  |
| case series | Sparks | 1974 | Aphasia rehabilitation resulting from melodic intonation therapy |  |  |  |  | 1 |  |  |
| case series | Wambaugh | 2012 | Acquired Apraxia of Speech: The Effects of Repeated Practice and Rate/Rhythm Control Treatments on Sound Production Accuracy | 1 |  |  |  |  |  |  |
| controlled before and after study | Wan | 2014 | Intensive therapy induces contralateral white matter changes in chronic stroke patients with Broca’s aphasia |  | 1 |  |  |  |  |  |
| controlled before and after study | Osisanya | 2012 | Effectiveness of melodic intonation therapy in the management of communication difficulty of pupils with non-fluent aphasia in the classroom setting |  |  |  |  |  | 1 |  |
| Cross-over trial | Brendel | 2008 | Effectiveness of metrical pacing in the treatment of apraxia of speech | 1 |  |  |  |  |  |  |
| RCT | Conklyn | 2012 | The Effects of Modified Melodic Intonation Therapy on Nonfluent Aphasia: A Pilot Study |  | 1 | 1 |  |  |  |  |
| RCT | Raglio | 2016 | Improvement of spontaneous language in stroke patients with chronic aphasia treated with music therapy: a randomized controlled trial | 1 |  |  |  |  |  |  |
| RCT | Zumbansen | 2017 | Effect of choir activity in the rehabilitation of aphasia: a blind, randomised, controlled pilot study | 1 |  |  |  |  |  |  |
| RCT | Vines | 2011 | Non invasive brain stimulation enhances the effects of melodic intonation therapy | 1 |  | 1 |  |  |  |  |
| single case | Hough | 2010 | Melodic Intonation Therapy and aphasia: another variation on a theme |  | 1 |  |  |  |  |  |
| single case | Jungblut | 2009 | Long-term recovery from chronic global aphasia: A case report |  |  |  | 1 |  |  |  |
| single case | Lagasse | 2012 | Evaluation of Melodic Intonation Therapy for Developmental Apraxia of Speech |  |  |  |  | 1 |  |  |
| single case | Zipse | 2012 | When right is all that is left: plasticity of right-hemisphere tracts in a young aphasic patient |  |  |  |  |  |  | 1 |
| single case | Fountura | 2014 | Efficacy of the Adapted Melodic Intonation Therapy: a case study of a Broca`s Aphasia Patient |  |  |  |  |  | 1 |  |
| single-case study | Goldfarb | 1979 | Espousing melodic intonation therapy in aphasia rehabilitation: a case study. |  | 1 | 1 | 1 |  |  |  |
| single-case study | Morrow-Odom | 2013 | Effectiveness of melodic intonation therapy in a case of aphasia following right hemisphere stroke |  | 1 |  |  |  |  |  |
| single-case study | Wambaugh | 2000 | Eﬀects of rate and rhythm control treatment on consonant production accuracy in apraxia of speech | 1 |  |  |  |  |  |  |
| uncontrolled before and after study | Bonakdarpour | 2003 | Melodic intonation therapy in Persian aphasic patients |  | 1 | ? |  |  |  |  |
| uncontrolled before and after study | Lim | 2013 | The Therapeutic Effect of Neurologic Music Therapy and Speech Language Therapy in Post-Stroke Aphasic Patients |  |  |  | 1 | 1 |  |  |
| uncontrolled before and after study | Hurkmans | 2016 | The treatment of apraxia of speech: Speech and music therapy, an innovative joint effort | 1 |  |  |  |  |  |  |
|  | Keith | 1975 | Singing as therapy for apraxia of speech and aphasia: Report of a case | 1 |  |  |  |  |  |  |
|  | Krauss | 1982 | Melodic intonation therapy with language delayed apraxic children |  |  |  |  |  |  | 1 |
|  | Marshall | 1976 | Melodic Intonation Therapy: Variations on a Theme |  |  | 1 |  |  |  |  |
|  | Mauszycki | 2008 | The effects of rate control treatment on consonant production accuracy in mild apraxia of speech | 1 |  |  |  |  |  |  |
|  | Springer | 1993 | Training in the use of wh-questions and prepositions in dialogues: A comparison of two different approaches in aphasia therapy |  | 1 |  |  | 1 |  |  |
|  | Tonkovich | 1977 | The Effects of Stress and Melodic Intonation on Apraxia of Speech |  |  |  |  |  |  |  |
|  | Darland | 2021 | The Effects of Varying Melodic Intervals in Melodic Intonation Therapy for Persons with Aphasia | 1 |  |  |  |  |  |  |
|  | Martzoukou | 2021 | Adaptation of Melodic Intonation Therapy to Greek: A Clinical Study in Broca’s Aphasia With Brain Perfusion SPECT Validation | 1 |  |  |  |  |  |  |

# Tests and outcome measures in primary studies

eTable 3: List of all tests considered.

| **Test battery abbreviation** | **Test battery full name** | **Validation study exists** |
| --- | --- | --- |
| - | Farsi aphasia test | No |
| - | Apraxia Battery for Adults | No |
| AABT | Aachener Aphasie Bedside Test | Yes6 |
| AAT | Aachen Aphasia Test | Yes7,8 |
| ADP | Aphasia Diagnostic Proﬁles | No |
| ANELT | Amsterdam-Nijmegen Everyday Language Test | Yes9 |
| BDAE | Boston Diagnostic Aphasia Examination | Yes10,11 |
| BNT | Boston Naming Test | Yes12,13 |
| CAL | Communicative Activity Log | No |
| CIU | Sabadel CIUs/min | No |
| DIAS | Diagnostic Instrument for Apraxia of Speech (AoS) | Yes14 |
| HWL | Hierarchical Word List | Yes15 |
| MT86 | Montréal–Toulouse Aphasia Battery | No |
| PALPA | Psycholinguistic assessments of language processing in aphasia | Yes16 |
| PICA | Porch Index Of Communicative Ability | Yes17,18 |
| PPTT | Pyramids and Palm Trees Test | Yes16 |
| SLTA | Standard Language Test of Aphasia | Yes19 |
| WAB | Western Aphasia Battery | Yes20 |

eTable 4: Categorisation scheme showing how, for each target syndrome, Subtests → Tests → Abilities → Domains.

| **Target syndrome** | **Domain** | **Ability** | **Test battery** | **Subtest** |
| --- | --- | --- | --- | --- |
| Aphasia | Aphasia severity | Overall language performance | AAT | aphasia severity |
| Aphasia | Aphasia severity | Overall language performance | BDAE | aphasia severity |
| Aphasia | Aphasia severity | Overall language performance | PALPA | (no particular subtests) |
| Aphasia | Aphasia severity | Overall language performance | PPTT | (no particular subtests) |
| Aphasia | Aphasia severity | Overall language performance | WAB | aphasia quotient (AQ) |
| Aphasia | Communication | Everyday communication | ANELT | comprehensibility |
| Aphasia | Communication | Everyday communication | ANELT | intelligibility |
| Aphasia | Communication | Everyday communication | ANELT | verbal communication |
| Aphasia | Domain-general function | Cognitive-executive skills | AABT | BLIKO = Aufforderungen zu Blick- und Kopfbewegungen |
| Aphasia | Domain-general function | Cognitive-executive skills | AABT | IDENT = Identifizieren von Objekten |
| Aphasia | Domain-general function | Cognitive-executive skills | AABT | MUMO = Aufforderungen zu Mundbewegungen |
| Aphasia | Domain-general function | Cognitive-executive skills | AAT | token |
| Aphasia | Language comprehension | Auditory comprehension | AAT | auditory comprehension |
| Aphasia | Language comprehension | Auditory comprehension | BDAE | auditory commands |
| Aphasia | Language comprehension | Auditory comprehension | BDAE | auditory comprehension |
| Aphasia | Language comprehension | Auditory comprehension | BDAE | complex auditory material |
| Aphasia | Language comprehension | Auditory comprehension | WAB | auditory comprehension |
| Aphasia | Language comprehension | Written comprehension | AAT | written comprehension |
| Aphasia | Language comprehension | Written comprehension | AAT | written language |
| Aphasia | Language comprehension | Written comprehension | BDAE | reading comprehension |
| Aphasia | Language comprehension | Written comprehension | WAB | reading |
| Aphasia | Non-communicative language expression | Articulatory agility | BDAE | articulatory agility |
| Aphasia | Non-communicative language expression | Grammatical form | BDAE | grammatical form |
| Aphasia | Non-communicative language expression | Naming | AABT | BENENN = Benennen von Objekten |
| Aphasia | Non-communicative language expression | Naming | AAT | naming |
| Aphasia | Non-communicative language expression | Naming | BDAE | naming |
| Aphasia | Non-communicative language expression | Naming | BDAE | naming (confrontation ~) |
| Aphasia | Non-communicative language expression | Naming | BDAE | naming (responsive ~) |
| Aphasia | Non-communicative language expression | Naming | BNT | naming |
| Aphasia | Non-communicative language expression | Naming | SLTA | picture (manga) description test |
| Aphasia | Non-communicative language expression | Naming | WAB | naming |
| Aphasia | Non-communicative language expression | Phrase length | BDAE | phrase length |
| Aphasia | Non-communicative language expression | Repetition | (trained) | repetition |
| Aphasia | Non-communicative language expression | Repetition | (untrained) | repetition |
| Aphasia | Non-communicative language expression | Repetition | AABT | SIREI = Singen, Reihen- und Floskelsprechen |
| Aphasia | Non-communicative language expression | Repetition | AAT | repetition |
| Aphasia | Non-communicative language expression | Repetition | BDAE | repetition |
| Aphasia | Non-communicative language expression | Repetition | WAB | repetition |
| Aphasia | Non-communicative language expression | Spontaneous speech | AAT | automatic language |
| Aphasia | Non-communicative language expression | Spontaneous speech | AAT | communication |
| Aphasia | Non-communicative language expression | Spontaneous speech | AAT | phonetic language |
| Aphasia | Non-communicative language expression | Spontaneous speech | AAT | prosody |
| Aphasia | Non-communicative language expression | Spontaneous speech | AAT | semantic language |
| Aphasia | Non-communicative language expression | Spontaneous speech | AAT | syntactic language |
| Aphasia | Non-communicative language expression | Spontaneous speech | WAB | spontaneous speech |
| Aphasia | Non-communicative language expression | Syllable production | (trained) | correct syllables across test-phrases |
| Aphasia | Non-communicative language expression | Syllable production | (trained) | correct syllables per test-phrase |
| Aphasia | Non-communicative language expression | Syllable production | (untrained) | correct syllables across test-phrases |
| Aphasia | Non-communicative language expression | Syllable production | (untrained) | correct syllables per test-phrase |
| Aphasia | Non-communicative language expression | Verbal expression | BDAE | verbal expression |
| Aphasia | Non-communicative language expression | Word production | (trained) | proportion of words correct |
| Aphasia | Non-communicative language expression | Word production | (untrained) | proportion of words correct |
| Aphasia | Non-communicative language expression | Writing | WAB | writing |
| Apraxia of Speech | Speech-motor planning | Speech-motor planning | DIAS | articulation of phonemes |
| Apraxia of Speech | Speech-motor planning | Speech-motor planning | DIAS | articulation of words |
| Apraxia of Speech | Speech-motor planning | Speech-motor planning | DIAS | diadochokinesis (DDK) |
| Apraxia of Speech | Speech-motor planning | Speech-motor planning | HWL | number of assessable items |
| Apraxia of Speech | Speech-motor planning | Speech-motor planning | HWL | phonemic structure |
| Apraxia of Speech | Speech-motor planning | Speech-motor planning | HWL | phonetic structure |
| Apraxia of Speech | Speech-motor planning | Speech-motor planning | HWL | speech fluency |

# Supplementary meta-analysis methods

## RCTs

All RCTs were reported at the group-level. We computed effect sizes as the pretest-posttest-control group Hedges’ *g*21:

. We computed the variance for each *g* using the method of Morris (2008). We estimated multi-level mixed effects meta-regression models to account for effect size dependency, with random intercepts for each study. We first fit an overall meta-analysis combining all effect sizes. Second, we fit additional meta-regression models including potential moderator variables. For these meta-regression models, we included random slopes for the *Domain* moderator, nested within studies22. We used a homoscedastic compound symmetric structure for the random effects, estimating a single random effects variance and correlation for all abilities.[[1]](#footnote-1) We estimated the amount of heterogeneity (i.e., *τ*) using the restricted maximum-likelihood estimator23. We computed confidence intervals for meta-regression coefficients and mean treatment effects using the Knapp and Hartung *t*-distribution method24, and for the random effects components using profile likelihood. We estimated models using *R* version 4.1.025 and the *metafor* package version 3.-0126.[[2]](#footnote-2)

## Case reports

All case reports reported results as individual-level data, so we analysed these studies using IPD meta-analysis. We computed individual-level scores as the difference between pre-test and post-test *z*-scores (the mean difference in these scores is the pretest-posttest Hedges’ *g*, *gpp*). We then pooled data across studies using a three-level random-effects IPD meta-analysis, with individual scores again (see Figure 2 in main article) nested within patients nested within studies27. Similar to the group-level RCT meta-analyses, we first fit an overall model including all data points with no moderators, then fit additional models including potential moderator variables as predictors. For these models, we included random intercepts for patients and studies.[[3]](#footnote-3) We estimated random effects components using REML and computed confidence intervals using profile likelihood. We estimated models using *R*25 and the *lme4* package version 1.1-2728.

# Results tables

## Overall RCT meta-analyses

eTable 5: Overall RCT meta-analyses.

| Term | Estimate | *SE* | Statistic | *df* | *p* | 95% conf. int. |
| --- | --- | --- | --- | --- | --- | --- |
| *g̅* | 0.31 | 0.16 | 2.00 | 25 | 0.057 | [−0.01, 0.63] |
| τ | 0.25 |  | 212.08 | 25 | < 0.001 | [ 0.10, 1.11] |

*Note.* *g̅* = mean pretest-posttest difference (*gppc*; accounting for control group), where a value of *g̅* = 1 can be back-translated to 10 ANELT points9,29,30; τ = estimated random effects standard deviation across studies; Statistic = *t* value for *g̅* and *QE* value for τ; confidence intervals computed using *t* distributions for *g̅* and profile likelihood for τ and ρ.

## RCT meta-analyses of domain categories

eTable 6: RCT meta-analyses of domain categories.

| Term | Estimate | *SE* | Statistic | *df* | *p* | 95% conf. int. |
| --- | --- | --- | --- | --- | --- | --- |
| *g̅* (Non-communicative Language Expression) | 0.35 | 0.21 | 1.68 | 21 | 0.108 | [-0.08, 0.78] |
| *g̅* (Communication) | -0.04 | 0.27 | -0.14 | 21 | 0.893 | [-0.59, 0.52] |
| *g̅* (Language Comprehension) | -0.12 | 0.26 | -0.47 | 21 | 0.643 | [-0.67, 0.42] |
| ∆*g̅* (unvalidated measure with untrained items) | -0.15 | 0.15 | -1.06 | 21 | 0.300 | [-0.46, 0.15] |
| ∆*g̅* (unvalidated measure with trained items) | 0.99 | 0.19 | 5.24 | 21 | < .001 | [ 0.60, 1.39] |
| τ | 0.33 |  | 158.71 | 21 | < .001 | [ 0.15, 1.01] |
| ρ | -0.05 |  |  |  |  | [-0.52, 0.93] |

*Note.* *g̅* = mean pretest-posttest difference (*gppc*; accounting for control group), where a value of *g̅* = 1 can be back-translated to 10 ANELT points9,29,30; τ = estimated random effects standard deviation across studies; ρ = estimated correlation among *g* treatment effects between measures of different ability domains across studies; Statistic = *t* value for *g̅* and *QE* value for τ; confidence intervals computed using *t* distributions for *g̅* and profile likelihood for τ.

## Overall IPD meta-analyses

eTable 7: Overall IPD meta-analyses.

| Term | Estimate | *SE* | *t* | 95% conf. int. |
| --- | --- | --- | --- | --- |
| *g̅* | 1.72 | 0.35 | 4.91 | [1.00, 2.42] |
| τ | 1.25 |  |  | [0.75, 1.90] |
| σ (person) | 0.75 |  |  | [0.35, 1.16] |
| σ (measure) | 2.02 |  |  | [1.87, 2.20] |

*Note.* *g̅* = mean pretest-posttest difference (*gpc*; not accounting for any control group), where a value of *g̅* = 1 can be back-translated to 10 ANELT points9,29,30; τ = estimated random effects standard deviation across studies; σ (person) = estimated random effects standard deviation across persons (within study); σ (measure) = estimated random effects standard deviation across measures (within person); confidence intervals computed using profile likelihood; *p* values omitted as the appropriate denominator degrees of freedom for linear mixed effects models is ill-defined 31,32; inference should be based on the profile likelihood confidence intervals.

## IPD meta-analyses of domain categories

eTable 8: IPD meta-analyses of domain categories.

| Term | Estimate | *SE* | *t* | 95% conf. int. |
| --- | --- | --- | --- | --- |
| *g̅* (Non-communicative Language Expression) | 2.01 | 0.42 | 4.79 | [ 1.17, 2.82] |
| *g̅* (Aphasia Severity) | 0.94 | 0.60 | 1.57 | [-0.23, 2.11] |
| *g̅* (Communication) | 1.46 | 0.60 | 2.42 | [ 0.29, 2.63] |
| *g̅* (Domain-General Function) | -0.07 | 0.61 | -0.12 | [-1.27, 1.12] |
| *g̅* (Language Comprehension) | 0.52 | 0.46 | 1.11 | [-0.40, 1.41] |
| *g̅* (Speech-Motor Planning) | 1.42 | 0.58 | 2.46 | [ 0.29, 2.53] |
| ∆*g̅* (unvalidated measure with untrained items) | -0.47 | 0.99 | -0.48 | [-2.40, 1.46] |
| ∆*g̅* (unvalidated measure with trained items) | 2.37 | 0.99 | 2.38 | [ 0.44, 4.31] |
| τ | 1.41 |  |  | [ 0.89, 2.05] |
| σ (person) | 0.82 |  |  | [ 0.49, 1.20] |
| σ (measure) | 1.86 |  |  | [ 1.70, 2.01] |

*Note.* *g̅* = mean pretest-posttest difference (*gpc*; not accounting for any control group), where a value of *g̅* = 1 can be back-translated to 10 ANELT points9,29,30; ∆*g̅* = estimated difference in *g̅* between validated and unvalidated measures; note that only Non-communicative Language Expression included unvalidated measures; τ = estimated random effects standard deviation across studies; σ (person) = estimated random effects standard deviation across persons (within study); σ (measure) = estimated random effects standard deviation across measures (within person); confidence intervals computed using profile likelihood; *p* values omitted as the appropriate denominator degrees of freedom for linear mixed effects models is ill-defined 31,32; inference should be based on the profile likelihood confidence intervals.

## IPD meta-analyses with aphasia stage (MPO) as a moderator

eTable 9: IPD meta-analyses with aphasia stage (months post-onset, MPO) as a moderator.

| Term | Estimate | *SE* | *t* | 95% conf. int. |
| --- | --- | --- | --- | --- |
| *g̅* (Non-communicative Language Expression) | 1.97 | 0.29 | 6.74 | [ 1.39, 2.54] |
| *g̅* (Aphasia Severity) | 1.08 | 0.51 | 2.13 | [ 0.14, 2.07] |
| *g̅* (Communication) | 2.10 | 0.45 | 4.62 | [ 1.21, 3.05] |
| *g̅* (Domain-General Function) | 2.00 | 0.56 | 3.58 | [ 0.96, 3.15] |
| *g̅* (Language Comprehension) | 0.74 | 0.35 | 2.10 | [ 0.05, 1.43] |
| *g̅* (Speech-Motor Planning) | 1.96 | 0.41 | 4.74 | [ 1.14, 2.83] |
| ∆*g̅* (unvalidated measure with untrained items) | -0.14 | 0.65 | -0.22 | [-1.41, 1.07] |
| ∆*g̅* (unvalidated measure with trained items) | 2.70 | 0.65 | 4.15 | [ 1.43, 3.91] |
| ∆*g̅* (per month post-onset) | -0.02 | 5.00e-03 | -3.07 | [-0.03, -0.01] |
| τ | 0.32 |  |  | [ 0.00, 0.82] |
| σ (person) | 1.01 |  |  | [ 0.69, 1.38] |
| σ (measure) | 1.57 |  |  | [ 1.40, 1.71] |

*Note.* *g̅* = mean pretest-posttest difference (*gpc*; not accounting for any control group), where a value of *g̅* = 1 can be back-translated to 10 ANELT points9,29,30; ∆*g̅* = estimated difference in *g̅*; note that only Non-communicative Language Expression included unvalidated measures; τ = estimated random effects standard deviation across studies; σ (person) = estimated random effects standard deviation across persons (within study); σ (measure) = estimated random effects standard deviation across measures (within person); confidence intervals computed using profile likelihood; *p* values omitted as the appropriate denominator degrees of freedom for linear mixed effects models is ill-defined 31,32; inference should be based on the profile likelihood confidence intervals.

## IPD meta-analyses with MIT protocol as a moderator

eTable 10: IPD meta-analyses with MIT protocol as a moderator.

| Term | Estimate | *SE* | *t* | 95% conf. int. |
| --- | --- | --- | --- | --- |
| *g̅* (Non-communicative Language Expression) | 1.71 | 0.58 | 2.93 | [ 0.59, 2.83] |
| *g̅* (Aphasia Severity) | 0.64 | 0.73 | 0.88 | [-0.75, 2.03] |
| *g̅* (Communication) | 1.16 | 0.73 | 1.60 | [-0.22, 2.55] |
| *g̅* (Domain-General Function) | -0.37 | 0.74 | -0.50 | [-1.78, 1.04] |
| *g̅* (Language Comprehension) | 0.22 | 0.62 | 0.35 | [-0.97, 1.40] |
| *g̅* (Speech-Motor Planning) | 1.11 | 0.71 | 1.55 | [-0.25, 2.47] |
| ∆*g̅* (unvalidated measure with untrained items) | -0.50 | 1.00 | -0.50 | [-2.42, 1.40] |
| ∆*g̅* (unvalidated measure with trained items) | 2.35 | 1.00 | 2.35 | [ 0.42, 4.25] |
| ∆*g̅* (modified MIT protocol) | 0.56 | 0.77 | 0.73 | [-0.92, 2.03] |
| τ | 1.42 |  |  | [ 0.84, 2.00] |
| σ (person) | 0.82 |  |  | [ 0.49, 1.21] |
| σ (measure) | 1.86 |  |  | [ 1.70, 2.01] |

*Note.* *g̅* = mean pretest-posttest difference (*gpc*; not accounting for any control group), where a value of *g̅* = 1 can be back-translated to 10 ANELT points9,29,30; ∆*g̅* = estimated difference in *g̅*; note that only Non-communicative Language Expression included unvalidated measures; τ = estimated random effects standard deviation across studies; σ (person) = estimated random effects standard deviation across persons (within study); σ (measure) = estimated random effects standard deviation across measures (within person); confidence intervals computed using profile likelihood; *p* values omitted as the appropriate denominator degrees of freedom for linear mixed effects models is ill-defined 31,32; inference should be based on the profile likelihood confidence intervals.

## Meta-analyses with only the change in control groups (taken from the RCTs).

eTable 11: Meta-analyses with only the change in control groups (taken from the RCTs).

| Term | Estimate | *SE* | Statistic | *df* | *p* | 95% conf. int. |
| --- | --- | --- | --- | --- | --- | --- |
| *g̅* (Non-communicative Language Expression) | 0.35 | 0.23 | 1.53 | NA | 0.14 | [-0.12, 0.81] |
| *g̅* (Communication) | 0.33 | 0.24 | 1.37 | NA | 0.19 | [-0.17, 0.82] |
| *g̅* (Language Comprehension) | 0.38 | 0.23 | 1.61 | NA | 0.12 | [-0.11, 0.86] |
| ∆*g̅* (unvalidated measure with untrained items) | 0.03 | 0.11 | 0.31 | NA | 0.76 | [-0.20, 0.26] |
| ∆*g̅* (unvalidated measure with trained items) | -0.55 | 0.10 | -5.59 | NA | < .001 | [-0.75, -0.34] |
| τ | 0.38 |  | 113.00 | 21.00 | < .001 | [ 0.17, 1.61] |
| ρ | 1.00 |  |  |  |  | [ 0.14, 1.00] |

eTable 11 shows that the estimated change for control groups is about .35 across categories. This accounts for some but not all of the difference in results between the g̅ values from the RCT meta-analysis of pretest-posttest-control group, and those of the case series.

## IPD meta-analyses with aphasia stage (months post-onset, MPO) as a moderator for pretest scores only.

eTable 12: IPD meta-analyses with aphasia stage (months post-onset, MPO) as a moderator for pretest scores only.

| Term | Estimate | *SE* | *t* | 95% conf. int. |
| --- | --- | --- | --- | --- |
| *g̅* (Non-communicative Language Expression) | -0.19 | 0.35 | -0.54 | [-0.86, 0.48] |
| *g̅* (Aphasia Severity) | -0.66 | 0.66 | -0.99 | [-1.90, 0.63] |
| *g̅* (Communication) | 0.55 | 0.58 | 0.94 | [-0.57, 1.67] |
| *g̅* (Domain-General Function) | -0.92 | 0.74 | -1.24 | [-2.34, 0.51] |
| *g̅* (Language Comprehension) | 2.34 | 0.50 | 4.68 | [ 1.38, 3.30] |
| *g̅* (Speech-Motor Planning) | 1.55 | 0.53 | 2.95 | [ 0.54, 2.56] |
| ∆*g̅* (unvalidated measure with untrained items) | -0.53 | 0.84 | -0.62 | [-2.15, 1.10] |
| ∆*g̅* (unvalidated measure with trained items) | 0.55 | 0.84 | 0.65 | [-1.08, 2.18] |
| ∆*g̅* (per month post-onset) | 0.01 | 0.01 | 0.97 | [-0.01, 0.03] |
| τ | 1.18 |  |  | [ 0.75, 1.61] |
| σ (person) | 0.00 |  |  | [ 0.00, 0.90] |
| σ (measure) | 2.18 |  |  | [ 1.94, 2.37] |

eTable 12 shows that pretest scores appear to increase by about .01 SDs per month post onset.

# Supplementary References

1. Brady, M. C., Kelly, H., Godwin, J. & Enderby, P. Speech and language therapy for aphasia following stroke. *Cochrane Database Syst. Rev.* (2016) doi:10.1002/14651858.CD000425.pub3.

2. Hurkmans, J. *et al.* Music in the treatment of neurological language and speech disorders: A systematic review. *Aphasiology* **26**, 1–19 (2012).

3. van der Meulen, I., van de Sandt-Koenderman, M. E. & Ribbers, G. M. Melodic Intonation Therapy: Present Controversies and Future Opportunities. *Arch. Phys. Med. Rehabil.* **93**, S46–S52 (2012).

4. Zumbansen, A., Peretz, I. & Hébert, S. Melodic Intonation Therapy: Back to Basics for Future Research. *Front. Neurol.* **5**, (2014).

5. Zumbansen, A. & Tremblay, P. Music-based interventions for aphasia could act through a motor-speech mechanism: a systematic review and case–control analysis of published individual participant data. *Aphasiology* **33**, 466–497 (2018).

6. Biniek, R., Huber, W., Glindemann, R., Willmes, K. & Klumm, H. [The Aachen Aphasia Bedside Test--criteria for validity of psychologic tests]. *Nervenarzt* **63**, 473–479 (1992).

7. Huber, W., Poeck, K. & Willmes, K. The aachen aphasia test. *Adv. Neurol.* **42**, 291–303 (1984).

8. Willmes, K. An approach to analyzing a single subject’s scores obtained in a standardized test with application to the aachen aphasia test (AAT). *J. Clin. Exp. Neuropsychol.* **7**, 331–352 (1985).

9. Blomert, L., Kean, M. L., Koster, C. & Schokker, J. Amsterdam—Nijmegen everyday language test: construction, reliability and validity. *Aphasiology* **8**, 381–407 (1994).

10. Goodglass, H., Kaplan, E. & Barresi, B. BDAE: The Boston Diagnostic Aphasia Evaluation. (2001).

11. Goodglass, H., Kaplan, E. & Weintraub, S. *Boston naming test*. (Lea & Febiger Philadelphia, PA, 1983).

12. Theodoros, D., Hill, A., Russell, T., Ward, E. & Wootton, R. Assessing acquired language disorders in adults via the Internet. *Telemed. J. E-Health Off. J. Am. Telemed. Assoc.* **14**, 552–559 (2008).

13. Pedraza, O., Sachs, B. C., Ferman, T. J., Rush, B. K. & Lucas, J. A. Difficulty and discrimination parameters of Boston naming test items in a consecutive clinical series. *Arch. Clin. Neuropsychol. Off. J. Natl. Acad. Neuropsychol.* **26**, 434–444 (2011).

14. Feiken, J. Diagnostic Instrument Apraxia of Speech (DIAS). (2009).

15. Liepold, M., Ziegler, W., Brendel, B. & Ziegler, W. *Hierarchische Wortlisten: Ein Nachsprechtest für die Sprechapraxiediagnostik*. (Borgmann, 2003).

16. Pinto-Grau, M. *et al.* Validation and standardization of the Psycholinguistic Assessments of Language Processing in Aphasia (PALPA). *Aphasiology* **35**, 1593–1610 (2021).

17. Sanders, S. B. & Davis, G. A. A comparison of the Porch Index of Communicative Ability and the Western Aphasia Battery. in *Clinical Aphasiology: Proceedings of the Conference 1978* 117–126 (BRK Publishers, 1978).

18. Duffy, J., Keith, R. L., Shane, H. & Podraza, B. L. Performance of normal (non-brain injured) adults on the Porch Index of Communicative Ability. in *Clinical Aphasiology: Proceedings of the Conference 1976* 32–42 (BRK Publishers, 1976).

19. Tamura, A., Shichijo, F. & Matsumoto, K. A study on simplification of the Standard Language Test of Aphasia (SLTA). *Tokushima J. Exp. Med.* **43**, 39–46 (1996).

20. Wallace, S. J. *et al.* A core outcome set for aphasia treatment research: The ROMA consensus statement. *Int. J. Stroke* **14**, 180–185 (2019).

21. Morris, S. B. Estimating effect sizes from pretest-posttest-control group designs. *Organ. Res. Methods* **11**, 364–386 (2008).

22. Konstantopoulos, S. Fixed effects and variance components estimation in three-level meta-analysis: Three-level meta-analysis. *Res. Synth. Methods* **2**, 61–76 (2011).

23. Viechtbauer, W. Bias and efficiency of meta-analytic variance estimators in the random-effects model. *J. Educ. Behav. Stat.* **30**, 261–293 (2005).

24. Knapp, G. & Hartung, J. Improved tests for a random effects meta-regression with a single covariate. *Stat. Med.* **22**, 2693–2710 (2003).

25. R Core Team. *R: a language and environment for statistical computing*. (R Foundation for Statistical Computing, 2021).

26. Viechtbauer, W. Conducting meta-analyses in *R* with the *metafor* package. *J. Stat. Softw.* **36**, (2010).

27. Riley, R. D., Lambert, P. C. & Abo-Zaid, G. Meta-analysis of individual participant data: rationale, conduct, and reporting. *BMJ* **340**, c221 (2010).

28. Bates, D., Mächler, M., Bolker, B. & Walker, S. Fitting linear mixed-effects models using *lme4*. *J. Stat. Softw.* **67**, (2015).

29. van der Meulen, I., van de Sandt-Koenderman, W. Mieke. E., Heijenbrok-Kal, M. H., Visch-Brink, E. G. & Ribbers, G. M. The Efficacy and Timing of Melodic Intonation Therapy in Subacute Aphasia. *Neurorehabil. Neural Repair* **28**, 536–544 (2014).

30. Van Der Meulen, I., Van De Sandt-Koenderman, M. W. M. E., Heijenbrok, M. H., Visch-Brink, E. & Ribbers, G. M. Melodic Intonation Therapy in Chronic Aphasia: Evidence from a Pilot Randomized Controlled Trial. *Front. Hum. Neurosci.* **10**, (2016).

31. Bates, D. [R] lmer, p-values and all that. https://stat.ethz.ch/pipermail/r-help/2006-May/094765.html (2006).

32. Bates, D., Mächler, M., Bolker, B. & Walker, S. Fitting Linear Mixed-Effects Models Using lme4. *J. Stat. Softw.* **67**, 1–48 (2015).

1. For comparison, we also estimated models with unequal random effects variances across dependent variables. This did not improve model fit based on AICc comparison or likelihood ratio tests. [↑](#footnote-ref-1)
2. As only three RCT studies were identified, it was not possible to apply methods to detect publication-bias or other small-sample effects (e.g., tests of funnel plot asymmetry). [↑](#footnote-ref-2)
3. Models with random slopes for the *Domain* variable did not converge, likely due to the limited co-occurrence of specific pairs of those within any one study. [↑](#footnote-ref-3)