Form Approved Through 5/2004

OMB No. 0925-0001

Department of Health and Human Services
Public Health Services

# Grant Progress Report

| Review Group | Type | Activity | Grant Number |
|---|---|---|---|
| | | | 5RO1HD42386-4 |

Total Project Period
From: 09/25/2001 Through: 08/31/2006

Requested Budget Period:
From: 09/01/2004 Through: 08/31/2005

1. TITLE OF PROJECT
fMRI & Sports Related Concussion

2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Name and address, street, city, state, zip code)
Mark R. Lovell, Ph.D., ABPN
UPMC Center for Sports Medicine
3200 South Water Street
Pittsburgh, PA 15203

2b. E-MAIL ADDRESS
lovellmr@msx.upmc.edu

2c. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT
Orthopaedic Surgery

2d. MAJOR SUBDIVISION
School of Medicine

3. APPLICANT ORGANIZATION (Name and address, street, city, state, zip code)
University of Pittsburgh
Office of Research
350 Thackeray Hall
Pittsburgh, PA 15260

4. ENTITY IDENTIFICATION NUMBER
EIN/TIN Number

5. TITLE AND ADDRESS OF ADMINISTRATIVE OFFICIAL
Michael M. Crouch
Director, Office of Research
350 Thackeray Hall
Pittsburgh, PA 15260
E-MAIL: ornih@offres.pitt.edu

6. HUMAN SUBJECTS
☐ No ☒ Yes
6a. Research Exempt ☒ No ☐ Yes
6b. Human Subjects Assurance No. FWA00006790
If Exempt ("Yes" in 6a): Exemption No.
6c. NIH-Defined Phase III Clinical Trial ☒ No ☐ Yes
If Not Exempt ("No" in 6a): IRB approval date: 11/19/03
☐ Full IRB or ☒ Expedited Review

7. VERTEBRATE ANIMALS
☒ No ☐ Yes
7a. If "Yes," IACUC approval Date
7b. Animal Welfare Assurance No.
A3187-01

8. COSTS REQUESTED FOR NEXT BUDGET PERIOD
8a. DIRECT $408,792
8b. TOTAL $571,292

9. INVENTIONS AND PATENTS
☐ No ☒ Yes If "Yes," ☒ Previously Reported ☐ Not Previously Reported

10. PERFORMANCE SITE(S) *(Organizations and addresses)*
UPMC Center for Sports Medicine
3200 South Water Street
Pittsburgh, PA 15203

UPMC Presbyterian Hospital
MR Research Center, 200 Lothrup St.
Pittsburgh, PA 15213

Brain Imaging Research Center
3025 E. Carson Street, Room 143
Pittsburgh, PA 15203

11a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR *(Item 2a)*
Mark R. Lovell, Ph.D.
TEL 412-432-3670
FAX 412-432-3686

11b. ADMINISTRATIVE OFFICIAL NAME *(Item 5)*
Michael Crouch
TEL 412-624-7405
FAX 412-624-7414

11c. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION *(Item 14)*
NAME Michael Crouch
TITLE Director, Office of Research
TEL 412-624-7405 FAX 412-624-7414
E-MAIL offres@offres.pitt.edu

12. Corrections to Page 1 Face Page

13. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

SIGNATURE OF PI/PD NAMED IN 2a. *(In ink. "Per" signature not acceptable.)* Mark R. Lovell

DATE 7/8/04

14. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN 11c. *(In ink. "Per" signature not acceptable.)* Michael M Crouch

DATE 7-9-04

| DETAILED BUDGET FOR NEXT BUDGET PERIOD – DIRECT COSTS ONLY | FROM 09/01/2004 | THROUGH 08/31/2005 | GRANT NUMBER 5R01HD42386-4 |
|---|---|---|---|

| PERSONNEL (Applicant organization only) | | TYPE APPT. (months) | % EFFORT ON PROJ. | DOLLAR AMOUNT REQUESTED (omit cents) | | |
|---|---|---|---|---|---|---|
| NAME | ROLE ON PROJECT | # | % | SALARY REQUESTED $ | FRINGE BENEFITS | TOTALS |
| Mark Lovell,PhD | Principal Investigator | | | | 20,219 | 108,129 |
| Michael Collins, PhD | Co-Principal Investigator | | | | 8,522 | 45,572 |
| Fernando Boada, Ph.D. | Co-Principal Investigator | | | | 3,300 | 17,646 |
| V. Andrew Stenger, Ph.D. | Co-Principal Investigator | | | | 648 | 3,467 |
| Howard Yonas, M.D. | Co-Principal Investigator | | | | 1,625 | 8,690 |
| James Becker, Ph.D. | Co-Principal Investigator | | | | 639 | 3,416 |
| Jamie Stump, Ph.D. | Study Coordinator | | | | 13,139 | 48,843 |
| Rebecca Roush | Research Associate | | | | 11,148 | 41,442 |
| Tara Rockasey | Research Associate | | | | 3,014 | 11,204 |
| Denise Davis | Research Faculty | | | | 708 | 3,786 |
| **SUBTOTALS** | | | | $229,233 | $62,962 | $292,195 |

CONSULTANT COSTS

None

EQUIPMENT *(Itemize)*

None

SUPPLIES *(Itemize by category)*

**FMRI studies**

$42,570 — $42,570

TRAVEL

None

PATIENT CARE COSTS

INPATIENT None

OUTPATIENT None

ALTERATIONS AND RENOVATIONS *(Itemize by category)*

None

OTHER EXPENSES *(Itemize by category)*

Patient Parking $285 — $285

**SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD** — $335,050

CONSORTIUM/CONTRACTUAL COSTS

DIRECT COSTS — $49,825

FACILITIES AND ADMINISTRATIVE COSTS — $23,917

**TOTAL DIRECT COSTS FOR NEXT PROJECT PERIOD** *(Item 9a, Face Page)* — **$408,792**

| BUDGET JUSTIFICATION | GRANT NUMBER<br>5R01HD42386-4 |
|---|---|

Provide a detailed budget justification for those line items and amounts that represent a significant change from that previously recommended. Use continuation pages if necessary.

There is a significant increase in line amounts covering personnel from the applicant organization, as well as in the line amount for subcontracts. In total, there is an approximate $64,621 increase. This increase is due to several factors: 1) staff salaries for the P.I., Dr. Collins, and the subcontract employee were listed and paid incorrectly due to an accounting error in the department last year, and are corrected for the budget this year; 2) Most applicant organization employees, as well as the contractual employee received small institution approved salary raises, typically less than 5%, 3) We hired a part-time employee, as described below, so that we can run participants simultaneously at both fMRI sites during our busy football season.

| CURRENT BUDGET PERIOD | FROM<br>09/01/2004 | THROUGH<br>08/31/2005 |
|---|---|---|

Explain any estimated unobligated balance (including prior year carryover) that is greater than 25% of the current year's total budget.

There remains an unused balance from the previous budget period. This is most closely tied to our initial difficulties in subject recruitment, some MR technical difficulties, and some department accounting errors in listing faculty salaries, all of which have been resolved. This amount, therefore is not unobligated, as we still intend to meet our stated goal of 250 participants by the project's end. We are requesting a carry over of unused funds allocated for fMRI and ImPACT procedures, as well as for parking, control subject payment, etc., from the past budget period to the budget period covered by this non-competing renewal. We are also not requesting additional funds for ImPACT studies or control subject payments, in anticipation of budget carryover funds availability. We have had great success in significantly increasing subject recruitment over the past year, and through the use of two fMRI sites and the addition of part-time assistance with running the scanners, we can now scan two participants at the same time, though at different sites.

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

| NAME | POSITION TITLE |
|---|---|
| | |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | YEAR(s) | FIELD OF STUDY |
|---|---|---|---|
| | | | |

* There are no changes in key personnel, therefore, no biographical sketches are attached.

# PHS 2590 OTHER SUPPORT

Provide active support for all key personnel. **Other Support includes all financial resources, whether Federal, non-Federal, commercial or institutional, available in direct support of an individual's research endeavors, including but not limited to research grants, cooperative agreements, contracts, and/or institutional awards.** Training awards, prizes, or gifts do not need to be included.

**Becker, James T** → Please see corresp. Section of file for explanation. ew 8/30/04

**ACTIVE**

5 K02 MH01077-10 (Becker) 07/01/99 – 12/31/04 %
NIMH $77,594
Natural History of Dementia
The data gathered from this project will address the question on how the HIV virus affects higher thought processes and why there is individual variation in the behavioral effects.

5 R01 AG21431-02 (Becker) 09/30/02 - 08/31/06 %
NIA $224,749
Age Moderates HIV-Related CNS Dysfunction
The purpose of this study is to compare and contrast neuropsychological deficits, including brain structural and functional abnormalities associated with HIV/AIDS as a function of chronological age.

1 R01 AG20098-01 (Lopez) 04/01/02 - 02/28/07 %
NIA $308,210
Alzheimers Disease in Mild Cognitive Impairment
This study focuses primarily in early detection and modification of progression in AD and disability, and raises the question of whether we can improve the identification of individuals in the earliest stages of AD.

1 R01 HD42386-01 (Lovell) 09/25/01 - 08/31/06 %
NIH $367,704
fMRI and Sports-Related Concussion
To explore the impact of concussion on cognitive processes through fMRI, as well as to determine the correlation of a computerized neuropsychological test with cognitive and physiological indicators of recovery.

1 R01 MH64921-01A1 (Wiley) 09/05/02 - 08/31/05 %
NIH $250,000
Monocytes in HIV Encephalitis

To test the hypothesis that the radioligand 11C-PK11195 in 3D-PET will detect the presence of activated macrophages in the CNS of HIV infected subjects.

5 P50 AG05133-18 (DeKosky) 6/1/00 - 3/31/05 %
NIA $193,598
ADRC--Administrative Core
The Administrative Core provides the organizational structure and leadership for planning and implementation of all activities directed toward the fulfillment of the ADRC aims.

**Overlap:** There is no scientific or budgetary overlap between any of these projects and the current project.

% = Percentage of Effort

## Boada, Fernando

**Ongoing**

R01 NS044818-01 (Boada) 4/1/2003-3/31/08 %
National Institutes of Health $241,837.00
Ischemic Brain Damage and Triple/Single Quantum Sodium MRI
The specific aim of this project is to investigate the relationship between the increase in TSC during focal cerebral ischemia, as measured by single an triple quantum filtered sodium MRI, and the development of infraction after tissue reperfusion in a non-human primate model of reversible middle cerebral artery (MCA) occlusion.
Overlap: There is no overlap with the current.

R01HL64205-01 (Boada) 1/18/00-12/31/04 %
National Institutes of Health $122,043.00
Methodology for In Vivo 3D Triple Quantum Sodium MRI
Normal cells maintain a relatively low intra-cellular sodium concentration (10-40mM) against a large sodium pool in the extra-cellular space. The large concentration gradient that develops across the cell membrane is critically important for...
Overlap: There is no overlap with the current proposal.

2R01NS30839-07 (Jones) 4/1/2001-3/31/05 %
National Institutes of Health $59,273.00
Sodium Accumulation During Ischemia
This proposal addresses the problem posed by a stroke victim who is a candidate for thrombolysis, but whose onset time is not known. A sizeable fraction of patients fall into this category, estimated in several studies to be from 20 to 45%. Using experimental stroke models and external factors, we propose to define, understand, and validate a system to estimate the time after stroke onset.
Overlap: There is no overlap with the current proposal.

1R01HD42386-07 (Lovell) 9/1/2001-8/31/06 % This grant
National Institutes of Health $367,704.00
fMRI and Sports-Related Concussion

National Institutes of Health (Stenger) 12/1/2002-11/30/06 %
fMRI Acquisition Informatics Tool $150,000.00
The purpose of this R01 proposal is to develop an fMRI acquisition informatics tool for the quantitative evaluation of neuroimaging tools routinely sued in the analysis of fMRI data. This tool will also allow an investigator to predict what effect their acquisition parameters have on their fMRI data.
Overlap: There is no overlap with the current proposal.

%

National Institutes of Health (Stenger) 7/1/2002- 6/30/06 %
fMRI Acquisitions in regions with Field Inhomogeneity $175,000.00
The purpose of the proposal is to develop novel methods for the mitigation of magnetic susceptibility artifacts in T2 funcitonal MR imaging. The primary goal is to develop a rapid fMRI data acquisition strategy that is robust to local field inhomogeneity in both the in-plane and through-plane directions.
Overlap: There is no overlap with the current proposal.

% = Percentage of Effort

**COLLINS, M.W.**
**ACTIVE: project amount is for total project period**

CCU323352-01 09/30/03-09/29/07 %
Centers for Disease Control and Prevention $1,940,360
Development and Validation of Measures to Assess Outcomes of Mild Traumatic Brain Injury
The purpose of this study is to develop computer-based neuropsychological testing for children ages 5 to 13, with a specific focus on concussion and other traumatic brain injury.

CCR323155-01 10/01/03-09/31/07 %
Centers for Disease Control and Prevention $492,250.00
Managing Return to Play Decisions Following Mild Traumatic Brain Injury
The purpose of this study is to examine concussion management protocols in Australia using a large sample of athletes.

HD42386-10
~~NS-01-007~~ 09/01/01-09/01/06 %
NIH/NINDS $2,856,387.00
fMRI and Sport-Related Concussion

%

Private Support 08/14/02-01/30/05 %
$87,000
Private Support
The purpose of this study is to examine differential effects of helmet type on the frequency or severity of concussion, as well as on duration of recovery time.

**OVERLAP:** There is no scientific or budgetary overlap.

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**Eddy, William**
**Active: Amount listed is for total project period**

DMS-9819950 (Eddy) 1/1/99 - 6/30/04 %
NSF $472,008
VIGRE-Vertical & Horizontal Integration of Research and Education in Statistics and Mathematical Science
This proposal describes a project for training post doctoral fellows and train and retain US graduate students, avoiding excess time to complete a Ph.D.
OVERLAP: There is no scientific or budgetary overlap.

107468-1 (Eddy) 6/01/97 - 5/31/07 %
University of Pittsburgh (NIH 5 U19 HD35469-07 PI Minshew) $1,620,872
Neurologic and Cognitive Mechanisms of Autism
The major goals of this project are to provide statistical support for the various projects and to develop new, relevant statistical methods.
OVERLAP: There is no scientific or budgetary overlap.

106667-1 Eddy (PI) 9/25/02 – 8/31/06 %
University of Pittsburgh (NIH R01 MH67166-01 PI Stenger) $216,539
FMRI Acquisition Informatics Tool
The PI will provide advice on the statistical aspects of the fAIT model.
OVERLAP: There is no scientific or budgetary overlap.

% = Percentage of Effort

104923-1 Eddy (PI) 9/25/01 – 8/31/06 %
University of Pittsburgh (NIH 5 RO1 HD42386-03 PI Lovell) $554,652
FMRI and Sports Related Concussion
The PI provides statistical consultation and supervision of data analytic support.
OVERLAP: There is no scientific or budgetary overlap.

%

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**LOVELL, M.R.**
**ACTIVE: project amount is for total project period**

NIH/NINDS HD 42386 09/01/01-09/01/06 %
fMRI and Sports-Related Concussion $2,856,387.00

Dept of Health and Human Services/Center for Disease Control 09/30/03-09/29/07 %
Development and Validation of Measures to Assess Outcome of Mild TBI $1,940,360
The purpose of this study is to develop computer-based neuropsychological testing for children ages 5 to 13, with a specific focus on concussion and other traumatic brain injury.

%

Private Support 08/14/02-01/30/05 %
$87,000
The purpose of this study is to examine differential effects of helmet type on the frequency or severity of concussion, as well as on duration of recovery time.

**Overlap:** There is no scientific or budgetary overlap.

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**V. Andrew Stenger**

ACTIVE

1 R01 MH66066-01 (Stenger) 7/1/02-6/30/05 %
National Institute of Mental Health $175,000.00
fMRI Acquisitions in regions with Field Inhomogeneity
The purpose of the proposal is to develop novel methods for the mitigation of magnetic susceptibility artifacts in T2 funcitonal MR imaging.

1 R01 MH067166-01 (Stenger) 7/1/02-6/30/06 %
National Institute of Mental Health $150,000.00
fMRI Acquisition Informatics Tool
The purpose of this R01 proposal is to develop an fMRI acquisition informatics tool for the quantitative evaluation of neuroimaging tools routinely used in the analysis of fMRI data. This tool will also allow an investigator to predict what effect their acquisition parameters have on their fMRI data.

1 R21 DA015900-01 (Stenger) 7/1/02-6/30/05 %
National Institute of Drug Abuse $100,000.00
Pediatric fMRI Technology Development
The purpose of this proposal is to develop special methodology for functional MRI in pediatric subjects. Specifically we propose to test a novel rapid event-related paradigm, develop a specialized data acquisition method using 3D tailored RF pulses and SENSE, and a deformable image registration procedure.

% = Percentage of Effort

**V. ANDREW STENGER (cont'd)**

1R01HD42386-07 (Lovell) 09/01/00-6/30/05 %
National Institutes of Health $371,000.00
fMRI and Sports Related Concussions
The purpose of this proposal is to use fMRI to observe the effects of sports related concussion on working memory. The paradigms and behavioral testing will be accomplished with the software tool ImPACT, a widely used tool for monitoring sports related concussion.

5R01DA014103-02 (Fiez) 8/1/01-7/31/04 %
National Institute of Drug Abuse $150,000.00
fMRI Studies of the Neural Basis of Reward Processing

5K02MH064190-02 (Carter) 8/1/01-7/31/06 %
National Institute of Mental Health $150,000.00
Cognitive Neuroscience of Schizophrenia

5R01MH059883-03 (Carter) 3/15/00-2/29/04 %
National Institute of Mental Health $200,000.00
Pathophysiology of Cognitive Disability in Schizophrenia

R01 MH59256 (Fiez) 4/1/00-3/31/05 %
National Institute of Mental Health $150,000.00
Articulatory/Phonological Processes in Working Memory

%

%

**Howard Yonas, M.D.**
**ACTIVE**

K01-HL04037 (Pindzola) 4/01/99-3/31/04 %
National Heart Lung and Blood Institute $123,850
"Cerebrovascular Reserve by Xe/CT versus TCD and Oximetry"
The objective is to define the relationship between stable Xenon-enhanced/CT cerebral blood flow, transcranial Doppler ultrasonography, and near infrared spectroscopy measurements in order to best identify patients with symptomatic carotid stenosis or occlusion who have compromised cerebrovascular reserves.

R01 HD42386 (Lovell) 9/1/01 – 8/31/06 %
National Institutes of Health $371,005 ($8,646 sub)
"fMRI and Sports-Related Concussion"
Functional MRI (fMRI) will be used to study high school and college athletes who have suffered a concussion in order to characterize post-concussive abnormalities in brain activation patterns. Changes in fMRI activation patterns will be correlated with changes detected using a conventional test of working memory (N-Back), and also with the ImPACT battery. Using this paradigm, the effects of single vs. multiple concussions will be measured. How well changes in fMRI activation patterns, subjective symptoms of concussion, and objective neurocognitive abnormalities correlate with each other and with academic performance at six and 12 months after injury will be assessed.

50 NS30318-13 (Dixon) 9/30/91-2/28/05 %
National Institutes of Health $940,513
"University of Pittsburgh Brain Trauma Research Center – Core B"
The University of Pittsburgh Brain Trauma Research Center has been investigating the molecular and cellular mechanisms of secondary brain injury and the effects of therapeutic moderate hypothermia since its inception in 1991. The major goals of this project are to operate a core facility that continues the investigation of basic molecular mechanisms responsible for secondary injury.

% = Percentage of Effort

**Yonas, Howard (cont'd)**

U01NS43353 (Clifton) 04/01/02-09/30/05 %
National Institutes of Health $115,690 (subcontract only)
"National Acute Brain Injury Study: Hypothermia II" (Multicenter Clinical Trial)
This is a prospective trial based on the findings of NABIS:HI, a randomized, prospective, multi-center trial with specific aim to determine if surface-induced moderate hypothermia (33°C), begun within six hours of severe brain injury (Glasgow Coma Score, GCS, < 8) and maintained for 48 hours, would improve outcome with low toxicity. There was no difference in outcome and treatment with hypothermia blunted major elevations of intracranial pressure. The specific aim of NABIS:HII is to determine if surface-induced moderate hypothermia (33°C for 48 hours) reached within four hours after severe brain injury improves outcome with low toxicity in patients age 16 – 45 years and a low admission temperature (< 35.0°C).

R01 NS421676 (Powers) 10/01/01- 9/30/07 %
National Institutes of Health $20,007
"Carotid Occlusion Surgery Study"
The goal of this multi-center, randomized study is to test the hypothesis that surgical anastomosis of the superficial temporal artery to the middle cerebral artery (STA-MCA) when added to best medical therapy can reduce by 40%, despite perioperative stroke and death, subsequent ipsilateral ischemic stroke (Fatal and Non-fatal) at two years in patients with recently (less than 120 days) symptomatic internal carotid artery occlusion ipsilateral increased oxygen extraction fraction measured by positron emission tomography (PET).

RO1 NR04801 (Kerr) 7/1/99 -6/30/04 %
Agency: National Institutes of Health $97,282
"The Effect of APOE on Outcomes in TBI Adults"
This goal of this proposal is to determine whether outcome after TBI is related to the presence of the APOE allele.

R01 HL074316 (Horowitz) 4/1/04 – 3/31/09 %
National Institutes of Health $365,895
Myocardial Ischemia and Vasospasm in Aneurysmal SAH
The specific aims are to 1) determine the association between the magnitude of the catecholamine release (NE,EPI), the occurrence of myocardial ischemia and infarct [as detected by ECG arrythmias (ST changes and T wave inversion), decreased ventricular function; elevated CB-K, CPK, and cTnl levels)] and 2) determine whether the presence of myocardial ischemia and infarct within the first five days after SAH increases the risk of SV within 14 days following SAH. A prospective, longitudinal, within-subject between-group repeated measure design will be used in that all subjects will undergo serial sampling of serum (NE, EPI, cardiac enzymes) concurrent with intense neurophysiologic monitoring, daily bedside portable echocardiography screening and clinical examinations in order to detect the presence of the outcomes of myocardial infarct and ischemia and SV.

1 T32 HD40686 (Kochanek) 5/30/05- 4/30/10 %
NIH $297,754 %
Pediatric Neurointensive Care and Resuscitation Research
This is a postdoctoral training program for resuscitation and treatment of children with severe traumatic brain injury (TBI) and in hospital cardiopulmonary arrest (CA). The research focus is on injury mechanisms, novel therapies and outcomes after TBI and CA.

**Overlap:**
There is no scientific or budgetary overlap between this grant and any other funding source for Dr. Yonas.

% = Percentage of Effort

**PROGRESS REPORT SUMMARY**

GRANT NUMBER
5R01HD-42386-4

PERIOD COVERED BY THIS REPORT

| PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR | FROM | THROUGH |
|---|---|---|
| Mark R. Lovell, Ph.D. | 09/01/2004 | 08/31/2005 |

APPLICANT ORGANIZATION
University of Pittsburgh

TITLE OF PROJECT (Repeat title shown in Item 1 on first page)
fMRI and Sports Related Concussion

A. Human Subjects (Complete Item 6 on the Face Page)
Involvement of Human Subjects ☒ No Change Since Previous Submission ☐ Change

B. Vertebrate Animals (Complete Item 7 on the Face Page)
Use of Vertebrate Animals ☒ No Change Since Previous Submission ☐ Change

SEE PHS 2590 INSTRUCTIONS.

**Has there been a change in the other support of key personnel since the last reporting period?** Yes. Dr. James Becker's NIMH grant titled the "Natural History of Dementia" is scheduled to expire December 31, 2004. This grant had allowed him to be fully funded, and therefore he was not financially compensated through this grant for his % effort. Beginning January 1, 2005, he will begin receiving compensation. Otherwise, there is no change in other support.

**Will there be, in the next budget period, a significant change in the level of effort for key personnel from what was approved for this project?** No, there will not be a significant change in effort level for any key personnel.

**Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25 percent of the current year's total budget?** There will likely be a carryover of a balance greater than 25 percent of the current year's total budget, though most of this balance is obligated in that the funds are designated for the fMRI scans, ImPACT tests, parking costs, and control participant reimbursement for remaining participants. Though we are still slightly behind schedule on the recruitment of concussed individuals, we have made great progress and continue to implement new measures to increase our subject pool (see below). Our control recruitment is on schedule. Therefore, we would like to have permission to carryover the balance as we do feel we will be able to recruit all anticipated 250 participants before the study's end and will need those funds for that data collection and completion of the study. In addition, we are relying on availability of carryover funds for fMRI, ImPACT, etc., in order to balance our budget this year, in light of corrections and increases in personnel costs. Approval of the use of carryover funds will allow the study to continue to run without difficulty in light of new budget issues.

**A. Specific Aims:** The overall specific aims for the project have not been modified. Our aims continue to include the following: (1) to describe fMRI patterns of brain activation that typically occur with specific cognitive deficits identified using a traditional (n-back) and new (ImPACT) test of neuropsychological function in individuals sustaining sports-related concussion, (2) to describe typical fMRI activation associated with subjective components of sports-related concussion and post-concussion syndrome, (3) to determine the effect of multiple sports-related concussions on cognitive functioning and fMRI activation, (4) to define gender and age effects on concussion-related changes in fMRI activation and cognition, and (5) to correlate concussion-related fMRI, cognitive, and symptomatic changes with academic performance. We plan to study 250 high school and college athletes over five years in order to address these specific aims.

**B. Studies and results:** We are currently in the final stages of our third year of the project. This past year represented the project's second football season, Fall, 2003. Due to the resolution of early technical difficulties in the fMRI laboratory, as well as to our acquisition of an additional scanning site, we were able to substantially increase enrollment in the study throughout the year to our present enrollment of 93. Overall referrals to our sports concussion clinic continue to increase, many more area schools have adopted the ImPACT software program, and we expect even higher numbers of potential participants in the coming football season, as well as throughout the year. In addition, to address the issue of being able to scan more than one or two concussed athletes per day, we have trained an additional part-time research associate in the administration of the fMRI protocol. Therefore, we will this year be able to have two athletes running through the study at the same time, though at two different sites. This should further increase our number of participants. During the previous football season, we had to turn away a few participants because scan times were full, and we had only one research associate to run the protocol. Regarding non-injured control participants, we have been quite successful in recruiting controls, and have nearly 2/3 of our control subjects who have completed or are in the process of completing the study.

At the time of our previous progress report, we were in the process of adding the "color match" test for use within the scanner. Initial testing appeared to demonstrate activation in expected areas, though examination of additional data showed that this go-no-go type of task was not consistently demonstrating these activation patterns. Therefore, we are modifying a different go-no-go task, an "arrow" task to be administered both in the scanner and during the ImPACT evaluation. This task has been demonstrated in other brain activation studies to produce activation in the prefrontal cortex, as had the "color match" task. In addition, changes in activation on this task with various disease states have been demonstrated in other studies.

Regarding initial analyses, we have begun examining the functional and ImPACT data from many of the early participants. At this point, the functional overlays for most participants have been completed, and initial comparisons on the n-back tasks both within and between subjects have been made. Our core group has been meeting on an almost weekly basis to address statistical issues, as well as issues that surround the acquisition, coding, and interpretation of fMRI data. The initial analysis was focused on determining if the control group and the concussed had similar activation patterns at time point two, the "recovered" time point. We have been pleased with these initial results, as the activation patterns at time two are similar as hypothesized. These results provide early validation for ImPACT as a good measure of recovery, and therefore potentially safer return to play. In addition, we are examining details of individual cases (such as concussion history and severity of present concussion), to gain more insight into activation pattern as it corresponds to ImPACT data. We also discovered a "teepee" pattern in the voxel time series which because of our experimental design is confounded with our current TR. In the "off season" (e.g., non-football season), we have been preparing a new design paradigm that will allow us to increase precision with discerning the motion artifact from real activation. In addition, early analysis of ImPACT data, indicates expected patterns in both control and concussed participants.

**C. Significance:** The potential implications of our project remain highly significant in the medical and sports medicine fields. Through our large sample size, as well as through using control subjects and obtaining data from concussed athletes once recovery is achieved, we will develop an understanding of some of the physiological changes in cognition that occur with concussion. In addition, we will be able to provide information about cognitive functioning in concussed athletes once the athlete has healed, in order to determine if there are any differences between controls with no concussion history and recovered concussed athletes. In addition, we also hope to document changes in a computerized neuropsychological test (ImPACT) that correspond with changes in functional MRI data during concussion,that return to baseline levels at recovery. Close correspondence of cognitive test performance and functional performance will increase our understanding of recovery, as well as assist healthcare practitioners in making more accurate and safer return-to-play decisions. By examining gender and age differences, we will gain even more detailed insight into the physiological and cognitive effects of concussion, as well as insight into the duration and pattern of recovery in these different groups. This study may also have a significant impact in the research area of registration, analysis, and interpretation of fMRI data across large groups of subjects. There are many intricacies and issues regarding normalization of functional activity across group, developing new ways to address and interpret idiosyncratic functional data, and determining optimal methods of acquisition, interpretation, and comparison.

**D. Plans:** During the next year, we plan to continue accruing both control and concussed participants, and expect to be especially busy during the upcoming football season. In addition, we are in the process of preparing our first manuscript introducing the study and initial findings to the scientific community. Abstracts for conference presentations have been prepared and will be presented at local, national, and international conferences. Also, data analysis will continue, as will our weekly statistics meetings addressing issues specific to data interpretation. Overall, we hope to accrue most of our remaining subjects in the coming year, as well as complete a great deal of data analysis, all while presenting initial findings to the scientific community.

**E. Publications:** There are currently no publications resulting directly from this grant, though the initial manuscript introducing the study and presenting initial findings is in preparation.

**F. Project-Generated Resources:** There are no project-generated resources.

# Targeted/Planned Enrollment Table

**This report format should NOT be used for data collection from study participants.**

**Study Title:** fMRI and Sports-Related Concussion

**Total Planned Enrollment:** 250

| TARGETED/PLANNED ENROLLMENT: Number of Subjects | | | |
|---|---|---|---|
| **Ethnic Category** | **Sex/Gender** | | |
| | **Females** | **Males** | **Total** |
| Hispanic or Latino | 0 | 0 | 0 |
| Not Hispanic or Latino | 60 | 190 | 250 |
| Ethnic Category Total of All Subjects* | 60 | 190 | 250 |
| **Racial Categories** | | | |
| American Indian/Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 10 | 30 | 40 |
| White | 50 | 160 | 210 |
| Racial Categories: Total of All Subjects * | 60 | 190 | 250 |

*The "Ethnic Category Total of All Subjects" must be equal to the "Racial Categories Total of All Subjects."

# Inclusion Enrollment Report Table

**This report format should NOT be used for data collection from study participants.**

**Study Title:** fMRI and Sports-Related Concussion

**Total Enrollment:** 93 **Protocol Number:** 111

**Grant Number:** 5R01HD42386-4

**PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race**

| Ethnic Category | Sex/Gender | | | |
|---|---|---|---|---|
| | Females | Males | Unknown or Not Reported | Total |
| Hispanic or Latino | 1 | 0 | 0 | 1 ** |
| Not Hispanic or Latino | 24 | 68 | 0 | 92 |
| Unknown (Individuals not reporting ethnicity) | 0 | 0 | 0 | 0 |
| Ethnic Category: Total of All Subjects* | 25 | 68 | 0 | 93 * |
| **Racial Categories** | | | | |
| American Indian/Alaska Native | 0 | 0 | 0 | 0 |
| Asian | 1 | 0 | 0 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 | 0 |
| Black or African American | 1 | 1 | 0 | 2 |
| White | 22 | 67 | 0 | 89 |
| More than one race | 1 | 0 | 0 | 1 |
| Unknown or not reported | 0 | 0 | 0 | 0 |
| **Racial Categories: Total of All Subjects*** | 25 | 68 | 0 | 93 * |

**PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)**

| Racial Categories | Females | Males | Unknown or Not Reported | Total |
|---|---|---|---|---|
| American Indian or Alaska Native | 0 | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 | 0 |
| White | 0 | 0 | 0 | 0 |
| More Than One Race | 1 | 0 | 0 | 1 |
| Unknown or not reported | 0 | 0 | 0 | 0 |
| **Racial Categories: Total of Hispanics or Latinos**** | 1 | 0 | 0 | 1 ** |

* These totals must agree.
** These totals must agree.

GRANT NUMBER
5R01HD42386-4

# CHECKLIST

**1. PROGRAM INCOME** ***(See instructions.)***

All applications must indicate whether program income is anticipated during the period(s) for which grant support is requested. If program income is anticipated, use the format below to reflect the amount and source(s).

| Budget Period | Anticipated Amount | Source(s) |
|---|---|---|
| | | |

**2. ASSURANCES/CERTIFICATIONS** ***(See instructions.)***

The following assurances/certifications are made and verified by the signature of the Official Signing for Applicant Organization on the Face Page of the application. Descriptions of individual assurances/ certifications are provided in Section III of the PHS 398. If unable to certify compliance, where applicable, provide an explanation and place it after this page.

•Human Subjects •Research Using Human Embryonic Stem Cells •Research on Transplantation of Human Fetal Tissue •Women and Minority Inclusion Policy •Inclusion of Children Policy• Vertebrate Animals

•Debarment and Suspension •Drug- Free Workplace *(applicable to new [Type 1] or revised [Type 1] applications only)*; •Lobbying •Non-Delinquency on Federal Debt •Research Misconduct •Civil Rights (Form HHS 441 or HHS 690); •Handicapped Individuals (Form HHS 641 or HHS 690) •Sex Discrimination (Form HHS 639-A or HHS 690) •Age Discrimination (Form HHS 680 or HHS 690); •Recombinant DNA and Human Gene Transfer Research •Financial Conflict of Interest (except Phase I SBIR/STTR)
•STTR ONLY: Certification of Research Institution Participation.

**3. FACILITIES AND ADMINSTRATIVE (F&A) COSTS**

Indicate the applicant organization's most recent F&A cost rate established with the appropriate DHHS Regional Office, or, in the case of for-profit organizations, the rate established with the appropriate PHS Agency Cost Advisory Office.

F&A costs will ***not*** be paid on construction grants, grants to Federal organizations, grants to individuals, and conference grants. Follow any additional instructions provided for Research Career Awards, Institutional National Research Service Awards, Small Business Innovation Research/Small Business Technology Transfer Grants, foreign grants, and specialized grant applications.

☒ DHHS Agreement dated: 07/29/2003 ☐ No Facilities and Administrative Costs Requested.

☐ No DHHS Agreement, but rate established with _____ Date _____

CALCULATION*

Entire proposed budget period: Amount of base $ 335,050 x Rate applied 48.50 % = F&A costs $ 162,499

Add to total direct costs from Form Page 2 and enter new total on Face Page, Item 8b.

*Check appropriate box(es):

☐ Salary and wages base ☒ Modified total direct cost base ☐ Other base *(Explain)*

☐ Off-site, other special rate, or more than one rate involved *(Explain)*

Explanation *(Attach separate sheet, if necessary.):*

# PERSONNEL REPORT

GRANT NUMBER
5R01HD42386-4

Place this form at the end of the signed original copy of the application. Do not duplicate.

**All Key Personnel for the Current Budget Period**

| Name | Degree(s) | SSN | Role on Project *(e.g. PI, Res. Assoc.)* | Date of Birth *(MM/DD/YY)* | Annual % Effort |
|---|---|---|---|---|---|
| Mark R. Lovell | Ph.D. | SSN | P.I. | Date of Birth | % |
| Michael W. Collins | Ph.D. | | Co-Investigator | | |
| James Becker | Ph.D. | | Co-Investigator | | |
| Fernando Boada | Ph.D. | | Co-Investigator | | |
| V. Andrew Stenger | Ph.D. | | Co-Investigator | | |
| Howard Yonas | M.D. | | Co-Investigator | | |
| William Eddy | Ph.D. | | Consultant | | |
| Rebecca Roush | B.S. | | Research Assoc. | | |
| Denise Davis | B.S., R.T. | | Research Faculty | | |
| Jamie Stump | Ph.D. | | Project Coord. | | |
| Tara Rockasey | | | Research Assoc. | | |
| Jennifer Bakal | M.A. | | Consultant | | |



% = Percentage of Effort