Complex speech-language therapy interventions for stroke-related aphasia: the RELEASE study incorporating a systematic review and individual participant data network meta-analysis

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Scientific summary

The RELEASE study

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Scientific summary

Background

Aphasia (impairment of language) is a common and devastating long-term consequence of stroke. Its impact extends beyond the language domains of spoken language, auditory comprehension, reading comprehension and writing. Stroke survivors with aphasia experience poorer functional recovery (with comprehension deficits in particular affecting activities of daily living), continence and emotional well-being after stroke, than stroke survivors with intact language abilities. People with aphasia are also less likely to return to work or even return home.

Speech and language therapy benefits people with stroke-related aphasia. Maximising language recovery is a research priority for stroke survivors, carers and health-care professionals. We need greater insight into the contribution to recovery across language domains made by individual characteristics (e.g. age, stroke and aphasia profiles) and by the components of speech and language therapy (target and theoretical approach, delivery model and regimen).

Objectives

We aimed to explore:

- the pattern of language recovery following stroke-related aphasia
- the predictors of language recovery outcomes following aphasia
- the components of effective aphasia rehabilitation interventions
- whether or not some interventions (or intervention components) were more beneficial for some subgroups (individual, stroke or aphasia characteristics) than others.

Methods

We created an international aphasia database that included individual participant data on demographics, stroke profiles, language impairment, and speech and language therapy interventions and subsequent outcomes across a range of language domains. The database (Integrated Research Application System number 179505) met existing data-sharing guidelines and followed a prespecified protocol (PROSPERO CRD42018110947). Our reporting observes the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and relevant extensions. We employed Guidance for Reporting Involvement of Patients and the Public and referred to the grading quality of evidence and strength of recommendations [using the Grading of Recommendations Assessment, Development and Evaluation and the Risk Of Bias In Systematic reviews (ROBIS) tools] to support judgements of the impact of the quality of the evidence on our findings.

We systematically searched the following databases (from inception to September 2015) using a randomised controlled trial-optimised search strategy: Cochrane Stroke Group Trials Register, Cochrane Central Register of Controlled Trials and other Cochrane Library databases (Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects and Health Technology Assessment Database), MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature, Allied and Complementary Medicine Database, Linguistic and Language Behavior Abstracts and SpeechBITE. We imposed no language restrictions. We searched for data sets containing anonymised individual participant data on at least 10 people with aphasia following stroke (collected with ethics approval), including measures of language impairment and time since stroke.

The identified records were screened for eligibility. Full-text reports were reviewed by two independent researchers; disagreements were resolved through discussion with a third researcher when necessary. Randomised controlled trial, non-randomised controlled trial, cohort, case series and registry data sets were included. Primary researchers of identified records were invited to contribute electronic data sets. Eligible data sets in the public domain were also identified and transcribed. We developed and piloted a data extraction table, which supported retrieval of demographic, environmental, stroke and language data at individual participant data level, as well as descriptors at study level, including quality criteria (selection, detection and attrition bias). Speech and language therapy interventions from identified studies described targeted rehabilitation tasks that sought to enhance language abilities, activities or participation. These interventions were extracted using the Template for Intervention Description and Replication, and additionally categorised by impairment target and theoretical approach. Data extraction was rigorously checked by a second researcher. When possible, we confirmed data extraction with the primary researchers. Ensuring data integrity was essential to the project.

We converted all data sets into SAS® version 9.4 (SAS Institute Inc., Cary, NC, USA). Prior to analysis, we cleaned all data relating to prespecified variables required for our planned analyses. Across data sets, language abilities were captured on a range of different assessment tools (sometimes in various language adaptations). Language or version variations were treated as separate tools. For each domain, we identified the assessments used; calculated the median score, interquartile range, minimum and maximum; and identified an anchor measure for that domain (the measurement used by the most data sets). All other measures for that domain (minority measures) were transformed to match the format, distribution and range of each anchor measure, using a prespecified algorithm.

Our project aimed to generate hypotheses and to highlight important avenues for further research. We therefore did not employ a strict experimental, hypothesis-testing approach, but, instead, used statistical inferencing to inform the description of participant populations, data items and research questions for future large-scale definitive experimental investigations. We conducted one-stage, random-effects meta-analyses and network meta-analyses based on our individual participant data database. Analyses comprised individual participant data from both electronic data sets and the public domain; these combined data were filtered for relevance into analysis-specific data sets, which were then analysed using a model that considered the clustering of individual participant data in a study. In this way, we explored the subtleties of a highly heterogeneous group of people with aphasia after stroke, controlled for individual predictors. This supported detailed exploration of the influence of participant-level covariates on speech and language therapy treatment effects across a range of language domains.

Results

We created a database of 5928 individual participant data on people with aphasia after stroke, gathered from 174 data sets across 28 countries. Half of the data sets were based on an English-speaking population, 27% were randomised controlled trials and 7.5% were unpublished. Our search identified an additional 53 randomised controlled trials (of which 46 appeared to include a speech and language therapy intervention) as potentially eligible for inclusion, but their individual participant data were unavailable. Speech and language therapy interventions were described for half of the included data sets and almost half of the participants. Limited language individual participant data both at baseline and after an intervention restricted the data available for our meta-analyses of speech and language therapy interventions for aphasia.

Interventions were complex and wide-ranging. Classification of speech and language therapy by impairment target and theoretical approach required a consensus method. We considered risk of bias at both primary data set and meta-analysis level. We endeavoured to address any risk of bias methodologically and considered that risk in the interpretation of the findings.

Patterns of language recovery

A paucity of data on participants who received no speech and language therapy, enrolled within 15 days of stroke onset, and who had not received speech and language therapy in the past precluded analysis of the natural history of recovery or the nature of spontaneous recovery across language domains (individual participant data from one data set). Many participants in our database who were initially allocated to receive no speech and language therapy were permitted to receive speech and language therapy following the study's intervention period. Limited data at the post-intervention time point for those who were allocated to no speech and language therapy precluded effective comparison of the trajectory of language scores over time between those who were allocated to no speech and language therapy and participants who had access to speech and language therapy. Data on those who received only historical speech and language therapy (standard speech and language therapy prior to the research study start) were also limited [22 individual participant data from two randomised controlled trials and 34 individual participant data from three data sets (all study types)], as corresponding post-intervention follow-up values were unavailable or did not meet our minimum eligibility criteria for the analysis.

Among participants who were allocated to receive speech and language therapy, we observed an increase in scores over time. Language impairment scores were higher as time to study entry increased, particularly for measures of overall language ability and naming.

We noted that, across all language domains, the highest absolute proportions of changes in scores were seen in those participants enrolled in a study within 1 month of stroke and in those who were aged < 55 years. This proportion of change appeared to decrease with increasing time since stroke. Although many of these changes since baseline did not appear to be significantly different across different domains (e.g. the 95% confidence intervals overlapped), the estimated median changes in scores were notable from a clinical standpoint for some domains (e.g. 16.7% change on the Western Aphasia Battery-Aphasia Quotient from baseline for overall language ability, 207 individual participant data from 10 randomised controlled trials; 18.9% change in Aachen Aphasia Test-Spontaneous Communication for observer-rated activities, 318 individual participant data from nine randomised controlled trials).

Predictors of language recovery

Baseline language score, age, sex and time since stroke were significantly associated with absolute change in raw language domain scores (overall language ability, 418 individual participant data from 11 randomised controlled trials; auditory comprehension, 508 individual participant data from 17 randomised controlled trials; naming, 346 individual participant data from 14 randomised controlled trials; and functional communication, 608 individual participant data from 16 randomised controlled trials). These variables were included in the base statistical models in subsequent analyses of optimum speech and language therapy interventions. Optimum intervention parameters were identified as those that were associated with the greatest statistically significant mean differences in scores from baseline, which we present as 'peak' or 'highest gains' (or similar terms) in language recovery on these measures.

Effective aphasia rehabilitation interventions

To the base statistical model, we added speech and language therapy regimen (frequency, duration, intensity, dosage), approach (target and theoretical) and delivery (context, mode, expertise, tailoring) variables. The outcome measure of this model was change in absolute raw scores from baseline on the anchor measure, across each language domain. Relative variance was acceptable in these analyses (< 30%).

Speech and language therapy frequency (average number of therapy days weekly)

We observed that the greatest gains in functional communication [0.78 points on the Aachen Aphasia Test-Spontaneous Communication (95% confidence interval 0.48 to 1.09 points), 155 individual participant data from eight randomised controlled trials] and overall language abilities [14.95 points on the Western Aphasia Battery-Aphasia Quotient (95% confidence interval 8.67 to 21.23 points), 194 individual participant data from six randomised controlled trials] were associated with receiving speech and language therapy 4 or 5 days weekly. Peak gains in auditory comprehension [5.86 points on the Aachen Aphasia Test-Token Test (95% confidence interval 1.64 to 10.01 points), 114 individual participant data from five randomised controlled trials] occurred alongside speech and language therapy delivered 3 or 4 days weekly.

Duration (total number of weeks over which speech and language therapy was delivered)

The duration network geometry was unstable, with small numbers of participants and trials, and fewer connections between nodes; caution should be used when considering these data. We observed that the greatest gains in overall language abilities [17.27 points (95% confidence interval 9.71 to 24.82 points) on the Western Aphasia Battery-Aphasia Quotient, 45 individual participant data from three randomised controlled trials] and auditory comprehension [6.79 points (95% confidence interval 1.69 to 11.88 points) Aachen Aphasia Test-Token Test, 93 individual participant data from five randomised controlled trials] occurred when speech and language therapy was of > 10–20 weeks' duration. The highest naming gains [8.38 points (95% confidence interval 1.24 to 15.51 points) on the Boston Naming Test, 134 individual participant data from three randomised controlled trials] were associated with > 20 weeks of speech and language therapy, and the best functional communication gains [0.8 points (95% confidence interval 0.29 to 1.31 points) on the Aachen Aphasia Test-Spontaneous Speech Communication, 57 individual participant data from two randomised controlled trials] occurred for people receiving speech and language therapy for more than 4 weeks.

Intensity (average number of speech and language therapy hours weekly)

Optimal speech and language therapy intensity varied by language domain. We observed the greatest gains on overall language abilities [15.85 points (95% confidence interval 8.06 to 23.64 points) on the Western Aphasia Battery-Aphasia Quotient, 74 individual participant data from three randomised controlled trials], functional communication [0.77 points (95% confidence interval 0.36 to 1.19 points) on the Aachen Aphasia Test-Spontaneous Speech Communication, 83 individual participant data from four randomised controlled trials] and naming [13.23 points (95% confidence interval 5.83 to 20.64 points) on the Boston Naming Test, 18 individual participant data from two randomised controlled trials] in the context of speech and language therapy for 2 hours weekly. Clinically similar gains were observed alongside 4 and > 9 hours weekly. Naming findings were informed by small numbers of individual participant data and randomised controlled trials, and unstable network geometry, and should thus be treated cautiously. In contrast, the highest auditory comprehension gains [7.30 points (95% confidence interval 4.09 to 10.52 points) on the Aachen Aphasia Test-Token Test, 141 individual participant data from six randomised controlled trials] were associated with > 9 hours of speech and language therapy weekly.

Dosage (total number of therapy hours delivered)

A speech and language therapy dosage of more than 20–50 hours was associated with the greatest gains on overall language ability [18.37 points (95% confidence interval 10.58 to 26.16 points) on the Western Aphasia Battery-Aphasia Quotient, 31 individual participant data from four randomised controlled trials] and auditory comprehension [5.23 points (95% confidence interval 1.51 to 8.95 points) Aachen Aphasia Test-Token Test, 90 individual participant data from seven randomised controlled trials]. The greatest functional communication gains were seen alongside 14–20 hours of speech and language therapy [0.94 points (95% confidence interval 0.34 to 1.55 points) on the Aachen Aphasia Test-Spontaneous Speech Communication] and the greatest naming gains [12.48 points (95% confidence interval 1.34 to 23.63 points) on the Boston Naming Test, 28 individual participant data from two randomised controlled trials)] were seen alongside up to 5 hours of speech and language therapy. The numbers of individual participant data and randomised controlled trials, however, were small and the networks unstable in both analyses. In both functional communication and naming, the second-highest gains were noted to occur alongside 20–50 hours of speech and language therapy [naming: 9.23 points (95% confidence interval 1.75 to 16.7 points) on the Boston Naming Test, 81 individual participant data from five randomised controlled trials; functional communication: 0.77 points (95% confidence interval 0.43 to 1.1 points) on the Aachen Aphasia Test-Spontaneous Speech Communication, 96 individual participant data from nine randomised controlled trials].

The prescription of home practice tasks which augments the speech and language therapy dose contributed to the base model for auditory comprehension scores ($p = 0.019$), as did tailoring of speech and language therapy interventions for functional relevance ($p = 0.029$) and by level of difficulty ($p = 0.043$). Prescribed home practice was associated with the greatest gains in overall language ability [16.69 points (95% confidence interval 10.01 to 23.37 points) on the Western Aphasia Battery-Aphasia Quotient, 87 individual participant data from two randomised controlled trials] and auditory comprehension [5.28 points (95% confidence interval 2.19 to 8.37 points) on the Token Test-Aachen Aphasia Test; 278 individual participant data from seven randomised controlled trials].

Tailoring by functional relevance was associated with the best overall language ability [16.47 points (95% confidence interval 10.95 to 21.99 points) on the Western Aphasia Battery-Aphasia Quotient, 232 individual participant data from six randomised controlled trials], naming [8.79 points (95% confidence interval 1.95 to 15.63 points) on the Token Test-Aachen Aphasia Test, 113 individual participant data from five randomised controlled trials], auditory comprehension [5.26 points (95% confidence interval 2.05 to 8.47 points), 194 individual participant data from seven randomised controlled trials] and functional communication gains [0.74 points (95% confidence interval 0.38 to 1.10 points), 249 individual participant data from six randomised controlled trials]. Tailoring by level of language difficulty was associated with the best gains on auditory comprehension [4.57 points (95% confidence interval 1.55 to 7.60 points), 331 individual participant data from 10 randomised controlled trials]. Notably, adding the speech and language therapy theoretical approach (limited individual participant data), the provider's expertise (professional vs. trained non-professional or family member), the mode of speech and language therapy (face to face, computer based, self-managed) or therapy context (inpatient or outpatient) to the base model made no significant contribution to language outcomes.

Optimal speech and language therapy interventions for subpopulations of people with aphasia

We explored the impact of speech and language therapy interventions on people with aphasia with respect to their age, time since stroke, aphasia severity, sex and changes in language outcomes from baseline. The data from our subgroup analyses were informed by limited numbers of suitable individual participant data from randomised controlled trial data sets and should be cautiously interpreted in the context of the exploratory nature of this work. Relative variance was modest to low in most analyses.

Across subgroups (and when significant changes from baseline were observed), we noted the highest gains in language performance from baseline occurred among the participants aged < 55 years, female participants and in the context of early (< 3 months since aphasia onset) speech and language therapy intervention.

Both young participants (aged ≤ 65 years) and those in the older age group made optimal gains on language outcomes in the context of speech and language therapy interventions of a similar frequency and dosage. Where differences were noted, older participants' language improvements were generally greatest when speech and language therapy regimens were lower in intensity, whereas the younger group had highest language gains alongside more intensive speech and language therapy. Auditory comprehension, however, demonstrated the greatest improvements for both groups along with highly intensive speech and language therapy (of > 9 hours per week).

When speech and language therapy was delivered > 3 months after stroke, optimal gains were observed when therapy was frequent and at a high dosage. The best language gains within 3 months of aphasia onset were associated with less frequent and up to 50 hours of speech and language therapy.

People with mild to moderate aphasia were observed to have the highest change in scores from baseline in the context of speech and language therapy that was at a high intensity (e.g. interventions in excess of 9 hours weekly). However, some of the group's language gains from baseline were non-significant, a finding possibly limited by assessment ceiling effects. For people with moderate to severe aphasia, language gains were highest when associated with speech and language therapy for up to 4 hours weekly over 3–5 days.

Male participants made their greatest language gains in the context of speech and language therapy that was more frequent and intensive than the speech and language therapy interventions associated with female participants' best language gains.

Strengths

The international, multidisciplinary data sets, obtained in people with aphasia after stroke in clinical and research settings across several language domains, supported rigorous one-stage individual participant data meta-analyses and network meta-analyses and provides important insights into aphasia recovery after stroke. The database included high-quality randomised controlled trials and was developed using rigorous systematic review, data extraction and checking procedures, informed by the primary research teams when possible. We standardised multiple language measures to a single anchor measure for each domain, supporting clinical interpretation of the findings. We extended the Template for Intervention Description and Replication checklist to assist data extraction, synthesis and meta-analyses of complex speech and language therapy rehabilitation interventions. We explored patterns and predictors of recovery, and optimal speech and language therapy interventions for aphasia by language domain and participant subgroup. The findings provide important insights into the understanding of aphasia recovery after stroke.

Limitations

The exploratory findings require confirmation in definitive research designs. In some cases, the individual participant data database was insufficient to support the planned analysis; therefore, caution should be used when interpreting those data. We observed considerable variation in the collection and reporting of demographic, language and therapy intervention data in the aphasia data sets included. Similarly, reading and writing interventions and outcomes relating to communication participation or activities were rarely available. More than half of the individual participant data were English-language based, with limited individual participant data available in any one other language. Such gaps in the data collection, reporting and evidence syntheses highlight important methodological developments and topics for investigation in future definitive aphasia research.

Implications for people with aphasia after stroke and for health-care professionals

- We observed an increase in scores over time for participants allocated to receive speech and language therapy, which is probably inclusive of spontaneous recovery alongside early speech and language therapy interventions.
- Given the lack of available natural history data by language domain, distinguishing spontaneous recovery from therapeutic gains may continue to be a challenge. In our data, speech and language therapy access for stroke survivors with long-standing aphasia led to increased scores, supporting therapeutic gains. Nevertheless, clinical interventions are typically delivered in a context of spontaneous recovery. Identifying maximum gains in this context is clinically relevant.

- Language performance at baseline, age and time since stroke were significantly associated with recovery in selected domains.
- Optimal language gains from baseline for people with aphasia after stroke varied by language domain and in response to different levels of speech and language therapy frequency, intensity and dosage.

Research recommendations

- The data informing the analysis of optimum speech and language therapy interventions for reading and writing were limited. More randomised controlled trials of the effectiveness of speech and language therapy interventions for these language domains are required.
- Data on non-English-speaking populations were severely deficient. Given greater movement of people and languages internationally, more data on aphasia recovery in non-English languages are required.
- Generally, the greatest language improvements were seen in the context of therapy over several days a week, for several hours weekly, for up to 50 hours. Exceptions to this pattern were typically associated with data from a small number of participants, specific subgroups of participants or unstable networks.
- Targeted investigations of dose–response relationships, with specific consideration of subgroups of people with aphasia, are required.
- Development of our understanding of complex rehabilitation interventions in a complex population can be enhanced and methodologically addressed through improvements in research design, data capture, description and reporting, and continued international, multidisciplinary, collaborative initiatives such as the REhabilitation and recovery of peopLE with Aphasia after StrokE study and others supported by the Collaboration of Aphasia Trialists.

Study registration

This study is registered as PROSPERO CRD42018110947.

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