A comparison of aphasia therapy outcomes before and after a Very Early Rehabilitation programme following stroke

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Conflict of Interest Statement
None declared.
Abstract

**Background:** Very early aphasia rehabilitation studies have shown mixed results. Differences in therapy intensity and therapy type contribute significantly to the equivocal results.

**Aims:** To compare a standardised, prescribed very early aphasia therapy regimen to a historical usual care control group at therapy completion (4-5 weeks post-stroke) and again at follow-up (six months).

**Method and Procedures:** This study compared two cohorts from successive studies conducted in four Australian acute/subacute hospitals. The studies had near identical recruitment, blinded assessment and data collection protocols. The Very Early Rehabilitation (VER) cohort (N=20) had mild-severe aphasia and received up to 20 one-hour sessions of impairment-based aphasia therapy, for up to five weeks. The control cohort (n=27) also had mild-severe aphasia and received usual care (UC) therapy for up to four weeks post-stroke. The primary outcome measure was the Aphasia Quotient (AQ) and a measure of communicative efficiency (DA) at therapy completion. Outcomes were measured at baseline, therapy completion and six months post stroke and were compared using Generalised Estimating Equations (GEE) models.

**Outcomes and Results:** After controlling for initial aphasia and stroke disability the GEE models demonstrated that at the primary endpoint, participants receiving VER achieved 18 percent greater recovery on the AQ and 1.5 percent higher DA scores than those in the control cohort. At six months, the VER participants maintained a 16 percent advantage in recovery on the AQ and 0.6 percent more on DA scores over the control cohort participants.

**Conclusions and implications:** A prescribed, impairment-based aphasia therapy regimen, provided daily in very early post-stroke recovery, resulted in significantly greater communication gains in people with mild-severe aphasia at completion of therapy and at six months, when compared to a historical control cohort. Further research is required to demonstrate large-scale and long-term efficacy.
What this paper adds
What is already known about the subject:
The outcomes of very early aphasia therapy are the subject of ongoing debate. Given the potentially devastating impact of aphasia, very early rehabilitative therapy for people with aphasia requires further investigation.

What this study adds:
Very early aphasia intervention, provided as 20 sessions over 4-5 weeks, resulted in significantly greater communication gains than usual care. It adds to evidence suggesting increased aphasia therapy (intensity, frequency and amount) in the very early and early recovery phases are important for augmenting the effects of spontaneous recovery.

Background

Aphasia is a devastating condition that affects up to 42% of first-ever stroke survivors (Engelter et al, 2006). Up to 50% of these people may still suffer aphasia at 18 months (Davidson et al. 2008). The negative effects of aphasia have wide ranging social and financial implications with few people with aphasia regaining full independence (Davidson et al, 2008). People with aphasia consume greater healthcare resources (Morris, Franklin & Menger, 2011), report higher levels of social and emotional isolation (Davidson et al, 2004; Kauhanen et al. 2000) and higher incidences of major depression within the first 12 months post stroke, than stroke survivors without aphasia (Kauhanen et al. 2000).

The mainstay for aphasia recovery is rehabilitation. The "earlier is better" concept is supported by small randomised controlled trials (Bakheit et al, 2007; de Jong-Hagelstein et al, 2011; Godecke et al. 2012) and comparative studies, which suggest that 2-5 hours of impairment based therapy per week, provides improved recovery (Bhogal et al. 2003, Robey 1998). The first 90 days post stroke are believed to be the "window of opportunity" for neuronal changes to occur as part of neuroplasticity (Meyer et al, 2010). The positive effects of early aphasia rehabilitation are thought to be underpinned by neural substrates that enable brain recovery in the immediate post stroke period. Very early (acute) and early (subacute) post stroke aphasia rehabilitation is believed to harness the effects of spontaneous recovery through therapeutic activities that include high levels of "repetition and intensity", "task specific practice" and therapy "saliency" (Raymer et
al, 2008). The process of recovery is thought to be driven by the strengthening of neural networks. Neural strengthening requires repeated, synchronous firing of a group of neurons (Berthier & Pulvermuller, 2011). This repeated synchronous neuronal firing is achieved through high frequency task repetition, and is thought to minimise independent neuronal activation that potentially produces maladaptive behaviours (Berthier & Pulvermuller, 2011). Implementation of the above neuroplasticity principles is aimed at strengthening the neural networks, used for communication, when the brain has its greatest potential for recovery (Kreisel, Hennerici & Hansjorg, 2007). It is believed that these activities lead to significant changes in communication abilities when delivered in manageable doses starting within the first two weeks post stroke (Godecke et al. 2012).

The clinical effects however, of very early aphasia therapy are equivocal. This is due to methodological difficulties related to the implementation of large scale trials to address the aphasia efficacy debate. In particular, issues in early recovery include identifying: i) the optimum therapy intensity, ii) the ideal therapy type to accommodate the enormous variability in aphasia presentation and iii) selecting people with aphasia who will benefit from rehabilitation. The Cochrane Review (Brady et al. 2012) reported a trend in evidence to support aphasia intervention, with further research required to confirm these findings. There is little evidence from the Cochrane Review (Brady et al. 2012) regarding the efficacy of aphasia therapy started in the very early or early recovery phase.

**Current Research on Early and Very Early Aphasia Therapy**

The following summary provides an overview of the most recently published clinical trials in early aphasia rehabilitation. For a comprehensive overview see Brady et al. (2012). de Jong-Hagelstein et al. conducted a RCT to investigate the role of therapy type in early aphasia recovery, with aphasia therapy commencing within three weeks of stroke onset. Participants (N=80) received an equal amount of therapy (mean of 45.4 hours) at a low intensity level (2.1 hours per week). The primary outcome measure was the Amsterdam-Nijmegen Everyday Language Test ANELT (Blomert, Koster & Kean 1995) at three and six months post stroke. The intervention
group received a cognitive linguistic approach to treatment consisting of a semantically based treatment, BOX and/or a phonological treatment programme, FIKS. The control group received PACE therapy (Promoting Aphasic Communication Effectiveness) (Davis & Wilcox 1985), role playing and conversational coaching. Both groups (N=80) made positive change on the ANELT at three and six months post stroke, with the majority of recovery occurring within the first three months. There were no between group differences at three and six months. The authors (de Jong-Hagelstein et al. 2011) suggested that the low level of early aphasia therapy intensity and the fact that the two therapy types were not sufficiently different may have contributed to the findings.

Two published randomised controlled trials (RCTs) showed that very early aphasia therapy is feasible (Godecke et al. 2012; Laska et al. 2011). The Scandinavian study by Laska et al. (2011) and the Australian equivalent study by Godecke et al (2012) were strikingly similar in design, baseline aphasia severity, therapy intensity and overall amount of intervention. The studies differed in the type of therapy provided to the intervention groups and the overall outcome of these studies was disparate. The difference in the nature of the treatment approaches and the outcome measures used in these studies may explain some of the discrepancy in the reported results.

Stroke severity in the Scandinavian study appears to be slightly less than that of the Australian study, despite participants being recruited and treated within the first two weeks post stroke in both studies. Participants in the Laska et al. (2011) trial received either daily Language Enrichment Therapy (LET) or no therapy for the period of intervention. LET comprised exercises for comprehension with some (though limited) naming tasks included. The intervention group in this study received a minimum of 10 hours and a maximum of 12.5 hours of direct therapy over 15 working days. The control group received no speech and language therapy for the intervention period of the study. After controlling for baseline aphasia and stroke severity, Laska et al. (2011) found no significant difference between those who received LET and those who received UC, on the ANELT.

In comparison, the Australian study (Godecke et al. 2012) provided impairment-based therapy which targeted increased verbal production and connected speech using predominantly
Semantic Feature Therapy (Boyle & Coelho, 1995) or a combination of Semantic Feature Therapy (SFT) and BOX therapy (Visch-Brink, Bajemal & van de Sandt-Koenderman, 1997), or SFT and Mapping therapy (Schwarts et al. 1994). Each therapy session also included a picture description task which was used to enhance verbal output through a structured and supported conversational approach. The intervention group in Godecke et al. (2012) received an average of 5.6 hours of direct therapy provided by a speech-language therapist over an average of 7.5 working days (overall mean length of stay – 22 days). Participants (and families) received education, counselling, case management and discharge planning however these data were not included in the 5.6 hours of direct therapy. Twenty-three (85%) of the 27 participants in the UC group in this trial received no therapy during the intervention phase (22 days) (Godecke et al. 2012). The four participants in UC who were treated received on average less than 14 minutes of 1:1 direct therapy per week and therapy tasks matched those used in the intervention group.

Godecke et al. (2012) reported that those receiving daily therapy showed immediate and positive effects of very early aphasia therapy when compared with UC participants. Unfortunately due to the application of mixed therapy types for participants in this study, little can be said about the effects of discrete therapy types in this recovery phase.

The pragmatic randomised controlled trial (ACTNoW) by Bowen et al (2012a) compared enhanced speech and language therapy (SLT) with attention control (AC) in stroke survivors with aphasia and dysarthria. The intervention in this trial commenced on average 15 days after hospital admission for acute stroke and lasted for 16 weeks. The intervention group received a less intensive (or dispersed) therapy regimen of a mean of 1.3 hours of SLT per week over 16 weeks (18 hours total) when compared to Laska et al. 2011 and Godecke et al. 2012 who provided more intensive therapy over a shorter duration. More importantly, the 1.3 hours of intervention time recorded in the ACTNoW study incorporated all elements of communication intervention which included assessments, provision of communication materials and education, carer contact, indirect patient contact and direct therapy (Bowen et al, 2012b). Consequently, when compared to other studies which demonstrated a positive therapy effect, (de Jong-Hagelstein et al. 2011; Godecke
participants in the intervention arm of ACTNoW received substantially reduced direct therapy intensity.

The AC group in ACTNoW received an average of 15 hours of social contact from a paid visitor over 16 weeks (Bowen et al, 2012b). The intervention for the AC group consisted of a structured program including: i) *rapport building* of 2-4 sessions, ii) *regular contact* sessions involving conversation, the visitor reading from books, magazines, newspapers to create conversation topics, watching tv, listening to music, playing games of tactics and strategy or creative activities such as crafts or gardening and iii) *winding down* sessions (2-4 sessions) which included preparation for the visitor’s time with the participant to come to an end. At six months post stroke, this study found no significant difference in communication outcomes, between those in the SLT intervention group and those who received the attention control intervention.

More recently, Sickert et al. (2013) completed a single-blind RCT investigating a modified dose of intensive aphasia therapy in first-ever stroke survivors when therapy was started in the sub-acute phase (mean of 34.8 days post-stroke). One hundred participants with mild to Global aphasia were randomised to either CIAT or standard treatment. Treatment for both groups was provided for 2 hours per day over 15 (working) days for a total of 30 hours of therapy or a mean of 10 hours per week. CIAT was provided as per Pulvermuller et al. 2001 with the addition of the use of conventional treatment in a group setting (p.2). “Standard treatment consisted of aphasia exercises including sentence completion, improving patients’ retrieval of words, learning sentence patterns, conversation on current topics, listening to words, and repeating and following instructions”. (p.2)

At therapy completion the authors found both groups made significant recovery on all sub-tests of the Aachener Aphasia Test (Huber, Poeck, Weniger et al. 1983). Twenty-six of the original 100 participants were reassessed at eight weeks and one year post-stroke and the authors report further significant gains at both time points with no between group significance. Therefore they concluded that both CIAT and standard therapy lead to significant improvements in language function and that people in the sub-acute phase of recovery tolerated two hours of therapy each
day for three weeks (five days per week), regardless of aphasia type/severity (classification) (Sickert et al. 2014, pg.5).

Limitations of existing aphasia research and future research directions

While preliminary research for early aphasia intervention has shown positive results (de Jong-Hagelstein et al. 2011; Godecke et al. 2012; Sickert et al. 2013) there is no evidence (Brady et al. 2012) to support the efficacy of very early post-stroke aphasia treatments in the long-term. This is a result of limitations in study methodology, difficulties with participant selection, reduced sample size, inconsistent application and description of aphasia therapy types and use of low intensity aphasia rehabilitation.

Aims

This study aimed to show that a prescribed, standardised and intensive very early aphasia therapy regimen would provide better communication outcomes when compared to a historical usual care control cohort at therapy completion. In doing so this study aimed to validate previous positive very early rehabilitation (VER) findings related to therapy type, therapy intensity, and overall amount of direct therapy.

Methods

Design

This study compared the communication outcomes of two independent cohorts in the very early post-stroke recovery phase. The primary endpoint for this study was at therapy completion (four to five weeks post stroke) and follow up was at 26 weeks post stroke.

The intervention cohort (VER, n=20) was taken from a study that controlled for therapy intensity in very early aphasia rehabilitation. The historical usual care (UC) comparison (n=27) was derived from a previous RCT reported in full in Godecke et al. (2012). Ethical approval was obtained from hospitals before each study commenced.

Setting

VER Cohort: Participants in this study were identified from patients admitted to either
Royal Perth Hospital (RPH) or Sir Charles Gairdner Hospital (SCGH) in metropolitan Perth, Western Australia between December 2008 and September 2009. Both facilities are acute care teaching hospitals with over 400 stroke admissions each year. Stroke specific subacute rehabilitation was provided by RPH – Shenton Park Rehabilitation Hospital and Osborne Park Stroke Rehabilitation Unit (OPH), as required. Therapy was initiated in the acute facility as soon after recruitment as possible. Therapy continued without interruption or re-assessment on transfer to the subacute facility. The treating therapists changed from acute to post-acute setting however the participants’ therapy was seamless.

Control Cohort: Participants were recruited from RPH, SCGH and Fremantle Hospital (FH) between 2000 and 2003. Participants in this cohort were assessed at a mean (SD) of 3.4 (2.2) days post-stroke and the intervention period commenced the day following assessment. Stroke specific and general rehabilitation was provided by metropolitan sub-acute sites as required.

Participant recruitment

Both studies: Participants for both studies were identified from the hospital generated daily admissions list from each recruiting hospital. Medical notes were screened for all admissions with diagnoses of stroke, falls, headache, confusion and seizures on the day of admission or the next working day. Patients with a possible or confirmed stroke were identified as prospective study participants. Prior to enrolling in each study, all candidates and their families/Next of Kin (NoK) were informed that the main goal of each project was to increase the accuracy and amount of verbal output.

Inclusion criteria

The following criteria were identical for both studies: i) aphasia caused by an acute stroke as outlined by Warlow et al. (2001) and diagnosed by a neurologist or stroke physician, ii) a clinical stroke diagnosis confirmed by computer tomography and/or magnetic resonance imaging within 48 hours of hospital admission, iii) aphasia identified by a score of less than 13/20 on the shortened Frenchay Aphasia Screening Test (FAST) (Enderby, Wood & Wade, 1987) which is a reliable and valid aphasia screening tool comprising auditory comprehension and verbal
expression tasks used to identify aphasia in the early phase of recovery, iv) medical stability (measured by the Glasgow Coma Scale score of >10 which indicates moderate level of alertness), v) wakefulness – able to maintain sufficient alertness to interact for 30 minutes and vi) aphasia severity score (less than 93.8 on the Aphasia Quotient (AQ) of the Western Aphasia Battery (WAB) (Kertesz, 1989). The VER cohort selection criteria were broadened slightly from that of the Control cohort in Godecke et al (2102) to include people with fluent English and those who were appropriate for the study up to fourteen days post stroke onset. A comparison of selection criteria for each trial is presented in Table 1.

*Insert Table 1 about here.*

The exclusion criteria for both trials were: i) a previous diagnosis of aphasia, mental illness or dementia, ii) a previous history of sub-arachnoid and/or sub-dural haemorrhage or neurosurgical intervention and iii) uncorrected hearing or vision impairment.

**Baseline data**

Patient characteristics including demographic factors, stroke features, stroke classification according to Oxfordshire Community Stroke Project Classification (Bamford et al. 1991) and the modified Rankin Scale (mRS) (Rankin, 1957) were collected at baseline for both studies. Table 2 shows the baseline characteristics and comparisons for the VER and control cohorts.

*Insert Table 2 about here.*

**Speech and Language service delivery and direct aphasia therapy intensity**

Participants in each study received dysphagia management, patient and family education (for example education regarding stroke, secondary prevention, aphasia, and dysphagia), counselling and support, case management, discharge planning and all other interventions as they required. These data were collected but only the direct aphasia therapy data are presented in this paper.

**VER Cohort:** Therapy was commenced as soon as possible after recruitment and assessment. Intervention started on or before day 14 post-stroke for all participants. The target therapy regimen was defined as between 900 and 1200 minutes (15-20 hours) therapy, provided over five days per
week for a total of 20 sessions in four weeks (4-5 hours of therapy per week). All attempts were made to complete the 20 therapy sessions within four working weeks (Monday -Friday) the fifth week was made available to complete any outstanding sessions. If more than two sessions were missed in any week, the participant was deemed as not tolerating the intervention. Six trained non-assessing speech pathologists treated the participants.

*UC Cohort:* This cohort (N=27) received an average of 11 minutes of therapy per week for an average of three weeks (22 days).

**Type of aphasia therapy provided in each trial**

The therapeutic approaches used in both studies adhered to the general principles of neurorehabilitation. Therapy types were designed for use with people with mild aphasia through to severe global aphasia. The therapies provided in each trial were impairment-based and believed to harness neural recovery through restitution via high frequency (massed practice), use-dependent, task-specific repetition (Berthier & Pulvermuller 2011). Strategies to minimise speech production errors and to promote self-correction were used to enhance correct production of speech and language targets. The speech pathologist pre-empted and avoided consistent task failure to ensure participants were supported as needed. This support included prompting, modelling and cueing to produce an appropriate verbal response. These strategies are thought to enhance ‘synchronous neuronal firing’ to strengthen neural networks and minimise independent neuronal activation that could potentially produce maladaptive behaviours (Berthier & Pulvermuller, 2011).

*VER cohort:* Participants in this study received either group or 1:1 therapy. Group therapy consisted of Constraint Induced Aphasia Therapy (CIAT) (Pulvermuller et al. 2001) in a modified dose. Individual therapy consisted of Semantic Feature Therapy (SFT) (Boyle & Coelho 1995), Cued Naming therapy (Nettleton & Lesser 1991), Lexical-semantic (BOX) therapy (Visch-Brink, Bajema & vande Sandt-Koenderman (1997), Mapping therapy (Schwartz et al. 1994) and/or Phonological Feature Therapy (Raymer et al. 1993).

Treatment integrity was addressed by training all treating therapists to ensure equivalent use
of stimuli and therapy type and therapy targets were identical across all therapy sites. All therapy tasks (CIAT and 1:1) were structured to promote and scaffold connected speech production.

**CIAT (Group)**

Therapy was based on the CIAT outlined by Pulvermuller and colleagues (2001). The therapy took place in small groups of 2–4 participants and one speech pathologist who provided language support appropriate to each participant's needs. The stimuli and language support were designed to accommodate all levels of aphasia severity in the same group. The group members were dealt a set of picture cards, the aim being to collect pairs of cards. Each pictured item allowed a verbal response ranging from a single word to complex sentences. Barriers prevented the participants from seeing each other's cards. The 'constraint' of the therapy was provided by the requirement of verbal-only interaction. The group language dynamics included politeness markers, requesting items, listening, clarification of other’s responses and negating requests. The complexity of verbal output required from each participant and the level of cueing and support provided was tailored to each individual’s communicative ability as established at assessment and through ongoing performance within therapy sessions.

**Individual therapy (1:1)**

Each participant receiving 1:1 therapy had a program tailored to suit their needs. Based on the participant's assessment results, the treating therapist selected the appropriate therapy from those previously listed. All 1:1 therapies were provided as per published instructions (Boyle & Coelho 1995, Nettleton & Lesser 1991, Visch-Brink et al. 1997, Schwartz et al. 1994, Raymer et al. 1993). Participants received either a single therapy, or a combination of therapy types such as cued naming therapy and semantic feature therapy.

**Control cohort:**

As previously outlined, 85% of participants in this cohort received no direct therapy. When participants received therapy it consisted of individual (1:1) cognitive-neuropsychological and neurolinguistically based therapy. Therapists used one or more of the following therapies: lexical-semantic (BOX) therapy (Visch-Brink et al 1997), Mapping therapy (Schwartz et al 1994) and
Semantic Feature Therapy (Boyle & Coelho 1995). Participants also attempted a picture
description task aimed at increasing connected speech in a supported and structured environment.
See Godecke et al. (2012) for further detail.

**Recording of speech pathology service delivery data**

The type and duration of speech pathology interventions for both studies were recorded via
the Allied Health System (AHS). This software package records intervention in five minute units.
All interventions for each participant were coded for aphasia/dysphagia/dyspraxia/dysarthria and
time spent in each activity was categorised into assessment, therapy, education/counselling, case
planning/consultation and documentation.

**Outcome assessment**

Both cohorts were assessed at acute hospital admission, immediately following intervention
(after four-five weeks therapy) and 26 weeks post stroke. All assessments were completed and
analysed by blinded assessors.

**Primary Outcome Measures**

The primary outcome measures were the AQ score of the Western Aphasia Battery (WAB)
(Kertesz, 1982) and the Discourse Analysis (DA) score at therapy completion. All discourse
samples were collected as per Godecke et al. (2012) and consisted of picture descriptions, personal
and procedural narratives (Kertesz, 1982; Nicholas & Brookshire, 1995). DA is the total percent
Correct Information Units produced s per minute (% CIU/MIN) per sample and is calculated by
dividing the total %CIUs (Nicholas & Brookshire, 1995) by the total time taken to produce the
discourse. The measure adds a communication efficiency/temporal element that is considered an
important communicative measure not captured in the AQ scores. CIUs are topic specific words
that provide detail and are not repetitious, exclamatory, additive or commentary in nature
(Nicholas & Brookshire, 1995). A count of 200 or more intelligible words across picture
description, personal and procedural narrative tasks was required for a representative and reliable
speech sample.
All discourse samples for the VER cohort were audio-recorded using a lapel microphone and digital recorder (Olympus-DM550). The recordings were transcribed verbatim and analysed as per Godecke et al (2012).

**Secondary outcome measures**

Secondary outcomes were the AQ (Kertesz, 1982) score and DA score at six months post stroke.

**Statistical analyses**

The VER and UC cohorts were compared at baseline using two-tailed t-tests and chi-square tests for independence. Generalised estimating equations (GEE) models were developed to compare the cohorts on AQ and DA scores at therapy completion and at 26 weeks post stroke. Generalized linear models are a class of statistical model that extend the general linear model (regression, ANOVA and ANCOVA) to handle non-normal data. Generalized estimating equations are a further extension of generalized linear models to account for longitudinal and clustered data. GEE models are preferred to repeated measures ANOVA approaches because of their flexibility in modelling complex covariance structures that arise in longitudinal and clustered data. Furthermore, GEE models are robust against misspecification of the covariance structure and are also more robust than repeated measures ANOVA in handling missing data (Ballinger 2004). GEE have also been found to be more efficient in that they are able to achieve higher power with smaller sample size or lower number of repeated measurements in both complete and missing data scenarios (Ma, Mazumdar & Memtsoudis, 2012). In the current work, separate GEE models were developed to compare the cohorts on the primary outcome measure (AQ) and the secondary outcome measure (DA). Missing data were treated with the last observation carried forward approach where appropriate. This complies with the intention to treat principle (Jansen et al. 2006).

Due to the possible ceiling effect in the AQ score, the AQ model involved transforming these
scores to the percent of maximum potential recovery (AQ%MPR) as per Lazar et al, (2010). The score for each participant was calculated as the ratio of the achieved improvement in AQ to the maximum achievable improvement at baseline. The ratio was then multiplied by 100 to convert it to a percentage score.

There was a larger number of people with mild aphasia in the VER cohort (n=6; 30%) than in the UC cohort (n=3; 11%) and therefore the two cohorts were expected to significantly differ on baseline aphasia severity. Since baseline aphasia and stroke severity/disability are universal predictors of aphasia recovery, the baseline AQ and mRS (Rankin, 1957) scores were included as covariates in both GEE models to control for these differences. Baseline DA was not included as a covariate in the models because it was correlated with baseline AQ (r = 0.6, p < 0.001).

**Results**

**Baseline**

Over the ten month recruitment period for the VER cohort, the medical notes of 1006 admissions to Royal Perth Hospital were screened for collapse, falls, seizures, headache, confusion and stroke. A total of 236 people were admitted with an acute stroke with 88 (37.2%) of these people having confirmed aphasia. We recruited 18 (20.4%) of the people with confirmed aphasia from Royal Perth Hospital to this study. Two participants from Sir Charles Gairdner Hospital met the selection criteria and were recruited taking the total number of participants to 20. The majority (n = 17; 85%) of participants in the VER cohort required full assistance (including aphasia friendly forms) to complete the informed consent procedure.

The baseline characteristics between VER and UC cohorts were not significantly different except for the time to initial assessment and baseline AQ score. The VER cohort had a mean age (±SD) of 70.7 (±14.3) years and was slightly older than the UC cohort who had a mean age of 67.7 (±15.4) (Table 2). Ninety percent of the VER cohort had an ischaemic stroke compared to 89% of the UC cohort. The majority of the VER cohort (80%) and the UC cohort (82%) had severe stroke-related disability as indicated by a score of 4 or 5 on the modified Rankin Scale (mRS). A clinical
but non-significant difference in the mRS is noted. The difference in the time to initial assessment reflects an increase in the length of time to recruitment for the VER cohort which included people with aphasia who were recruited up to 14 days post-stroke.

The difference in baseline AQ scores is reflective of the increased number of people with mild aphasia in the VER cohort (n=6; 30%) when compared to the number of people with mild aphasia (n=3; 11%) in the UC cohort. Table 2 shows the baseline characteristics and comparisons for the VER and UC cohorts.

Two (10%) of the 20 participants in the VER cohort did not reach the minimum intervention requirement (both participants were randomised to receive 1:1 intervention). One participant suffered a further stroke after completing a single 40 minute session of therapy. The second completed 13 sessions and 780 minutes (13 hours) of therapy, then suffered a gastric haemorrhage and was unable to complete the intervention. Table 3 outlines the therapy compliance for participants in the VER and control cohorts. Table 4 shows group raw and transformed scores at baseline, therapy completion and follow up. The participants in the VER study tolerated approximately 4.25 hours of therapy per week for an average of 4.5 weeks (32 days). During this time, the average number of therapy sessions was 18.65, and each session averaged 53.5 minutes.

Insert Table 3 about here.

Twenty-three of the 27 participants (85%) in the UC cohort received no direct therapy during the intervention period (Godecke et al. 2012) (Table 3). The collective amount of direct therapy time provided to the four UC participants who received aphasia therapy was 295 minutes (4.9 hours) over 7 sessions, equating to an average of 11 minutes of therapy per week for each of the UC participants.

Insert Table 4 about here.

Primary End-Point

The GEE models showed (see Tables 5 and 6) that after controlling for baseline aphasia severity and stroke related disability, VER was a significant predictor of recovery on the AQ (p=0.006) and on the DA score (%CIU/Min) (p=0.034). Specifically, participants receiving VER
achieved 18 percent greater recovery on AQ and 1.5 percent more on the DA score (%CIU/Min) than those in the UC Cohort at therapy completion. These results indicate that people who received VER had improved communication impairment measures (AQ%MPR) on standardised testing (AQ scores) and produced significantly more accurate and efficient verbal language (DA scores) than those who received UC at therapy completion. Table 4 outlines the descriptive data for the AQ, DA and the AQ percent of maximum potential recovery (AQ%MPR) scores for the VER and UC cohorts at baseline, post therapy and 26 weeks post stroke. As expected, these data indicate that the historical UC cohort had more severe communication impairment at baseline than the VER cohort. When the AQ data are transformed to (AQ%MPR), baseline scores are returned to zero corresponding to a maximum potential recovery of 100% for each participant.

Insert Tables 5 and 6 about here.

Follow-up

At follow-up assessment 26 weeks post-stroke, the GEE model (see Tables 5 and 6) for AQ showed that after controlling for baseline aphasia severity and stroke related disability, participants receiving VER maintained a statistically significant advantage in recovery ($p=0.017$) over those receiving UC, with the VER cohort scoring 16 percent higher on the AQ than those who received UC (Figure 1). The difference between the cohorts on DA scores was not statistically significant ($p=0.249$) at the six month follow up. However, the VER cohort showed 0.6 percent greater recovery on DA than the UC cohort (Figure 2). The dosage of aphasia therapy was not controlled after the four-five week intervention period, and participants from both cohorts received UC therapy as per their available services.

Insert Figures 1 and 2 about here

Discussion

The present study showed that impairment-based aphasia therapy provided by a speech pathologist for 45-60 minutes per day for up to 20 sessions, commencing in the first two weeks of
stroke recovery, improved communication outcomes at therapy completion in people with mild, moderate and severe aphasia when compared to a historical usual care control. Interestingly, the communication gains achieved for those treated in the very early recovery period were sustained at six months when measured by the AQ score, but despite a clinically meaningful improvement in the DA score at six months, this outcome did not reach statistical significance.

*Therapy intensity*

Only the hours of *direct patient therapy* have been reported in this study, in Laska et al. 2011 and in Godecke et al (2012). In comparison, Bowen et al. 2012 reported on all aspects of speech and language intervention as contributing to therapy intensity. When considering direct aphasia therapy only, Laska et al. (2011) and Godecke et al. (2012) provided an average of 3.75 and 3.6 hours per week respectively; this study provided an average of 4.25 hours per week; Bowen et al. (2012b) provided 1.3 hours (combined intervention) per week and Sicket et al. (2013) provided 10 hours per week in the sub-acute recovery phase. The total amount and duration of the intervention in each trial varied, and the outcomes of these studies were mixed. Previous reviews (Bhogal et al. 2003; Robey, 1998) have found that an average of 2.5 - 5 hours of aphasia therapy per week produced significantly better communication outcomes than therapy provided at lower intensity level. The results of this study support previous work that highlights the importance of therapy intensity in enhancing spontaneous recovery in very early aphasia after stroke. An interesting point to also consider here is that people with aphasia in *very early recovery* can and do tolerate daily aphasia therapy of up to 60 minutes per day if the service is provided.

*Therapy type*

Therapy for the VER participants was structured, tailored therapy, based on psycholinguistic principles and targeted verbal production (output) at the impairment level of communication. People in this study who received very early intervention, consisting of either 1:1 or group therapy demonstrated superior communication outcomes at therapy completion and at six months (AQ scores) when compared to the historical control group. Results of this study support de Jong-Hagelstein et al. 2011; Godecke et al. 2012 and Sicket et al. 2013 which show positive results.
using a variety of therapy types. No research to date has determined the most beneficial therapy
type for the various aphasia severities and types. A definitive answer to address this complex issue
is expected to be some time off and will likely require the pooled efforts of multiple data sources.

*DA score at six months*

The very large clinically meaningful but non-significant improvement in the mean DA
scores in the VER group when compared to the UC group at the same period is an interesting
finding (Table 4). Seeing a 25% improvement in any score is a welcome result, (Figure 2)
especially if that score represents: i) the accuracy and efficiency of connected speech and ii) the
amount of improvement that was made when recovery is thought to be all but completed (Lazar 2010). The factors that contribute to this recovery remain unclear. The fact that this amount of
clinical change does not represent a statistical difference is likely to be multifactorial and is best
explained through the large natural variation seen in the standard deviations, coupled with the
small sample size in the study.

**Study Limitations**

Due caution regarding the comparative use of a historical control group is warranted given
that the original population from which the samples in the VER and control cohorts are taken are
at least five years apart. We acknowledge improvements in the systems of hospital care are likely
to have occurred in the period 2000-2009 when these data were collected. These changes are likely
to include increased rates of thrombolysis, improved management of stroke related complications
and reduction of stroke related morbidity and mortality. It is also possible that these changes will
have contributed in some way to the results presented here. Unfortunately, the large scale systems
audit required for monitoring service delivery and organisational changes in stroke services was
not available at the time these data were collected. Some reassurance is provided, given the fact
that there was no statistical between group significance in stroke type, stroke classification and
mRS score between the VER and control cohorts at baseline.

The VER rehabilitation study design would have been strengthened by including a third
arm of randomisation that measured usual care alone and with stratification of aphasia severity.
Additionally, the results of the VER cohort should be interpreted with caution due to the small number of participants who completed the six month follow-up. Whilst the statistical modelling for this paper was conservative and vigilant, the highly variable nature of aphasia requires large scale clinical trials before clinical efficacy and/or effectiveness can be established.

**Conclusion and future directions**

Very early, impairment-based aphasia therapy resulted in superior communication outcomes which were sustained at six months post-stroke when compared to a historical control cohort. This paper provides support for very early impairment-based aphasia therapy provided between 45-60 minutes per day, when commenced within the first two weeks post-stroke. Importantly this study found the timing and intensity of very early therapy is feasible and beneficial for people with mild to severe aphasia (Godecke et al, 2012). It also adds evidence to suggest that increased aphasia therapy (intensity, frequency and amount) in the very early and early recovery phases is important for augmenting the effects of spontaneous recovery.

Given the ongoing debate surrounding the benefits of very early aphasia intervention, we must focus further research attention to unpacking the elements of the optimal aphasia therapy type, intensity, and timing to best facilitate the natural mechanisms of very early aphasia recovery. If healthcare funding bodies are to be convinced of the benefits of very early aphasia rehabilitation we must determine the right combination of aphasia therapy for the right person, provided at the right time.

**References**


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Kertesz A. Western Aphasia Battery. New York: Grune and Stratton; 1982


Lazar RM, Minzer B, Antoniello D, Festa JR, Krakauer JW, Marshall RS. Improvement in aphasia scores after stroke is well predicted by initial severity. Stroke. 2010;41:1485-1488


Morris J, Franklin S, Menger F. Returning to work with aphasia: A case study. Aphasiology. 2011; iFirst,1-18


<table>
<thead>
<tr>
<th>Criteria</th>
<th>VER cohort</th>
<th>Control cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission to hospital (days)</td>
<td>&lt;14</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Frenchay Aphasia Screening test (days)</td>
<td>&lt;14</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Conscious/Medically stable (days)</td>
<td>&lt;14</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Wakeful state &gt;30 minutes (days)</td>
<td>&lt;14</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Aphasia severity</td>
<td>Mild –Severe</td>
<td>Mild - Severe</td>
</tr>
<tr>
<td>English as a second language</td>
<td>yes</td>
<td>no</td>
</tr>
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</table>
Table 2. Baseline demographic and stroke characteristics and comparisons for the VER and control cohorts

<table>
<thead>
<tr>
<th></th>
<th>VER cohort n = 20</th>
<th>Control cohort n = 27</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Mean (SD)</td>
<td>70.7 (14.3)</td>
<td>67.7 (15.4)</td>
<td>.499*‡</td>
</tr>
<tr>
<td>Female (%)</td>
<td>8 (40)</td>
<td>12 (44)</td>
<td>.761†</td>
</tr>
<tr>
<td>Previous Stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>17</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Stroke type</td>
<td></td>
<td></td>
<td>.903†</td>
</tr>
<tr>
<td>Ischaemic (%)</td>
<td>18 (90)</td>
<td>24 (89)</td>
<td></td>
</tr>
<tr>
<td>Haemorrhagic (%)</td>
<td>2 (10)</td>
<td>3 (11)</td>
<td></td>
</tr>
<tr>
<td>Stroke classification</td>
<td></td>
<td></td>
<td>.298†</td>
</tr>
<tr>
<td>PACI (%)</td>
<td>1 (5)</td>
<td>9 (33.5)</td>
<td></td>
</tr>
<tr>
<td>TACI (%)</td>
<td>17 (85)</td>
<td>14 (52)</td>
<td></td>
</tr>
<tr>
<td>PoCI (%)</td>
<td>0</td>
<td>1 (3.5)</td>
<td></td>
</tr>
<tr>
<td>LACI (%)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Non-classified</td>
<td>2 (10)</td>
<td>3 (11)</td>
<td></td>
</tr>
<tr>
<td>Stroke Hemisphere:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left (%)</td>
<td>18 (90)</td>
<td>26 (96)</td>
<td></td>
</tr>
<tr>
<td>Right (%)</td>
<td>2 (10)</td>
<td>1 (4)</td>
<td></td>
</tr>
<tr>
<td>Mortality within 28 days</td>
<td></td>
<td></td>
<td>.458†</td>
</tr>
<tr>
<td>Number (%)</td>
<td>1 (5)</td>
<td>3 (11)</td>
<td></td>
</tr>
<tr>
<td>Admission mRS score: Number (%)</td>
<td></td>
<td></td>
<td>.676‡</td>
</tr>
<tr>
<td>2</td>
<td>1 (5)</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3 (15)</td>
<td>4 (15)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>9 (45)</td>
<td>8 (30)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>7 (35)</td>
<td>14 (52)</td>
<td>.898‡</td>
</tr>
<tr>
<td>Admission to assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean days (SD)</td>
<td>6.1 (2.3)</td>
<td>3.4 (2.2)</td>
<td>.000‡</td>
</tr>
</tbody>
</table>

PACI: partial anterior circulation infarct; TACI: total anterior circulation infarct; PoCI: posterior circulation infarct; LACI: Lacunar infarct; Non-classified = haemorrhage

*‡ Chi-Square test for independence
*† 2tailed t-test comparing Very Early Rehabilitation cohort with Control cohort
* Overall mRS score comparison
^ mRS categorised comparisons: Categories 2-3 indicate mild to moderate disability; Categories 4-5 indicate severe disability
**Table 3.** Descriptive data for intervention compliance, total therapy time (minutes) and number of sessions in the intervention phase

<table>
<thead>
<tr>
<th>Therapy details</th>
<th>VER cohort</th>
<th>Control cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 20</td>
<td>n= 27</td>
</tr>
<tr>
<td>Met intervention compliance</td>
<td>18 (90%)</td>
<td>n/a</td>
</tr>
<tr>
<td>Received therapy</td>
<td>20 (100%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Intervention phase language therapy (total mins)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1070.25 (267.44)</td>
<td>10.92 (38.73)*</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>1167.5 (131.25)</td>
<td>47.5(86.25)</td>
</tr>
<tr>
<td>Intervention phase language number of therapy sessions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>18.65 (4.44)</td>
<td>0.3 (.99)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>8 (5.25)</td>
<td>1 (.75)</td>
</tr>
</tbody>
</table>

* indicates the overall mean for all participants (n=27) in control cohort
IQR – interquartile range
Table 4. Group raw-scores comparisons for communication outcomes between Very Early Rehabilitation participants and the Control Cohort.

<table>
<thead>
<tr>
<th></th>
<th>VER Cohort</th>
<th>Control Cohort</th>
<th>p-value*</th>
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</thead>
<tbody>
<tr>
<td><strong>Baseline AQ</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>20</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>43.53 (27.02)</td>
<td>19.62 (26.26)</td>
<td>.009</td>
</tr>
<tr>
<td><strong>Therapy completion AQ</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>17</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>67.55 (30.16)</td>
<td>31.37 (32.83)</td>
<td>.001</td>
</tr>
<tr>
<td><strong>Follow-up (26 weeks) AQ</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>8</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>89.01 (11.96)</td>
<td>45.62 (39.64)</td>
<td>.001</td>
</tr>
<tr>
<td><strong>Baseline AQ%MPR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>20</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Therapy completion AQ%MPR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>17</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>46.72 (35.43)</td>
<td>17.92 (23.18)</td>
<td>.007</td>
</tr>
<tr>
<td><strong>Follow up (26 weeks) AQ%MPR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>8</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>77.60 (20.45)</td>
<td>38.77 (37.08)</td>
<td>.002</td>
</tr>
<tr>
<td><strong>Baseline DA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>20</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>3.26 (5.0)</td>
<td>1.18 (4.06)</td>
<td>.123</td>
</tr>
<tr>
<td><strong>Therapy completion DA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>17</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>8.36 (8.54)</td>
<td>2.37 (5.60)</td>
<td>.012</td>
</tr>
<tr>
<td><strong>Follow up (26 weeks) DA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>8</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>33.90 (17.9)</td>
<td>7.74 (12.87)</td>
<td>.004</td>
</tr>
</tbody>
</table>

n.b These scores are unadjusted for baseline differences in aphasia severity and stroke disability. * t-test; significance p=.005
Table 5. GEE Model for Percent of Maximal Potential Recovery on AQ

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Confidence Limits</th>
<th>Wald Chi-Square</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline AQ</td>
<td>.32</td>
<td>.09</td>
<td>.15</td>
<td>.49</td>
<td>13.96</td>
</tr>
<tr>
<td>Baseline mRS</td>
<td>-2.64</td>
<td>2.94</td>
<td>-8.41</td>
<td>3.14</td>
<td>.801</td>
</tr>
<tr>
<td>Primary End-point</td>
<td>17.70</td>
<td>4.58</td>
<td>8.73</td>
<td>26.68</td>
<td>14.94</td>
</tr>
<tr>
<td>Follow-up</td>
<td>39.21</td>
<td>7.46</td>
<td>24.59</td>
<td>53.82</td>
<td>27.65</td>
</tr>
<tr>
<td>VER</td>
<td>-8.27</td>
<td>3.19</td>
<td>-14.52</td>
<td>-2.01</td>
<td>6.71</td>
</tr>
<tr>
<td>Primary End-point * VER</td>
<td>26.19</td>
<td>9.52</td>
<td>7.52</td>
<td>44.86</td>
<td>7.56</td>
</tr>
<tr>
<td>Follow-up * VER</td>
<td>24.22</td>
<td>10.17</td>
<td>4.28</td>
<td>44.15</td>
<td>5.67</td>
</tr>
</tbody>
</table>

n.b Primary End-point: Therapy Completion (4-5 Weeks post-stroke); Follow-up: 6 months post-stroke; VER: Very Early Rehabilitation Group; Primary End-point * VER: Very Early Rehabilitation group compared to Usual Care group at Therapy Completion; Follow-up * VER: Very Early Rehabilitation group compared to Usual Care Group at 6 months
### Table 6. GEE Model for Recovery on DA

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Confidence Limits</th>
<th>Wald Chi-Square</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline AQ</td>
<td>.20</td>
<td>.03</td>
<td>.146</td>
<td>.26</td>
<td>49.62</td>
</tr>
<tr>
<td>Baseline mRS</td>
<td>-.51</td>
<td>.94</td>
<td>-2.34</td>
<td>1.33</td>
<td>.29</td>
</tr>
<tr>
<td>Primary End-Point</td>
<td>.53</td>
<td>.81</td>
<td>-1.06</td>
<td>2.12</td>
<td>.43</td>
</tr>
<tr>
<td>Follow-up</td>
<td>6.21</td>
<td>1.85</td>
<td>2.59</td>
<td>9.83</td>
<td>11.31</td>
</tr>
<tr>
<td>VER</td>
<td>-3.05</td>
<td>1.48</td>
<td>-5.96</td>
<td>-.14</td>
<td>4.21</td>
</tr>
<tr>
<td>Primary End-Point * VER</td>
<td>4.56</td>
<td>2.15</td>
<td>.34</td>
<td>8.78</td>
<td>4.49</td>
</tr>
<tr>
<td>Follow-up * VER</td>
<td>3.61</td>
<td>3.13</td>
<td>-2.52</td>
<td>9.73</td>
<td>1.33</td>
</tr>
</tbody>
</table>

n.b  Primary End-point: Therapy Completion (4-5 Weeks post-stroke); Follow-up: 6 months post-stroke; VER: Very Early Rehabilitation Group; Primary End-point * VER: Very Early Rehabilitation group compared to Usual Care group at Therapy Completion; Follow-up * VER: Very Early Rehabilitation group compared to Usual Care Group at 6 months
Figure 1. AQ%MPR comparisons at baseline, therapy completion and follow-up (26 weeks)
Figure 3. Discourse Analysis comparisons at baseline, therapy completion and follow-up (26 weeks)

Figure 2. DA comparisons at baseline, therapy completion and follow-up (26 weeks)