Albert Einstein Healthcare Network

Annual Progress Report: 2011 Formula Grant

Reporting Period


Formula Grant Overview

The Albert Einstein Healthcare Network received $52,011 in formula funds for the grant award period January 1, 2012 through December 31, 2013. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

Task-switching: A Window to Cognitive Control Deficits in Aphasia – Although aphasia has been characterized as a language disorder, the affected individuals show various non-linguistic problems, especially with cognitive control functions such as holding and manipulating information in working memory, and switching between tasks. A clearer understanding of these problems will bring us closer to understanding aphasia syndromes, and is likely to open new doors for rehabilitation methods that go beyond traditional linguistic therapies. This study launches a new investigation of task switching in aphasia, using a simple, well-controlled experimental design that has the potential to pinpoint the reasons why task-switching deficits arise in aphasia.

Anticipated Duration of Project

1/1/2012 – 12/31/2013

Project Overview

Objective #1: assessing a non-linguistic cognitive control ability (task-switching) in individuals with aphasia.
Objective #2: breaking down task-switching to more simple cognitive processes and investigating each in turn in individuals with aphasia.

The specific aims are:
1. Assessing transient vs. sustained switching costs in individuals with aphasia, and comparing each type of cost to normal age-matched controls (Experiment 1). Transient effects assess trial by trial performance, while sustained effects address the ability to keep a certain mentality throughout the task. For example, that the probability of performing task A is 100% when only one task is demanded, but 50% under circumstances when one of the two tasks may be demanded on each trial.
2. Determining the contribution of working memory load to sustained and transient costs in individuals with aphasia, and comparing it to normal age-matched controls (Experiment 2).

3. Determining the contribution of response conflict to sustained and transient costs in individuals with aphasia, and comparing it to normal age-matched controls (Experiment 3).

4. Investigating individual differences in the effects listed in 1-3, with regard to the size and site of the lesion.

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**Expected Research Outcomes and Benefits**

Left frontal cortex is a common site of lesion in individuals with non-fluent aphasia. This is the same region that hosts many executive abilities necessary to control primary cognitive modules such as language production. It is therefore expected that individuals with aphasia have various degrees of cognitive control problems that are masked by the more prominent language impairment. Even though researchers have investigated (and endorsed) the existence of these non-linguistic deficits in the past, the tasks used are often too complex, and involve too many mental processes to allow for a clear interpretation of the underlying deficits leading to impaired performance.

In the proposed study, we plan to (1) focus on one crucial executive ability, task switching, which has a direct bearing on the life of the aphasic individuals, since conversation, by definition, involves constantly switching between listening and speaking. (2) adopt a simple paradigm, used successfully in neurologically healthy adults, to thoroughly examine the cognitive components involved in successful task-switching.

**Summary of Research Completed**

Our proposal outlined an investigation of executive-function deficits in aphasia utilizing a sensitive experimental procedure called “task-switching”. An initial pilot phase (2 patients, 2 controls) led to some changes in the experimental design, and, more importantly helped generate a specific hypothesis that thereafter framed the project. The hypothesis is that executive deficits are causally related to the clinically significant condition known as “non-fluency”. The project
has proceeded in several steps, each of which is detailed below. First, we refined and operationalized the construct of fluency. Next, we conducted a group-level lesion-symptom mapping analysis that confirmed a significant correlation between non-fluency and lesions in brain areas that are deemed crucial for executive control. The third step, which is ongoing, is an experimental investigation of task-switching performance in three participants with aphasia – two non-fluent and one fluent – along with neurologically healthy, age-matched controls. Preliminary analyses support the prediction that the non-fluent participants are selectively impaired in executive functions.

The widely used Western Aphasia Battery (WAB) bases the measurement of fluency (speech rate) on the aphasic person's conversational speech and complex-picture description. Fluency is rated on a 10 point scale, based on criteria that deliberately conflate disruptions in the speech flow arising at the levels of single words and multi-word utterances. For present purposes, this is a critical distinction: We hypothesize that non-fluency results from an executive deficit that specifically impacts the ability to produce multi-word phrases efficiently and correctly, i.e., a grammatical deficit. Testing this hypothesis requires a measure of fluency that is not contaminated with the person’s ability – or lack thereof – to produce single words. To create such a measure, archived WAB fluency scores for 139 individuals with aphasia in the Moss database (www.mappd.org) were regressed on their picture-naming scores. The beta derived from this regression model was used to calculate an expected fluency score for each patient, based on his/her picture naming ability. Specifically, we created a new measure expressing the discrepancy between the expected fluency score and the actual fluency score (Expected – Actual), where a positive value indicates that the actual fluency is lower than what is expected based on the patient's single word production abilities. We hypothesize that this refined measure of verbal non-fluency — which can no longer be attributed to word finding deficits — is due to executive deficits.

To test this hypothesis at the group level, we used the archived lesion files of 107 patients in the Moss registry. These lesions were traced by trained research staff at Moss, and reviewed by an experienced neurologist, all blinded to the behavioral data. The lesions were then warped onto the standard MNI (Montreal Neurological Institute) space, which makes it possible to overlay different individuals’ lesions for the sake of group analysis. Using these lesion files, we performed a voxel-based lesion symptom mapping (VLSM) analysis, a statistical technique in which one measures the correlation between lesion presence and behavioral scores voxel-by-voxel across the whole brain (or left hemisphere, in this case) and identifies regions in which the correlation exceeds a threshold that is appropriately corrected for the multiple comparisons. If our hypothesis about the relationship between fluency and executive ability is correct, we expect the correlation with non-fluency to be carried by voxels in brain regions that are known to be crucial for executive functions. The results confirmed this prediction. With the statistical threshold set to a level that insures no more than 1% false positives among voxels identified as significant (i.e., False Discovery Rate correction, q = .01) we found significant effects in frontal areas, specifically left middle frontal and inferior frontal gyri, as well as the underlying white matter (Figure 1). Both middle and inferior frontal gyri have been previously implicated in studies of task-switching, which, as we noted, is sensitive to a variety of executive functions.
Having found support for our hypothesis at the group level with VLSM, we embarked on single-subject experiments to establish the relationship between non-fluency and executive functions, as measured by task-switching. While group level analyses have the benefit of detecting effects that prevail among a large group of subjects, single-subject analysis has the advantage of tighter and better experimental control. In our case, we selected three patients, two non-fluent, and one fluent (according to our refined non-fluency measure), who were carefully matched on demographic information, as well as on comprehension and single-word naming and repetition scores. This matching is crucial, because when comprehension and word production abilities are matched, we can make the clear prediction that the two non-fluent patients should show poor executive abilities, while the fluent patient should not; that is, if our hypothesized relationship between fluency and executive ability is correct.

Before testing the patients in the task-switching paradigm, we collected additional information to have a more complete picture of their production/fluency profile. All three patients completed a free narrative of Cinderella after reviewing a picture book to remind them of the story. The production rate for narrative words (i.e., non-repeated words that represent the propositional speech used to tell the story) was calculated for each patient, to ensure that the non-fluent patients produced fewer narrative words/min. These data are summarized in Table 1. The Quantitative Production Analysis (QPA), which quantifies aspects of grammatical production in terms of the lexical and structural complexity, was also applied to the Cinderella speech sample. The QPA was originally designed to characterize abnormalities found in agrammatic sentence production, but it can be useful for comparing and contrasting grammatical production abilities in different patients, especially the non-fluent ones. Table 2 presents the data. As expected from their matching word production scores, the non-fluent patients do not differ from the fluent patient in the production of open-class words, including nouns and verbs, or in the generation of simple sentences. However, they do score consistently lower than the fluent patient on indices of grammaticality, such as inflection, embedding and sentence well-formedness. We have also tested seven neurologically-healthy adults as controls, and are continuing to test others.

We used the task switching paradigm, described in detail in the grant, in which participants were asked to judge either the size or category (natural/man-made) of pictured objects. On single-task blocks, all trials involved the same type of judgment (“repeat” trials). In switch-task blocks, the required judgment switched across trials, as signaled by a cue. On half of these trials, the judgment was the same as the trial before (“repeat”) and on half of the trials it switched to the other judgment (“switch”). After piloting 2 patients and 2 controls, we made a few changes to the original proposal, while keeping the task structure essentially the same: (1) We eliminated the manipulation of working memory, because the longer duration of the cue caused no change in performance. (2) Instead we increased the number of sessions from 3 to 4 to increase the reliability of the results (an IRB modification was submitted for this). Participants were tested in four sessions, two using button-press and two, using verbal responses. Figure 2 shows the response modality and the item-list for each session.

The data from the button-press sessions were analyzed for response times (RTs) with two types of costs of interest: transient costs (difference between mean RTs in switch vs. repeat trials in the switch-task blocks), and sustained costs (difference in mean RTs between repeat trials in the switch-task and single-task blocks). The data from the verbal sessions were analyzed for two
error types: within-task errors (e.g. “small” for “large”), and between-task errors (e.g. “small” for “natural”). Patients’ log RT-based costs were individually compared to controls’ using a t-test with small sample size correction. None of the patients showed significantly larger sustained costs than controls. However, the two non-fluent patients, but not the fluent patient, showed exaggerated transient costs (tNF1(7) = 3.2; tNF2(7) = 6.5; p<.02). The exaggerated transient cost observed only in the non-fluent patients confirmed our hypothesis about the relationship between fluency and executive deficit, when other factors are controlled for.

According to their structural MRI scans (Figure 3), NF1 had a large lesion effacing left inferior frontal gyrus, and possibly severing it from the outflow from the anterior temporal lobe. NF2, on the other hand, had damage in his left middle frontal gyrus, with some involvement of inferior frontal gyrus. Note that both frontal areas were implicated in our VLSM analysis, as showing correlation with non-fluency. And, in agreement with that, both NF1 and NF2 did show exaggerated switching costs. Interestingly, the difference in the anatomy of the lesion generated two different response patterns when verbal responses of the 2nd and 4th sessions were analyzed: Although both NF1 and NF2 made considerably more errors than controls, especially in the switch-task blocks (Figure 4), NF1’s errors were almost entirely (98%) within-task (e.g., ‘small’ for ‘large’, or ‘natural’ for ‘man-made’, but not ‘small’ for ‘natural’), while 58% of NF2’s errors on the switch blocks were between-task (e.g., ‘small’ for ‘natural’). The error data suggest problems in controlling conflict at two different levels: task and response. There might be parallels to this in language production.

In summary, this project is generating behavioral and neuroimaging data in support of the hypothesis that executive deficits are associated with non-fluency – a clinically significant component of aphasia. The single-subject experiments on task switching additionally produced an unexpected dissociation in the two non-fluent aphasic participants, raising the interesting possibility that multiple levels of conflict control are necessary to insure normal speech fluency.

**TABLES**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Demographic information</th>
<th>Word Production</th>
<th>Comprehension</th>
<th>Fluency</th>
<th>Exaggerated Cost/error</th>
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<td>Ed (yrs)</td>
<td>MPO (yrs)</td>
<td>PNT (%)</td>
<td>PRT (%)</td>
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Table 1- Background Information and results for the two non-fluent (NF1, NF2) and the fluent (F) patient.

Ed = Education; MPO = Months post-onset; PNT = Philadelphia Naming Test; PRT = Philadelphia Repetition Test; Sem = Semantic; W/min = (Narrative) words per minute; yrs = years.

† Sem-Word composite comprehension score was created by averaging comprehension of semantics (using Camels and Cactus Test, and Pyramids and Palm Trees Test) and single words (using Auditory discrimination test (Non-delayed), Lexical decision task (word and nonword
variants), Peabody picture-vocabulary test (Third Edition), and Philadelphia picture-name verification test).

† W/min was obtained by counting the number of narrative words during free narration of Cinderella.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Open class words</th>
<th>Verbs</th>
<th>Sentences</th>
<th>Mean NP length</th>
<th>Closed class words</th>
<th>Inflection index</th>
<th>Mean VP length</th>
<th>Mean sentence length</th>
<th>Proportion of well-formed sentences</th>
<th>Embeding index</th>
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Table 2- QPA results. The columns in purple are indices of speech complexity.
FIGURES

Figure 1- VLSM results at the FDR of 0.01.

Figure 2- Sessions 1-4. Two lists of pictured items were used. Response modality could be either button-press or verbal.
Figure 3- Structural MRI of the two non-fluent patients. NF1 (above) has a large lesion in left inferior frontal gyrus. Nf2 (below) has lesions in both left middle frontal and inferior frontal gyri.
Figure 4- Error rates in the verbal sessions (2 and 4) for single and switch blocks. The blue bars show averaged error rates over seven control participants (error bars reflect 95% confidence interval). The other bars are net error rates for the Fluent (purple), NF1 (red) and NF2 (orange) patients.