

Albert Einstein Healthcare Network

Annual Progress Report: 2009 Formula Grant

Reporting Period

July 1, 2010 – June 30, 2011

Formula Grant Overview

The Albert Einstein Healthcare Network received \$119,376 in formula funds for the grant award period January 1, 2010 through December 31, 2012. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

A Feasibility Study of Fruit and Vegetable Consumption in Low Income Communities - The purpose of this project is to collect preliminary data from supermarket shoppers in a low income community about their purchasing of fruits and vegetables and to assess the feasibility of our methods. The results will provide us with preliminary data that will be used in designing a larger intervention study on the use of incentives to promote healthier eating, particularly in low income populations.

Anticipated Duration of Project

1/1/2010 - 12/31/2012

Project Overview

The broad research objective is to identify effective methods and approaches to improve healthier eating, particularly for low income populations. The specific research aims are: 1) To collect pilot data on purchase and consumption of fruits and vegetables in a low-income community and assess the feasibility of our research methods; 2) To describe healthy foods purchasing patterns, examining which individual and household characteristics are independent predictors of greater purchases of fruits and vegetables; and 3) To assess whether incentives in the form of discount coupons for fruits and vegetables can be studied as a potential intervention to encourage family members to buy more healthy foods.

The project will help us to determine the feasibility of using electronic supermarket data to obtain information about grocery purchasing behaviors. This is a 12 month trial examining food purchases in a cohort of adult shoppers who have at least one child living in the home. We will enroll 15-25 individuals who conduct the majority of their grocery shopping at the Fresh Grocer and examine their food purchase patterns over three time periods. We will also examine the use and impact of an incentive in the form of discount coupons for fruit and vegetable purchases. We

will analyze self-report data as well as purchase data obtained from the Point of Sale system maintained by the Fresh Grocer, which records all purchases made with frequent shopper cards.

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Expected Research Outcomes and Benefits

Identifying effective strategies for improving healthier eating for low income populations is both a clinical challenge and a public health priority. Approximately, only 38% of Americans consume the recommended servings of vegetables and only 23% consume the suggested amount of fruit. In low income households, close to 20% of households do not purchase fruits and vegetables at all. The consumption of fruits and vegetables is strongly associated with the prevention and management of chronic diseases such as diabetes, cardiovascular disease, and obesity. Low-income populations are disproportionately affected by these health conditions.

The overall objective of this project is to build the foundation for a more formally organized randomized controlled trial to determine the effectiveness of incentives to improve healthy eating, targeting increased consumption of fruits and vegetables, particularly for low income populations.

Summary of Research Completed

We successfully recruited and enrolled our study cohort and have completed all data collection.

In terms of recruitment: Since the last report, we recruited, consented, and enrolled all participants. They have been interviewed at the beginning of the study and their purchases have been tracked as detailed in the research plan. We were able to conduct follow up interviews with most but not all participants.

Data Collection and Management: The collection of electronic supermarket data as the primary source of data for this investigation has been a formidable task. We have developed a very strong relationship with the study supermarket and, because of this, have been able to obtain data and transfer it into a workable format for analysis. Transaction data were extracted from the study store's point-of-sale (POS) system over the course of the study period.

The presence of transaction data was used to confirm the eligibility of the participant as being a shopper and customer loyalty card user at the store. These data from the first export also provided baselines for the food shopping practices that will be discussed later in this update. The store's data manager extracted the transactions of enrolled participants from the POS system and sent the individual data files via email to the research data manager.

We developed and implemented a multistep process to create a longitudinal record of a participant's food shopping practices. The data extracted from the store's POS system were text files that closely resembled a typical grocery store receipt. The individual text files were converted into a study dataset through a sequence of four main data steps: (1) imported the POS files into one row-wise database, (2) standardized the fields into uniform variables, (3) linked the POS data to a nutrition reference file, and (4) generated study specific variables for the primary study outcomes (i.e., number of servings, dollars spent on fresh fruit and percent of total food dollars spent on fresh produce). The participants' customer loyalty card numbers were used as unique identifiers to relate multiple transaction files to individual participant households. The final study database contained all food and grocery items purchased at the store during the study period. These data were merged with self-report data obtained from the baseline and follow-up surveys of participants.

Because of the extensive amount of data collected through the above procedures, we have approached the data analysis in phases. We decided to analyze data collected during the baseline period and to write our first manuscript on the study. That paper, entitled, "Fresh fruit and vegetable purchases in an urban supermarket by low income households," was completed and was recently submitted to a peer-review journal. An abstract of our study, focusing on the participant experience or social validity of the study, was accepted for poster presentation at the 2011 American Public Health Association National Meeting to be held in Washington, DC. We are currently analyzing data for the full study and preparing the second manuscript.

Research Project 2: Project Title and Purpose

The Role of Left Inferior Frontal Cortex in Sequencing and Language - The project purpose is to explore an important component of language - the sequencing of words in a sentence - that is commonly impaired in non-fluent aphasia. Non-fluent aphasia is a stroke-related disability that features poor grammatical structure, effortful speech and impaired comprehension under some conditions. It is a complex syndrome that may consist of dissociable components. Understanding the cognitive and neuroanatomical bases of these components is critical for the accurate categorization of aphasic impairments and their subsequent treatment. A preliminary study suggested a key role for the left inferior frontal cortex (LIFC) of the brain in sequencing. This project aims to reproduce those results, clarify the relationship between the sequencing of words and sentence production, and test whether the sequencing deficit is specific to language.

Anticipated Duration of Project

1/1/2010 – 12/31/2012

Project Overview

Objective #1: To clarify the role of left inferior frontal cortex (LIFC) in sequencing for language.

Objective #2: To clarify the relationship between such sequencing impairments and deficits in other linguistic and non-linguistic functions.

Specific aim #1: To determine whether damage to a specific sub-region of LIFC (posterior portion, Brodmann area 44/6/9) is predictive of impairment in flexibly sequencing words. We will compare patients with damage to this region of LIFC with patients who have damage to other areas of the brain. This will provide more accurate information about the anatomical basis of such impairments.

Specific aim #2: To correlate impairment in sequencing words with difficulty in producing complete, grammatical sentences during other tasks. We will compare patients' performance in multiword naming with their performance in describing events and scenes and telling stories. This will clarify current theories of the relationship between different components involved in sentence production.

Specific aim #3: To correlate impairment in sequencing words with impairment in sequencing non-linguistic items such as tones and visual stimuli. This will allow us to determine the extent to which patients' impairments are language-specific.

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Expected Research Outcomes and Benefits

Persons with mild or moderate non-fluent aphasia are able to function independently in many everyday situations, but they either avoid interactions that require prolonged or subtle spoken language communication or are dependent on others to “translate” for them in such situations. This can have a negative impact on psychosocial wellbeing and quality of life. This project seeks to understand whether an impairment in flexibly sequencing words lies at the core of patients' grammatical difficulties. Previous research and a preliminary study conducted prior to this project have validated the tasks that we will use. The preliminary study implicated a specific area of the brain within the left inferior frontal cortex. If successful, this project will a) allow us to predict specific impairments in patients from their anatomical profiles; b) use the tasks developed herein to diagnose more accurately the cognitive deficits of patients; and c) determine

whether the sequencing difficulties are circumscribed to language and if so, possibly harness patients' preserved abilities in sequencing other kinds of stimuli (e.g., pictures) to design therapy.

Summary of Research Completed

Specific aim #1: To determine whether damage to a specific sub-region of LIFC (posterior portion, Brodmann area 44/6/9) is predictive of impairment in flexibly sequencing words.

Data collection and analysis for this specific aim are complete. Participants completed the multiword priming task, where they produced two nouns in a "X and Y" phrase. We manipulated whether a repeated noun appeared in a consistent or inconsistent position compared to previous prime trials. We measured patients' impairment in flexibly sequencing words by computing the increase in reaction time for inconsistent compared to consistent trials as a percent of patients' baseline latencies. A higher percent increase indicates greater difficulty in flexible sequencing.

We had previously finished testing 7 patients with damage to different areas of the brain. In this reporting period, we finished collecting the same kind of data from 8 healthy controls. We used the mean (4.19) and standard deviation (5.05) from this control population in a Crawford t-test to determine whether each patient's score was significantly different from the controls. Table 1 shows the p values from this analysis in parentheses next to the reaction time measure.

Our results are partially consistent with our predictions. As predicted, non-frontal damage patients (5 and 6) did not have any particular difficulty with this task. Also as predicted, patients 1-3 (damage to posterior LIFC) had the most exaggerated difficulty. However, patient 4 (damage to another part of LIFC) also was significantly different from the controls. It is possible that patient 4's difficulty arises not from an impairment in flexible sequencing, but an impairment in overriding prepotent responses. Under specific aim #3, we discuss a sequencing task without a priming manipulation that might tease apart these mechanisms.

Specific aim #2: To correlate impairment in sequencing words with difficulty in producing complete, grammatical sentences during other tasks.

Data collection and analysis for this specific aim are complete. We evaluated whether the frontal patients who showed difficulty in flexible sequencing in the multiword priming task above also showed difficulties in other language production tasks.

We previously reported that there was no special relation between performance in the multiword priming task above and two other language production tasks (verbal fluency and scene description). In this reporting period, we finished collecting and analyzing data from two other tasks.

In the story-telling task, well-formedness of the sentences did not correlate with impairment in the multiword task. Only patient 1 had a score (0.78) that was (slightly) more than 2 standard deviations from the control norm ($M=0.95$, $SD=0.08$). The other patients had scores that fell within the 2 standard deviation range (0.81 to 1).

In the moving picture task, patient 3, who had considerable damage to the premotor cortex, showed large latencies in general (Patient filler latency = 2007.9 ms; Control mean = 885.5 ms; SD = 135 ms). This suggests a difficulty in motor/speech planning in general (see more below). Patients 1 and 2 on the other hand had elevated latencies particularly when they had to sequence multiple nouns compared to the filler trials. None of the other patients showed this pattern. This is consistent with our hypothesis that damage to posterior LIFC leads to difficulty in sequencing co-activated, competing representations.

Overall, examining the relation between the different language production tasks revealed that the sequencing of words (multiword priming, moving picture) was dissociable from other forms of executive function (verbal fluency) and the production of infrequent structures (scene description). It was also dissociable from the production of sentences in a naturalistic story-telling context. Future testing should explore whether the semantic support available in naturalistic situations but not in some experimental tasks is responsible for this difference (see more below).

Specific aim #3: To correlate impairment in sequencing words with impairment in sequencing non-linguistic items such as tones and visual stimuli.

Data collection is nearly complete for this specific aim (one control participant remains to be tested).

We previously reported that our original sequence manipulation task was subject to the use of strategies and was therefore difficult to interpret. We designed and implemented a new sequence manipulation task. Participants reproduced four-item sequences shown on the screen using the keyboard. Stimuli were letters (A, B, C), colored squares (blue, yellow, red) or color names (“blue,” “yellow,” “red”). Items appeared one at a time (sequential) or all at once (simultaneous). Healthy controls are known to slow down in the simultaneous condition for item 1 (cost for planning) but go faster for subsequent items (benefit from planning ahead). In contrast, frontal patients may incur initial interference costs without reaping much subsequent benefit. We computed the difference between cost (item 1 simultaneous minus sequential) and benefit (item 2 simultaneous minus sequential), normalized by the baseline reaction time (RT) to item 1 in the sequential condition.

We only tested the four frontal patients (1-4) on this task because we were interested in exploring sub-specialization within the frontal cortex for those patients who had shown impairment in the multiword priming task. Patients with different frontal lesion profiles showed different patterns (Table 2). Patient 3, who had the most damage to premotor cortex, showed substantial interference for all three types of stimuli (letters, colors, color names). As in the moving picture task, this might reflect a general motor planning difficulty. Patient 4, with damage to anterior and not posterior frontal cortex, was within the control range for all three types of stimuli. Thus, her difficulty in the multiword priming task may have arisen from difficulty overriding a prepotent response and not difficulty in sequencing. Interestingly, patients 1 and 2 were the only patients who showed exaggerated difficulty on the letters version of the task, but not the colors or color names versions. This together with their multiword and moving picture performance suggests

that they might have specific difficulty in sequencing, particularly when there is not much semantic support and/or prior orders have to be overridden.

Table 1. Multiword priming scores

Patient #	Description of brain lesion	% increase in reaction time (inconsistent minus consistent)
1	Extensive damage to posterior LIFC	23.18* (p<.01)
2	Extensive damage to posterior LIFC	36.76* (p<.01)
3	Some damage to posterior LIFC	24.58* (p<.01)
4	Damage to LIFC, but not posterior parts	17.51* (p<.05)
5	No damage in LIFC. Posterior brain regions only.	-2.37 (p>.05)
6	No damage in LIFC. Posterior brain regions only.	3.50 (p>.05)
7	No damage in LIFC. Posterior brain regions only.	N/A*

* Reaction time data from patient 7 were not usable due to too many naming errors.

Table 2. New Sequencing Task Scores

Patient #	Letters	Colors	Color names
Control mean (SD)	0.60 (3.32)	9.93 (9.64)	1.45 (13.15)
1	20.43*	9	12.49
2	19.12*	6.17	13.22
3	30.95*	44.11*	45.36*
4	-0.54	25.65	0.37

* Indicates scores more than 2 standard deviations from the control mean

Research Project 3: Project Title and Purpose

Longitudinal Multi-modal Neuroimaging of Natural Recovery after Traumatic Brain Injury: A Pilot Study - This project will provide pilot data for a large-scale future study whose aims include 1) determining the pattern of longitudinal changes in structural and functional neuroimaging indices associated with traumatic brain injury (TBI) and their relationship with behavioral improvements and 2) developing a “recovery potential” index, based on the difference between structural and functional imaging measures obtained at different points of post-injury, and collect data on its relationship with behavioral recovery. This project will demonstrate our capability to collect and analyze longitudinal multi-modal neuroimaging data and to estimate the appropriate sample size for the larger study to be proposed for NIH funding.

Anticipated Duration of Project

1/1/2010 - 12/31/2012

Project Overview

The specific aims of this project are 1) to demonstrate, under our recruitment and neuroimaging infrastructure, the feasibility of longitudinal, multi-modal neuroimaging data collection to study neural recovery after TBI, 2) to develop and validate the “recovery potential index” that is based on the difference between structural and functional imaging measures obtained at different points of post-injury, and 3) to estimate, for each neuroimaging modality, the sample size necessary to demonstrate longitudinal changes between 3 and 6 months.

To achieve these goals, we will test 4-9 survivors of TBI on four neuroimaging measures twice, at 3 and 6 months from the date of injury. To measure longitudinal improvements in behavior, a global behavioral outcome measure and a neuropsychological test battery consisting of six executive function tests will be administered at each time point. Recovery potential index will be calculated from the difference between the masks covering significant areas of hypoperfusion at 3 months and the masks covering significant atrophy at 6 months for each individual. Then, the variability of the index across subjects will be assessed. Regarding sample size calculation, using obtained estimates of the magnitude of longitudinal changes (i.e., difference between 3 and 6 months) and their variances, we will calculate necessary sample sizes for each imaging indices with a type I error level 0.05 and a power of 0.8.

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Expected Research Outcomes and Benefits

The “recovery potential” index to be developed and validated in this project has a potential to be used as a biomarker to predict future recovery from traumatic brain injury. This index may ultimately contribute to the development of efficient intervention by helping to reveal the neural mechanism of recovery and to predict its individual differences.

Summary of Research Completed

Although we have not begun testing patients, we have made progress in the following areas.

Training research staff on neuropsychological testing: Two research assistants have been trained by our neuropsychologist (Tessa Hart, PhD) in regards to the administering and scoring of our neuropsychological battery.

Preparation of MRI pulse sequences: The MRI pulse sequences required to collect structural and functional MRI data were assembled at the University of Pennsylvania.

Refining recruitment and screening procedures: Our bi-weekly recruitment meeting was launched, and many issues have been resolved that required refinements in recruitment and screening processes. For example, we needed to modify existing substance abuse screening tools for our purpose. To achieve this, we conducted an in-depth literature review regarding the degree of substance abuse resulting in brain damage. We did this to be able to determine what and how past or current drug abuse may affect a participant's brain. This review helped us to pinpoint what substances would lead to a participant being ineligible to participate in our study due to the possibility of brain damage resulting from substance abuse. We started by reviewing a wide range of substances including alcohol, inhalants, cocaine, marijuana, and amphetamines to name a few. We narrowed down the substances to focus on the type, amount and likelihood of brain damage that may result from their abuse. We have decided to screen our patients for alcohol, solvents, amphetamines, opiates, benzodiazepines and PCP substance abuse. We have also developed a tracking sheet which allows us to keep track of the participants that do or do not meet our inclusion and exclusion criteria, which may change from week to week. This way we are able to know immediately if a participant is no longer appropriate for our study. Along with the development of our tracking sheet, we created and made modifications to our screening form. We have made the screening form specific to our study's inclusion and exclusion criteria resulting in a more streamlined and efficient way for us select appropriate participants for the study.

No-cost extension: Due to the following three main reasons, a no-cost extension was requested in June, 2011. First, the approval of the subcontract at the University of Pennsylvania for MRI scanning is taking a very long time (more than 3 months). This was caused by an unfortunate administrative oversight at the University of Pennsylvania. It is expected to be approved before August 2011. Second, training the research assistants (RAs) for the neuropsychological assessments took a longer time than expected. An RA who was hired last year quit shortly after he was hired for personal reasons. Third, we had to go through an IRB modification multiple times (see below) to accommodate several procedural changes and new IRB requirements.

Modification of the protocol and consent forms: The following are the highlights of IRB modifications and protocol changes during the reporting period.

1. Approval date: February 2nd 2011

- a. Consent modification:

- Modified withdrawal information:

- Adult consent: "In the event that you withdraw from the study, the principal investigator will ask your permission to continue study follow-up. All clinical data, as it relates to the study, will continue to be collected from your medical records. All clinical data already collected will continue to be used."

Addition of “relationship to kin” for signature lines -- The adult consent form has been revised to now include “(relationship of kin)” for all appropriate signature lines.

Addition to description of procedures -- We have added “Participants will be interviewed about their medical history, current health problems, and current medications, and scheduled for their testing session(s). Some of this will be dealt with by telephone but in some cases, in-person screening interviews may be required. These will take place at MossRehab or at the University of Pennsylvania Hospital, depending on convenience” to our description of procedures.

Center for Advanced Magnetic Resonance Imaging and Spectroscopy (CAMRIS) clause -- We’ve made a change to the CAMRIS experimental device clause. We removed the term “non-significant risk” of the CAMRIS experimental device clause and replace it with “no more than minimal risks.”

Confidentiality -- We’ve added “If you are also enrolled in the Moss Traumatic Brain Injury Model System, information collected as part of your participation in that project (such as medical and rehabilitation chart information, demographic information and social history, cognitive test results, and information gathered during regular follow-ups) can also be shared.” This will allow us to be able to share data across projects.

To reflect the addition of a new neuropsychological test, we have created a new caregiver consent to be used in addition to the existing consents. The reason for this request is because we are modifying the neuropsychological battery we are administering to the subjects and one of the new assessments requires caregiver participation.

b. Protocol modification:

The protocol modifications are related to the neuropsychological battery and global outcome assessments we administer to the study subjects. These changes reflect the recommendations recently made by the TBI Outcomes Workgroup supported by the National Institute of Health.

- We dropped Brown-Peterson Auditory Consonant Trigrams, Regard’s 5-point and the Stroop Test.
- We added: Digits Backward, Letter Number Sequencing (LNS) and Processing Speed Index (PSI) from the Wechsler Adult Intelligence Scale IV (WAIS-IV) (which will be replacing the Wechsler Memory Scale III), the Rey Auditory Verbal Learning Test (RAVLT) and the Family Rating Scale Behavioral Evaluation (FrSBe).
- We added a second global outcome assessment, the Extended Glasgow Outcome Scale (GOS-E).

2. Approval date: May 3rd 2011

- a. Consent modifications: Changes to “Procedure” section to inform our participants about the possibility of them being dropped from the study even after they consent, and that they will still be compensated. We also modified our “Description of Procedures” to provide more information to our participants about testing and scanning procedures.