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CLINICAL AND PHYSIOLOGICAL MEASURES
OF THE EFFICACY OF
PROSPECTIVE MEMORY TREATMENT

BY

Tessa Bloomquist

A THESIS SUBMITTED TO
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Clinical and Physiological Measures of the Efficacy of Prospective Memory Treatment

BY

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ABSTRACT

Prospective memory (PM) involves the ability to form and realize intentions after a time delay (Einstein & McDaniel, 1990). This study examines the relationship between clinical measures of PM and an event-related potential paradigm (West & Ross-Munroe, 2002) before and after Cognitive Rehabilitation Therapy (CRT). Participants with traumatic brain injury (TBI) were assigned to one of two groups, CRT and an active control condition. Electrophysiological and behavioral data were collected while subjects performed a computerized PM measure and the Memory for Intentions Screening Test (MIST) (Raskin, Buckheit, & Sherrod, 2011), a clinical measure. The results from the two groups were compared to determine physiological and clinical change as a result of treatment.

INTRODUCTION

Acquired brain injury (ABI), which includes both stroke and traumatic brain injury, is a leading cause of disability in the United States and worldwide. Prospective memory, the ability to remember to do things in the future, is one of these cognitive functions that is affected by an acquired brain injury. Cognitive rehabilitation is the most accepted form of therapy to try and regain an individual's prospective memory. This study aims to determine the efficacy of cognitive rehabilitation by testing individuals electrophysiologically before and after therapy to see if there is any physiological change.

Acquired Brain Injury

ABI is defined as a brain injury that occurred after birth (Brain Injury Association of America, 2012). ABI is a very broad definition and the type of injury can vary widely. ABI can cover etiologies including cerebrovascular accidents (CVAs) or strokes, traumatic brain injury and encephalitis (Brain Injury Association of America, 2012). While the term ABI excludes injuries induced by trauma during birth, or any injury that is congenital, hereditary, or degenerative it does include structural injury induced traumatically or a physiological disruption of brain function as the result of an external force (Vincent, Roebuck-Spencer & Cernich, 2014).

After acquiring an ABI it is common that the individual loses consciousness for a period of time, loses memories from directly before or after the incident, feels perplexed and disoriented from the time of the incident, and neurological deficits such as a change in vision, sensory loss, aphasia, loss of balance and weakness. These deficits can last for weeks, months, or sometimes even years (American Congress of Rehabilitation Medicine, 2012).

Severe Acquired Brain Injuries

There are five major groups of sABI which are coma, vegetative state, persistent vegetative state, minimally responsive state, akinetic mutism, and locked-in syndrome. These five groups all share some similar symptoms. All are between 8-13 on the GCS (Brain Injury Association of America, 2014), have confusion lasting upwards of a week, and physical, cognitive, and behavioral impairments that can span for weeks or even months (Vincent et al., 2014).

The prognosis for individuals with sABI depends on age, GCS score, papillary response and size, high intracranial pressure, hypoxia and hypothermia (Jiang et al., 2002). After an sABI many preventative measures can be taken to reduce negative effects. One study was conducted on a very large sample size of TBI and after one year of injury there was 31.56% good recovery, 14.07% moderate disability, 24.35% severe disability, 0.58% vegetative status, and 29.43% died (Jiang et al. 2002).

Recovery is difficult because, typically, numerous brain regions are damaged in a sABI (Vincent et al., 2014). These variations lead to an array of similar cognitive defects that many individuals seem to experience. Many report symptoms of anhedonia, apraxia, aphasia, and amnesia (Dawkins, Cloherty, Gracey, & Evans, 2006). Beyond these neurological symptoms an individual's behavior is likely affected and individuals will experience disinhibition or emotional flooding, the unconscious release of repressed feelings or fears (Tonks, Williams, Frampton, Yates, & Slater, 2007).

Prospective Memory

PM is the ability to form and realize intentions after a time delay, or the ability to remember to do things in the future (Einstein &McDaniel, 1990). In contrast, retrospective memory is remembering events from the past. Both prospective and retrospective memory are integral parts of everyday life. It is a crucial skill to possess if an individual is able to function independently.

PM can be split into time-based and event-based tasks. Time-based PM refers to the ability to remember to do a task at a specific time in the future. An example of a time-based PM is remembering to go to the hairdresser at noon. Event-based PM is remembering to perform an action in response to an external cue. If an individual is driving through town and passes the library, and event-based PM would be remembering to return a library book after seeing the library.

PM has five different stages; intention formation, a delay period, a performance interval, realization, and monitoring (West & Ross- Monroe, 2002). These five stages can be seen through distinctive characteristics. First, there is the formation of a conscious intention, then a delay between the realization of the intention and performing the intention, monitoring is occurring throughout this delay period, a continuous task within the delay, and then a final cue or reminder (Raskin, 2009). All PM tasks go through the same stages but healthy adults (HA) vary in PM performance between event-based and time-based cues, long and short delay periods, and action versus verbal responses (Koriat et al. 1990). A time-based task is more difficult to remember than an event-based task because there is no external cue to remind the individual of the intended action and it therefore requires more self-initiation (Tay et al., 2010).

There are two major theories of prospective memory, Preparatory Attention and Memory Theory (PAM) (Smith, 2003) and Multi-Process Theory (McDaniel & Einstein, 2000). PAM suggests that prospective remembering is sometimes aided by strategic monitoring of the environment for appropriate and helpful cues. These cues tend to be a specific event or the passage of a certain amount of time for the completion of an activity and then retrospective memory is used to distinguish between wanted PM intention and unwanted thoughts (Smith, 2003). The multi-process PM theory states that there are both automatic and strategic processes used for memory retrieval. When PM target events are not salient or if there is no pre-association between target event and intended action monitoring is used (Einstein and Mc Daniel, 2007).

While there is still much to be learned about PM, multiple studies have revealed that the various phases of PM are mediated by prefrontal lobe activity, both through functional magnetic resonance imaging (fMRI) (Volle, Gonen-Yaacovi and Burgess, 2011) and electroencephalogram (EEG) (West & Ross-Munroe, 2002, West, 2011). The details of the EEG and its pertinence to this study will be discussed later in the introduction.

Measurements of PM

Memory for Intentions Screening Test (MIST)

Investigating PM can be done through investigating established stages of PM through event and time-based tasks. The Memory for Intentions Screening Test (MIST) (Raskin & Buckheit, 1998) is designed to evaluate these stages. The MIST is specifically valuable as it is not specific to one group of patients or test subjects, the test is versatile (Raskin, 2011).

The MIST lasts 30 minutes and has clinical sensitivity and specificity (Raskin, 2009). The ongoing task within the MIST is a word search As the participant completes this task, the MIST assesses the two cue types, event and time-based, PM cues, verbal and action responses, different time delays, and specific PM errors. PM errors in the MIST include PM failure (PF), task substitution (TS), loss of content (LC), loss of time (LT), place losing error (PL), and random errors (RE) (Raskin, 2009). PF is when the subject does not respond. TS occurs when the participant performs an action rather than a verbal item or response. LC is when the subject remembers that a task needs to be completed at a certain time but cannot place what the task is. LT is when a task is completed at the incorrect time. PL is if the participant only performs part of the task or repeats a previous task. RE is when the subject's response does not fit into any of the above categories.

The MIST also allows for comparisons between different populations. In this study it allows for the comparison of HA and ABI before and after treatment. Previous studies have been conducted comparing healthy adults to those with TBI (Raskin, 2011). In these studies, the results from the MIST have shown that individuals with TBI have significant impairment on event-based tasks as well as the 24-hour trial (Raskin, 2004). Both the healthy and TBI groups performed better on action-based tasks over verbal, and the only errors were in PM. Attention is necessary to observe time and keep the intention throughout PM tasks but individuals with TBI may have difficulty performing tasks that require complex action (Raskin, 2011).

*Electrophysiological Correlates of PM*

PM can also be measured using electrophysiological correlates, a method of measuring event-related potentials (ERPs). ERPs are electrical brain responses that result from an external

stimulus such as a sound or visual cue. An ERP is identified as a positive or negative voltage deflection during a course of time (West, 2011). Studying ERPs is useful in discovering the brain regions and activity related to PM.

ERPs can be measured from the scalp using an encephalogram (EEG) machine that records the response to an event at a specific time. West's ERP studies (West, 2001, West and Ross-Munroe, 2002) measure ERPs to examine the five-phases of PM. Both event and time-based PM are tested in these studies by combining an ongoing activity with a PM cue (West, 2003). West's studies (West, 2001, West and Ross-Munroe, 2002) include a computer-based test where the participant completes an ongoing task with PM tasks scattered throughout. The ongoing activity is categorizing words as semantically related or unrelated. An individual's accuracy in categorizing words as related or unrelated as well as their reaction time is measured to provide a measure of ongoing activity engagement. These measures are used to provide insight into the participant's active involvement in the ongoing task. While an individual is completing this ongoing task, the PM cue, or intention formation trial, is presented. If the participant correctly remembers the task, and responds correctly to the PM cue, they have realized the intention and their response will be recorded as a "hit." If they fail to press the correct key they have not realized the intention and have their response recorded as an incorrect PM response or a PM miss.

During the task, ERP's are recorded. Behavioral and electrophysiological measures can then be compared. ERPs produced during the ongoing activity and PM cue trials are different (West, 2001, West and Ross-Munroe, 2002). The differences in ERPs can aid in discovering the process behind remembering an intention and then performing it (West, 2003). When comparing the ERPs elicited during the intention formation trials associated with realized intentions,

unrealized intentions, and the ongoing activity (Figure 1) to those ERPs elicited in PM hit trials,

PM miss trials, or the ongoing activity (Figure 2).
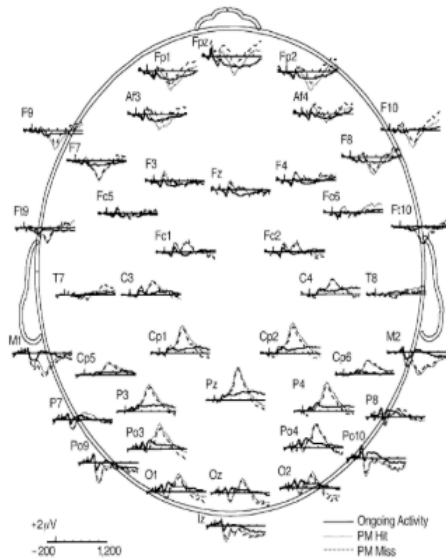
Figure 1. Grand averaged ERPs for ongoing activity trials preceding intention formation trails, realized intention trials, and unrealized intention trials and their approximate spatial locations on the scalp (West & Ross-Munroe, 2002).
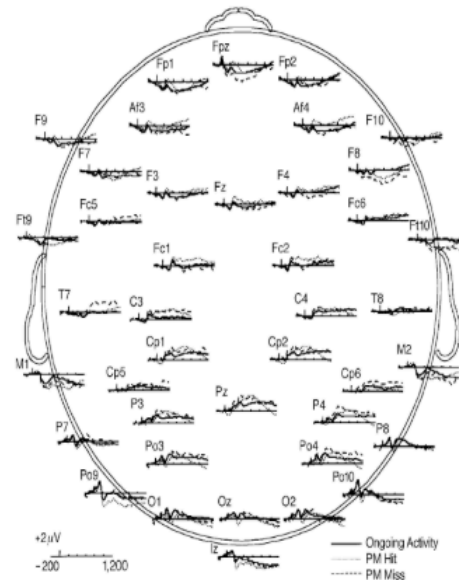
Figure 2. Grand averaged ERPs for ongoing activity trials preceding PM cue trials, PM hit trials, and PM miss trials and their approximate spatial locations on the scalp (West & Ross-Munroe, 2002)

For each phase, specific PM ERPs were identified. The ERPs associated with PM are

N300, parietal positivity, the late positive component (LPC), and slow waves (West, 2003). Both

N300 and parietal positivity are neural correlates associated with the realization of intentions.

The N300 is a phasic negativity that happens 300 ms after the stimulus onset and peaks over the

occipital parietal region (West & Ross-Munroe, 2002) (Figure 3 & 4). The N300 is specifically

useful in alerting the neural system to the presence of a possible cue (West & Ross-Munroe,

2002). The N300 did not differentiate the ERPs demonstrated during intention formation trials

where the intention was realized when the cue was present versus those trials where the intention

was not realized in the presence of a cue.
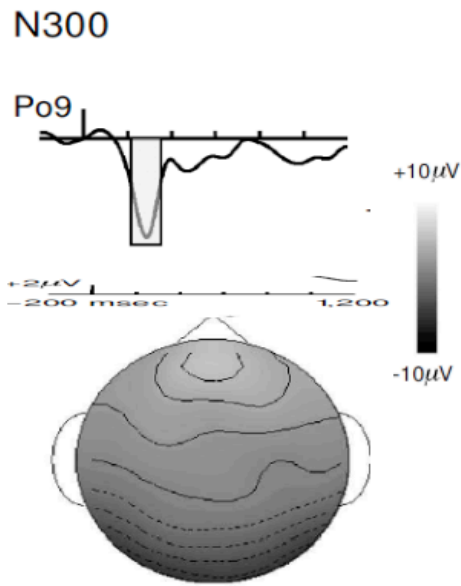
Figure 3. ERP difference waves and spline voltage maps reflecting the N300 for the intention formation trials. The waveform reflects the difference between realized intentional trials and unrealized intention trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002).
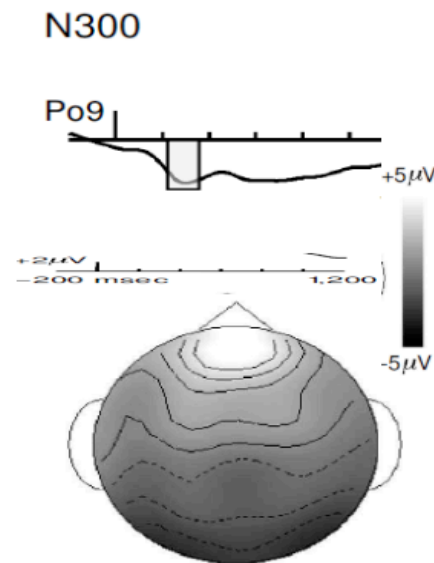
Figure 4. ERP difference waves and spline voltage maps reflecting N300 for PM cue trials. The waveform reflects the difference between the PM hit trials and ongoing activity trials. The topography reflects the activity of the bounded area for each modulation (West & Ross-Munroe, 2002).

Parietal positivity is positivity that happens between 400 and 1200 ms after stimulus onset and peaks over the parietal region of the scalp. (West, 2011). The Late Positive Component (LPC) is the ERP associated with recovering an intention from one's memory. The LPC happens 575 ms after stimulus onset and is seen as a positivity over the parietal region of the scalp and negatively over the lateral frontal regions (West and Ross-Munroe, 2002). (Figures 5 & 6) The LPC, similarly to the N300 did not differentiate between trials where the intention was realized or not and this indicates that it may not be indicative of the later realization of an intention.
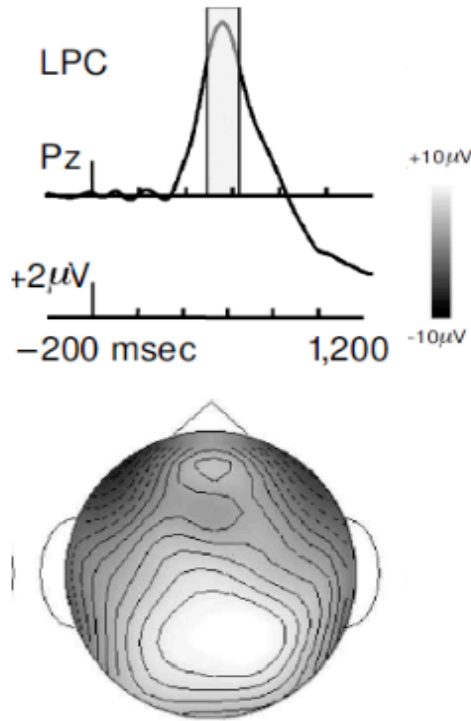
Figure 5. ERP difference waves and spline voltage maps reflecting LPC for intention formation trials. The waveform reflects the difference between the realized intention trials and ongoing activity trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002)

Figure 6. ERP difference waves and spline voltage maps reflecting LPC for PM cue trials. The waveform reflects the difference between PM hit trials and ongoing activity trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002)

Lastly, the slow wave (SW) is associated with stopping the ongoing activity to be alerted to a potential cue (West & Ross-Munroe, 2002; West, 2003). (Figure 7 & 8) The slow wave occurs 400 ms after stimulus onset and appears as a negativity over the frontal-central region of the scalp (West & Ross-Munroe, 2002). The ERPs from the SW demonstrated greater negativity for those elicited on realized intention trials than for those elicited on unrealized intention trials, indicating that it was predictive of the later success of PM.

Slow wave

Af3

+10μV

+2μV

−200 msec 1,2(

−10μV

Figure 7. ERP difference waves and spline voltage maps reflecting slow wave for intention formation trials. The waveform reflects the difference between the realized intention trials and unrealized intention trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002).
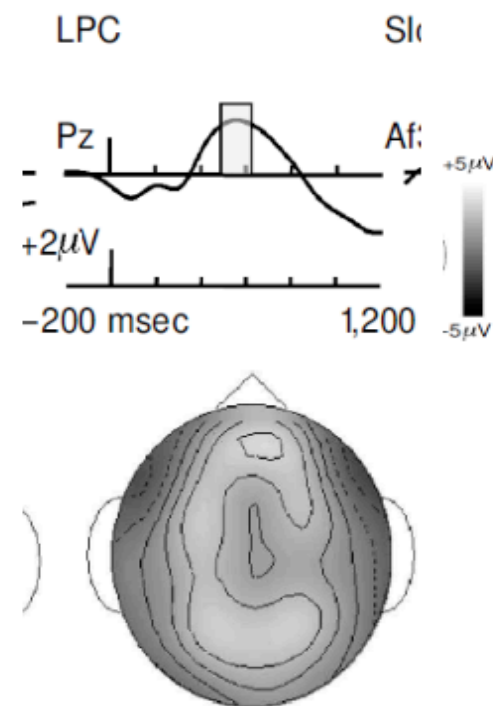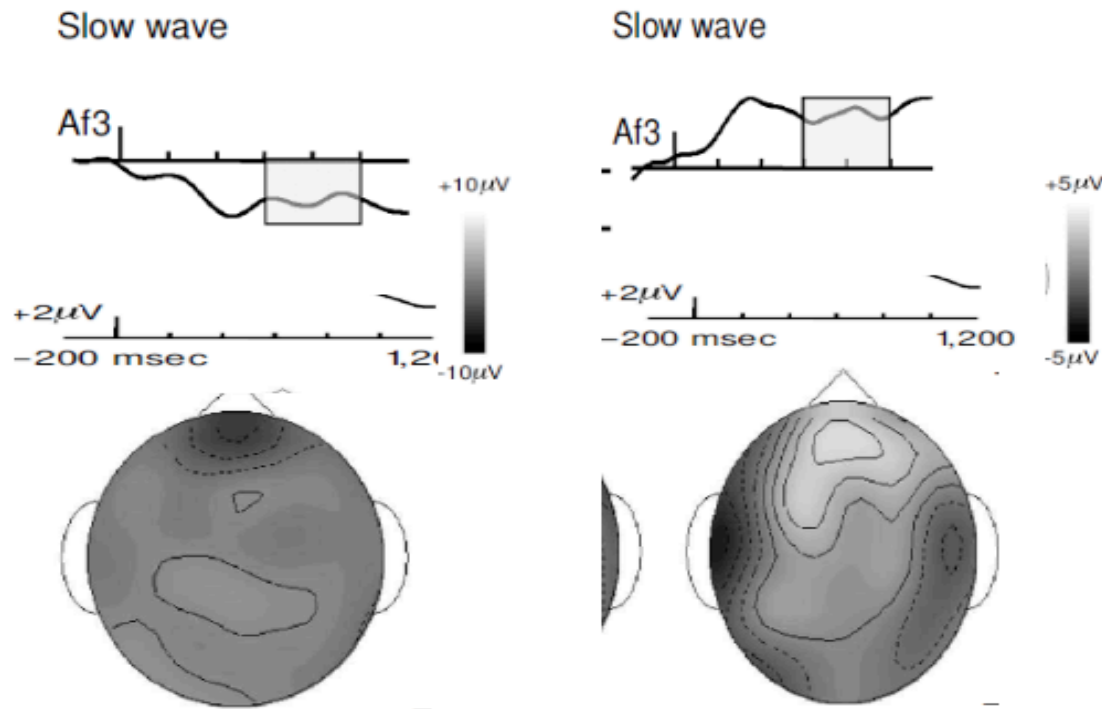
Slow wave

Af3

+5μV

+2μV

−200 msec 1,200

−5μV

Figure 8. ERP difference waves and spline voltage maps reflecting slow wave for PM cue trials. The waveform reflects the difference between PM hit trials and PM miss trials. The topography reflects the average of the bounded area for each modulation (West & Ross-Munroe, 2002).

Treatment of PM Deficits in Individuals with ABI

Cognitive Rehabilitation

Individuals with ABI struggle significantly more with PM tasks compared to healthy adults. In both time-based and event-based PM, healthy adults outperform those with sABI (Shum et al., 2010). Those with ABI, specifically severe traumatic brain injury, have also been shown to experience great difficulty allocating attention resources to a PM task and differentiating targets from non-targets during PM trials (Pavawalla, Schmitter- Edgecombe &

Smith, 2012). There has also been impairment on time, event, and activity based PM compared to controls (Vakil, 2005). Other studies have gathered results demonstrating a clear PM deficit in individuals with ABI.

In an effort to minimize these PM deficits, a common treatment method for those with ABI is cognitive rehabilitation (CR). Rehabilitation of any impaired cognitive process has become a standard component of care after ABI (Mazmanian, Kreutzer, Devany, & Martin, 1993; McCrea et al., 2008).

Cognitive rehabilitation (CR) has shown the potential to reduce disability and improve the quality of life in individuals with neurological disorders (Harley, et al., 1992). CR is defined as services that are directed to achieve functional changes by (1) reinforcing, strengthening, or reestablishing previously learned patterns of behavior, or (2) establishing new patterns of cognitive activity or compensatory mechanisms for impaired neurological systems (Harley et al., 1992). CR is done in four components. First, the problem has to be addressed and the individual is educated about their cognitive weaknesses and strengths. Then, skills are retrained or practiced so the problem can be improved. Once the fundamental skills are regained, environmental, internal, and external strategies are used so the problem can be studied in more depth. Lastly, the first three components are combined to imitate real life

Previous studies using imaging to measure changes following CR have demonstrated many improvements in cognition. One study showed an increased activation in vigilance and orienting networks following attention training in TBI through the EEG (Moore, McLaughlin, Pavese, Heidrich, and Posner, 2000). It has also been shown that CR, specifically attention process training (APT-III), causes increased activation in the frontal and tempoparietal regions in the brain of individuals with TBI as seen through an fMRI, another imaging technique (Kim,

Whyte, Patel, Avants, Europa, Wang, Slattery, Gee, Coslett, and Detre, 2010) Most of the studies using imaging have been conducted on the efficacy of CR in individuals with Parkinsons, multiple sclerosis, and schizophrenia (Costa, Carlesimo, & Caltagirone, 2012).

This study will aim to fill the gap in research as to how effective CR is in aiding individuals with PM after ABI. Through testing individuals electrophysiologically pre and post treatment, any areas of the brain changing through therapy may be identified. Clinically there may also be evidence that CR helps to improve cognitive function, specifically PM.

QUESTION AND HYPOTHESIS

Question

What are the specific electrophysiological correlates associated with prospective memory (PM)

that change throughout cognitive rehabilitation (CR) in ABI patients?

Hypothesis

1. There will be significant differences in the frontal lobe (Fp1, Fp2, and F4) and in the parietal

lobe (P3 and P4), post treatment in the active treatment group but no notable changes in the

attention control group.

2. There will also be significant changes in the LPC and parietal positivity in the active treatment

group but not in the attention control group

METHODS

This study was conducted at Trinity College in Hartford, CT after being approved by Trinity College's Institutional Review Board. The study aimed to realize the difference in clinical and physiological measures of PM over the course of time and treatment. The study used two different tests to compare the clinical and physiological differences in an individual's brain and lasted approximately two hours. The first test administered was the MIST to test clinical measures. The MIST was then followed by an electrophysiological paradigm mirroring the West & Munroe (2002) design. These two tests were then repeated approximately five weeks after the initial testing, or after the participant had completed their respective treatment. Results from pre- and post-treatment were then analyzed.

Participants

Nine participants were enrolled in this study. All participants were right handed and visually unimpaired. Five healthy participants from within the Trinity College community were recruited as the control group and four individuals with a severe acquired brain injury were enrolled as the experimental group. Within the experimental group there were two sub-categories. Half of the individuals were assigned to an active treatment group receiving actual CRT while the other half received a "brain education" active placebo treatment.

Not all participants that began the study completed the process. One individual did not return after pre testing.

Healthy Criteria

A healthy adult (HA) in this study was identified as an individual older than 18 whose native language is English, had more than 12 years of education, adequate visual and auditory functioning, and the absence of neurological or psychological illness.

Experimental Participant Criteria

Participants in the experimental group had to meet criteria for ABI. Eligibility was determined through an extensive phone-screening questionnaire. Additionally, individuals had to speak English as their native language, have no other neurological or psychiatric condition, 12 years or more of education, adequate visual and auditory functioning and be at least one year post-injury.

Exclusion Criteria

Subjects were excluded from the study if they have significant difficulty functioning independently, a diagnosis of HIV/AIDS, loss of oxygen to the brain (anoxia), a severe head injury, severe visual and hearing impairment that interferes with participation in daily activities, treatment for substance abuse or dependence, hospitalization for a psychiatric condition, or were younger than 18.

All participants provided written, informed consent prior to testing. Participants received

financial compensation of a $15 gift certificate to a campus bookstore or restaurant. Detailed

information about demographics are summarized in the below table.

	Healthy Adults	ABI Treatment	ABI Control
n	5	2	1
Age (years)	19.6 ± 1.075	39 ± 4.61	52
Years of Education	15.6 ± 1.074	13 ± 1.15	11
Etiology	-------	2 MVA	1 Fall

Cognitive Rehabilitation

Participants were randomly selected from the experimental group to receive cognitive

rehabilitation therapy (CRT). Participants were called and given a phone screening to determine

eligibility. After meeting eligibility criteria, participants were invited to take pre-treatment

assessments. These assessments included gathering background information, measures of

generalization including the Prospective Memory Questionanaire (Smith, Della Sala, Logie, &

Maylor, 2000), Everyday Memory Questionnaire (Royle & Lincoln, 2008), Dysexecutive

Questionnaire (Burgess, Alderman, Wilson, Evans, & Emslie, 1996), APT-II Questionnaire

(Sohlberg & Mateer, 2001), and Quality of Life Survey (Cohen, 1997). Neuropsychological

assessment included the Trail making Test (Reitan, 1979), Stroop Color-Word Test (Golden,

1978) Brief Test of Attention (Schretlen, 1989), Hopkins Verbal Learning Test (Brandt &

Benedict, 2001), and the Brief Visuospatial Memory Test (Benedict, 1997), and the MIST

(Raskin, 2004). Then, participants were randomly assigned to the active treatment group

receiving cognitive rehabilitation or an active control group that was receiving a brain education program. The brain education program consists of informational presentations, videos, and quizzes to help further an individual's understanding of the brain. Topics include the history of neuroscience, neuroanatomy, neurophysiology, neurochemistry, sensory systems, attention, memory and learning, executive functions, understanding ABI and ABI general resources. Cognitive rehabilitation is focused on Attention Process Training (APT-III) (Sohlberg & Mateer, 2009), Rote Repetition PM Training, and General Management Training.

After completion of 10 sessions, individuals are given a post assessment with all the same measures of generalization, Neuropsych, and the MIST.

Brain Education

Half of the ABI adults received lectures on the brain and general science as an active control condition. The same assessment tools were used pre and post testing and the process lasted for 10, hour-long sessions.

Clinical Measures of Prospective Memory

The clinical aspects of PM were measured with the MIST. In the MIST, participants are given a word-search that they spend 30 minutes completing. During this block of time, participants are instructed to complete a number of time and event-based prospective memory tasks. An example of a event based task is, "When I hand you an envelope, self-address it." An example of a time-

based prospective memory task is "In fifteen minutes, tell me it is time for a break." Depending on the participant's response, their performance is scored on a scale of zero to two. An example of the task is included as Figures 9 and 10.

If an individual doesn't respond to the cue, gives the incorrect response to an event-based cue, or gives and incorrect response at the wrong time, they are given a zero. A score of one is given for time trials only. If the participant remembered they were supposed to perform a task at the right time but gave the wrong response, or if the participant has the wrong time but a correct response they are given a one. The best score, a two, is given for any correct response to a time or event based cue with a grace period of one minute.

After the MIST eight multiple-choice questions are asked. These questions probe at the participant's recognition of the tasks they were just asked to complete. An example of a "recognition multiple-choice question is "At any point during this test were you asked to 1) Ask me when the session ends, 2) Ask me when the office closes, 3) Ask for your medical records?" The MIST Professional Manual (Raskin, Buckheit and Sherrod, 2010) suggests that high scores on the recognition questions means an individual encoded the intention, whereas a low score means they did not realize the intention. There is one final task that requires a response in 24 hours, which simulates prospective memory tasks in every day life.

	TASK TIME	PROSPECTIVE MEMORY TASKS	SCORE/RESPONSE	E.C.
A	Time at start A:_____	**"In 15 minutes, tell me to check my mail."**		
B	(A+:01):	**"When I hand you a red pen, write today's date on your paper."** [*Point to examinee's word search puzzle*]		
C	(A+:02):	**"In 2 minutes, tell me a time of day when I can call you tomorrow."**		
D	(A+:03):	**"When I hand you an envelope, self-address it."**		
CC	(C+:02):	Examinee should tell examiner when they can be called tomorrow.	**TRIAL 1** Correct ☐ 2 Incorrect ☐ Time: 0 1	

Figure 9: A sample page of the MIST which includes event-based and time-based cues, delay periods of varying times, and different verbal and physical response types.

TRANSPORTATION

U	E	E	Z	W	F	B	O	A	T	T	M	Y	X	M	I	N	I	V	A	N	M	D	R	L	E
E	S	C	A	L	A	T	O	R	S	B	L	O	R	X	P	Y	C	Z	F	S	E	M	M	W	Q
Q	C	Q	S	J	N	S	U	B	W	A	Y	K	Y	B	D	O	S	K	I	P	P	I	N	G	V
W	A	C	R	Z	Y	C	A	R	R	I	A	G	E	P	O	I	J	F	R	A	P	M	E	W	B
S	N	K	P	D	U	H	A	L	X	G	D	R	I	W	E	A	Y	B	A	C	T	X	D	J	L
A	O	W	P	O	R	X	D	M	O	T	O	R	C	Y	C	L	E	A	Q	E	P	T	S	C	I
P	E	M	I	V	J	A	Y	E	P	O	M	P	T	K	X	E	K	R	C	S	I	F	O	V	M
T	R	U	C	K	F	J	D	S	B	E	S	U	B	M	A	R	I	N	E	H	L	W	I	X	P
R	S	C	H	O	O	L	B	U	S	A	R	U	V	L	F	Z	T	M	C	I	T	N	R	V	K
E	A	E	N	V	O	R	K	L	P	R	S	A	R	E	F	E	R	R	Y	P	O	S	U	N	A
Z	F	N	T	R	A	I	N	E	W	C	W	E	T	H	W	V	O	N	E	Q	P	E	N	W	A
N	P	L	A	N	E	J	K	X	H	Q	O	A	Q	N	Z	U	L	A	R	M	O	T	N	E	M
Y	W	E	M	T	U	Q	E	B	N	E	S	Q	L	B	I	M	L	V	K	E	W	S	I	X	B
I	U	I	S	A	E	M	X	I	E	N	W	N	B	K	O	X	E	I	N	Z	P	I	N	S	U
W	N	E	N	X	R	S	I	M	N	E	B	E	X	W	I	A	Y	T	M	E	B	K	G	P	L
S	I	A	X	I	W	Q	H	A	L	J	E	W	E	W	Z	N	B	R	B	O	F	P	S	E	A
Q	C	W	N	R	L	E	X	E	Y	C	B	Z	H	A	O	M	G	N	I	I	U	W	I	Z	N
E	Y	O	C	S	Q	Z	B	U	L	I	L	M	T	E	B	E	Y	Z	U	O	K	S	U	T	C
T	C	N	O	R	B	M	T	J	N	I	F	I	K	H	E	W	P	Q	X	L	K	E	I	U	E
Z	L	E	W	T	Y	P	R	O	T	B	C	N	M	O	R	L	W	J	Z	L	U	H	R	N	Z
C	E	D	S	Z	E	H	A	Y	R	I	T	O	M	B	N	Q	C	Z	V	P	O	E	K	D	E
A	P	W	S	I	R	R	C	A	M	U	O	E	P	D	I	E	N	H	R	Y	W	P	A	S	D
R	I	X	H	E	M	R	T	W	X	P	M	K	E	T	U	N	S	K	A	T	E	S	J	S	L
F	L	Y	I	N	G	H	O	R	S	E	X	O	C	K	E	F	G	A	H	I	Q	N	X	I	H
S	Q	W	P	J	W	M	R	K	P	C	L	K	H	W	O	R	K	L	F	V	R	I	X	A	Q
R	P	R	T	L	X	B	O	N	I	V	H	C	R	A	W	L	I	N	G	I	W	A	G	O	N
Z	N	R	O	W	I	N	G	W	X	Z	B	U	L	L	D	O	Z	E	R	W	B	P	O	T	R

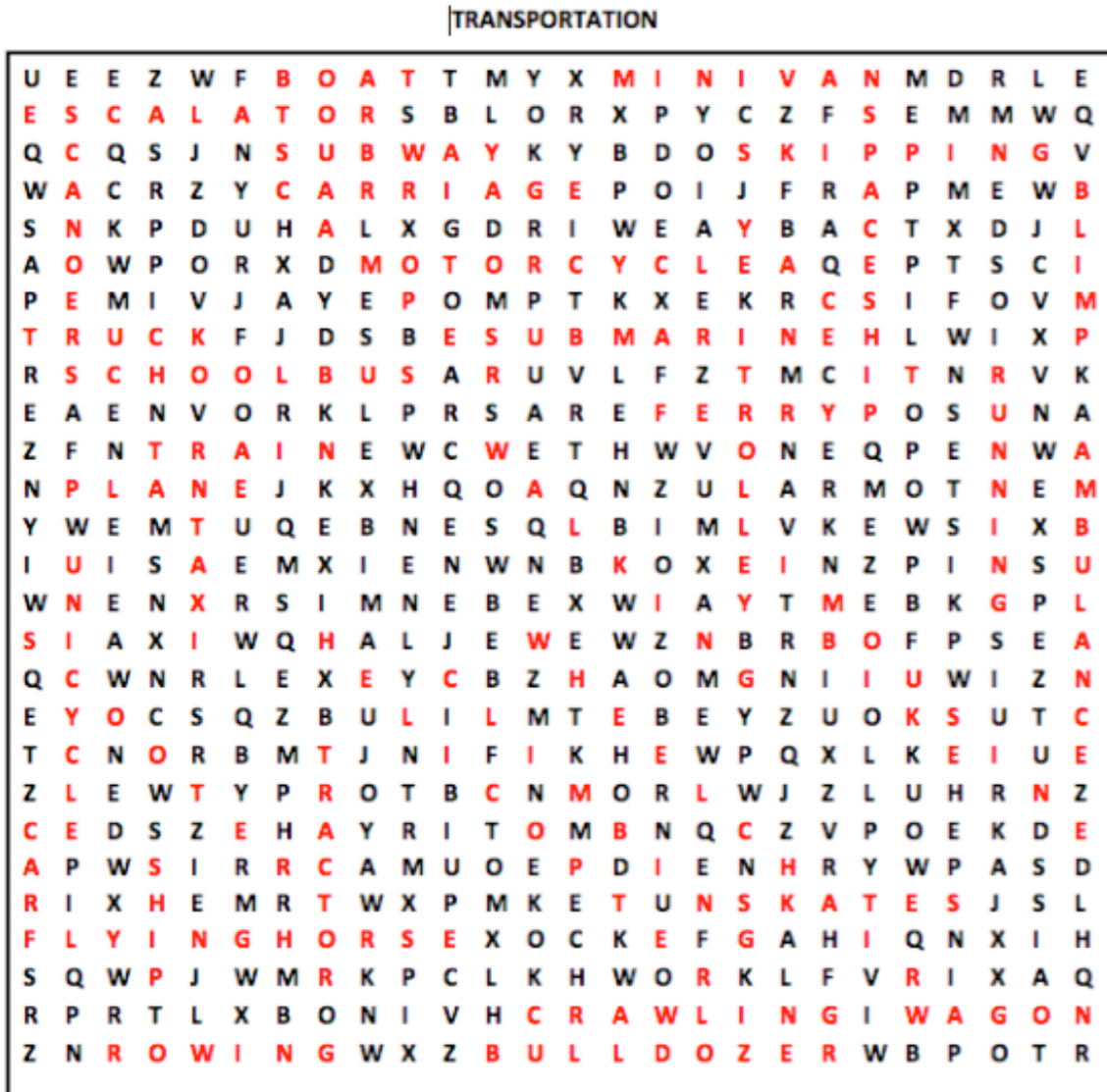|				
BIKE	CANOE	RUNNING	TROLLEY	YACHT
BOAT	CAMPER	SKATES	ESCALATOR	SHIP
SCHOOLBUS	CRAWLING	SPACESHIP	WAGON	MOTORCYCLE
BULLDOZER	FLYING	SUBWAY	WALKING	HELICOPTER
CAR	HORSE	TAXI	WHEELCHAIR	TRUCK
CARRIAGE	PLANE	SUBMARINE	UNICYCLE	AMBULANCE
CLIMBING	MINIVAN	TRAIN	TRACTOR	BLIMP
LIMOUSINE	SKIPPING	ROWING	FERRY	SCOOTER

Figure 10: The MIST Ongoing Task. A sample of the word search puzzle used as the ongoing activity during the MIST.

Electrophysiological Measure of Prospective Memory

The physiological measures of PM were recorded using an encephalogram (EEG). In this study a Compumedics Neuroscan Quick-cap with 64 electrodes sewn-into the cap and six external electrodes was used. Each electrode was gelled to the scalp with a blunt syringe (BD 16G 3⁄4 Blunt Square Grind *Precision Glide* Needle attached to BD 10ml Syringe *Luer-Lok* Tip, Latex free) and Compumedics Neuromedical Supply Supplies *Quik Gel*. The computer test that each participant took was modeled after West and Ross-Muroe (2002) on E-prime. Throughout the test, stimuli were displayed on the computer screen and participants were instructed to respond by pressing one of four marked keys. Three of the external electrodes were positioned around the left eye while one was placed to the side of the right eye to measure vertical and horizontal eye movement. The other two external electrodes were gelled to the participant's mastoid bones. These data points were used as a reference when it was time for data to be analyzed.

To begin each testing session, twenty-five milliliters of the conductive gel along with five milliliters of water were mixed in a microwave safe container and heated for 30 seconds. A blunt syringe was then filled to facilitate the gelling process. Before the cap was placed on the participant's head, a makeup-removing wipe was used to clean the skin around the participant's forehead and eyes to create the most effective surface. Additionally, participants were asked to abrade their head by taking a hairbrush to gently scratch their head and tussle their hair.

There were a few measurements taken before placing the cap on the participant's head. The subject's head is measured from the nose to the back of the participant's head to establish the correct position of the cap. The circumference of the subject's head is also measured. Then,

10% of the circumference is calculated and that distance is measured from the back of the head to the front of the head. The cap is then placed to fit these measurements. Once on the participant's head, the cap fit such that the forward most electrodes just reached the forehead and the strap snuggly framed the participant's chin. The external electrodes can then be placed in accordance to their individual code. Each is securely fastened with a Compumedics v-shaped electrode washer. One electrode was placed on the side of the left eye (HEOL), another on the side of the right eye (HEOR), one above the left eye (VEOU), and one below the left eye (VEOL). The other two external electrodes, M1 and M2 were placed on the respective left and right mastoid bones.

After attaching the external electrodes, the cap was plugged into the Neuroscan head box through a SynAmpRT amplifier. To see the connection between the cap and the scalp, the "acquire impedance" screen through Scan 4.5 was used. When the cap is connected and there is no gel, each electrode appears as a magenta box and signifies an impedance of approximately 50.0 (kOhms).

To lower the impedence, gel was inserted into each electrode. Each electrode was gelled to the scalp with a blunt syringe (BD 16G 3⁄4 Blunt Square Grind *Precision Glide* Needle attached to BD 10ml Syringe *Luer-Lok* Tip, Latex free) and Compumedics Neuromedical Supply Supplies *Quik Gel*. Using the blunt syringe, gel was carefully placed in the electrodes such that it did not leak out from underneath. Great caution was taken to prevent gel from spreading between the electrodes and creating a salt bridge that compromises the readings. As the gel was inserted, the impedance reading starts to drop below 50 kOhma and the diagram on Scan 4.5 changes color. The darker the color, black being the darkest, the better as it represents an impedance of 5kOhms. Once all the electrodes appeared as a darker color it was time to start the computer test.

The computerized experiment lasts approximately 45 minutes. The experimental design followed that created by West and Ross-Munroe (2002). Each test consisted of ten trials, each trial containing 102 word pairs, with some as intention formation, ongoing activity, and PM cues.

The first information to appear on the computer screen is a standard set of instructions. These instruct the participant to use their right index finger to press the key labeled "same" (the "n" key with a label) whenever the word pair flashed on the screen is related. When the word pair is not related, they were instructed to press the key labeled "different" (the "m" key with a label) using their right middle finger. Each pair was flashed in different colors including green, blue, red, and purple but semantically could be differentiated as related or non-related. Each pair of words was also presented horizontally, in the center of the screen, with one positioned on top of the other. For example, when the word pair of *opal* in blue and *topaz* in purple appears, the participant should press the *same* key since they are both in the same category, or are semantically related. Conversely, when the word pair of *physics* in red, and *rose* in green is presented, the participant should press the different key since they are semantically unrelated.

The intention-formation trials used a string of letters (either c-c-c-c-c-c-c or v-v-v-v-v-v-v). Rather than being shown in different colors, as the ongoing activity and PM cues were, the string of letters appears in either gray or magenta. When this happens, the participant is instructed to remember the letter that appeared in either color and press that key when a pair of words appears in that color. For example, if c-c-c-c-c-c appears in gray, the participant should press "c" to recognize they saw a string of c in gray. Then, the test will continue on with pairs of words in different colors being sorted as related or unrelated. When a pair of words appears in

gray though, rather than determining if they are related, the participant is asked to press the letter "c".

A practice trial began to familiarize the participant with the experiment and eliminate any error from not understanding the instructions. The trial is very similar to the actual experiment and contains each type of trial.

RESULTS

Clinical Measure of PM

Data for the pre and post testing for all three groups (HA, ABI with active CRT, ABI with active control) on the MIST is presented in Figures 1 and 2. The means and standard errors of the three groups were calculated. Student's t-test (t(8)=1.21; p< .05) indicated that the ABI treatment group performed significantly better on MIST action scores after treatment as compared to before treatment. There were no other significant differences between any of the three group's pre and post scores on the MIST. These data are shown in Figures 11 and 12.
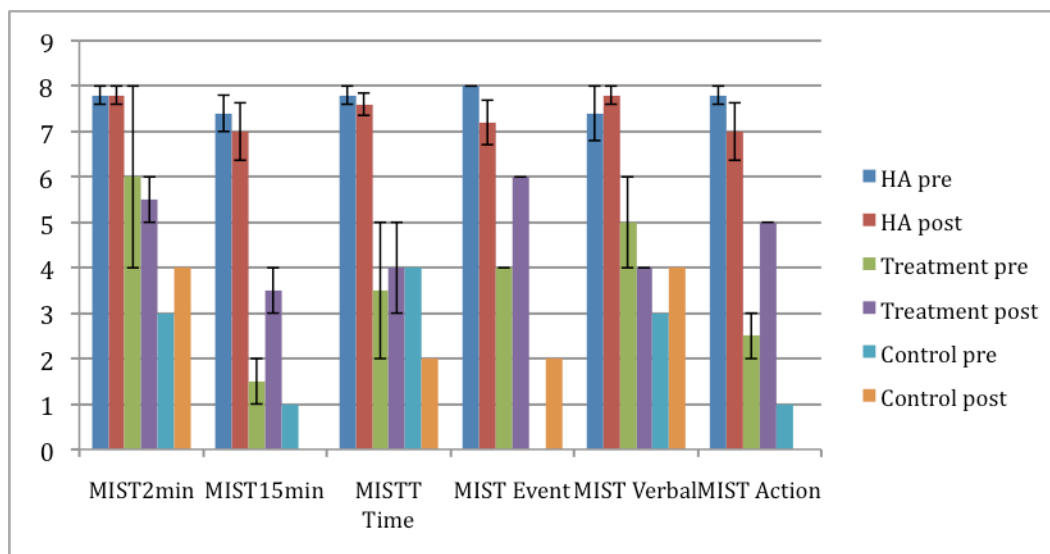
Figure 11: Mean scores in performance on MIST variables in HA, individuals with ABI receiving CRT, and control ABI receiving brain education.
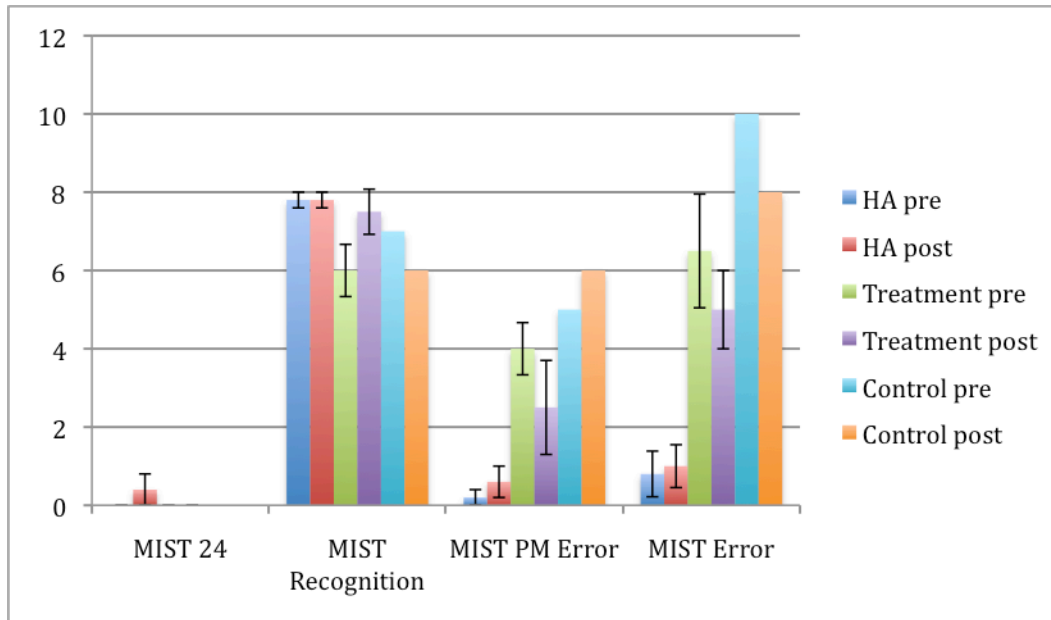
Figure 12: Mean Scores in Performance on MIST 24 hour, recognition and errors for HA, individuals with ABI receiving CRT, and control ABI receiving brain education.

Computerized PM Task

Behavioral Measures

The data for the computerized behavioral measures are presented in Figures 13 and 14. Student's

t-test revealed no significant differences between the groups.
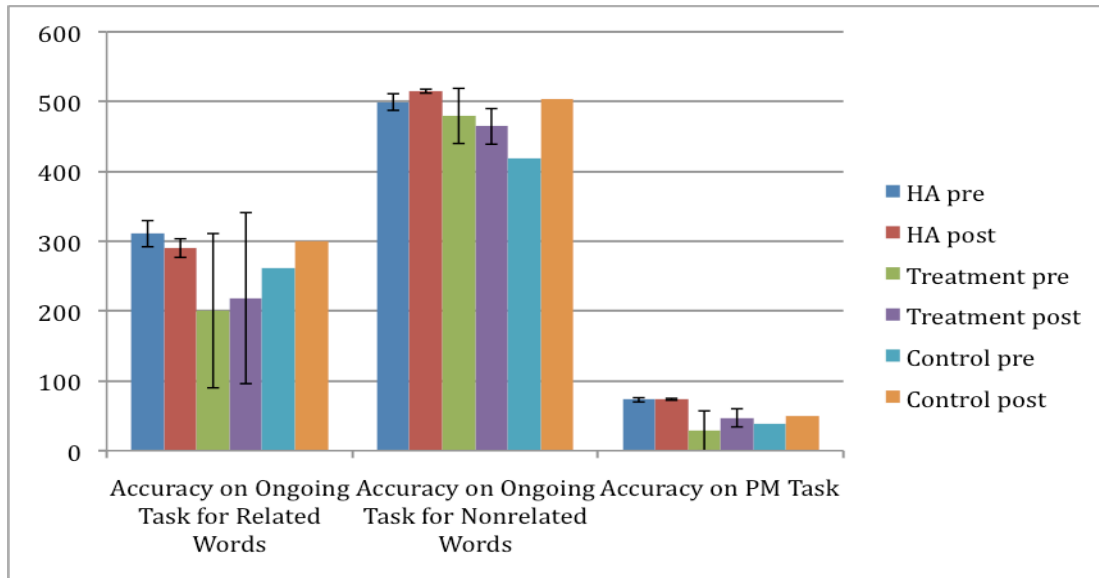
Figure 13: Mean Scores on the Computerized Behavioral Data in HA, individuals with ABI receiving CRT, and control ABI receiving brain education.

Student's t-test (t(8)=2.41; p< .05) demonstrated that HA participants differed from the other groups only in terms of reaction time on the RT PM Miss trials, with HA participants showing a significantly shorter reaction time when compared to both groups of ABI.
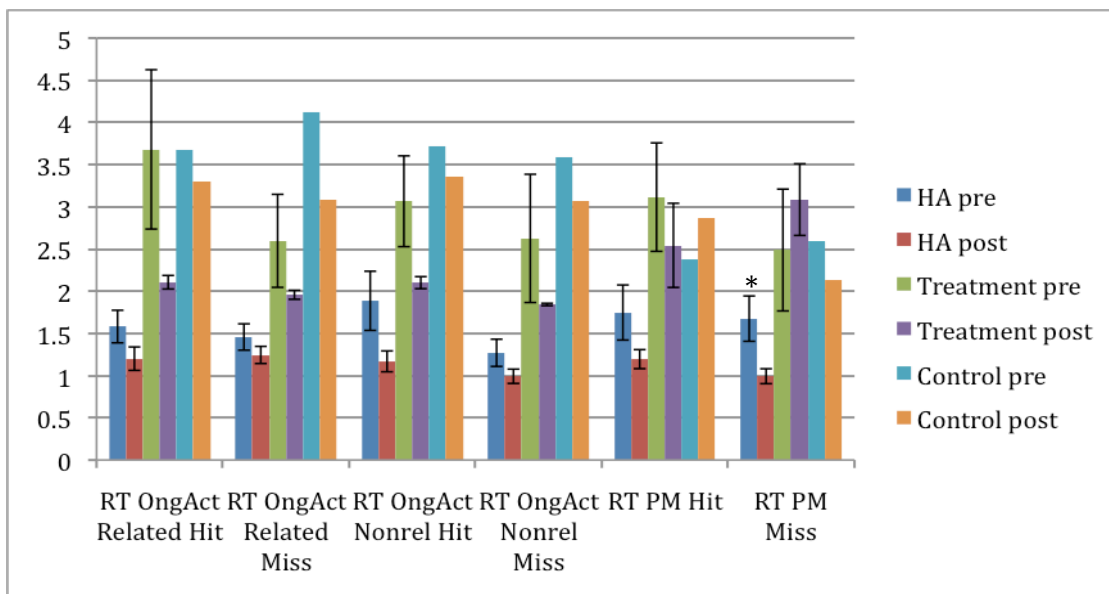
Figure 14: Mean Score in the Reaction Time for Hit and Miss Responses Obtained from the Computerized Data in HA, individuals with ABI receiving CRT, and control ABI receiving brain education.

Electrophysiological Measures

Mean amplitudes and standard error for the N300 ERP at specific electrodes are presented in Figure 15. Both of the groups with ABI showed unexpected ERP amplitudes at the N300 in comparison to healthy adults. A t-test was conducted to compare means and no significance between the pre and post trials for any group was demonstrated.
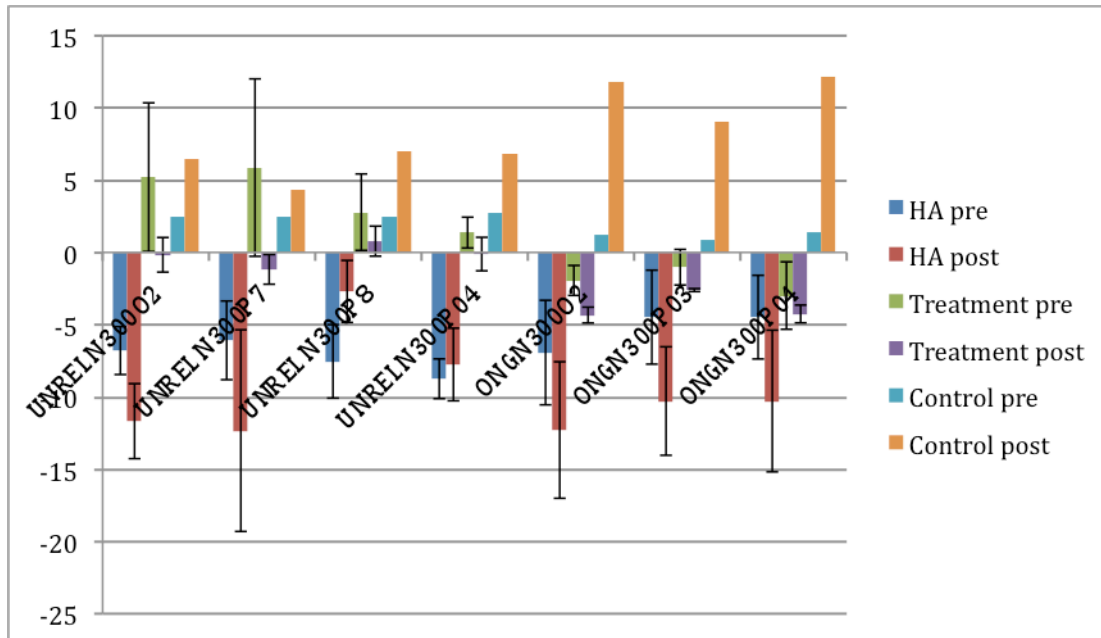
Figure 15: Amplitude (mV) at the N300 Time Span (275-325 ms after stimulus onset) for ERPs at electrodes O2, P7, P8, PO4, 02, PO3, PO4.

Mean amplitudes and standard error for the electrodes in the parietal lobe are presented in Figure 16. A t-test was conducted to compare means and no significance between the pre and post trials across a group was determined.
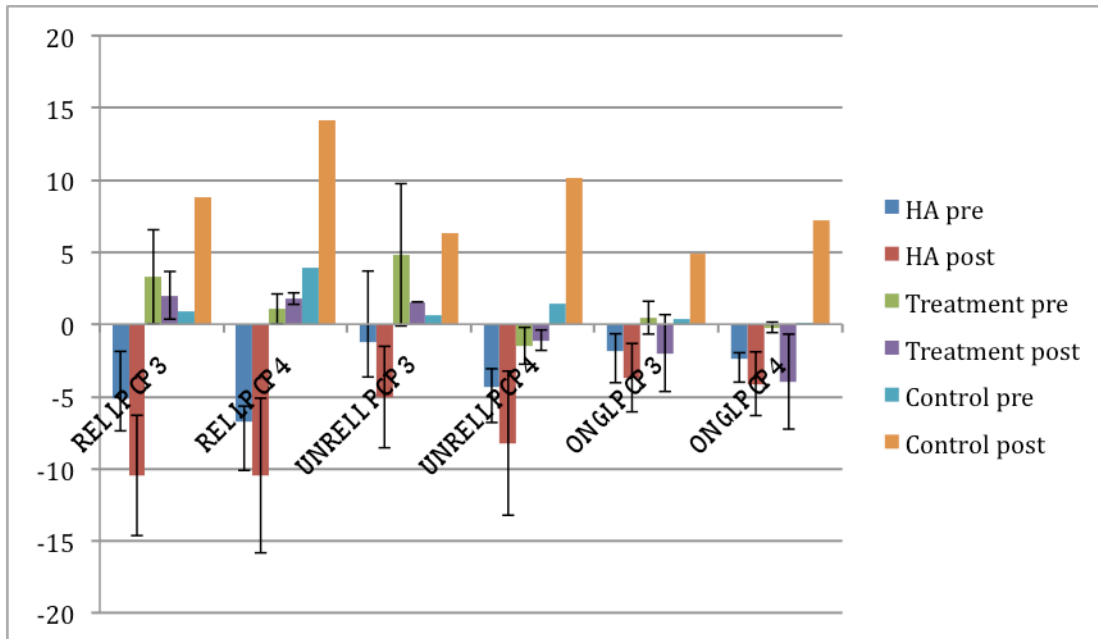
Figure 16: Amplitude (mV) for ERP at electrodes in the Parietal lobe P3 and P4.

Mean amplitudes and standard error for the electrodes in the frontal lobe are presented in Figure

17. A t-test was conducted to compare means and no significance between the pre and post trials

across any group were demonstrated.
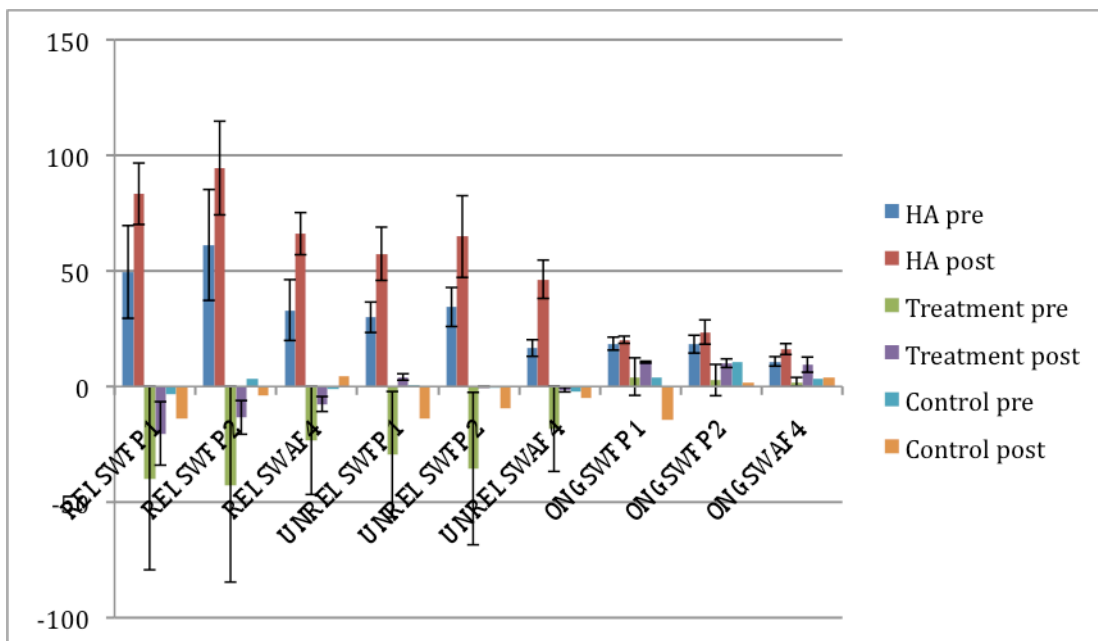
Figure 17: Amplitude (mV) for ERP at electrodes in the Frontal lobe FP1, FP2, AF4

Mean amplitudes for the ERP across the brain is presented in Figure 18. A t-test was conducted

to compare means and no significance between the pre and post trials across a group was

determined.
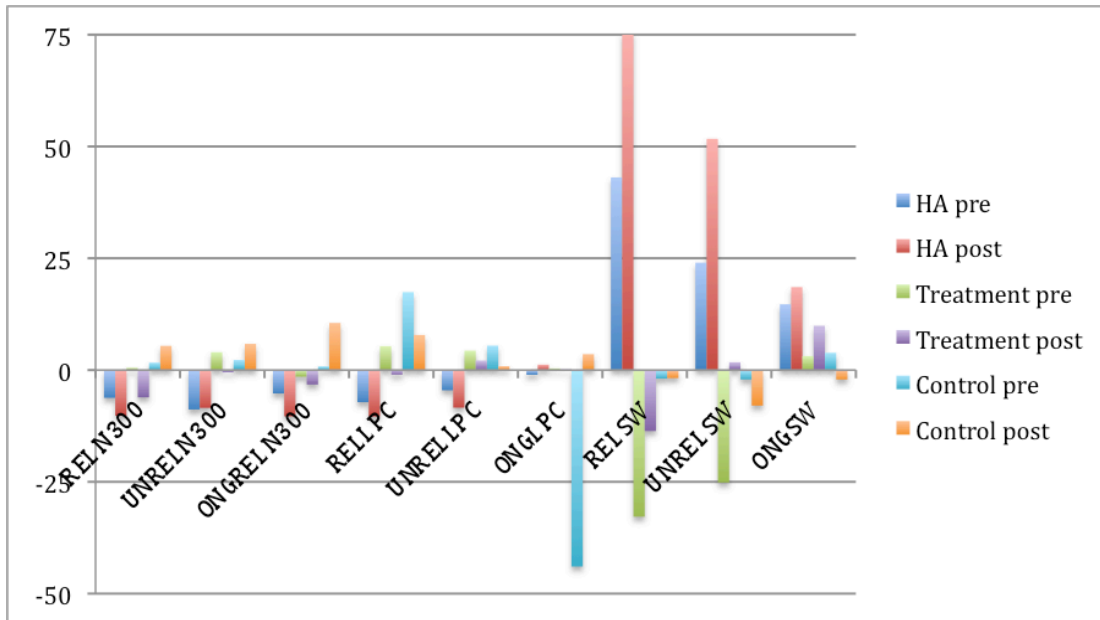
Figure 18: Average Amplitudes (mV) for ERPs at electrodes positioned across the brain

DISCUSSION

In the initial MIST given before treatment, individuals with ABI, in both the treatment and control group displayed impaired PM compared to HA on all measures of the MIST. At post testing, HA performed at a similar level to their pretest scores, which demonstrates that taking the test for a second time does not mean an individual will naturally perform better or be familiar with the questions being asked. In the MIST given after treatment, both groups of individuals with ABI still performed at a lower level than the HA participants. The ABI treatment group did show improvement on many measures of the MIST, but the only measure that improved significantly at post treatment was the ABI treatment group on MIST action trials.

There are some trends in the data that might be worth noting as the low power in the sample could explain the lack of significant findings. Individuals in the treatment group performed better on all measures of the MIST after treatment except for the MIST 2 minute trials and verbal cues. Of real interest is the reduction in number of PM errors and general errors after treatment.

The individual in the ABI control group performed at a lower level on almost all measures of the MIST at post testing. Categories of particular interest include the MIST 15 minute delay periods and MIST actions, in which the individual did not score any points during post testing. This suggests the possibility of specificity for the treatment.

Computerized differences among groups

In accuracy of performance, there were no significant differences between the pre and post data for HA or either of the ABI groups. Each of the groups improved on the accuracy of the PM task but not significantly from their pre performances.

Interestingly, the individual in the ABI control group improved on all measures of accuracy. While this is only the data from one individual, it is possible that simply engaging your brain could lead to improvements in accurately completing this task.

Reaction Times

Individuals with ABI had pronounced deficits in reaction time compared to HA which agree with the findings of Carroll et al. (2004), Pavawalla et al. (2012) and Vakil et al. (2005). All groups decreased their reaction time in post testing. While these individuals reacted more quickly, this does not indicate that they improved on the task. In completing this long test for a second time, it is possible that participants became frustrated and preferred to react more quickly knowing that the test would then be over sooner. While this trend is observed for all groups, it is of particular interest in the ABI treatment group. Reaction time dropped considerably for the ABI individuals on all tasks except for the PM trials that they answered incorrectly. One possible explanation for this could be that the participants realized they needed to respond in a way other than "same category or different category" and spent more time trying to determine what the correct response would be.

Variation in N300 Amplitude on Computerized Tests

ERP results revealed varied amplitudes across all trials. Healthy adults demonstrated the expected negative waveform across all trials, specifically over the leads O2 and P7 (*Kim et al., 2009*). For HA, more negative amplitudes were also found during ongoing trials compared to unrealized trials over the same lead.

The N300 represents a phasic negativity that peaks over the occipital-parietal region of the scalp around 300 milliseconds after stimulus onset (West & Ross-Munroe, 2002). When participants have a PM hit, the amplitude for the N300 ERP will be greater in amplitude than if the participant made a response that was a prospective miss or an ongoing activity response (West, 2005). As all three groups improved on the accuracy of the PM task, the N300 ERP should be greater in all three groups. The amplitude of ABI receiving brain education does increase but is not the expected negative amplitude. For HA and ABI receiving CRT, the amplitude is larger during post testing for most measures, demonstrating that this area of the brain may have been impacted during the time between pre and post testing.

ABI in both the active treatment and control group did not demonstrate the expected negative waveform. Previous studies West and Covell (2001), Herndon et al. (2003), and Zollig et al. (2012) found attenuated amplitude of the N300 in individuals with ABI that was not present in HA. It is hypothesized that the most prominent negative waveform for these participants is likely delayed because of the individual's impairments. Additional tests are being conducted to determine if this waveform appears as late as 500 ms after stimulus onset. The ABI treatment group's ERP does decrease after treatment, appearing more normalized. These

differences are not significant but it is possible that with more participants, this trend would develop into significance.

Variation in Amplitude of Electrodes in Parietal Lobe on Computerized Tests

ERP results in the parietal lobe vary across the different electrodes. In this study, HA demonstrated a negative amplitude of LPC within the parietal region and the ABI treatment group experienced a more negative waveform during post testing. In West (2011) the LPC is defined as a negativity over the frontal regions of the scalp and a positive waveform over the parietal region of the brain. It is possible that the window of time when the LPC was measured in this study is too delayed for a healthy brain. The peak in the wave may come earlier and therefore the time of the analysis may capture the negative waveform that comes after the peak. Additionally, there could have been salt bridging, when the gel inserted into the electrodes spreads to collect a single signal for multiple electrodes, between the electrodes of the frontal and parietal regions which resulted in an inaccurate reading. To further understand the role of a significantly more negative LPC, more research needs to be conducted on HA with high scores of PM.

The parietal lobe is very important for processing sensory information and therefore would hopefully improve through therapy. Brain changes in the parietal region would have been expected to show increased activation, specifically in the inferior parietal lobe in patients after CRT (Wei, Wang, Yan, Li, Pan, Gui, Su, Liu, & Tang, 2016). While the EEG is not sensitive enough to pick up these differences, they would have been seen as larger amplitudes from the electrodes placed near the parietal lobe. Changes in this region may imply that the individual is using this brain region more efficiently.

Variation in Amplitude of Electrodes in Frontal Lobe on Computerized Tests

In the frontal lobe, various ERP relating to the slow wave were measured. As defined by West (2011), the FSW is associated with disengagement from ongoing activity and alerting to a possible cue. In this study, HA demonstrated positive amplitude within the frontal region and the ABI groups had a more negative waveform. Not only did HA show more positive waveforms, but also waveforms with a larger amplitude. This higher amplitude correlates to an individuals' increased ability to disengage from the ongoing activity, especially relative to those with ABI.

Across all groups, the FSW for the ongoing trials had smaller amplitudes than the realized trials. As shown in previous studies (West, 2011), this may reflect the participant's focus on the ongoing task as the FSW is linked to disengaging from this distraction for the ongoing activity. The more positive amplitudes for the individuals in post testing indicate that the frontal lobe may be more active after treatment.

As the frontal lobe is so pertinent to executive functioning, it would be important to improve the brain activity through treatment. The frontal lobe is the front part of the brain involved with planning, organizing, problem solving, and personality. Through CRT it is expected that the frontal lobe, specifically the left medial frontal gyrus, left inferior frontal gyrus, right middle frontal gyrus, and the right postcentral gyrus (Wei, 2016). While these changes were not seen, if the EEG was a bit more sensitive, changes in these regions of the scalp may have been visible as larger amplitudes in the electrodes in the frontal region. Changes in this brain region may also imply that individuals are better able to use the functions of their frontal lobe after treatment.

Variation in Average Amplitude of Electrodes across the brain on Computerized Tests

The averages of the electrode amplitudes in the N300, LPC, and FSW were compared across the three groups. There were no significant differences between pre and post testing for any of the groups.

Across the ongoing and PM task for the N300, LPC, and FSW, the waveforms of the ABI treatment group becomes more normalized while the ABI in the control group appear more abnormal. HA differed the most from the ABI in the treatment group in regards to the FSW. It appears that individuals with ABI were not using the frontal region of their brain before treatment, as evidenced by the negative waveform. After treatment, the means appeared much more similar to the HA as many waveforms were positive. If the positive waveform shown for HA is the norm, individuals who receive CRT are better able to disengage from the ongoing task and appear more normal in the FSW.

Age Influence on MIST, Behavioral and Electrophysiological correlates of PM

While most of the analyses were run to determine the difference between a group's pre and post scores, HA are used as a baseline for almost all of the measures. The difference in age of HA and individuals with ABI is significantly different which may lead to issues in comparing the three groups. Cona et al. (2012) showed that younger individuals demonstrated more prefrontal sustained PM ERPs than older adults. This same study, Cona et al. (2012), also found that without these PM ERPs, older adults are impaired on strategic monitoring systems during the ongoing task. This difference in age and therefore PM function may make the comparison of HA to ABI more of a confounding variable than desired. It is logical that the healthy, younger

individuals performed better than the ABI on all tasks because their initial PM functioning may have been much better even without a brain injury.

Time of Treatment Influence on MIST, Behavioral and Electrophysiological correlates of PM

HA were tested with a five week break period for a uniform testing period but not all of the participants were on the same schedule and time frame to completing the treatment or brain education. This could have affected the observed changes. Some participants took up to six weeks to complete the 10-hour CRT or brain education while other completed the training in three weeks. Initial plans for the study had aimed to include 20 hours of CRT over a 10-week period, which may result in more significant findings. In the future, the time between pre and post testing could be extended and made uniform for more accurate results.

CONCLUSION

The results of our study do not successfully support the hypotheses. While very little of the data demonstrated significant differences in pre and post testing, the results of the experiment showed that individuals with ABI receiving CRT are improving clinically and physiologically in their PM performance. The data was not significant but this shows promising signs for individuals with ABI receiving CRT. If a 10-hour treatment regimen can result in an increase in PM performance, it is possible that spending more time completing CRT could lead to significant results. More significant results could also be seen with more participants. Brain injury is difficult to study because individuals are affected in different ways depending on where their injury occurred and at what age the injury occurred. With more participants, some of the trends that were observed could have been confirmed.

An interesting finding in this study was the positive amplitude observed in the HA participants for the LPC and SW over the frontal and parietal regions of the brain. Further analysis is needed to examine these waveforms as the treatment group moves towards this normalized but unexpected positive amplitude.

Additional studies could be conducted in which the different groups are all around a similar age. According to previous studies older adults are more cognitively impaired on PM tasks and therefore the difference in age may have affected the results. The time between pre and post testing could also be standardized to standardize the gap in time between pre and post testing. Further research using these two improvements to the study could shed further light on the efficacy of CRT after a ABI.

IMPLICATIONS

The findings of this study have potential merit in determining the effectiveness of a widely used treatment technique for individuals with ABI. While no significance was determined with these results, it is possible that with a larger sample size, larger trends would be identified. If CRT is not as effective, it is possible that the treatment techniques should be altered to more efficiently target the areas of the brain that are impaired.

ACKNOWLEDGEMENTS

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