

Stress and language recovery in individuals with aphasia: constraint induced aphasia therapy

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Objective: Constraint induced aphasia therapy (CIAT) is a more intensive form of language treatment for aphasia as compared to traditional treatments. This study examined whether there are differences in cortisol stress levels between the two methods of aphasia treatment as well as effects on language skills.

Design: Randomized controlled trial.

Methods: A total of 20 participants with expressive aphasia were randomly placed into one of the two treatment groups. The CIAT group received 10 days of intensive treatment over two weeks. The traditional therapy group received 6 days of treatment over 2 weeks. All participants in each group provided salivary cortisol samples before treatment, at the mid-point of treatment, and at the conclusion of treatment. Language skills were assessed before treatment and at the conclusion of treatment.

Results: A significantly higher proportion of individuals in the CIAT treatment group had increased salivary cortisol stress levels when compared to the traditional treatment group at the mid-point of the program (80% versus 30% respectively, $p < 0.05$). There was no significant difference in the proportion of individuals with increased cortisol stress by the end of the treatment. Language scores for word repetition and overall aphasia quotient significantly improved for the CIAT group when compared to the traditional group ($p < 0.05$).

Conclusions: The CIAT treatment appears to initially create increased psychophysiological stress as compared to the traditional treatment. In spite of the initial increases in psychophysiological stress, participants appear to become conditioned to the challenge and ultimately have enhanced benefit from CIAT treatment.

Key Words: Aphasia, Stress, Constraint induced aphasia therapy, Cortisol

Introduction

Aphasia

Aphasia is a language disorder that is usually caused by a cerebral vascular accident (CVA, or stroke). Nearly one-third of individuals who suffer CVA will develop some degree of aphasia [1-4]. Individuals with aphasia typically have difficulty processing and expressing language [5] and will need some type of speech and language therapy.

Traditional aphasia treatment has focused on models that

use retraining (restoration of function) and compensation (use of alternative modes of communication). In traditional models, if stimulation and cueing do not restore functional communication, patients are taught compensatory techniques [5]. Classically, compensatory techniques include simple tools (communication boards, gestures, etc.), as well as more complex tools (electronic speaking devices, for example). According to traditional models, theoretically, when retraining is unsuccessful, tools that require the least amount of effort are preferred [6]. Additionally, Levine and Page cit-

Received: 2 May, 2013 Revised: 5 June, 2013 Accepted: 10 June, 2013

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ed Wolf in their article noting that the impact of limited time and resources for rehabilitation push clinicians to move quickly to use compensatory techniques, often at the expense of restoration of language function [7]. It is a widely accepted notion that spontaneous recovery occurs in the first six months, with minimal spontaneous improvement within one year post [8]. Conventional wisdom seems to promote compensatory techniques in order to facilitate communicative functionality as rapidly as possible. However, recent research suggests that bypassing the impaired system may lead to learned non-use [9,10]. Individuals who are repeatedly unsuccessful in their attempts to communicate quite naturally learn to avoid use of the impaired neurological pathway. This avoidance is called, “learned non-use.” Ironically, avoiding the use of the impaired neurological pathway actually promotes chronic neurological impairment (in this case, chronic aphasia) [3].

The latest research in the fields of physical therapy and occupational therapy targets traditional models, which seem to abandon restoration too quickly. Taub *et al.* [11] suggests that individuals who are forced to use the impaired system exhibit improved function, provided there is a high level of intensity (length of therapy session) and a high level of frequency (number of therapy sessions). Forced use of the impaired system, combined with high intensity and high frequency of treatment seems to prevent or reverse learned non-use, according to Taub and others [12-14]. This concept of forced use, high intensity, high frequency was introduced to the field of aphasia therapy by Pulvermüller *et al.* [6] and has been replicated by others, with verbal communication as the targeted outcome [15-17]. Forced use of the impaired communication system, with high frequency and high intensity therapy is now known as constraint induced aphasia therapy (CIAT) [6,18,19]. Subsequent studies that compared CIAT with conventional therapy showed that CIAT resulted in greater improvement of language skills [3,6,9,16,18]. In the Meinzer *et al.* [19] study, participants demonstrated improved neurological activity, confirmed by abnormal slow wave activity mapping, as well as improved functional language performance on at least one subtest of a standard language test [19]. Meinzer *et al.*'s findings [19] suggest that CIAT may assist neural plasticity in the process of restoration of language function by restoring or reintegrating the language network.

Stress

Stress, which may be triggered by internal or external fac-

tors, causes a psychophysiological response [20]. When the body is under stress, allostasis, the body's ability to adapt to environmental demands [21], is threatened. When allostasis is threatened, undesirable changes may occur in the immune system [22]. Glucocorticoids (GCs), which are steroid hormones that have both enhancing and inhibiting effects on the immune system, inhibit pro-inflammatory cytokines, which, in turn, helps to balance the immune system when it is under stress [23], thus, keeping the immune system from overshooting [24].

GCs include the steroid hormone cortisol. An increase in cortisol levels may influence immune system modulation. Thus, increased levels of cortisol may indicate stress [25,26]. As stress increases, the production of cortisol increases via the hypothalamic-pituitary-adrenal axis [26].

Not all stress is harmful, and, cortisol levels normally fluctuate. However, failure to recover from stress is abnormal and potentially harmful. Recovery from stress (allostasis) occurs when the body is capable of maintaining stability. When the body is unable to maintain stability, *allostatic load* occurs. Allostatic load is defined as the wear and tear on the body created by stress [27]. In other words, allostatic load is the consequence of the body's inability to reestablish homeostasis from the stress [28].

McEwen [29] refers to five (5) stress recovery patterns (labeled A through E for the purpose of clarity here). Pattern A is the pattern for normal recovery. Patterns B through E are patterns that cause allostatic load. Pattern B (repeated hits) occurs when there are successive multiple novel stressors. This is chronic stress. Pattern C (lack of adaptation) occurs with failure to adapt to repeated occurrences of the same stressor. Pattern D (prolonged response) occurs when there is no recovery, which induces a prolonged state of stress. Pattern E (inadequate response) occurs when there is diminished or no response to stress.

These patterns of allostatic load (abnormal recovery from stress) may affect the success of communication therapy. For example:

Pattern B (repeated hits): A variety of activities, at mixed levels of difficulty, is presented to a patient who is consistently performing poorly. Failure on item after item creates a succession of new stressors; thus, the patient has no opportunity to recover.

Pattern C (lack of adaptation): A patient with aphasia is repeatedly presented with the same failed activity day after day. The failure creates stress, but recovery follows. Yet, upon presentation of the same activity the next day, the same

stress response occurs when failure occurs. Failure to adapt to the stressful situation makes each failure an essentially new failure.

Pattern D (prolonged response): A patient with aphasia continues to worry about failed responses to therapy tasks. No recovery from stress occurs.

Patterns E (inadequate response): The patient with aphasia may exhibit no response to failure or success in therapy. This may be an indication that the immune system could eventually be compromised.

Methods

Subjects

Participants in this study were recruited through local, outpatient speech-language pathology departments and local community stroke support groups. The participants were recruited through the use of flyers that were given to speech-language pathologists and support group facilitators. The inclusion criteria for participation in the study were: (1) medical diagnosis of left hemisphere CVA with an onset of six months or more; (2) diagnosis of aphasia at least six months prior to the study; (3) English as primary language; and, (4) non-verbal communication as either a primary or secondary form of communication.

Participants were excluded from the study if they were: (1) taking corticosteroid medications; (2) diagnosed with any neurological condition other than CVA; (3) diagnosed with a cognitive disorder that prevented participation in aphasia therapy; and, (4) diagnosed with a cognitive disorder that would prevent being able to answer questionnaires. The inclusion and exclusion criteria were sent to the referral sources to allow for pre-screening. Eligible participants were scheduled for an initial consultation with the principle investigator to complete an informed consent packet as well as a demographic information form. The initial consultation served as an opportunity to review the inclusion and exclusion criteria in order to determine candidacy for the study. Once enrolled, the participants were randomly assigned to one of two treatment groups.

A total of 20 participants were included in this study, 10 of whom were assigned to each of the two groups. Age range of participants was 50 to 70 years, with a mean age of 65.0 ± 5.6 years for the traditional aphasia treatment group and 66.8 ± 3.6 years for the CIAT group. Time post onset ranged from six to 27 months, with a mean of 11.5 ± 4.6 months for the traditional aphasia treatment group and 14.0 ± 6.3 months for

the CIAT group.

Procedure

All procedures used in this study were reviewed and approved by the institutional review board of Loma Linda University. As subjects were identified and placed on the pre-randomized list, groups of 2-3 subjects were created and treatment was initiated.

Pre-treatment salivary cortisol testing

Once identified and placed in one of the two treatment groups, the participants were provided with a saliva cortisol collection package for pre-treatment levels. The saliva collection packet contained instructions from Salimetrics (State College, PA, USA), regarding how to collect saliva via the passive drool method (Saliva Collection and Handling Advice, 3rd edition, Salimetrics, State College, PA, USA). All participants and their caregivers reviewed the instructions and were asked to collect the sample at home at the appropriate times. Home collection was chosen in order to obtain a baseline assessment in the least stressful environment possible. The passive drool collection method at home required the participants to drool through a straw into a vial which was pre-coded with a sticker that contained their participant number followed by their sample number (1=pre, 2=mid, 3=post). All participants were instructed to collect the salivary samples at noon so as to control for diurnal variability. The participants were instructed to bring the saliva sample the morning of their language pre-testing. Once received, the salivary samples were double checked for volume, correct labeling and collection time. All samples were then placed in a -80°C freezer in the Molecular Research Lab in the School of Allied Health Professions, Loma Linda University for storage prior to ELISA testing (Salimetrics, State College, PA, USA).

Language pre-treatment testing

The Western Aphasia Battery (WAB) test was administered according to test protocol. Participants were given the following subtests: 1) spontaneous speech, 2) word repetition, 3) word finding, and 4) auditory comprehension. All of the scores were analyzed and an aphasia quotient score was obtained and recorded for each participant.

Treatment

The goal for the participants in the traditional aphasia treatment group was to produce functional communication

by any means necessary. The participants in the traditional aphasia treatment group completed language activities, such as naming, picture description, sentence formulation and conversational speech. Various types of cueing were provided, and participants were allowed to use gestures or other non-verbal modes of communication in order to make communication easier. Treatment was conducted three times a week for two weeks, with each participant receiving 45-60 minutes per session for a total of six sessions. The total treatment time in the traditional aphasia treatment group ranged from five to six hours with an average of 5.5 hours.

The goal for the participants in the CIAT group was to produce verbal communication. The participants in the CIAT group complete language activities. The therapeutic activity consisted of a deck of 40 object cards with a total of 20 different pictures. There was one pair of cards for each target item/stimulus. This activity was also conducted with two-to-three participants in each group. In this activity the participants were instructed to request a card that they had in their hand from another person in the group. The request had to be made verbally without the use of any non-verbal communication. A barrier was used to constrain non-verbal modes of communication. In order to ensure that each participant actually employed forced use, additional rule constraints were devised in order to raise the difficulty level of language activities and criteria for success. When participants reached performance levels of 80% or higher on verbal targets, new rule constraints were added or adjusted. The additions and adjustments changed the criteria for a correct response. For example, when a one-word target presented no challenge for the participant, an additional constraint increased the difficulty and criteria for success. The criteria for success were modified to requiring the participant to produce a verbal request at the phrase or sentence level. Additions and adjustments in constraint were continually fine tuned. CIAT treatment was conducted five times a week for two weeks, with each participant receiving 2.5 to 3 hours of treatment per session. The total treatment time in the CIAT group ranged from 25 to 30 hours with an average of 26.5 hours.

Mid-treatment and post-treatment cortisol testing

Each participant underwent cortisol testing at the midpoint (conclusion of the first week) and again at the end of treatment (conclusion of the second week). For the traditional aphasia treatment group, midpoint testing occurred at noon after the third treatment session. The CIAT group received their midpoint testing at noon after the fifth treatment

session. Participants provided a saliva sample collected using the passive drool method. Post-testing was conducted at the end of the treatment programs. Post-treatment testing was conducted for both groups at noon in order to maintain consistency with the prior testing parameters. Participants provided a saliva sample collected using the passive drool method.

Language post-treatment testing

The WAB was administered to participants in order to obtain receptive and expressive language scores as well as an aphasia quotient.

Data analysis

Data were analyzed using IBM SPSS Statistics 20.0 (IBM Co., Armonk, NY, USA). One sample Kolmogorov Smirnov test was used to examine the distribution of the continuous variables. Chi-square Fisher exact test was used to examine the differences in gender, marital status, and work status by treatment group. Differences in race by treatment group were assessed using Pearson's chi-square. Mean age, time post onset, baseline cortisol levels, and language scores were compared between the traditional aphasia treatment group and the CIAT group using independent t-test. Changes in language subtest scores and aphasia quotients by treatment group were examined using Mann-Whitney U-test. For cortisol levels, we calculated the percent change between pre- and mid-, pre- and post-, and mid- and post-testing; then, we calculated the number of participants who had an increase, no change, or a decrease at all times in both treatment groups. A chi-square test of independence was used to examine differences in proportions of participants who experienced a percent change in cortisol level by treatment group. The level of significance was set at $p < 0.05$.

Results

There were no significant differences in mean age and time status post onset between treatment groups (Table 1). There were no significant differences between groups with regards to gender, marital status, race and work status ($p > 0.05$; Table 1). Results revealed no significant difference in baseline testing of cortisol or language skills between the two groups ($p > 0.05$; Table 2).

Stress levels were examined between groups by comparing pre-treatment, mid-treatment, and post-treatment cortisol levels. As Figure 1 illustrates, between baseline and mid

Table 1. Frequency distribution of characteristics of study sample by treatment type (N=20)

Demographics	Traditional group (n=10)	CIAT group (n=10)	<i>p</i>
Age (y)	65.0 (5.6)	66.8 (3.6)	0.42 ^a
Time post onset (mo)	11.5 (4.6)	14.0 (6.3)	0.36 ^a
Gender			
Male	6 (60)	7 (70)	0.65 ^b
Female	4 (40)	3 (30)	
Married			
Yes	7 (70)	6 (60)	0.50 ^b
No	3 (30)	4 (40)	
Race			
White	5 (50)	4 (40)	0.61 ^c
Black	3 (30)	2 (20)	
Other	2 (20)	4 (40)	
Work			
Yes	2 (20)	1 (10)	0.50 ^b
No	8 (80)	9 (90)	

Values are presented as mean (SD) or n (%).

CIAT: constraint induced aphasia therapy.

^aMann-Whitney U-test. ^bFishers exact test, ^cPearson's chi-square.

Table 2. Mean (SD) of baseline outcomes by treatment type (N=20)

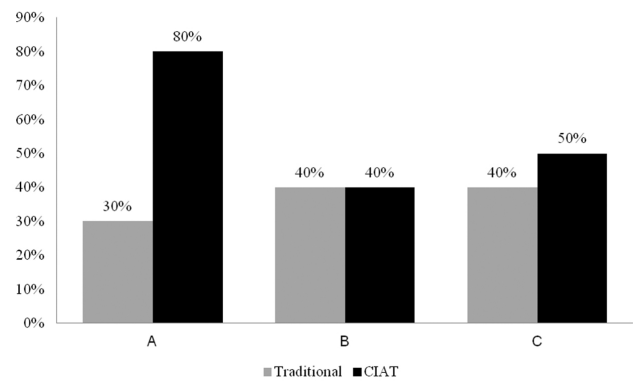
Pre-testing results	Traditional group (n=10)	CIAT group (n=10)	<i>p</i> ^a
Cortisol	0.37 (0.19)	0.21 (0.17)	0.06
Spontaneous speech	10.4 (3.5)	9.0 (3.0)	0.35
Repetition	5.7 (1.8)	6.3 (1.2)	0.39
Word finding	5.2 (1.7)	5.6 (1.3)	0.55
Auditory comprehension	7.6 (1.08)	7.5 (0.9)	0.88
Aphasia quotient	57.6 (15.6)	56.7 (12.0)	0.89

CIAT: constraint induced aphasia therapy.

^aIndependent t-test.

treatment, 80% (n=8) of participants in the CIAT group showed increased cortisol levels, compared to 30% (n=3) in the traditional therapy group ($\chi^2=3.2$, $p=0.03$). Between mid-treatment and post-treatment, 40% (n=4) of participants in the CIAT group showed increased cortisol levels, compared to 40% (n=4) in the traditional therapy group ($\chi^2=0.2$, $p=0.68$). From pre-treatment to post-treatment, 50% (n=5) of the CIAT group showed increased cortisol levels, compared to 40% of the traditional aphasia therapy group ($\chi^2=0.1$, $p=0.50$).

Observation of individual participants' cortisol levels (not shown in Figure 1) revealed that 100% (n=10) of the participants in the CIAT group showed an increase at some

**Figure 1.** Percentage of subjects with increased salivary cortisol by treatment periods. (A) Pre treatment to mid treatment, (B) mid treatment to post treatment, (C) pre treatment to post treatment.**Table 3.** Mean (SD) changes (post-pre) of language task scores by treatment type (N=20)

Language task	Traditional group (n=10)	CIAT group (n=10)	<i>p</i> ^a
Spontaneous speech	5.54 (2.67)	4.02 (2.50)	0.14
Word repetition	0.40 (0.16)	0.70 (0.27)	0.02
Word finding	0.50 (0.29)	0.76 (0.27)	0.06
Auditory comprehension	0.07 (0.08)	0.10 (0.11)	0.53
Aphasia quotient	3.58 (1.47)	5.72 (2.13)	0.02

CIAT: constraint induced aphasia therapy.

^aMann-Whitney U-test.

point during treatment. Eight showed an increase during the first half of treatment. Two of those continued to show an increase during the second half, while the other six showed a decrease. Of the original 10, the remaining two showed an initial decrease during the first half of treatment, with a subsequent increase during the second half.

In the traditional aphasia therapy group, seven of the participants showed increased cortisol levels at some point during treatment. Three showed an increase in the first half of treatment; all three of these showed decreased levels in the second half. Four who had a decrease in the first half showed an increase during the second half. Thirty percent (n=3) of this group actually showed a continual decrease in cortisol levels during treatment.

The mean difference between pre-treatment and post-treatment scores on the WAB were compared between groups using the Mann-Whitney U-test. Participants in the CIAT had significant pre-test/post-test improvement compared to the traditional group in both word finding and overall aphasia quotient ($p < 0.05$; Table 3).

Discussion

The purpose of this study was to determine if CIAT increases stress significantly more than traditional aphasia treatment. Increases in cortisol reactivity represented increased psychophysiological stress. Percentages of increased stress are shown in Figure 1. Other studies have shown that CIAT achieves greater effects than traditional therapy approaches. Studies have shown that cortisol is a psychophysiological indicator of stress, and that it can be measured. To our knowledge, this is the first study that examined cortisol levels (as an indicator of stress) during CIAT and traditional aphasia therapy. Analysis of cortisol levels in this study suggests that CIAT may increase stress during the initial week of treatment, compared with traditional aphasia treatment. However, by the end of the treatment, CIAT participants showed no significant difference in cortisol levels from the participants in the traditional aphasia treatment. In other words, CIAT participants showed increased stress initially, but were able to recover.

Additionally, the language testing provided information about stress and language treatment. The CIAT group did receive more hours of therapy, which may have impacted the increased language scores; however the purpose of the study was to determine if language skills can improve in a stressful therapy program. It appears that recovery of language may be stressful, but improvement is possible, provided stress recovery and the ability to adapt to the treatment occurs. It should be noted that stress management is influenced by many factors, including psychological factors, such as depression and quality of life. Those factors may play a significant role in one's ability to adapt to the CIAT program.

A limitation of this study was the sample size (20 participants). Although 10 subjects in a group does not present with enough power to generalize, the study has identified that stress management does play a role in recovery, and it is an important factor to consider when choosing a therapy procedure. Researchers must further examine the concepts of forced use, stress, and aphasia treatment to determine if there are psychological predictors that will allow clinicians to be better informed in their treatment choices.

This study has initiated the bridging of aphasia therapy and psychoneuroimmunology (the relationship between mind and body and the determinants of a healthy system). The CIAT treatment appears to initially create increased psychophysiological stress as compared to the traditional treatment. In spite of the initial increases in psychophysio-

logical stress, participants appear to become conditioned to the challenge and ultimately have enhanced benefit from the CIAT treatment.

Acknowledgements

The present work was supported by the Department of Communication Sciences and Disorders at Loma Linda University in the School of Allied Health Professions in conjunction with the Faculty Graduate Studies. The authors would like to give special acknowledgment to the Speech Pathology Department at St. Bernadine's Medical Center and Villa Healthcare Center of Riverside for their support and assistance. This work was supported by the Department of Communication Sciences and Disorders at Loma Linda University and the Office of the Dean of the School of Allied Health Professions at Loma Linda University.

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