

# **Pennsylvania Department of Health Final Performance Summary Report Formula Grants**

## **Overview of the Health Research Project Performance Review Process and Criteria**

An applicant that receives a health research grant under Tobacco Settlement Act / Act 77 of 2001, Chapter 9, is subject to a performance review by the Department of Health upon completion of the research project. The performance review is based on requirements specified by Act 77 and criteria developed by the Department in consultation with the Health Research Advisory Committee.

As part of the performance review process, each research project contained in a grant is reviewed by at least three experts who are physicians, scientists or researchers. Reviewers are from the same or similar discipline as the research grant/project under review and are not from Pennsylvania. Reviewers use the applicant's proposed research plan (strategic plan), the annual progress report and final progress reports to conduct the review. A grant that receives an unfavorable performance review by the Department may be subject to a reduction in funding or become ineligible for health research funding in the future. The overall grant evaluation rating is based on the ratings for the individual research projects contained in the grant.

This performance review report contains the outcome of the review for the grant as a whole (outstanding, favorable, or unfavorable), strengths and weaknesses of each research project, as well as recommendations for future improvement.

The following criteria were applied to information submitted by research grant recipients:

- **Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?**
  - Did the project meet the stated objectives?
  - Were the research design and methods adequate in light of the project objectives?
  - Consider these questions about data and empirical results: Were the data developed sufficiently to answer the research questions posed? Were the data developed in line with the original research protocol?
  - If changes were made to the research protocol, was an explanation given, and, if so, is it reasonable?
  - Consider (only for clinical research projects) the extent of laboratory and clinical activities initiated and completed and the number of subjects relative to the target goal.
  - Were sufficient data and information provided to indicate or support the fact that the project met its objectives or made acceptable progress?
  - Were the data and information provided applicable to the project objectives listed in the strategic research plan?

- **Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?**
  - What is the significance of this project for improving health?
  - Consider the value of the research completed towards eventual improvement in health outcomes.
  - Consider any changes in risk factors, services provided, incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of impact and effectiveness of the research being conducted.
  - Consider any major discoveries, new drugs and new approaches for prevention, diagnosis and treatment, which are attributable to the completed research project.
  - What are the future plans for this research project?
  
- **Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?**
  - If leveraging of funds were expected, did these materialize?
  - Are the researchers planning to apply for additional funding in the future to continue or expand the research?
  
- **Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted/filed?**
  - If any of the above listed were expected, did these materialize?
  - Are the researchers planning to submit articles to peer-reviewed publications, file for any licenses, or patents or begin any commercial development opportunities in the future?
  - Consider the number/quality of each.
  
- **Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?**
  - Were there improvements made to infrastructure?
  - Were any new investigators added or were any researchers brought into the institution to help carry out this research?
  - Were funds used to pay for research performed by pre- or post-doctoral students?
  
- **Criterion 6 - Did the project lead to collaboration with research partners outside the institution, or new involvement with the community?**
  - Are the researchers planning to begin any collaborations as a result of the research?
  - For clinical research only: consider the number of hospitals and health care professionals involved and the extent of penetration of the studies throughout the region or the Commonwealth.

## **Overall Evaluation Rating**

An overall evaluation rating is assigned to each research project. The rating reflects the overall progress the project attained in meeting the stated goals and objectives. The rating is based on a scale of 1–3, with 1 being the highest. An average rating is obtained from all the reviews (minimum of 3) of each project and is the basis for the determination of the final overall rating for each project as follows:

1.00 – 1.33 = *Outstanding*

1.34 – 2.66 = *Favorable*

2.67 – 3.00 = *Unfavorable*

The grant level rating is an average rating from all projects as above. The numerical rating appears in parentheses for the grant and each project in the ***Overall Grant Performance Review Rating*** section of the report.

### ***Overall Grant Performance Review Rating***

**Grant Rating:** Favorable (1.45)

**Project Rating:**

<b>Project</b>	<b>Title</b>	<b>Average Score</b>
0988601	A Feasibility Study of Fruit and Vegetable Consumption in Low Income Communities	Outstanding (1.00)
0988602	The Role of Left Inferior Frontal Cortex in Sequencing and Language	Favorable (1.67)
0988603	Longitudinal Multi-modal Neuroimaging of Natural Recovery after Traumatic Brain Injury: A Pilot Study	Favorable (1.67)

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**Project Number:** 0988601  
**Project Title:** A Feasibility Study of Fruit and Vegetable  
Consumption in Low Income Communities  
**Investigator:** Phipps, Etienne

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## ***Section A. Project Evaluation Criteria***

***Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?***

### **STRENGTHS AND WEAKNESSES**

#### Reviewer 1:

The project successfully met all stated objectives related to the three specific aims.  
The research design and methods were adequate for research objectives.  
The data were analyzed according to analysis plan in the proposal.  
No changes were made in the protocol.

Strength: The recruitment goal was 15-25 participants and more participants than planned (30) were recruited.

Sufficient data were provided to support that the project met its objectives.  
The data and information provided were applicable to the program objectives.

#### Reviewer 2:

The researchers followed their research protocol and met their stated objectives with rigorous methods and data analysis procedures.

They acknowledged some limitations of their study in their manuscript published in the *Journal of Nutrition Education and Behavior*; specifically, (1) people may purchase fruits and vegetables (and other foods) from sources other than the grocery store for which they have electronic data and (2) people may have bought foods from the grocery store in question, but may not have used their shopping rewards card that tracks purchases.

#### Reviewer 3:

Strengths: Aims 1–3 were completed. The team’s goal for recruitment was 15-25 customers, and they enrolled 29 participants (the number 30 was seen in a few places). The research design was adequate to answer the research questions. The data that were collected and analyzed were sufficient to answer the research questions posed. Particularly innovative was the use of electronic supermarket data and frequent shopper cards to track produce purchases.

Weaknesses: The research team did not control for seasonality of fruit/vegetable consumption. They did not examine concurrent shifts in sugary beverages and other less healthy food purchases in tandem with fruit/vegetable purchases, although this was proposed in the strategic

plan. The research team also proposed to examine the relationship between self-report food consumption data and purchase data, but it is unknown if they were able to accomplish this. Although the focus is on low-income consumers, and the Fresh Grocer is located in a low-income area in Philadelphia, the inclusion criteria for the study do not include any income criteria (annual household income, Supplemental Nutritional Assistance Program (SNAP) participation, etc.).

***Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?***

## **STRENGTHS AND WEAKNESSES**

### Reviewer 1:

This project is significant in that it provides the researchers with pilot data related to the impact of providing financial incentives to low-income participants to improve healthy eating (specifically fruit and vegetables [F&V] consumption). The study also provided the researchers with expertise in using data obtained from “frequent shopper cards.” This method of data collection can provide more objective data than self-report, and therefore is a potentially valuable data collection method.

Given the current statistics regarding low F&V consumption among low-income participants, finding effective strategies to increase F&V consumption among this population is significant. Participants increased their fresh produce purchases during the intervention period. This increase was not significant, but this was most likely due to the small sample size.

No major discoveries are attributable to this project but that was not the purpose of this study.

Strength: Researchers have already applied for funding for a larger scale study.

### Reviewer 2:

Developing a system for coding and analyzing the electronic supermarket data was an ambitious and productive undertaking that will allow these researchers and others to use electronic supermarket data to analyze the relationship between food purchases and a variety of health conditions.

### Reviewer 3:

Significance: Obesity negatively affects the health of several individuals in the U.S. Fruit and vegetable consumption can reduce risk of obesity and related chronic diseases, yet consumption is woefully low in Americans, particularly low-income Americans. Cost is one major barrier to fruit and vegetable consumption, an issue that has been cited by many. This was a feasibility study which sought to determine if provision of coupons for fruits and vegetables would result in increased purchase of fruits and vegetables among low-income Pennsylvanians.

Changes in risk factors: The intervention results indicated that among the study participants (n = 29), produce consumption increased; specifically, fresh fruit consumption increased in the intervention period as compared to the baseline period.

New approaches: The study showed the feasibility of using store point-of-sale data to evaluate the intervention. The study also provided coupons for produce, which is not necessarily a new approach but one that simulates what it might be like to have greater incentives for produce purchase in SNAP.

The future plans of this project include completion of a Robert Wood Johnson Foundation (RWJF) randomized trial, and submission of other grant proposals for further work, including partnering with the City of Philadelphia for a proposal to the RWJF for a city-wide supermarket program to increase sales of healthy foods and partnering for additional funding from the African American Collaborative Obesity Research Network (AACORN).

Strengths: The intervention resulted in an increase in fruit purchases, which would hopefully lead to greater fruit consumption (and lower consumption of less healthful foods) among low-income adults and children.

The study also contributed valuable information as to the feasibility of partnering with supermarkets to collect point-of-sale data to evaluate the intervention. From a research perspective, this work is innovative and can provide a model for others conducting similar studies.

Weaknesses: Demonstrating an increase in fruit purchases in the intervention period may not lead to improvements in health if not accompanied by reductions in less healthy food purchases/consumption.

An increase in fruit purchases does not necessarily translate into greater fruit consumption.

The investigators proposed to study both of the aforementioned points, but there was no evidence of analyses to investigate these issues in any of the reports.

***Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?***

### ***STRENGTHS AND WEAKNESSES***

#### **Reviewer 1:**

Additional funding has been received from the RWJF and through the AACORN grant. Another proposal that was submitted was not funded.

Researchers have been asked to collaborate with the City of Philadelphia Department of Public Health to submit another grant to the RWJF.

Strength: Two additional grants have been funded.

Reviewer 2:

These researchers were awarded approximately \$188,000 in additional funds and plan to apply for additional funding to continue this line of research.

Reviewer 3:

The investigators sought and were awarded an RWJF grant for \$168,489 and an AACORN grant from the RWJF (\$20,000) to further the work. They are currently working on additional grant proposals including partnering with the City of Philadelphia for a proposal to the RWJF for a city-wide supermarket program to increase sales of healthy foods and partnering for additional funding from the AACORN. In addition, the group has expanded their healthy eating research to include worksites with funding from the Kynett Foundation and the Albert Einstein Society.

Strengths: Given the resources allotted to this study, the funding outcomes (return-on-investment) are impressive.

Weaknesses: None.

***Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted / filed?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

Two peer-reviewed articles have been accepted for publication. In addition, two poster presentations have been presented.

Strength: Two articles from this relatively small study have already been accepted which is a major strength. It indicates that the researchers are very productive.

Reviewer 2:

At the time of the final report, one paper had been published in the *Journal of Nutrition Education and Behavior*, a well-respected journal in health education/behavior research. Another publication was under review, and the researchers were collaborating with the University of Pennsylvania researchers doing other analyses that could result in additional publications.

Reviewer 3:

The project resulted in two peer-reviewed papers, one published (in the *Journal of Nutrition Education and Behavior* and one accepted (in the *Journal of Health Care for the Poor and Underserved*). The impact factor for the *Journal of Nutrition Education and Behavior* is 1.549 and the impact factor for the *Journal of Health Care for the Poor and Underserved* is 1.102.

The project also resulted in two presentations.

Strengths: The research team published two papers, which was over and above what was set forth in their strategic plan.

Weaknesses: It would have been nice if the papers had addressed the two innovative ancillary research questions the team had regarding: shifts in sugary beverages and other less healthful food and beverage purchases in tandem with fruit/vegetable purchases; and the relationship between self-report food consumption data and purchase data.

***Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?***

### ***STRENGTHS AND WEAKNESSES***

#### Reviewer 1:

No improvements were made to the infrastructure due to this grant.

No new investigators were added or brought to the institution.

No funds were used to support students.

The project did strengthen the research skills of junior and senior faculty which has contributed to additional grant funding and research capacity at the researchers' institution.

Weakness: Although it is not surprising that no changes in the infrastructure or investigators were made because of this study, I would have expected to see some funds go to pay for student research. This is the only weakness found with this study.

#### Reviewer 2:

No improvements were made to the infrastructure; no new investigators were added or brought into the institution to help carry out the research; and no funds were used to support any students. However, the project did strengthen the skills of new junior investigators and developed the skills of senior investigators, resulting in the development of additional projects and the award of extramural funds which contributed to the quality and research capacity of the institution.

#### Reviewer 3:

Strengths: The skills of both junior and senior investigators were strengthened, resulting in increased funding to further their research.

Weaknesses: Funds were not used to pay for pre- or post-doctoral students, and no new researchers were brought into the institution to help conduct the research. However, this is a minor weakness, given the level of funding for the current project.

***Criterion 6 - Did the project lead to collaboration with research partners outside of the institution or new involvement with the community?***

### ***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The project did contribute to an active collaboration with researchers at the University of Pennsylvania and Arcadia University.

In addition, the researchers have been consulting with community organizations and have helped these organizations in the development of their evaluation plans.

Strength: Increased collaboration with community partners is a strength of this project.

Reviewer 2:

The project did lead to collaboration with other researchers at the University of Pennsylvania and Arcadia University as well as community organizations that are involved in increasing access to healthy foods in low-income communities. These collaborations should continue to improve community capacity to provide effective solutions for health disparities.

Reviewer 3:

Strengths: The team reported an active collaboration with the University of Pennsylvania (Center for Clinical Epidemiology and Biostatistics) and Arcadia University.

As a result of the project, the research team helped community organizations to design outcome evaluations for projects related to increasing access to healthy foods in low-income communities.

The team also recruited a group of lower-income, minority supermarket shoppers for the study.

Weaknesses: None.

### ***Section B. Recommendations***

#### **SPECIFIC WEAKNESSES AND RECOMMENDATIONS**

Reviewer 1:

None.

Reviewer 2:

Designing future studies to overcome some of the limitations identified in the present manuscripts is recommended.

Reviewer 3:

1. Since the investigators did not examine changes in the purchase of less healthful foods in response to the intervention, this should be explored further, because, if fruit and vegetable

purchase/consumption increases without resulting in decreases in purchase/consumption of other less healthful foods, obesity will not be affected.

2. Because an increase in fruit purchases does not necessarily translate into greater fruit consumption, investigators should study the correlation between fruit purchases and fruit consumption in their sample.

### **Generic Recommendations for the Institution**

#### Reviewer 1:

This was an important pilot study and the researchers should be commended for their productivity.

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**Project Number:** 0988602  
**Project Title:** The Role of Left Inferior Frontal Cortex in Sequencing and Language  
**Investigator:** Schwartz, Myrna

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## ***Section A. Project Evaluation Criteria***

***Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?***

### **STRENGTHS AND WEAKNESSES**

#### Reviewer 1:

The strategic research plan employed a design and methods that were consistent with the project objectives. These methods appear to be well-considered and tailored to some extent to address a well-detailed hypothesis about neuroanatomical specialization that might be present in the left inferior frontal cortex (LIFC) as one moves from anterior sections of this region to more posterior and dorsal parts of LIFC. Three specific aims were proposed.

The data obtained from this study were in line with the original research proposal. A strength of the research is that the specific patient population that was proposed, highly-localized LIFC stroke patients, was successfully recruited. The collected data addressed the specific hypothesis that selective posterior/dorsal LIFC lesions would impair linguistic sequencing in particular. The major change to the protocol, and a resulting weakness, was the reduction in the recruitment from 30 to 15 subjects. Originally, 20 stroke patients with aphasia were proposed, but only seven were recruited with two lost to poor performance. Also, 10 controls were proposed but only eight were recruited, with one lost to the exclusion criteria at a later review point.

The major apparent limitation in the recruitment process for patients appeared to result from two factors. First, although over 300 new patients were recruited into Dr. Schwartz's stroke registry, only 85 met the criteria for this study at the time of its implementation. As opposed to altering admissions criteria for any of the three patient groups, anterior LIFC, posterior/dorsal LIFC and non-LIFC strokes or adding new lesion types, the research team chose to alter the statistical methodology from a group approach to a case-control approach. The combination of maintaining strict admissions criteria and having only a limited number of patients to choose from posed a significant difficulty to recruiting the originally-proposed study population. Using the available patients, the research team acquired the proposed data and was able to obtain limited support for the hypothesis of neuroanatomical specialization in the posterior/dorsal regions of LIFC for language-specific sequencing deficits. This support is limited by the relatively small sample size. Of the seven recruited patients, two had unusable data, one had a non-LIFC posterior cortical lesion, one had an anterior-LIFC lesion not including posterior LIFC and three had lesions including posterior LIFC lesions.

It appears that only about \$40,000 was spent on this project. Given the limited recruitment, a limited expenditure would seem reasonable. Although the project did not meet the goals of the original research plan in terms of recruitment, those recruited were tested as proposed, and the data indicates that some of the project objectives were met and progress toward the stated aims of the research plan was achieved, including the publication of the results in a well-established peer-reviewed journal.

Reviewer 2:

The project met the stated objectives based on the number of subjects enrolled. The plan was to enroll 20 stroke patients and 10 normal controls based on the results of four subjects in the pilot study. They have a very large population of stroke patients willing to participate in research studies. However, the researchers did not realize, based on the good pilot study findings, that many eligible subjects would not be able to comply with the testing paradigm. They were able to enroll seven subjects and a matching number of normal controls (eight).

The research design and methods were adequate in light of the project objectives.

For one of the paradigms testing word order, the researchers realized the subjects developed strategies to get the correct answer without doing the actual task; so, the paradigm was altered somewhat so the subjects had to do the actual task.

The seven patients were studied in great detail looking at the role of the posterior aspect of the left inferior frontal cortex.

Reviewer 3:

The goal of the proposed study was to investigate the role of Broca's area in word sequencing and how this function breaks down in patients with lesions to that region. The target enrollment was 30 participants, involving 10 controls, 10 patients with Broca lesions and 10 patients with lesions in other regions of the brain. A total of 15 patients were enrolled, eight controls and four patients with Broca lesions and three with lesions outside Broca's area.

The design of the experiment was changed to accommodate the finding that many patients could not perform the task well enough.

Though enrollment numbers were considerably below the stated goal, they yielded enough data for a research article to be published in a well-respected journal.

***Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The project did make limited progress toward the first aim and the second aim. Progress toward the third goal was achieved with only partial success in that the results provided some evidence for language-specific sequencing deficits in dorsal/posterior LIFC stroke patients, but the

knowledge was not substantial enough to indicate how that could be used to individualize therapy, which was one of the expected research outcomes and benefits proposed in the research plan. The benefit is judged small and in line with the hypotheses and predictions. Expenditures appear to be reasonable for this level of impact.

Reviewer 2:

Language is the main mode of communication for humans. These patients post-stroke could function in many daily life situations except those requiring extensive language communication, which then limited which activities they could participate in. This study attempted to better understand the nature of these language deficits, in a manner that could later be used for therapeutic approaches.

The findings for the seven subjects showed that indeed the patients lacked some language word order skills, but had some skills they were hypothesized not to have based on other studies. This information might help in planning therapy time for the patients in the correct categories for skill improvement; however, therapy was not a part of this study.

There was no risk to the subjects in this study and no increase in risk during the study. The major discoveries were that the subjects did not have all of the deficits in word manipulation that they were expected to have. In the future, this finding may be helpful for planning therapy.

For the PI's lab, this research project completed its goals. The post-doc associated with the study, completed the post-doc and moved to another institution, and will be able to continue this research at the other site.

Reviewer 3:

The impact of brain lesion studies such as this one is high, because they have a lot of external validity compared to neuroimaging studies. This is an important study.

***Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The project did not leverage any additional funding, and there was no expectation of future grant applications. Contributions (co-funding) from the PI's R01 and the co-PI's T32 grants were leveraged to accomplish the research, specifically patient recruitment and testing. No further federal funding proposals are planned at this time to expand the research; although, it is stated that the co-PI is continuing this line of research at her new institution as a new faculty member.

Reviewer 2:

Additional funds were not leveraged in the PI's laboratory in Pennsylvania. The post-doc who is now in another state may apply for funding through that new institution.

Reviewer 3:

No.

***Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted / filed?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The project resulted in a single peer-reviewed publication in *Neuropsychologia* in 2012, 50:3284-3294. This was an expected outcome. No licenses, patents, or commercial development opportunities are expected.

Reviewer 2:

The single peer-reviewed publication was able to present and discuss all the findings. This very high-quality article was published in *Neuropsychologia*, a typical and high-quality journal for publishing neurocognitive studies.

Reviewer 3:

The research project resulted in a peer reviewed publication.

***Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The final progress report indicates that no improvements were made to the infrastructure, nor were any researchers brought into the institution to help carry out the research. However, funds were used to pay for the research/training of a post-doctoral student (Dr. Thothathiri). The study did implement a refined approach to testing LIFC aphasic patients. This approach may be used by Dr. Thothathiri in subsequent research on this topic as she seeks funding to support her own lab.

Reviewer 2:

The PI is very experienced and already had an adequate infrastructure for this kind of study.

Reviewer 3:

No, but the funding amount was comparably low, so this can't be expected.

***Criterion 6 - Did the project lead to collaboration with research partners outside of the institution or new involvement with the community?***

### **STRENGTHS AND WEAKNESSES**

Reviewer 1:

There were no new collaborations or community involvement in this work.

Reviewer 2:

This study was done at the PI's hospital and home institution. There was no outside collaboration. However, the post-doc involved with the study moved to a faculty position in the Speech and Hearing Sciences Department at George Washington University, and may collaborate with the PI of this study in the future.

Reviewer 3:

No.

### ***Section B. Recommendations***

### **SPECIFIC WEAKNESSES AND RECOMMENDATIONS**

Reviewer 1:

Although it could be suggested that loosening recruitment criteria might improve recruitment (because that's the method that might be taken in a psychiatric research protocol), that approach might be fraught with additional unknown hazards, like a consequential loss in the specificity of the patient populations and the resulting lack of interpretability in the data. It does seem unusual and a weakness that more information was not provided about why limitations existed in the registry population. Were there too many patients with big lesions, aphasia that was too severe (seems likely based on the loss of two non-LIFC patients' data), or other reasons? Another weakness was that there was no information provided as to whether community or hospital-based recruitment strategies were considered, and if so, why they were not pursued.

Reviewer 2:

The specific weakness in retrospect, which the investigators did not expect in advance based on their pilot study, was that despite the large number of potential subjects screened based on having the correct locations of the anatomical stroke, only seven were able to finally participate. The method to resolve this is collaborative studies across multiple institutions to accrue sufficient subjects with both the correct locations of the anatomical stroke and the ability to finally participate in the paradigms.

Reviewer 3:

This study was done well and finished with a publication that disseminates the gained knowledge to the wider clinical and scientific community.

## **ADDITIONAL COMMENTS**

### Reviewer 1:

This study achieved some success in identifying the appropriate population for the study and did observe findings that would support their hypothesis that patients with posterior LIFC lesions have selective difficulty in sequencing linguistic material. The findings were obtained from several individual and heterogenous cases rather than three groups of relatively homogeneous patients. This recruitment change resulted in a change to the statistical analysis approach, which employed a case-control methodology. The significance of the results, while interesting and supportive of the overall hypothesis, may not have the kind of impact on the field that the proposed larger group study would have provided.

The weakness of the study was that the recruitment strategy was unable to support the proposed sample sizes. Only seven of the 20 proposed stroke patients were recruited. In part, this was the result of strict adherence to lesion-based recruitment criteria. It also partly resulted from the limited number of potential participants that were available via the MRRI database overseen by Dr. Schwartz. It is stated that 300 participants are added to this database yearly, but the total average size in any one year was not stated. These two factors, strict recruitment criteria and limited population, conspired to significantly impair recruitment. There was no indication as to whether loosening the lesion-based criteria or identifying other recruitment populations were considered or examined in detail as alternatives to the cessation of recruitment, which appears to have taken place prior to the second progress report. The concern over this may be mitigated by what appears to be a limitation in expenditures to \$40,573.83 according to the final progress.

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**Project Number:** 0988603  
**Project Title:** Longitudinal Multi-modal Neuroimaging of  
Natural Recovery after Traumatic Brain Injury: A Pilot Study  
**Investigator:** Kim, Junghoon

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### ***Section A. Project Evaluation Criteria***

***Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?***

#### **STRENGTHS AND WEAKNESSES**

##### Reviewer 1:

The project partially met its objective by demonstrating the feasibility of obtaining different imaging modality measures on traumatic brain injury (TBI) patients (Aim 1). However, one of the main objectives of the project, the development of the “recovery potential index” (Aim 2) was not successfully completed.

This study was originally planned to be completed in the first two years of the funding cycle. However, this was not completed until the fourth year of the grant cycle (last two years no-cost extension). This shows that investigators can be ambitious and underestimate the logistics including the enormous effort that go into recruiting the right patient population and the fulfillment of institutional safety requirements such as the IRBs. However, the extension of time to complete the project had no impact on the result of the study.

The main attraction of this project was the potential to develop and validate an index that can be used as a biomarker to predict recovery from TBI. Potentially, this could be used in combination with other indices to form a predictive model. Given the description of the method used to develop the index, it is not clear that the problem is tied to the variation of threshold value used. The researchers should at least point out alternative ways of establishing this, maybe even based on only the CBF result.

The estimation of sample size (Aim 3) is simply a consequence of the data obtained from the last two aims. The parameter that would be most helpful for future studies is the effect size or its components, mean and standard deviation rather than sample size should be reported. Looking at the estimated sample size, it would be hard to say what kind of differences one might obtain using the proposed sample size.

In terms of collecting and analyzing the data, the project is complete. The investigators obtained additional funding for a larger trial from the NIH. They plan to submit a manuscript combining the data obtained from this grant and the newly-awarded NIH funding. Although they published a review article on existing methods of longitudinal imaging studies, it is not based on data collected with funding from this grant.

Reviewer 2:

The investigators successfully achieved their stated goals. They have tested six patients both at three- and six-month post-injury. They have refined their proposed *RI* measure to avoid the limitation of signal thresholding. They have also calculated the sample size for the larger clinical study. Moreover, they extended their original aims and analyzed the relationship between longitudinal imaging measures with improvement in patient function measured by Disability Rating Scale.

Weaknesses: None.

Reviewer 3:

The project almost met its stated objectives and went a bit further, partly because it also garnered additional funding. (Funding was successful for this project with an R01 obtained soon after pilot funding was obtained from the State of Pennsylvania.) The investigators provided a good deal of detailed information on their progress, and included a single publication.

Strengths: The number of subjects studied was as proposed. The method of automated region of interest identification has appeal. Normalization of brains is avoided, which is important given the fact that brains have lesions and atrophy; although, one wonders how critical this problem really is in the milder cases and how important prediction is in the more severe ones.

Weaknesses: The thresholding issue affecting Aim 2 should have been anticipated, with the long history of threshold issues affecting functional imaging.

***Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The main impact of this protocol would have been the development of the “recovery potential index,” which is not completed in this project. In the absence of this, the demonstration of obtaining images from TBI patients longitudinally by itself (since this has been accomplished in other institutions) and the estimated sample size have little or marginal effect.

Reviewer 2:

The project has significant beneficial impact for improving the health of brain injury subjects. Longitudinal structural and functional MR imaging studies allow the elucidation of the brain recovery process. A continuation of the author's research through the NIH-funded study is likely to identify clinically-relevant biomarkers of the recovery.

There were no weaknesses.

Reviewer 3:

This is essentially a study regarding the prediction of functional outcomes after traumatic brain injury, and as such, has an impact mainly on prognosis. But, the imaging methodological development has more far-reaching consequences on this and other fields, and there is potential mechanistic knowledge gained regarding the pathophysiology of traumatic brain injury. The investigators plan to recruit more subjects; they have made adjustments to their imaging methods, and know the number of subjects needed to answer the questions they put forth.

***Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?***

**STRENGTHS AND WEAKNESSES**

Reviewer 1:

There was a successful application for funding (NIH) to conduct a larger expanded study using a similar design as the pilot study.

Reviewer 2:

Dr. Junghoon Kim received from the NIH five-year funding to develop and validate neuroimaging markers of successful recovery from brain injury.

There were no weaknesses.

Reviewer 3:

Funding was successful for this project with an R01 obtained soon after pilot funding was obtained from the State of Pennsylvania. There are plans for future applications as well.

***Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted / filed?***

**STRENGTHS AND WEAKNESSES**

Reviewer 1:

There is one published review article inspired by this project. This is a review article on the consideration of different methodologies used to analyze longitudinal imaging data. No publication which utilizes the data obtained from this project was published.

Reviewer 2:

The investigators have published a paper in a peer-reviewed journal *Frontiers in Human Neuroscience*. The funding from the Pennsylvania Department of Health was acknowledged in that paper.

There were no weaknesses.

Reviewer 3:

It resulted in a publication in *Frontiers in Human Neurosciences*. This paper included both theoretical considerations as well as actual analysis of eight subjects with reasonable confirmation of the method. The number of subjects is consistent with the number proposed in the project, but the behavioral outcome measures were not compared to the atrophy methods.

***Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

According to the final progress report, there were no new investigators, and no post-docs or pre-docs trained on this project.

Reviewer 2:

There was a significant improvement in the infrastructure of the grantee's institution through the present pilot grant and through subsequent NIH funding.

There were no weaknesses.

Reviewer 3:

There was no infrastructure change or new investigators added, or training, but there was development of a research team.

***Criterion 6 - Did the project lead to collaboration with research partners outside of the institution or new involvement with the community?***

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The project was conducted with consultation from the Penn Image Computing & Science Lab.

Reviewer 2:

The project involved collaborations with Drs. Brian Avants and James Gee from the Department of Radiology, the University of Pennsylvania.

There were no weaknesses.

Reviewer 3:

There was collaboration with the Penn Image Computing & Science Lab that should continue.

## ***Section B. Recommendations***

### **SPECIFIC WEAKNESSES AND RECOMMENDATIONS**

#### Reviewer 1:

1. At the design stage of the study it is important to anticipate many possible scenarios and plan accordingly how to handle them. Although the impact of conducting the study in four years rather than the planned two years didn't impact the outcome, it is a lesson every investigator needs to think about, i.e., the potential obstacle that goes with recruiting a patient population and fulfilling all institutional regulatory requirements.
2. It is puzzling that no attempt was made to summarize the data collected longitudinally (except for the sample size estimation). The main expected outcome from this study was the development of a utility index for recovery, but, citing threshold specific problems, the data was not presented or summarized in any form and as a result nothing was learned about the expected research outcome and benefits.

#### Reviewer 2:

None.

#### Reviewer 3:

1. The investigators made an issue regarding normalization. Normalization of brains is avoided, which is important given the fact that brains have lesions and atrophy; although, one wonders how critical this problem really is in the milder cases and how important prediction is in the more severe ones.
2. The investigators were able to show the relationship of volume reduction to functional disability but it sounds as if it's in the wrong direction (volume reduction correlating with functional improvement.) This needs to be addressed both in terms of confirmation and mechanistically.
3. Data from some of the imaging modalities touted in the strategic plan are not clearly presented (such as functional perfusion imaging). Although the sample size is limited, it would be useful to present data on which imaging modalities were useful and will be applied in the future.