

MPC Corporation

Annual Progress Report: 2006 Formula Grant

Reporting Period

July 1, 2009 – June 30, 2010

Formula Grant Overview

The MPC Corporation received \$160,944 in formula funds for the grant award period January 1, 2007 through December 31, 2010. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

Interactive Search-Assisted Diagnosis of Pigmented Skin Lesions - The ability to diagnose pigmented skin lesions, and in particular melanocytic neoplasms, with greater precision and accuracy, is a high health care priority. In addition to current methods of health care provider education, computer-aided diagnosis of the lesions has already been applied in radiology. The Jukic group has developed and used this approach for the analysis of dermatopathologic and pathologic images in the past and now intends to apply the approach to both dermatopathologic and dermatoscopic images of pigmented skin lesions. This approach is unique in that it will assist both the clinician and the pathologist, and in that the resulting database will consist only of those lesions with clinicopathologic correlation.

Duration of Project

7/1/2007 - 12/31/2010

Project Overview

The researchers will investigate and develop a new approach to dermatologic and dermatopathologic diagnosis called interactive search-assisted diagnosis (ISAD) for evaluation of pigmented cutaneous lesions depicted on dermatoscopic and dermatopathologic images. The software support for this new search capability is embodied in an open-source software prototype called Diamond, which has been created previously through a collaboration with Intel Research and Carnegie Mellon University. It is hypothesized that clinical decision making will be improved if the clinician is able to search a database of images with known diagnoses to find images that are similar in order to evaluate a lesion of unknown diagnosis. Not only has this approach not been tried previously, but there is currently no concept regarding the appropriate prototype for the graphic user interface (GUI) for image comparison in dermatopathology and dermatology. To use any software successfully, one needs to develop an acceptable GUI to ensure the success of the software application.

Specific Aims:

1. To build a database of at least 300, although ideally more, annotated dermatoscopic and dermatopathologic images of pigmented lesions paired with diagnosis.
2. To test the Diamond software's ability to process terabytes of data in the guise of dermatopathologic virtual slide images (aka whole slide images) that range in size from 50 MB to 10 GB.
3. To develop an interactive image-matching and pattern recognition scheme for dermatoscopic and dermatopathologic images based on Diamond and work toward the development of an ideal GUI for image comparison in dermatopathology and dermatology.

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Expected Research Outcomes and Benefits

The goal of this project is to deliver an information technology (IT) tool that will allow for the screening of pigmented lesions with greater precision in both dermatology and dermatopathology and be useful across the board for primary care physicians, general pathologists, dermatologists, and dermatopathologists. The medical community will benefit several-fold from this project. The outcome of the first specific aim, to build a database of pigmented and melanocytic lesions, will benefit the biomedical community as a whole. Even if one does not use Diamond or any software-assisted or guided diagnosis, there is no image database in the world that features dermatoscopic images of pigmented lesions paired with either still or whole-slide dermatopathologic images. From the software perspective, this will be the first orchestrated attempt for Diamond to compare processing of still images and virtual slide images. Thus, the investigators will develop and optimize the algorithm for the processing of whole slide images. Once the scheme for interactive matching of pigmented lesion images is actually developed, the creation of a graphic user interface (GUI), with input from both a dermatologist and a dermatopathologist, will ensure ease of implementation of this product in the clinical setting. The researchers believe that the Diamond-based approach will be used in the future for applications in dermatoscopy that will span clinical trials, therapeutic decision-making, and further analysis of dermatopathology images via whole slide images (WSI). The methodology developed in this study will be useful for other investigators who will adopt interactive search-assisted diagnosis (ISAD) or similar image-matching projects in other areas of medicine, including regular radiology, ultrasound imaging, CT scans, echocardiography, and other areas of pathologic

imaging. At the end of the project, the research team hopes to have both a database and a software product that will help in diagnosing pigmented lesions.

Summary of Research Completed

During the final months of funding, the team has met the study aims with few exceptions, and research and development continue. We continue to pursue opportunities to deliver outcomes and benefits indicated in the application. The first aim is in large part complete. The database, including correlated clinical and pathologic images with metadata enrichment, was created. The clinical images are paired with corresponding pathology whole slide images (WSIs). WSIs were annotated by pathologists, and search algorithms continue to be applied to these slides to determine their efficacy. There are more than 100 clinical images collected by Dr. Ferris that are correlated with pathology whole slides, and there are more than 500 available pathology WSIs.

In the first two years of this project, we used a 20X objective to obtain histopathology images, as our digital imaging technology was not advanced enough to allow us to scan slides at 40X magnification. We found, however, that some of the final cellular details (such as mitosis, individual chromosomes, and melanin granules) were, in fact, not visible with the 20X magnification. We determined that a 40X objective, which could be mounted on the digital imager, would greatly improve the quality of images obtained for this project. In April 2009, we purchased a 40X microscope objective with 0.95 numeric aperture (NA) for our Zeiss/Mirax robotic scanner.

Since the glass slides we initially scanned were still available for use, we re-scanned them at 40X magnification to create a dual-mode library. Data from slides scanned at both magnifications have allowed us to develop and test additional searchlets in the Diamond engine and to test Diamond's capability to process the additional, larger datasets (each 40X digital scan is four to five times larger than a 20X scan). Using information obtained from these datasets, we hope to apply for an R23 NIH award in the very near future.

As indicated in the second aim, the Diamond framework is capable of searching and processing terabytes of data, and work continues to improve the searching capacity of large WSIs (also referred to as digital slides). This framework allows for algorithm searches of individual slides, entire cases or WSI repositories for features or areas similar to regions of interest. Algorithms are developed through two parallel strategies: ImageJ feature algorithm development and pathologist training.

The CMU Computer Science Diamond Team has adapted the Intel Cloud for storing and sharing whole slide images (digital slides) as well as associated metadata. To improve the pathologist's experience, image mark-up and annotation tools are more intuitive, with right and left click functionality. The development of a MySQL database has begun to store these annotations, and metadata has been added to the cases.

Intel Labs at Carnegie Mellon received access to the HP Labs OpenCircus cloud (<http://opencircus.org/>). Cloud access makes a collection of computing assets available that can be rapidly allotted, and it is the goal of HP Labs to support research via OpenCircus. The CMU Diamond team recently began exploring ways to use the cloud. OpenCircus offers incrementally

provisioned computational resources for intensive tasks, which may provide significant benefit for classifier training. With continued research, more ISAD tasks, including workflow digitization, will be managed via cloud computing.

Basic image matching and feature-recognition algorithms have been developed for whole slide images, and research continues to refine these algorithms. The CMU Diamond team developed an unencumbered, user-optimized vendor-neutral slide viewer. In addition to the ease of use associated with the GUI design (including smooth zoom, smooth slide navigation, and side-by-side region of interest viewing), a unique feature of the viewer is that it can display digital slides from various vendors. Digital slide file formats are proprietary and vary significantly by vendor, and the CMU viewer allows users to view digital slides from a variety of vendors in one viewer. The viewer is open-source, which allows users to write code in order to display various image formats.

The graphical user interface (GUI) for uploading WSIs and region of interest (ROI) images via CMU Genie has been improved to allow pathologists to “batch upload” files. This GUI will be available to users as the application is expanded and will save a significant amount of pathologists’ time.

Additional algorithm development has occurred to refine sensitivity and specificity. The ImageJ-based eosinophil algorithm is compared to pathologists’ image mark-up (Figure 1) to determine the sensitivity and specificity. Currently a study is in the pre-design phase to compare algorithm-based and pathologist identification of eosinophils with consideration for time, sensitivity, and specificity. A video of the “Eosinophil Find” macro is available here: <http://diamond.cs.cmu.edu/movies/eosinophil-movie/Eosinophil.html>. Algorithms that locate eosinophils and melanocytes continue to be refined for accuracy. The identification of pagetoid spread (upward spread of melanocytes in the epidermis), along with single cell predominance and nest confluence, is the most important distinction in the diagnosis of melanoma versus benign lesions. The team has completed the pagetoid algorithms and is able to identify areas of pagetoid spread in WSIs, allowing retrieval via the Diamond engine. With further development, the algorithms have the potential to aid pathologists in diagnosis by reducing time spent on tedious, time-consuming tasks.

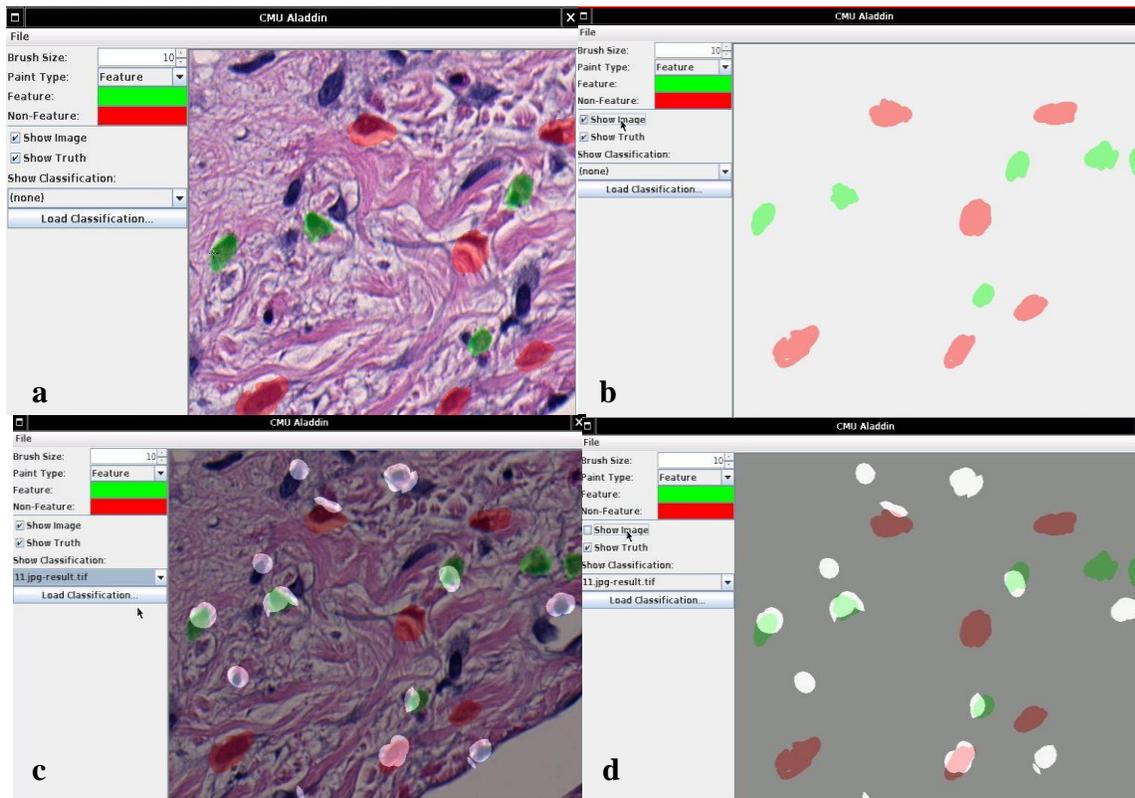


Figure 1: Image mark-up by a pathologist to indicate eosinophils (green highlight) versus non-eosinophils (red highlighting):”CMU Aladdin” image mark-up is created by pathologists. Green highlighting indicates “truth” (in this case, eosinophils are highlighted in green), while red highlighting indicates areas not containing “truths” (a). The mark-up can be reviewed without the underlying image (b). The bright areas (overlying the histologic section) indicate areas in which the ImageJ Eosinophil Find algorithm detected potential eosinophils (c), and the pathologists mark-up (highlighting) versus Eosinophil Find without the underlying histologic image (d). (Source: <http://diamond.cs.cmu.edu/movies/eosinophil-movie/Eosinophil.html>)

Research Project 2: Project Title and Purpose

Predicting Three-Dimensional Protein Structures - Automated structural prediction of tertiary and quaternary protein folding as well as finding corresponding coding motifs in the DNA sequence are crucially important in computational molecular biology. The research team had already made major inroads in precursor research, especially with respect to the computational mechanisms. The purpose of this project is to develop computational algorithms to predict the quaternary structure of multimeric protein strands.

Anticipated Duration of Project

7/1/2007 – 6/30/2010

Project Overview

Automated structural prediction for tertiary and quaternary protein folding is a great challenge for computational molecular biology. This research project will focus on computational techniques and build upon major findings from previous research in the laboratory. Prediction of protein structure bears strong similarity to natural language processing: both have atomic entities (words versus residues), sequential knowledge encoding, rules of combination (grammar versus biophysical rules), structure (syntax versus protein fold structure), and function (meaning versus binding affinities, conformational changes, and other protein functions). The challenge in both cases is to map sequences into higher-order structures, respecting linguistic (or biophysical) constraints and exploiting context to minimize residual ambiguity. Therefore, the specific aim of this project is to develop one or more algorithms to predict quaternary structure of multimeric protein strands like β -spirals in viral adhesions and interlocking viral capsid protein.

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Expected Research Outcomes and Benefits

The project's overall goal is to accelerate proteomics research by developing computational (or *in silico*) techniques that predict quaternary structure (the spatial arrangement of multiple three-dimensional protein sub-units) of proteins. In addition to providing fundamental advances in the emerging field of computational biology, the resulting techniques will be important to the discovery and testing of new drugs. We expect to apply the method to specific multimeric protein structural prediction.

Summary of Research Completed

The protein-structure prediction methods were completed and reported prior to this research period. In this period the prediction mechanisms were tested in the context of HIV-s drug effectiveness. HIV drugs address specific proteins (e.g. protease) required for the HIV mechanisms such as viral reproduction inside the host cell. We tested several predictive methods using viral-load and the response variables, and multiple features as the input variables, including viral-sequence amino-acid n-grams (corresponding to viral proteins and their mutations). The results were tested on data from the Detroit Medical Center, and we found

improvements ranging from 6.4% to 15.5% residual predictive error reduction compared to previous methods. The full results are shown in the table below.

| Feature source | # features | Train Accuracy | Test Accuracy | | # features | Train Accuracy | Test Accuracy | |
|------------------------------|------------|----------------|---------------|-------|--------------------------------------|----------------|---------------|-------|
| | | | ± 0% | ±2% | | | ± 0% | ±2% |
| <i>Decision Tree method</i> | | | | | <i>Support Vector Machine method</i> | | | |
| Patient | 10 | 0.543 | 0.510 | 0.614 | 10 | 0.534 | 0.527 | 0.641 |
| Patient | 60 | 0.648 | 0.546 | 0.619 | 90 | 0.653 | 0.551 | 0.636 |
| Patient | 110 | 0.693 | 0.537 | 0.609 | 110 | 0.663 | 0.549 | 0.623 |
| Virus | 50 | 0.565 | 0.528 | 0.567 | 50 | 0.536 | 0.514 | 0.564 |
| Virus | 250 | 0.694 | 0.554 | 0.612 | 250 | 0.672 | 0.568 | 0.629 |
| Virus | 500 | 0.703 | 0.527 | 0.597 | 500 | 0.729 | 0.542 | 0.608 |
| Both | 50 | 0.652 | 0.563 | 0.622 | 50 | 0.604 | 0.563 | 0.644 |
| Both | 250 | 0.710 | 0.578 | 0.647 | 100 | 0.653 | 0.585 | 0.651 |
| Both | 500 | 0.709 | 0.581 | 0.657 | 500 | 0.763 | 0.556 | 0.632 |
| <i>Naïve Bayesian method</i> | | | | | <i>Random Forest method</i> | | | |
| Patient | 10 | 0.525 | 0.523 | 0.614 | 10 | 0.548 | 0.524 | 0.627 |
| Patient | 60 | 0.552 | 0.538 | 0.605 | 40 | 0.793 | 0.547 | 0.622 |
| Patient | 110 | 0.565 | 0.530 | 0.598 | 110 | 0.832 | 0.534 | 0.618 |
| Virus | 50 | 0.510 | 0.491 | 0.538 | 50 | 0.598 | 0.504 | 0.548 |
| Virus | 350 | 0.612 | 0.583 | 0.642 | 250 | 0.755 | 0.549 | 0.619 |
| Virus | 500 | 0.616 | 0.577 | 0.634 | 500 | 0.756 | 0.544 | 0.614 |
| Both | 50 | 0.567 | 0.553 | 0.629 | 50 | 0.776 | 0.558 | 0.628 |
| Both | 350 | 0.632 | 0.600 | 0.653 | 100 | 0.809 | 0.572 | 0.642 |
| Both | 500 | 0.635 | 0.593 | 0.649 | 500 | 0.819 | 0.553 | 0.629 |

Research Project 3: Project Title and Purpose

Attentional Bias, Craving, and Smoking Related Cues: An fMRI Investigation - The purpose of this study is to further understand the mechanisms underlying self-regulation in people who smoke. The study will focus on the degree to which smoking-related items, or “cues,” draw and capture attention. This effect, termed attentional bias, is thought to play a critical role in generating and maintaining drug craving and, importantly, is correlated with smoking relapse. This project will contribute to the understanding of (1) the cognitive and brain-based underpinnings of attentional bias for smoking-related cues, and (2) the relationship between attentional bias, craving, and subsequent smoking behavior. The research findings will be applicable to many other conditions in which attentional biases are a factor (e.g., general drug addiction, mood disorders, and eating disorders).

Duration of Project

7/1/2007 - 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 4: Project Title and Purpose

The Life Events Assessment Profile (LEAP): A Preliminary Psychometric Analysis - This pilot project will be conducted in partnership with the Pittsburgh Mind-Body Center, a National Institutes of Health-funded center jointly operated by the University of Pittsburgh and Carnegie Mellon University. The project will systematically assess external environmental stressors (i.e., chronic burdens and resources) thought to result in adverse mental and physical health outcomes. Life stress has been posited as a key mechanism in the etiology and course of both psychological and physical health outcomes (e.g., depression and cardiovascular disease); however, research has been hampered by the limitations of available assessment methods. The purpose of this project is to test a newly developed instrument for assessing life stress, the Life Events Assessment Profile (LEAP).

Duration of Project

7/1/2007 – 12/31/2009

Project Overview

Two major methods have been used for life stressor assessment in adults. The first method uses self-report checklists. Although checklist methods are quite convenient and are, thus, widely employed, they have only been shown as modestly reliable. The second method uses investigator-based reports that have well-established coding systems with semi-structured prompts and memory aids to enhance assessment reliability. These investigator-based methods are reliable, but have not been widely adopted due to the costs associated with training, administering, and scoring. This project will examine the validity and reliability of LEAP, a new assessment instrument for adults, which was designed to incorporate the strengths of a comprehensive interviewer-based method without the associated costs. Specifically, LEAP involves a structured administration and scoring system designed to increase the efficiency and cost-effectiveness of the investigator-based method. The project's ultimate goal is to promote the feasibility of administering psychometrically sound life stress measures in the context of mind-body research.

The specific aims of the project are: (1) to demonstrate the concurrent validity of LEAP by comparing it with a standard checklist measure, the Psychiatric Epidemiology Research Interview Life Events Scale (PERI) and the gold standard for investigator-based measures, the Life Events and Difficulties Schedule (LEDS); (2) to compare LEAP's discriminant and convergent validity against PERI and LEDS by examining their associations with measures of social desirability and physical and psychological symptomatology in a community-based sample of adults; and (3) to determine LEAP's test-retest reliability and to compare it with the

test-retest reliability of the standard checklist measure. In order to accomplish these aims, research participants will be randomly assigned to one of three stress assessment conditions after completing a battery of measures to assess demographic and health outcomes. Participants will return for a second stress assessment administration at either one week (Group 1) or six weeks (Groups 2 and 3). Following data collection, statistical analyses will be performed to determine the psychometric utility of LEAP.

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Expected Research Outcomes and Benefits

Chronic exposure to psychosocial stress has been associated with various diseases that produce considerable public health burden (e.g., cancer, heart disease, substance abuse, and depression). However, the ability to precisely measure exposure to psychosocial stress has lagged behind the advances being made in the biological sciences, especially with respect to identifying genetic factors. This project makes a critical assessment of a novel environmental life stressor assessment tool, which has the potential to measure heterogeneous groups of adults (i.e., age, gender, ethnic/racial background, and socioeconomic status) as well as various physical and mental health outcomes related to stress. An economical method to assess life stressors (both acute and chronic) will help to facilitate further investigations into the relationship between life stressors and disease outcome and progression over the lifespan. Collecting normative data on the incidence of various life stressors will help to develop taxonomies to identify and follow groups at high risk for developing certain disease outcomes and to tailor specific intervention strategies.

Summary of Research Completed

Recruitment for the *Life Events Assessment Profile (LEAP)* pilot project began 9/5/2007 following receipt of funding. Since this time, we have refined the LEAP instrument; developed training procedures for LEAP administration; trained two research staff; created appropriate databases and scoring procedures associated with this tool; and recruited, enrolled, and collected data from participants (see below).

The recruitment phase and participant interviews have been completed, and we are in the data scoring, cleaning, verification, and analysis phase. Since 7/1/09, we have completed the process of writing scoring protocols and algorithms for the LEAP. We have offsite collaborators coding and scoring the measures in order to test the scoring algorithms and protocols being developed. In addition, we are continuing our work on the computerized version of the LEAP.

Subject Enrollment/Recruitment

We have met our recruitment goals in the project timeframe; we have not enrolled any participants in the timeframe 7/1/09–12/31/09. Ninety-nine participants have signed consent forms to participate in the study. Of these, 84 have completed the protocol, 14 have withdrawn their participation and one has dropped out of the study. The sample characteristics are representative of the Greater Pittsburgh area. See table below.

Databases and Data Management Strategies

Databases and electronic forms have been developed to collect, store, and score the life stress assessments (including the LEDS and PERI, a widely-used checklist measure of life stress, used as a validation standard) as well as the socio-demographic information and the various other psychosocial assessments. For future studies (with separate funding), we have been working in collaboration with the University Center for Social and Urban Research (UCSUR) to computerize the LEAP and develop data tables that will enable us to enter and score the LEAP instrument. To date, UCSUR has assisted us in computerizing nine domains; pilot testing these domains has facilitated scoring protocol and algorithm development as well as question enhancements to the original paper version. The development of the aforementioned databases has enabled us to track and monitor data quality. Reports regarding our recruitment efforts, missing data, and data discrepancies were generated on a weekly basis, allowing us to track our progress and readjust our recruitment and data management strategies.

We have completed our initial validation study, comparing this instrument to existing standard assessments of life stress (interview and self report format) in a community adult sample (n=99; subjects were paid from an existing grant that predated this project). Our analyses support the utility of this interview format. For example, a subset of this group (n=30) were administered the LEAP along with the LEDS (Life Events and Difficulties Schedule), the benchmark standard interview assessment device (which is, however, less structured and less efficient in terms of training and scoring than the LEAP). We found that standard assessments of life events exposure were comparable between the LEDS and the LEAP; measures of life events exposure in the past year from these two instruments were correlated at an $r=.83$ (see Fig. 1).

During the past year, we have made considerable progress on the development of the LEAP, including: 1) a major redesign of the interview content, refining questions and interview flow; 2) completion of scoring algorithm design for each content domain; 3) enhancements in the programming features for the computer administration version of the LEAP, including the development of an automated timeline with real-time update, the development of procedures to determine the chronology of events (to assist in scoring), and improved navigation to reduce

interview burden. We are in the process of developing a fully implementable version of the computer-based LEAP.

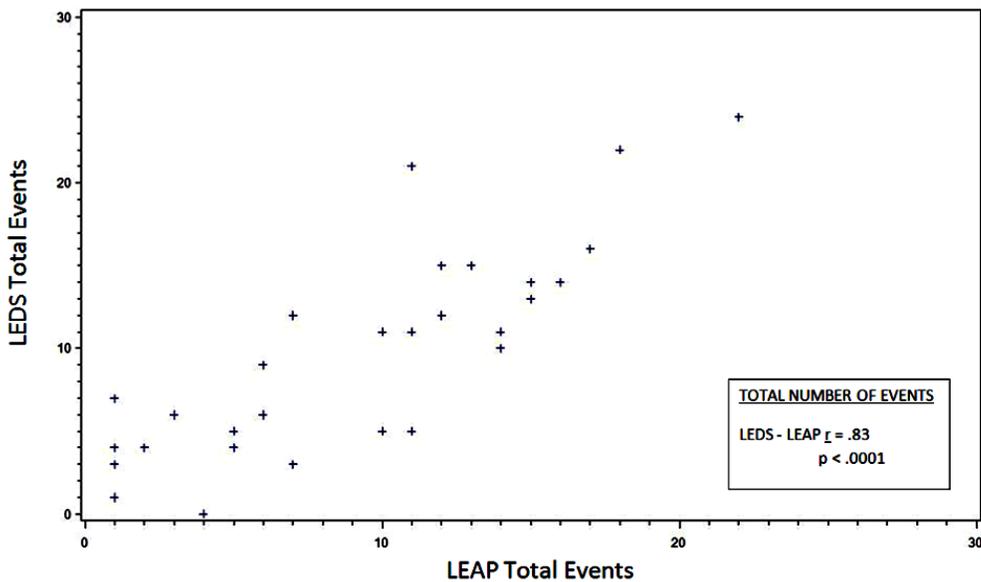
Data Analysis

Data quality was continually monitored throughout the data collection period. We have developed scoring protocols and algorithms for the paper-based version of the LEAP. We are still in the data analysis phase and anticipate this to be complete by 12/31/10.

Table 1. Race by Gender

| RACE | Gender | | Total (Percentage) |
|------------------------|------------|------------|-----------------------|
| | Male | Female | |
| White (Non-Hispanic) | 23 | 30 | 53 (54) |
| African American | 15 | 27 | 42 (42) |
| Asian | 0 | 1 | 1 (1) |
| Other | 0 | 3 | 3 (3) |
| Totals (Percentage) | 38 (38) | 61 (61) | 99 (100) |

Figure 1



Research Project 5: Project Title and Purpose

The Effect of Sleep Deprivation on Acute Stress and Emotional Reactivity - Sleep deprivation and stress are both associated with negative health outcomes and negative emotional responses. Few studies, however, have examined the incremental effect of stress under sleep-deprived conditions. The purpose of this project is to investigate the synergistic effect of stress and sleep deprivation by examining stress reactivity and emotional reactivity in healthy adults under both normal sleep and sleep-deprived conditions. The project also will examine the associations between stress reactivity and emotional reactivity. The ultimate goal of this research is to develop therapeutic and preventive strategies to reduce the psychiatric and physical consequences of sleep loss.

Duration of Project

7/1/2007 - 12/31/2009

Project Overview

Sleep plays an integral role in health and functioning. Sleep deprivation (SD) adversely affects systemic processes as diverse as immune function, endocrine activity, and glucose metabolism. The most well-documented effects of SD in humans are those on neurobehavioral function. The brain regions most sensitive to sleep loss are the prefrontal cortex (PFC), with corresponding impairments observed in PFC-associated executive functions. Even brief periods of SD are associated with impaired vigilance and cognition. However, another prominent effect of SD—the adverse effect of SD on mood and emotion (affect) regulation—has been less thoroughly explored in the experimental literature. SD is likely to have an effect on emotional function, given that PFC is strongly interconnected with brain structures linked to affect, like the amygdala. Conceivably, functional impairments in both cognition and affect associated with SD would have negative repercussions for a sleep-deprived individual when faced with environmental challenges that lead to stress. Stress increases inflammatory processes and has adverse effects on cardiovascular and immunological function. SD is also associated with proinflammatory responses, cardiovascular and immune system dysfunction, and emotional dysregulation. Understanding relationships between sleep, emotion regulation, and stress may reveal important pathways by which sleep disturbances lead to psychiatric disorders and other medical morbidities. The general aims of this project are to examine the additive, synergistic effects of sleep deprivation and stress and to explore mind-body relationships between stress reactivity and emotional reactivity. SD can be employed under strict experimental control conditions and offers a unique model to probe mind-body interactions involved in the generation of and recovery from stress. A two-condition (normal sleep, sleep deprivation) within-subject randomized crossover design will be used to assess the influence of SD on emotional reactivity and stress reactivity in healthy young adults. Stress reactivity will be examined by assessing physiological reactions to an acute stressor. Cardiovascular (blood pressure, heart rate variability), proinflammatory (the cytokine Interleukin-6 and C-Reactive Protein), and hormonal (cortisol) responses to psychological stress will be examined. The time course of psychophysiological reactivity (pupil dilation and heart rate variability) responses to emotional

pictures and sounds using methods previously developed and tested in sleep-deprived individuals will be used to examine emotional reactivity.

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Expected Research Outcomes and Benefits

The research project will examine both stress and emotional reactivity under normal sleep and sleep-deprived conditions. The hypothesis is that sleep deprivation will magnify both acute stress and emotional reactivity. If true, it suggests that educational or behavioral interventions that prevent sleep deprivation could buffer the adverse health outcomes associated with stress. Developing new ways to reduce the effect of stress on health is of tremendous public health significance. Sleep deprivation is an important public health concern, as rates of sleep deprivation appear to be increasing in adolescents and adults. This research may also benefit smokers, because individuals who smoke tobacco exhibit poorer sleep quality than non-smokers. If sleep deprivation exaggerates emotional reactivity and stress responses, it may provide further evidence for how smoking contributes to adverse health outcomes. Information obtained by this project may, therefore, be of particular relevance to alleviate some of the adverse effects of tobacco use.

Summary of Research Completed

For the past reporting period (July 1, 2009–December 31, 2009), 10 participants enrolled (i.e., completed informed consent procedures and underwent in-person screening assessments) in the study, and seven participants completed the entire study protocol (i.e., completed both the sleep deprivation and normal sleep experimental conditions). We successfully reached our targeted goal of having 20 participants complete the study protocol.

Other activities included processing and aggregating study data. All study data that were not collected electronically, including subjective ratings and blood pressure recordings, were entered into a database. Electrocardiographic data during the acute stress reactivity paradigm were processed and artifacts removed using the Mindware software suite. The analysis of blood serum samples that were collected and frozen was planned, and the assay kits were purchased.