SECTION III: STUDY PROTOCOL

1. **Study Abstract:** Provide a <u>brief</u>, non-technical summary of the study, including study purpose and methods.

   The purpose of this investigation is to examine the evidence on emotion, language, and music, and propose a first step, in the form of a single-subject research design, to determine the most effective and efficient method for application to the rehabilitation of patients with aphasia. A single-subject adapted alternating treatment design will be used to compare two music conditions, using music with sung lyrics simultaneously with silent reading of the lyrics, and priming with music and sung lyrics followed by reading of the lyrics, with a control condition using reading materials without music. Risks are expected to be minimal. The risk is confidentiality. Risk management procedures in this study include: assuring confidentiality of participants, assuring qualified personnel, assuring convenient location, ensuring adequate enrollment, continual monitoring, addressing potential conflicts of interest, and making a plan to manage problems. Continual monitoring will be used to assess whether study interventions appear to be interfering with normal speech therapy treatment. If the researcher sees any signs of interference, the subject will be withdrawn from the research and study interventions will be stopped.

2. **Background:** Summarize background information about the research question(s.) Tell why the research is needed and include the relevance of this research to the contribution of this field of study. Also, provide references to relevant articles in the literature. (If you have more than 10 references, please submit the list of references as a separate attachment. Otherwise, please insert them here.)

   Aphasia is a language disorder:
   • Caused by left cortical lesions;
   • Impacts all modalities of language including comprehension, expression, reading, and writing;
   • And affects language processing from single words through higher levels of semantic and syntactic processing.
   • Reading has been used effectively to improve language comprehension in patients with aphasia (Helm-Estabrooks, Albert, & Nicholas, 2014).
   Emotional words facilitate language in individuals with aphasia (Landis, 2006; Landis, Graves, & Goodglass, 1982):
   • Driven by activation of the amygdala;
   • Amygdala activation enhances memory for emotional scenes/pictures (Canli et al., 2000).
   • Lesions in the amygdala negate the emotional word response (Vuilleumier et al., 2004).
   • The amygdala also responded to nonlinguistic vocalizations (Fecteau, Belin, Joanette, & Armony, 2007).
   • The emotional word effect crosses languages (Herbert et al., 2009).
   • Labeling reduced amygdala activation and decreased affective response (Lieberman et al., 2007).
   • The emotional word effect has not been demonstrated beyond the word level.
   Music also evokes emotion and activates the amygdala (Blood & Zatorre, 2001).
   • Brain regions involved in music processing are mainly supplied by the middle cerebral artery (MCA) bilaterally (Ayotte et al., 2000).
   • Intensely emotional music activated brain structures involved in reward/motivation, emotion, and arousal (Blood & Zatorre, 2001).
   • Musical aspects of language provide scaffolding for later development of the semantic and syntactic aspects of language (Brandt et al., 2012).
   Music has been used for rehabilitation of patients with neurological impairments.
   • The amygdala and visual extrastriate areas are intact in many patients with aphasia.

•   Listening to music with lyrics was more effective than listening to language for improving language recovery in patients with aphasia in the early recovery period after stroke (Sarkamo et al., 2008).

In the Sarkamo et al. (2008) study, sixty-three percent of the music used contained lyrics.

•   Linguistic meaning is accentuated when lyrics are embedded in music, and repeated exposure to songs increased ratings of meaningfulness of the lyrics (Thompson & Russo, 2004).

•   Verbal material presented as song lyrics was learned and retrieved more efficiently than material presented verbally (Thaut et al., 2005).

•   Listening to music, especially with lyrics, activated a more widely and bilaterally distributed network than listening to verbal material alone (Callan et al., 2006).

•   Patients with aphasia repeat and recall more words from novel songs when singing than speaking along with a model (Racette et al., 2006).

Reading was not stimulated in the Sarkamo et al. (2008) study.

•   Training more complex language can result in generalization to less complex, untrained language (Kiran & Thompson, 2003; Thompson, Shapiro, Kiran, & Sobecks, 2003).

•   Reading is a more complex language activity than listening (Berl et al., 2011).

•   Musical training transferred to improved speech and language in children, including reading (Moreno et al., 2008).

There is controversy in the literature regarding whether language and music networks are independent or shared. Resource theory: "If two tasks demand separate resources, they will be performed together as efficiently as in isolation…" but competitieon for the same pool of resources would divide attention or direct attention to only one component (Bonnel, Faita, Peretz, & Besson, 2001).

1.   Evidence for independent language and music semantic processing (separate, independent domains):

•   Patients with selective loss of linguistic abilities without any accompanying music deficit, conversely patients with lost musical abilities who retained language.

•   Similar levels of performance were found on judgments of semantic incongruities in single-task vs. dual task music and language processing (Bonnel, Faita, Peretz, & Besson, 2001).

2.   Evidence for shared syntactic processing:

•   Both music and language can prime the semantic meaning of a word (Koelsh et al, 2004).

•   Linguistic syntactic processing and musical syntactic processing were both impaired in patients with aphasia (Broca's) (Patel, Iverson, Wassenaar, & Hagoort, 2008).

•   Sung material manipulated for linguistic syntactic complexity and musical syntactic complexity showed that more complex levels of structural integration in music and language appeared to be shared/additive, but lower levels (not structural) were not (Fedorenko et al., 2009).

The problem:

•   Sarkamo et al. (2008) demonstrated that listening to music with lyrics was more effective than listening to language alone to improve language recovery in patient with aphasia during the early recovery period after a left MCA stroke.

•   The proposed next step is to test the effectiveness of additionally stimulating reading as part of that language recovery using silent reading of the lyrics.

•   In application to treatment for patients with aphasia, will simultaneous processing of music and language (reading) enhance or overload the processing networks?

Purpose: The purpose of this study is to translate neuroscience on emotion, music, and cognition into application for rehabilitation of aphasia, and test the effectiveness and efficiency of a new treatment, using listening to music with lyrics, combined with silent reading of the lyrics, to evoke emotion, engage the amygdala-extrastriate cortical projections, and increase arousal and attention to the reading material, to promote recovery of reading and retention of phrase-level reading material in patients with aphasia.

Significance: The impact of this study is anticipated to be a demonstration of increased effectiveness and efficiency of therapy directed toward recovery of language including reading comprehension in participants with aphasia. In addition, new material will be developed to increase options for treatment. Further, it will provide behavioral evidence to support hypotheses of either independent or shared neural pathways for processing musical and linguistic semantic meaning.

3. **Objectives:** State the research hypothesis or the question that the research will answer. List the research objectives and expected outcomes. **A primary outcome or objective must be identified**. After the statement of the primary objective, secondary objectives may be listed. Objectives should be simple and specific.

   Primary objective: test the effectiveness and efficiency of a new treatment, using listening to music with lyrics, combined with silent reading of the lyrics, to promote recovery of reading and retention of phrase-level reading material in participants with aphasia.
   Research questions:
   1. Is music with lyrics (songs) presented simultaneously with written lyrics effective for facilitating recovery of reading of phrase-level material for participants with aphasia (independent processing)?
   2. Is music with lyrics followed by presentation of the written lyrics effective for facilitating recovery of reading of phrase-level material for participants with aphasia (shared processing)?
   3. Which procedure, simultaneous presentation or priming with the music/lyrics, is more effective for facilitating recovery of reading of phrase-level material for participants with aphasia?
   4. Is one method more efficient for facilitating recovery of reading of phrase-level material for participants with aphasia?
   5. Does one procedure result in greater retention of the trained material?

   Research Hypotheses:
   1. Music with lyrics (songs) presented simultaneously with written lyrics will be effective for facilitating recovery of reading of phrase-level material for participants with aphasia.
   2. Music with lyrics followed by presentation of the written lyrics will also be effective for facilitating recovery of reading of phrase-level material for participants with aphasia.
   3. Simultaneous presentation will be more effective than priming with the music/lyrics for facilitating recovery of reading of phrase-level material for participants with aphasia.
   4. Simultaneous presentation will be more efficient for facilitating recovery of reading of phrase-level material for participants with aphasia.
   5. Simultaneous presentation will result in greater retention of the trained material.

4. **Study Design:** Give a description of the research design including use of placebo, randomization and an explanation of what is experimental. Include type of study: descriptive, retrospective, cross-sectional, longitudinal, prospective observational, pilot, experimental (controlled or non-controlled) or pilot.

   This investigation uses a single-subject, adapted alternating research design to compare two different experimental conditions using music with lyrics combined with visual stimulation of the written lyrics, to extend the emotional word effect to phrases, in order to stimulate reading comprehension of the trained material for patients with aphasia. The two music conditions include 1) music with sung lyrics simultaneously with silent reading of the written lyrics; and 2) music with sung lyrics, followed by silent reading of the written lyrics (i.e. priming with the music). A control set without music will be used additionally within every third session to detect potential history and maturation effects. All conditions will be followed by a silent reading phrase-completion task composed of written words from the total combined sets of stimuli.

5. **Study Population:** Describe the subject population, including age, gender, ethnic characteristics and health status. State the inclusion/exclusion criteria along with how this was determined, and by whom. Please state whether pregnant women, children, or other vulnerable groups will be included or excluded. Provide rationale for using or excluding special populations. State the number of subjects or subject records necessary to complete the research.

Considerations in Participant Selection

The main neurological structures that must remain intact for the proposed treatment to work are lateralized left hemispheric, i.e. left amygdala and left extrastriate cortex. While it seems intuitive to choose patients with right cerebral vascular accident (CVA) as the trial subjects, deeper analysis of the fMRI results reveals that areas on the right middle and superior temporal gyri and bilaterally the superior parietal gyrus post central were simultaneously activated. In addition, it has been shown that reading comprehension is bilaterally organized. For example, Hauk et al. revealed that words are processed by distributed neuronal networks that reflect word semantics (Hauk, Johnsrude, & Pulvermuller, 2004). Specifically, event-related fMRI showed that action words/verbs presented in passive reading differentially activated areas in the motor strip involved in the actual movements. Further, the left hemispheric structures involved in re-entrant processing are not part of the primary speech/language areas, i.e. Broca's, conduction, or Wernicke's areas. Therefore, the population of subjects who could most benefit from the proposed treatment should be those with localized cortical aphasia.

Because the identification of the intact targeted structures, i.e. left amygdala to left extrastriate cortex, is the basis for inclusion in this study, signs/symptoms defining injury to those neuro-anatomical structures should also be the basis of exclusion criteria. Type of aphasia need not be a limiting factor. In single-subject research design, each subject serves as his/her own control, so severity levels need not be defining criteria, because the effect on the outcomes of both treatments would be the same. Hemianopsia or other visual field defects, unilateral hemi-neglect or inattention affecting vision for reading need to be excluded, and in particular right homonymous hemi- or inferior quadrantanopsia which would indicate a lesion of the left parietal or temporal lobes and involvement of the left optic radiations.

Inclusion Criteria

Participants will be post-hospitalization; premorbid reading at the 8th grade level or higher based on the participant's/family's stated years of formal education; post-stroke aphasia/left middle cerebral artery (MCA) CVA based on EMR and CT/MRI imaging reports, or consult with the neurologist; intact left amygdala and left extrastriate cortex based on EMR and CT/MRI imaging reports, or consult with the neurologist; reliability in answering yes/no questions as determined by a 80% score on yes/no comprehension therapy tasks during regular speech therapy.

Capacity to provide informed consent concerning a study involving an intervention with music therapy.

This will be determined by the physician who refers the patient. The physician's determination will be documented either through written communication with the researcher, including emails, or by a note to file by the researcher that documents a verbal communication from the physician.

Exclusion criteria

Co-morbidities diagnosed and reported in the EMR or shown on CT scan or MRI including past history of stroke affecting other brain areas with residual symptoms, dementia, Parkinson's disease, head injury, etc.; hemianopsia or other visual field defects affecting vision for reading, and in particular right homonymous hemi- or inferior quadrantanopsia; previous history of learning disabilities in reading/writing; significant psychiatric diagnosis; English as a Second Language or non-English language.

Sample Size

A minimum of four participants will be required to demonstrate replication of treatment effects (Gast & Ledford, 2014, p.327). A maximum of ten participants will be requested from the IRB to account for attrition.

6. **Methodology:** List all activities or procedures that will be performed (pre-treatment tests and medications, tests and medications used during therapy, diagnostic tests, x-rays, lab tests,

questionnaires and other forms, interviews, chart reviews etc.) Describe how, when and where research activities will be administered and analyzed. **Distinguish any standard processes from those that are research.** Please describe activities/procedures in a step-by-step chronological order. State the length of time subjects will be in the study and the expected amount of time required for each study visit or activity.

Procedures:

Research procedures for the study are described below. None of these procedures will be billed to the patient or third party insurers. When the patient is seen at CFMH Rehab or Roanoke Day Rehab, during the song testing, baseline, and intervention phases, the subject's normal speech therapy sessions will be cut from approximately 60 to 45 minutes. The research interventions will immediately follow. The research sessions will take, on average, an additional 45 minutes. When seen at CRCH Inpatient Rehab, the speech therapy sessions will not change other than reading. The Inpatient Rehab SLPs will receive the referral for ST and conduct an initial evaluation of patients for clinical purposes. This will include standard testing procedures for speech/language and swallowing. Patients with a diagnosis of left MCA CVA will be identified using the inclusion-exclusion checklist by the Inpatient Rehab SLPs who will then inform patients of the study and ask at a standard speech therapy session if the patient and legally authorized representative or person of the patient's choosing would agree to meet, via Carilion Secure Videoconferencing, with the Rehab Director to discuss the possibility of being in a research study. The treating SLP will notify the recruiter of the patient's decision. If the patient is recruited, the PI will be notified by the recruiter and the PI will schedule and conduct the Informed Consent interview. All research interventions will be scheduled after 2:30 pm and conducted by the PI onsite.

First Step--ST evaluation (standard procedure) and identification based on inclusion/exclusion criteria. (Expected length of time one visit).

Second Step—At CFMH Outpatient, Recruitment interview with Rehab Director. The treating SLP will inform the PI of new referrals. The PI will then check the EMR for preselection, and inform the recruiter of appropriate referrals to be contacted for recruitment. The Rehab Director will contact the potential participant to discuss the possibility of being in a research study. If the patient/representative agree, then a mutually agreeable time will be scheduled, probably before or after a standard therapy visit. The Rehab Director will notify the speech therapist researcher of the patient's decision on whether to further discuss participation in research.
AT CRCH Inpatient Rehab treating SLPs, which does not include the researcher, will inform patients of the study and ask at a standard speech therapy session if the patient and legally authorized representative or person of the patient's choosing would agree to meet, via Carilion Secure Videoconferencing, with the Rehab Director to discuss the possibility of being in a research study. The treating SLP will notify the recruiter of the patient's decision. If the patient/representative agree, then a mutually agreeable time will be scheduled.
At Roanoke Day Rehab the PI may or may not be the treating therapist. If the PI is the treating speech therapist, procedures to CFMH Oupatient will be followed. If the PI is not the treating therapist, procedures will mirror those used at CRCH Inpatient Rehab. The PI will set up the conference call but will not be present in the meeting, unless requested to come back in to assist given any problem with equipment. (Expected length of time one visit).

Third Step--Informed consent interview with SLP outside the patient's normal treatment time. SLP researcher will review consent document with patient and patient's representative. The informed consent discussion is expected to take 45 to 60 minutes. Patient will answer yes/no comprehension questions regarding the information presented, which will be documented in writing by the SLP researcher. Any questions answered in error will prompt a review of the information by the SLP. If the patient scores less than an average of 80% on the yes/no comprehension test after the review,

the patient will not be asked to participate in the study. Patient will have three days to review consent document at home and make a decision. (Expected length of time one visit plus three days)

Fourth Step--Administer pretest Boston Diagnostic Aphasia Examination (BDAE-3) full version Reading subtests (extended testing). (Expected length of time one visit)

Fifth Step--All songs will be pretested for familiarity and positive valence by questioning the participants (i.e. do you know this song? Do you like it?). Response data will be recorded. (Expected length of time 1-2 visits)

Sixth Step--Baseline phase, all 30 phrases (see attachment 1) will be tested using the phrase completion task (see attachment 2). Both correct responses and participation will be verbally reinforced. Results will be analyzed by the ST to ensure that the sets are of equal difficulty for each participant. (Expected length of time 5 visits or 2 weeks)

Seventh Step--Intervention phase (B) (see flowchart attached), each song (music with lyrics) from set 1 (B1 songs#1-10) will be played in its entirety. When the targeted verse or chorus plays, the written lyrics will be simultaneously shown along with the song lyrics. The ST will point to the words of the targeted verse/chorus which will be silently observed by the participant as they are sung. This will be repeated for all 10 songs. The phrase completion task will then be presented, including the ten phrases from the songs played that day and the five control phrases, without music. The participant will silently or orally read the phrase and orally read and/or circle or point to the phrase completion choice. Correct responses will be verbally reinforced. The next session, each song (music with lyrics) from set 2 (B2 songs #11-20) will be played in its entirety. After the song plays, the written lyrics from the targeted verse or chorus will be presented. The ST will point to the words of the targeted verse/chorus which will be silently observed by the participant. This will be repeated for all 10 songs. The phrase completion task will then be presented, including the ten phrases played that day and the five control phrases. The participant will silently or orally read the phrase and orally read and/or circle or point to the phrase completion choice. Correct responses will be verbally reinforced. This will be repeated for all 10 songs. For all interventions, the number of correct responses will be tallied on a LaPoint Base 10 form and the percent correct will be entered on the graph for that day. The same procedures will be repeated, alternating procedures on sets 1 and 2 on subsequent treatment visits, until a criterion of 9/10 (90%) x 3 consecutive visits is reached on both sets. If the criterion is not reached on one of the intervention sets, defined as no increase in percentage correct x 3 consecutive visits, a correction procedure will be applied using modeling of the correct response. If the criterion still is not reached, that intervention will be determined to be limited in effectiveness and discontinued. Every third session will be videotaped for a reliability check by the recruiter/research team member. When both of the sets (B1 and B2) have been acquired or one acquired and the other discontinued, the number of sessions to criterion will be counted for each intervention. (Expect length of time 2- 12 weeks)

Eighth Step--Posttest BDAE-3 full version Reading subtests (extended posttest). (Expected length of time one visit)

Ninth Step--Retest retention of 30 phrases 3-week follow-up. (Expected length of time one visit)

Total number of visits: 16-48; total length of time 10-20 weeks per patient.

For CFMH or Roanoke Day Rehab, the PI, who is also the treating SLP, will make clear to subjects each time when standard therapy has ended and a research study intervention is about to begin. The subjects will be told approximately how long the research intervention is expected to take. For CRMH Inpatients, research will be separated in time and completed by a different SLP (the PI).

7. **Data Collection:** Attach a copy of your data collection tool or spreadsheet listing exactly what data is to be gathered during this research study. Describe below the data collection methods and how data be compiled for assessment.

Outcome Measures and Time Points
   Pretest/post-test information on the ICF Body Functions/Structures, Activities, and Participation will be provided (Hurkmans et al. 2011).

   The Boston Diagnostic Aphasia Examination (BDAE) (Goodglass, Harold, & Kaplan, 1983): Pretest reading scores on the BDAE full version subtests, i.e. B. Word Identification: 1. Word-Picture Match, and 2. Lexical Decision; C. 1. Homophone Matching; D. Derivational and Grammatical Morphology: 1. Matching to spoken sample; E. Oral Reading: 1. Basic oral word reading; F. Oral Reading of Sentences with Comprehension; and G. Reading Comprehension-Sentences and Paragraphs; will be completed prior to baseline A and initiating intervention, and immediately following completion of intervention to assess generalization to non-trained stimuli.
   At three weeks follow-up the trained stimuli from all three interventions will be retested to assess retention (see Flow Diagram).

   The dependent variables, i.e. differential response to the two interventions (counted as the percent correct responses per day, number of sessions required to achieve mastery at each level (simple counting), retention of the material (number of items remembered).

Reporting Participant Characteristics
   Age; sex; time post onset of left MCA CVA; type of stroke; previous level of function including educational level; body functions/structures, activities, and participation will be reported for previous level of function and changes from the stroke per the World Health Organization (WHO) International Classification of Functioning Disability and Health (ICF) (World Health Organization, 2013).
   A meta-analysis of studies using music for the treatment of neurological language and speech disorders showed that although measurable improvement was reported, the methodological quality of studies was rated low (Hurkmans et al., 2011). Specific recommendations were made to report education, dominance, and musical background, all of which will be included in the current study. Education will be reported based on highest level of formal education attained. Dominance will be determined by premorbid handedness for writing. Musical background will include reporting previous formal instruction for singing/choir, playing an instrument, or reading music, and experience with performance of singing, dancing, and listening to music.

Carilion Clinic's REDCap software will be used as the central location for data collection. REDCap (research electronic data capture) provides a secure, web-based application designed to support data management and collection for research/QA/QI studies. Carilion's REDCap servers are securely housed on site in a limited access data center, and all data are stored on Carilions's firewall protected network. The Health Analytics Research Team suppports the proper development of projects and surveys in REDCap, observing appropriate change control and enforcing appropriate security controls. Data collection projects are built with a study-specific data dictionary, enforcing intuitive, accurate, consistent and complete data entry. REDCap also provides a survey tool for building and managing online surveys. Health Analytics Research team restricts user access to the IRB-approved project research team utilizing the approved processes and standards of TSG. REDCap is HIPAA compliant and provides audit trails. Data can be easily exported in several formats to a secure network directory for combination with extracted data, if appropriate, and analysis with common statistical packages.

8. **Statistical Analysis:** State how qualitative and/or quantitative data will be analyzed. This must include a statement from a statistician that there is sufficient power to determine the primary study

outcome or objective. Other outcomes may be listed as secondary and descriptive. If this is a proof of concept or feasibility study that includes limited efficacy testing, there must be a statistician statement that the appropriate design is in place to determine whether an intervention should be recommended for broader efficacy testing. If a study is meant to be solely descriptive, then results apply only to the sample being studied and conclusions cannot be drawn about the larger population; therefore, the primary outcome or objective must be limited in scope.

Data Analysis

Reliability of the items in the task assessment tool will be established using Cronbach's Alpha correlation coefficient once at the beginning of the baseline phase. Inter-observer reliability on the scoring of the tool will be determined weekly using the kappa coefficient, a.k.a. Cohen's Kappa. Reliability data will first be analyzed for normality/skewness, accuracy, and completeness. Outliers will be identified using the Outlier Labeling Rule based on rank and percentile. If data are incomplete, e.g. if the behavior cannot be clearly seen on the digital recording, the corresponding score from the other researcher will be eliminated from the reliability determination.

The correlation coefficient chosen is dependent on the scale of measurement of the variables being correlated. For the reliability of the task assessment tool it will be used to determine if scores recorded by one researcher are strongly correlated with scores recorded by the other. Scores will be recorded as correct vs. incorrect, which is a nominal scale. One classic correlation coefficient used with a nominal scale is Cronbach's Alpha, used when both X and Y are dichotomous variables. The assumption that the items of the test are unidimensional cannot be met, meaning that each item measures the same ability on the same scale, because many different mental processes may be used in various combinations from item to item. Cronbach's alpha provides a solution to this problem, so will be an appropriate measure of internal consistency (Cronbach, 2004, see p.8). Acceptable values of alpha range from .70 to .90 (Tavakol & Dennick, 2011). If alpha is below .70, either the task assessment tool will be revised or the assistant will be re-instructed.

Inter-observer reliability will be determined by the kappa coefficient, used when there are two observers. Again scores will be recorded as correct vs. incorrect, a nominal scale. Simple percent agreement cannot account for chance agreement/uncertainty. The kappa statistic was developed to control for random agreement. Interpretation will be based on the kappa coefficient squared to show the accuracy in the data due to conguence between data collectors. Acceptable kappa squared values will range from .90-1.00 (McHugh, 2012). If the accuracy is questionable, the cause will be determined, and may indicate the need for further instruction of the assistant(s) on data collection. If reliability is below simple percent agreement 80% or kappa squared .90 on any day, the recording will be reviewed again by both researchers and consensus reached.

Data analysis for treatment will include both visual analysis and quantitative statistical analysis as follows:
• Visual analysis will include graphing average (mean) correct responses on the multiple-choice reading comprehension questions each session during each phase. Trend will be described by celeration lines depicting slope in each phase with split middle lines to measure central tendency.
• Quantitative statistical analysis will include the binomial test for dichotomous outcomes, the two standard deviations band method, and statistical process control.
• The binomial test involves counting data points above and below the split middle line and comparing the total number of points above and below with the number with fewer points to determine Spearman's Rank Correlation Coefficient, one-tailed probabilities which show whether the response pattern could have occurred by chance (<0.05 is considered significant) (Portney & Watkins, 2009).
• Computer analysis will include statistical process control, to determine whether intervention represents special cause variation. Statistical process control plots the central line and upper- and lower-control limits at three standard deviations above and below the mean. Criteria for special

cause/significance include: 1) any point that falls outside the upper or lower control limits; 2) seven or more consecutive points all above or below the center mean line, called a "run;" 3) six or more consecutive points moving up or down across the center mean line, called a "trend" (Portney & Watkins, 2009).

• The difference in number of sessions/trials to achieve mastery at each level for each intervention, the difference in retention at three weeks follow-up, and generalization to words used in verbal expression, will be analyzed by comparison of the difference between data points for the control treatment and the two target intervention conditions. After the research design has been completed by a minimum of four subjects, data will be consolidated for group means.

Statistical review was conducted by: Thomas Cappaert, PhD, ATC, CSCS   (name of statistician)
Professor & Director of Post-Professional Research, Rocky Mountain University of Health Professions   (Department/Institution of statistician)