Adapting Acceptance and Commitment Therapy for Stroke Survivors With Aphasia
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4.4. Statistical Design and Power.

The purpose of this overall research agenda is to improve communication participation, psychosocial adjustment, and quality of life (QoL) for stroke survivors with aphasia by developing an effective new integrated language and counseling, *Act for Aphasia*. At this preliminary research stage, our primary goals are to develop and pilot this intervention, laying the groundwork for a subsequent larger-scale efficacy trial. Therefore, in **Aim 1**, we will engage a stakeholder advisory board to develop and revise the treatment manual. In **Aim 2a** we will establish primary outcomes of **acceptability** and **feasibility** of ACT for Aphasia. In **Aim 2b** we will estimate preliminary effect sizes on secondary outcome measures to inform power analyses for a subsequent randomized control trial.

Methods for Determining Intervention Acceptability. Acceptability will be assessed using the Client Satisfaction Questionnaire – 8[16]. It consists of 8 questions rated on a 4-point scale (summed scores range from 8 to 32). Participants will be given these questions at the end of follow-up assessment with an independent assessor. High scores indicate high satisfaction. We will consider *Act for Aphasia* to be acceptable if the group mean ≥28, a benchmark based on previous stroke rehabilitation work by project consultant Dr. Skidmore[17].

Methods for Determining Intervention Feasibility. Feasibility will be assessed by examining intervention adherence (the number of treatment sessions successfully completed), recruitment and participation rate (the number of eligible PWA identified and the percentage of PWA who choose to enroll), and completion rate (the percentage of enrolled participants who complete the follow-up assessment). The intervention will be considered to demonstrate adequate adherence if participants if participants complete at least 75% of weekly treatment sessions within a 12-week period[67]. We will not pre-determine cutoffs for other measures of intervention feasibility (recruitment, participation, and completion rate), but will take them into careful consideration when considering protocol modifications and study design considerations for the next phase of this research. For example, required sample size estimates for an efficacy trial will be compared against recruitment and participation rates to determine whether data collection could be successfully completed at a single Pittsburgh site, or require multiple sites. If multi-site research was required, it could take advantage of the University of Pittsburgh's status as a NIH Clinical and Translational Science Award Program Hub in the Trial Innovation Network, dedicated to supporting multi-center clinical trial research.

Initial estimates of treatment effects. We will assess change on two types of secondary outcome measures, ones that measure mechanisms of treatment action, and ones that measure functional outcomes. Assessments that measures mechanisms of treatment action will consist of the Acceptance and Action Questionnaire II, [73] which measures general psychological flexibility, the Acceptance and Action Questionnaire – ABI, [47] which measures psychological flexibility in relation to acquired brain injury, and the Values Tracker, [74] which measures values engagement. Functional outcome measures will consist of the K6, [75] which measures psychological distress, the Stroke and Aphasia Quality of Life – 39,[76,77] which measures QoL, the Aphasia Communication Outcome Measure,[78] which measures self-reported communication efficacy, and the Communication Participation Item Bank,[79,80] which measures communication participation. For these measures, we will calculate pre- to post-treatment changes by calculating standard effect sizes (Cohen's *d*[68]). These functional outcome measures will serve as primary outcome measures in planned Stage II efficacy research, should ACT for aphasia appear promising (see "Use of pilot data to inform development of a full-scale efficacy trial" below).

Statistical Approach. Primary outcomes will assess intervention feasibility and acceptability. Secondary outcome measures will provide initial estimates of participate response and variability. We will report means and standard deviations for continuous variables and frequencies and proportions for categorical variables, with 95% confidence intervals for both types of variables. As a preliminary check on treatment validity, we will explore the association between changes on mechanistic measures (i.e., psychological flexibility, values engagement) and secondary measures of functional outcomes (e.g., QoL) via multi-level regression models (please see Clinical Trials Information Section 4.4 for additional information). We will also examine whether biological sex exerts an effect on any primary acceptability and feasibility outcomes measures via appropriate statistical tests (e.g., a two-sample *t* test or nonparametric alternatives, depending on data distributions).

Sample size justification. Total sample size (N=21; N=5 for Cohort 1 and N=16 for Cohort 2) is considered to be realistic based on level of project staffing and previous experience recruiting PWA in the Pittsburgh area. The sample size for Cohort 1 was chosen to provide preliminary feedback for the first version of the treatment manual, while also making sure the size of the SAB stays manageable over time (should all five participants decide to join the SAB when invited, this would bring the total number of SAB members to nine). The sample size for Cohort 2 is considered adequate for providing a precise estimate of treatment acceptability. This is because even with an overly conservative attrition rate of 25%, final completion rates would still be N=12, which meets minimum recommendations for providing reasonably precise confidence intervals for continuous variables.[81]

Use of pilot data to inform development of a full-scale efficacy trial. The determination of whether a full-scale trial is warranted will be based on whether ACT for Aphasia meets our criteria for feasibility and acceptability (Aim 2a) and whether it appears to be promising in terms of promoting functional recovery (Aim 2b). We will also examine within-group effect sizes (with 95% confidence intervals to reflect uncertainty regarding the reliability of the treatment effects sizes for planning a subsequent trial). Should ACT for Aphasia appear promising, these data will be used to inform the power analysis to determine sample size for a subsequent efficacy trial.