Carnegie Mellon University

Annual Progress Report: 2005 Formula Grant

Reporting Period

July 1, 2009 – December 31, 2009

Formula Grant Overview

The Carnegie Mellon University received $737,186 in formula funds for the grant award period January 1, 2006 through December 31, 2009. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

Developing Methods and Software for the Analysis of Large and Sparse Contingency Tables - Log-linear models are a powerful statistical tool for the analysis of categorical data. Their use has increased greatly over the past two decades with the compilation and distribution of large sparse databases, especially in the medical and biological fields. Such databases often take the form of high-dimensional contingency tables with a large number of empty cells, a situation for which most existing statistical procedures cannot be applied. The purpose of this project is to derive and implement new statistical methodologies for the analysis of large sparse contingency tables.

Duration of Project

1/1/2006 – 6/30/2009

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement C.U.R.E. Annual Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 2: Project Title and Purpose

Changing Representational Codes in the Hippocampus - The hippocampus, located in the temporal lobe of the brain, plays an important role in memory formation, possibly by constructing compact representations for efficient coding of information by the cortex. The purpose of this project is to investigate computational theories of hippocampal coding in the rodent brain, in order to better understand how the hippocampus contributes to cognition.

Duration of Project

1/1/2006 – 3/31/2009

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement C.U.R.E. Annual Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 3: Project Title and Purpose

Effort of Thinking - A Neuroscience Approach - Many common mental operations, e.g., conversation, reading, and listening, are not accompanied by a subjective feeling of effort. However, some do invoke a feeling of effort; moreover, they become increasingly difficult to sustain the longer one has engaged in them. What types of mental operations produce mental fatigue? Is mental fatique associated with processing in specific brain regions? Why are our brains engineered such that some mental operations are tiring, but not others? This research will attempt to answer these questions. Given the increasing importance of mental effort in the workplace, this research could have implications for the formulation of work, in education and for understanding the cognitive effects of aging.

Duration of Project

1/1/2006 – 12/31/2009

Project Overview

Our first objective is to identify the types of mental operations that produce mental fatigue. We will conduct studies in which the mental exhaustion of human subjects is measured immediately after they have completed different types of mental tasks. These studies will measure mental effort using both the subjects' self-reports of mental tiredness and by measuring the impact of the intitial mental tasks on performance of subsequent ones.

Our second objective is to identify the brain regions associated with mental effort. Having identified what types of mental operations produce a feeling of effort, the next set of studies will use functional neuro-imaging to locate neural systems whose activation is correlated with mental effort.

Our long term goal is to develop a theoretical framework for understanding the function served by mental effort. The feeling of mental effort must have evolved to serve some function. Drawing on research concepts from economics and psychology, the goal of this theoretical model will be to shed light on why certain mental operations, but not others, are associated with a subjective feeling of mental effort.

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Expected Research Outcomes and Benefits

A better understanding of mental effort could yield numerous benefits. First, in our current 'information age,' most work involves mental rather than physical effort. A better understanding of the deterimants of mental effort could provide guidance for structuring work in a fashion that maximizes productivity while minimizing mental effort. This could be especially important for vocations, such as air traffic control and surgery, that require intense concentration. A better understanding of mental effort could also potentially yield educational benefits. The feeling of mental effort is undoubtedly a powerful deterrent to learning.

Summary of Research Completed

Previously we reported design of and recruitment for a study to explore incentives for older adults to use mental exercises, also known as "brain games." In this reporting period, we were forced to halt the study because we encountered a "ceiling effect." All participants used the brain games quite heavily, many doing the maximum 20 per day, regardless of which scheme they were enrolled in (Atomistic, Altruistic, or Cooperative/Competitive). It would seem that all of the subjects were motivated to perform the mental exercises.

This finding is important because prior investigations into the efficacy of mental exercises have been stymied by low rates of participation.

Research Project 4: Project Title and Purpose

Monitoring and Feedback to Support Physical Exercise Awareness - Being physically active is a critical component of fighting obesity. Reviews of studies on exercise have revealed that two factors promote and maintain appropriate levels of physical activity: point-of-decision prompts and individual activity programs. Most work in supporting physical activity has concentrated on non-computer based solutions for these factors. Our work is focused on conducting a rigorous user-centered design and development process to build technological support to automatically monitor physical activity and provide effective feedback to encourage engaging in appropriate

amounts of physical activity. In this project, we focus on sensing the activity levels of individuals dealing with obesity and use this information to sense patterns.

Duration of Project

1/1/2006 – 12/31/2008

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement C.U.R.E. Annual Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 5: Project Title and Purpose

MRI Detection of Cardiac Rejection in a Pig Model - The purpose of this research initiative is to support a pilot project using MRI techniques to detect cardiac rejection using a large animal model (namely pigs). Scientists working at the Pittsburgh NMR Center for Biomedical Research (NMR Center) and the University of Pittsburgh Medical Center will be conducting the research.

Duration of Project

1/1/2006 – 12/31/2009

Project Overview

The Pittsburgh NMR Center for Biomedical Research, which is a joint venture between Carnegie Mellon University and the University of Pittsburgh, is funded as a Biomedical Technology Research Center by the National Institute of Biomedical Imaging and Bioengineering of the National Institutes of Health. Tobacco settlement funding is being used to support a pilot project between scientists at the NMR Center and biomedical investigators at the University of Pittsburgh Medical Center to develop a large animal model (namely pigs) to detect cardiac rejection by MRI. The project will emphasize the development of non-invasive MRI techniques to detect rejection of a transplanted organ, specifically non-invasive MRI techniques to monitor functions of the cardiac transplanted organ *in vivo*, and non-invasive MRI techniques to track the movement of immune cells in the rejected heart *in vivo*.

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Expected Research Outcomes and Benefits

The NMR Center has been highly successful in developing state-of-the-art MRI techniques that have great potential in clinical medicine. The methods that the Center has applied are carefully controlled and reliable, facilitating the reproducible testing of therapies in the pre-clinical setting, which cannot otherwise be achieved except with large patient samples. In the area of organ rejection, the risks of biopsy of transplanted organs are considerable and, in some cases, have resulted in death. Reducing this risk by developing novel non-invasive imaging techniques that could replace biopsies for the evaluation of organ rejection would have great clinical benefit. Strong pre-clinical support in established models verified by clinically relevant MRI methods would be highly desirable to direct selection of agents for clinical testing. Progress in addressing either of these problems would greatly improve the medical care of affected patients. Over the long term, such advances would improve patients' quality of life and reduce health care costs due to the availability of less invasive, more specific, and more reliable treatments.

Summary of Research Completed

During grant period July 1, 2009 to December 31, 2009, we did not carry out any cardiac transplant experiments in our pig model. To track the accumulation of macrophages at the rejecting graft by MRI, we have been using the FDA approved iron-oxide contrast agent, Feridex I.V., obtained from Bayer Healthcare. The FDA approved Feridex in 1996 for detecting liver cancer by MRI. The decision to use Feridex in our pig experiments was driven by the fact that this agent was commercially available and FDA approved for human use, facilitating translation of the experimental methods to human patients. In November 2008, manufacturing of Feridex I.V. was discontinued, and has since become unavailable. We have turned our attention to finding another commercially available and suitable iron-oxide based cellular contrast agent for these experiments. Our focus is on obtaining clinically relevant results in the pig model for translational application. We have started to investigate the sensitivity and feasibility of using Molday ION, obtained from BioPAL, Inc. This is a nano-sized dextran-coated iron-oxide agent similar to the ultra-small paramagnetic iron-oxide (USPIO) particle we synthesize in our laboratory for our rodent experiments. Preliminary findings indicate that these particles are more sensitive than Feridex.