Mobile Scalable Device: Study 1

PI: Timothy Brown
IRB ID #: 201303742

Project Details

I. Project Introduction

I.1 ***Project to be reviewed by:***
IRB-01

I.2 ***Project Title:***
Quantification of Behavioral and Physiological Effects of Drugs Using a Mobile Scalable Device: Study 1

I.3 ***Short Title (optional):***
Mobile Scalable Device: Study 1

I.4 ***Provide a short summary of the purpose and procedures of the study proposed in this IRB application.***

- ***DO NOT include information on studies not proposed in this application.***
- ***Use LAY terminology only. This must be easily understandable by IRB community members and nonscientists.***
- ***DO NOT cut and paste technical abstracts from funding applications that may not be understood by a general audience.***

The overall study is designed to characterize the effects of common recreationally used prescription drugs (as well as Cannabis) with well known stimulant and sedating effects (Xanax and Adderall) and their relationship to results from the the Mobile Alertness Memory Profiler (M-AMP) which includes a set of vigilance and memory tasks. This study will test the effect of Adderall. This study will involve twenty subjects completing the protocol with up to twenty-six enrolled. This will involve testing using EEG, EKG, computerized assessment, blood sampling, and driving simulation.

The studies involve three visits, a screening visit as well as two dosing visits. The dosing visits will have a clean (placebo)and a drugged visit. The screening visit will last about two hours and will include drug and pregnancy testing as well as screening for physical/psychological health. Each of the dosing visits will last approximately five to six hours each and will involve baseline M-AMP assessment, a baseline drive, M-AMP assessment after dosing, a dosed drive, and dosed M-AMP assessment. There will also be blood sampling before dosing, before driving, and after driving.

I.5 ***Specify your research question(s), study aims or hypotheses (do not indicate "see protocol")***
The aim of this research is to assess drug effects on driving and to explore the utility of the Mobile Alertness Memory Profiler (M-AMP) application in detecting drug effects that effect driving.

I.6 ***Background and significance and/or Preliminary studies related to this project.***
(do not indicate "see protocol")
Many commonly used drugs including prescription, over-the-counter and illicit affect cognition, judgment, reflexes, and motor skills. Drug–related impairment while driving increases the potential for injuring others and causing fatalities (Walsh, de Gier et al. 2004). An estimated 18% of deaths caused by motor vehicle accidents are due to drug use (not including alcohol), and a 2008 survey revealed that over 10 million people in the US admitted to driving while under the influence of illicit drug (USDHHS 2009). The National Highway Traffic Safety Administration's (NHTSA) 2007 National Roadside Survey reported that more than 16% of weekend, nighttime drivers tested positive for illegal, prescription, or over-the-counter medications (NHTSA 2007). The impact of driving while intoxicated is of greatest concern amongst teenagers in part because they are the least experienced drivers and thus the most vulnerable to the effects of drugs and alcohol. According to the Centers for Disease Control and Prevention, vehicle accidents are the leading cause of death among young people age 16 to 19 (CDC 2008).

Marijuana is the most prevalent illegal drug detected in impaired drivers, fatally injured drivers, and motor vehicle crash victims. Evidence from both simulation-based and real world driving studies reveal that marijuana can negatively affect a driver's attentiveness, perception of time and speed, and the ability to recall and integrate prior experience. Marijuana has been shown to slow reaction time, impair concentration, induce sleepiness and may cause blurred vision and visual distortion. Other common drugs implicated most frequently in DUI arrests and motor vehicle crash victims (in addition to alcohol) belong to one of five classes: tranquilizers (i.e. benzodiazepines) , opioids, stimulants (i.e. amphetamine, cocaine, methamphetamine, and methylenedioxymethylamphetamine a.k.a.MDMA or ecstasy), antidepressants and antihistamines (Walsh, Flegel et al. 2004).

Although drugs and alcohol levels can be assessed using breath, saliva, blood, sweat, urine and hair tests, there are currently no devices for directly assessing the neurocognitive impairments associated with drug ingestion. There is a need for devices that can be easily

administered to assess the behavioral and physiological indices of drug use and the subsequent effect on driving and other task performance. Today's ubiquitous smart phone technologies offer a potentially rich platform for data acquisition and analysis with the benefit of instant connections worldwide. An evaluation test running on a smartphone platform could be used to administer assessments in the field. Additionally, a mobile evaluation platform would provide a tool for researchers to investigate the substance type and dose associated with driving related impairment and international comparative studies of drug induced intoxication. The information acquired from such studies would be invaluable in providing objective data on which to develop legislation and regulation, as well as educating law makers, insurance and healthcare providers, and consumers on the effects of drug intoxication on driving and other performance.

The proposed work for Phase II addresses this need with the Mobile Alertness and Memory Profiler (M-AMP), a system to be developed by Advanced Brain Monitoring (ABM) to provide a quantitative assessment of neurocognitive functions including alertness, attention, and memory. ABM will leverage prior work in developing platform technologies that facilitate high throughput data acquisition and analysis for human subject studies of brain and behavior. The Alertness and Memory Profiler (AMP) is an inexpensive, non-invasive solution that combines easy acquisition of EEG, EKG and actigraphy during a simple neurocognitive assessment using a single, integrated and synchronized system. The AMP approach facilitates rapid data collection from any size population, enabling large scale epidemiological studies, disease diagnosis, or treatment outcome evaluations. The AMP multivariate approach has been is proven sensitive and specific in characterizing the drowsiness-alertness continuum (Berka, Levendowski et al. 2005; Berka, Levendowski et al. 2007), discriminating drowsiness associated with sleep deprivation versus that caused by a sleep disorder and in identifying profiles associated with several commonly used anti-depressant drugs and nicotine. The M-AMP will employ a similar approach, integrating neural, physiological and performance measures into an easy-to-administer mobile platform.

Previous investigations conducted by ABM and others suggest that the M-AMP human cognition metrics will be highly sensitive to drug-induced stimulant and depressant effects. Many studies have evaluated EEG correlates of drug ingestion using EEG recorded from subjects that were passively resting with eyes closed and/or eyes open. More recent work reveals that EEG recorded concomitantly with cognitive tasks offers a rich source of data using a combination of EEG and performance metrics derived from the task (Gevins and Smith 1999; McEvoy, Smith et al. 2000; Berka, Levendowski et al. 2005; Berka, Levendowski et al. 2006; Berka, Ayappa et al. 2009). Multivariate analysis of EEG and performance metrics acquired during vigilance, attention, and memory tasks have been useful in distinguishing between alertness and drowsiness, mild, moderate and severe cognitive impairment and intoxicated states resulting from drug or alcohol ingestion (Gevins and Smith 1999; McEvoy, Smith et al. 2000; Berka, Levendowski et al. 2005; Berka, Levendowski et al. 2006; Berka, Ayappa et al. 2009).

The AMP system initially ran on a PC and acquired data that can be used to establish profiles associated with either stimulant or depressant drug ingestion providing an estimate of the level of intoxication. In Phase 1, the M-AMP was designed to run on a smart phone platform to facilitate the collection of epidemiological data on drug use patterns that could be easily applied to roadside evaluations worldwide.

In Phase 2 the M-AMP will be evaluated in combination with validated driving simulation protocols developed and tested at the University of Iowa. The team will also explore the utility of the M-AMP determining which substances impair driving-related behaviors with significantly powered human subject studies.

The current AMP includes: a) easily applied wireless acquisition of EEG, EKG, and optional respiration, GSR, and eye tracking; b) computerized subjective questionnaires that are autoscored and uploaded to the database; c) two preliminary report outputs; d) automated data quality evaluation with specific troubleshooting tips (e.g. an electrode needs to be reapplied or excessive EMG is identified indicating movement). Additional features include: allowing users to adjust AMP protocols and duration, automated self-report administration, and data quality procedures (60 s signal/artifact and impedance check). Multiple options for monitoring EEG quality were developed based on customer input, including simplified feedback to identify channels with significant data loss or instructing to restart a task if there is excessive data loss. Supplemental features include audio alerts, simplified user instructions and practice tests to ensure training-to-criterion on each of the AMP tasks.

Additional details about the M-AMP tasks are included in the AMP Task Details attachment.

I.7 ***Literature cited / references (if attaching a grant or protocol enter N/A).***
N/A

II. Research Team

II.1 ***Principal Investigator***

Name	E-mail	College
Timothy Brown	timothy-l-brown@uiowa.edu	College of Engineering

II.2 ***Team Members***

UI Team Members

Name	E-mail	College	Contact	Key Prsn	UI COI	VAMC COI	Consent Process Involvement	Activity Location	Subjects consented	Deactivated

Timothy Brown, PHD	timothy-l-brown@uiowa.edu	College of Engineering	Yes	Yes	No	Yes		No
Gary Gaffney, MD	gary-gaffney@uiowa.edu	Roy J. & Lucille A. Carver College of Medicine	No	Yes	No	Yes		No
David Kramer, BA, CCRC	david-kramer@uiowa.edu	College of Engineering	Yes	No	No	Yes		No
Gary Milavetz, BS, PharmD	gary-milavetz@uiowa.edu	College of Pharmacy	No	Yes	No	Yes		No
Andrew Spurgin, PharmD	andrew-spurgin@uiowa.edu	College of Pharmacy	No	No	No	Yes		No

Non-UI Team Members

Name	Institution	Location	FWA	Role	DHHS Contact	Key Prsn	UI COI	VAMC COI	Consent Process Involvement	Activity Location	Subjects consented
Nothing found to display											

II.3 ***The Principal Investigator of this study is:***
Staff

II.6 ***Identify the key personnel. The system will automatically designate the PI and all faculty members on the project as "key personnel." For information about other team members who should be designated as "key personnel" please click on the help information.***

Name	Is Key Personnel
Timothy Brown, PHD	Yes
Gary Gaffney, MD	Yes
David Kramer, BA, CCRC	No
Gary Milavetz, BS, PharmD	Yes
Andrew Spurgin, PharmD	No

III. Funding/Other Support

III.1 ***Funding Sources***

Type	Source	Grant Title	Name of PI on Grant	Status	Status Description
Federal Agency	US Department of Health & Human Services, National Institutes of Health	Quantification of Behavioral & Physiological Effects on Drugs Using a Mobile Scalable Device	Chris Berka	Awarded	

* new source name

III.2 ***Which office will process the agreement for this project***
Sponsored Programs - Federal/State/Local Agency Funded

III.3 ***Does any member of the research team have a financial conflict of interest related to this project according to the Conflict of Interest in Research policy? If yes, please indicate which members below.***

Name	Has Conflict of Interest	SFI	FCOI	Management Plan
Timothy Brown, PHD	No			
Gary Gaffney, MD	No			
David Kramer, BA, CCRC	No			
Gary Milavetz, BS, PharmD	No			
Andrew Spurgin, PharmD	No			

III.5 ***What is the current status of this funding source?***

Source	Status	Other Status Description

IV. Project Type

IV.1 ***Do you want the IRB to give this project***
Regular (expedited or full board) review

IV.2 ***Enter the date you will be ready to begin screening subjects/collecting data for this project.***
06/01/2013

IV.3 ***Are you requesting a waiver of informed consent/authorization (subjects will not be given any oral or written information about the study)?***
No

V. Other Committee Review

V.1 ***Does this project involve any substance ingested, injected, or applied to the body?***

- ***Do not answer yes, if the involvement includes a device, wire, or instrument***

Yes

V.1.a ***What is/are the substance(s):***
Adderall (amphetamine and dextroamphetamine)

V.2 ***Are any contrast agents used for any purpose in this study?***
No

V.4 ***Are all drugs or substances in this study being used within the FDA approved population (i.e., children, adults)?***
Yes

V.5 ***Are all drugs or substances in this study being used within the FDA approved indication (i.e., disease, condition)?***
No

V.6 ***Are all drugs or substances in this study being used within the FDA approved dose?***
Yes

V.7 ***Are all drugs or substances in this study being used within the FDA approved route of administration?***
Yes

V.8 ***Drugs Used In Study:***

Amphetamine/dextroamphetamine (Adderall)

Name of Sponsor

Investigator's Brochure Version

Investigator's Brochure Date

Planned Use in this Study

Condition/Disease Indication(s)	Normal/Healthy
Subject Population	18-40 Normal/Healthy
Dose(s)	30mg
Administration	Oral
Dosing Regimen	1 time use

FDA Approved Use

Approved Condition/Disease Indication(s)	ADHD
Approved Patient Population	12-65
Approved Dose(s)	10,20,30,40
Approved Administration	Oral

Approved Dosing Regimen	Daily
Is this study intended to be reported to the FDA as a well-controlled study in support of a new indication or a significant change in the labeling for this product?	No
Is this study intended to support a significant change in the advertising for this product?	No
Does this planned use of the product in this study, taking into consideration the route of administration, the dosage level, and the subject population, significantly increase the risk (or decrease the acceptability of the risk) associated with the use of this product?	No
Rationale:	The intention of this study is not to test any indications or efficacy of the medication being used.

V.9 ***Will any subject be asked to undergo a diagnostic radiation procedure (including radiographic, nuclear medicine, DEXA)?***
No

V.14 ***Will any subject be asked to undergo a radiation therapy procedure (including external beam therapy, brachytherapy, or nuclear medicine therapy)?***
No

V.20 ***Does this project involve the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research participant?***
No

V.21 ***Will any portion of this project be conducted in the CRU, or does it use any CRU resources?***
No

V.22 ***Will this project use any resource/patients of the HCCC?***
No

V.23 ***Will any part of this project be conducted on VAMC premises?***
No

V.24 ***Does this project involve VAMC patients or records?***
No

V.25.a ***Will the study involve <u>any</u> of the following activity at UI Health Care, even if subjects or their insurance will not be billed for the item or service, and regardless of the study funding source (including studies with departmental or no funding)?***
(for studies conducted entirely at the VAMC, the answer to this question is "no")

- ***Procedures, tests, examinations, hospitalizations, use of Pathology services, use of clinic facilities or clinical equipment, or any patient care services, including services conducted in the Clinical Research Unit; or***
- ***Physician services or services provided by non-physicians who are credentialed to bill (ARNPs, Physician Assistants, etc.)***

No

V.26 ***The study involves nursing, nursing resources or evaluates nursing practices.***
No

VI. Subjects

VI.1 ***How many adult subjects do you expect to consent or enroll for this project?***
26

VI.2 ***What is the age of the youngest adult subject?***
18.0

VI.3 ***What is the age of the oldest adult subject?***
40.0

VI.4 ***What is the percentage of adult male subjects?***
50

VI.5 ***What is the percentage of adult female subjects?***
50

VI.6 ***How many minor subjects do you expect to consent or enroll for this project?***
0

VI.13 ***Describe EACH of your subject populations***

- ***Include description of any control group(s)***
- ***Specify the Inclusion/Exclusion criteria for EACH group***

A total of twenty subjects are needed to complete study. It is anticipated that up to twenty-six will need to be enrolled to reach this target. Although an equal sample of males and female subject are desired for completing this study, some imbalance will be allowed. Subject progress will be tracked via an accountability spreadsheet. Recruitment effects will be modified based on the number of each gender enrolled and the number of each gender completed. For example, if five male subjects and only two females subjects have completed, recruitment efforts will be focused primarily on females.

No control group will be used for this study.

Inclusion Criteria:
Men and women 18 to 40 years of age in good health
Valid US driver's license and have been licensed driver for two years
Restrictions on driver's license limited to vision correction only
Drive at least 5,000 miles per year
Must be able to attend two morning daytime study visits lasting approximately 5 to 6 hours.
Live within 1 hour driving radius of NADS

Exclusion Criteria:

Females who are pregnant or test positive for pregnancy or lactating.
Any known sleep disorders, or family history of sleep disorders
Any neurological or pulmonary disorders (or taking medications for such)
Any psychiatric disorder (or taking medications for such)
Any eating disorder
Diagnoses of myasthenia gravis, glaucoma,hyperthyroidism, or cirrhosis of the liver
Regular use of pain medications other than OTC
Recent (past 5 yr) head injury, or older head injury with current symptoms
High blood pressure, Heart disease, diabetes, or history of stroke or taking medications to treat
Any known behavioral or attention disorder (or taking medications for such)
Untreated/Untreatable vision or auditory issues (because testing requires both of these senses at this time).
Seasonal allergies/taking allergy medications of any type
Excessive tobacco use (i.e. more than 10 cigarettes a day)
Excessive alcohol (20 or more drinks per week)
Excessive caffiene use (5 or more servings per day)
Any medication use that in causes drowsiness or is contraindicated for driving.
Prescribed MAOI's
Propensity to motion sickness (one single mode of transportation is high and present or more than 2-3 episodes where intensity is moderate or above)

VI.14 ***Provide an estimate of the total number of subjects that would be eligible for inclusion in each of your study populations (include your control population if applicable)***
There are approximately 133,000 people that reside in Johnson County Iowa. It is estimated that approximately 45% of the population is between the ages of 18 and 40. This would give us approximately 60,000 people in Johnson County that would be eligible for participation. Taking into account the inclusion and exclusion criteria, even if 75% were not eligible, that would still leave a study population from which to recruit of 15,000 which would provide a sufficient population from which to recruit.

Additionally, we will focus additional recruitment efforts in the Cedar Rapids Metropolitan Area(258,000), the Davenport-Moline-Rock Island Metropolitan Area (381,000), and in West Liberty (3,750). Assuming similar age and eligibility estimates as used for Iowa City, this would add another 72,000 from the population from which we will be recruiting.

VI.15 ***Describe how you will have access to each of your study populations in sufficient number to meet your recruitment goals.***
The primary recruitment tool to access the study population required for the main study will be the NADS database. A database query of the prospective age groups of people will be completed. From this query, a list of names will be generated. Emails will be sent out with study information to those with valid addresses while others will be called. Phone screenings will be conducted to determine if potential subjects meet study criteria.

In an effort to recruit a variety of racial/ethnic groups for this study, efforts will be focused in several ways to improve enrollment:
1) An intensive recruitment effort in larger population centers within a 1 hour drive to the research facility (Davenport, IA and Cedar Rapids, IA) which have more diverse demographics
2) An effort to recruit in a population area known to have a higher concentration of a particular ethnicity (West Liberty, IA)
3) A direct appeal to adult associations of certain ethnicities
a. Latino Service Providers
b. Iowa Asian Alliance
c. Iowa Chapters of the NAACP

VI.16 ***Do you plan to recruit/enroll non-English speaking people?***
No

VI.18 ***Do you propose to enroll any of the following in this study as subjects?***

- ***Employee of the PI or employee of a research team member***
- ***Individual supervised by PI or supervised by member of research team***
- ***Individual subordinate to the PI or subordinate to any member of the research team***
- ***Student or trainee under the direction of the PI or under the direction of a member of the research team***

No

VI.20 ***Will subjects provide any information about their relatives?***
No

VI.23 ***Will anyone (other than the subject) provide you with information about the subject (e.g. proxy interviews)?***
No

VI.26 ***Is this project about pregnant women?***
No

VI.27 ***Will this project involve fetuses?***
No

VI.28 ***Does this project involve adult subjects who may be incompetent or have limited decision-making capacity on initial enrollment into the study?***
No

VI.32 ***Does this project involve subjects whose capacity to consent may change over the course of the study?***
No

VI.37 ***Does this project involve prisoners as subjects?***
No

VII.A. Project Description (A)

VII.A.1 ***Where will project procedures take place (check all that apply)?***

- Other UI campus site - NADS, University Research Park

VII.A.2 ***Is this project also being conducted by other researchers at their own sites (e.g. a multi-site collaborative project)?***
No

VII.B. Project Description (B)

VII.B.1 ***Does this project involve any of the following:***

- ***clinical intervention***

- ***pharmacologic intervention***
- ***therapeutic intervention***
- ***physiology studies (e.g. studying the functions of organs, tissues, or cells)***

Yes

VII.B.2 ***Does this project involve a drug washout (asking subject to stop taking any drugs s/he is currently taking)?***
No

VII.B.6 ***Will any subjects receive a placebo in this study when, if they were not participating, they could be receiving an FDA-approved treatment for their condition?***
No

VII.B.11 ***Is there a separate, written protocol that will be submitted in addition to this IRB New Project form? (Note: a grant application is not considered to be a protocol)***
No

VII.B.18 ***Does this project involve testing the safety and/or efficacy of a medical device?***
No

VII.C. Project Description (C)

VII.C.1 ***Does this project involve any research on genes or genetic testing/research?***
No

VII.D. Project Description (D)

VII.D.1 ***Check all materials/methods that will be used in recruiting subjects (you will need to attach copies of all materials at the end of the application):***
- Posters -
- E-mail -
- Website - drivingstudies.com www.nads-sc.uiowa.edu
- Existing Registry/database - NADS database

VII.D.8 ***Will a member of the research team discuss the study with the subject in person prior to the subject agreeing to participate?***
Yes

VII.D.9 ***Describe the physical location where the consent process will take place:***
Informed consent will take place at the National Advanced Driving Simulator in the University of Iowa Research Park before any study procedures are conducted.

VII.D.10 ***Will a member of the research team discuss the study with the subject by phone prior to the subject agreeing to participate?***
Yes

VII.D.11 ***Describe:***
All potential subjects will be contacted by phone and study staff will conduct a phone screening which includes an overview of the study, inclusion/exclusion questions before a study appointment will be made.

VII.D.12 ***Who will be involved in the consent process (including review of consent document, answering subjects' questions)?***

Name	Consent Process Involvement
Timothy Brown, PHD	Yes
Gary Gaffney, MD	Yes
David Kramer, BA, CCRC	Yes
Gary Milavetz, BS, PharmD	Yes
Andrew Spurgin, PharmD	Yes

VII.D.15 ***Check all materials that will be used to obtain/document informed consent:***
- Consent Document

VII.D.16 ***Are you requesting a waiver of documentation of consent (either no subject signature or no written document)?***
No

VII.D.19 ***Before the subject gives consent to participate are there any screening questions that you need to directly ask the potential subject to determine eligibility for the study?***
Yes

VII.D.20 ***List any screening questions you will directly ask the potential subject to determine eligibility.***
Inclusion:
1) Do you possess a valid U.S. Drivers' License?
2) How long have you been a licensed driver?
3) What restrictions do you have on your license?
4) How many miles do you drive per year?
5) Do you require any special equipment to help you drive such as pedal extensions, hand brake or throttle, spinner wheel knobs or other non-standard equipment?

6) How old are you?

7) How far do you live from University of Iowa Research Park which is North of the Coral Ridge Mall?

8) Are you able to attend three study visits with one being approximately 45 minutes and two visits of approximately 5-6 hours?

Exclusion:
1) Females:Are you pregnant or lactating?
2) Do you have or have you been diagnosed with a sleep disorder, or do you have a family history of sleep disorders?
3) Do you have a neurological or pulmonary disorder or are you taking medications to treat such a disorder?
4) Have you been diagnosed with a psychiatric disorder or are you taking medications to treat such a disorder?
5) Do you have an eating disorder?
6) Do you regularly use prescription pain medication?
7) Have you had a head injury within the past five years, or are you still experiencing symptoms from a prior head injury?
8) Do you have a history of high blood pressure, heart disease, diabetes or stroke, or are taking medications to treat these conditions?
9) Do you have a behavioral or attention disorder or take medications to treat these conditions?
10) Do you have untreated or untreatable vision or auditory conditions?
11) Do you have seasonal allergies, or take medication to treat any type of allergies?
12) Do you smoke more than 10 times per day?
13) Do you have twenty or more alcoholic beverages per week?
14) Do you consume 5 or more servings of caffeinated beverages per day?
15) Do you use illicit drugs or taken prescription medications that were not prescribed for you?
16) Are you currently taking any prescription or over the counter medications?
17) Do you experience any kind of motion sickness?
18) Have you ever been diagnosed with any of the following: myasthenia gravis, glaucoma, or cirrhosis of the liver?

VII.D.21 ***Will you keep a screening log or other record that would include information on people who do not enroll in the study?***
No

VII.D.25 ***After the subject agrees to participate (signs consent), are there any screening procedures, tests, or studies that need to be done to determine if the subject is eligible to continue participating?***
Yes

VII.D.26 ***List and describe screening***
Screening visit:All subjects will first provide a urine specimen which will be screened for 10 types of drugs; methamphetamine, morphine/opiates, cocaine, marijuana, PCP, amphetamine, tricyclic antidepressants, benzodiazepines, barbiturates, methadone. Female subjects' urine specimen will be screened for pregnancy. If subject's drug screen is positive for a contraindicated drug, or a female screens positive for pregnancy, the subject will be excluded from continuing in the study and paid for their time and effort.

Subjects will have their height and weight recorded

Subjects will undergo a physical and psychological examination conducted by a medical professional.

Subjects will fill out a questionnaire on their driving history.

Subject will watch a PowerPoint slide show on the simulator

If subject drives the simulator and scores on Wellness survey indicate a potential for simulator sickness, the subject will be excluded

from continuing in the study and paid for their time and effort.

Subjects will have the B-ALERT® EEG Wireless Sensor Headset placed on their head and complete a 45 minute Mobile Alertness Memory Profiler (M-AMP) Assessment

VII.D.27 ***Discuss how much time a potential subject will have to agree to consider participation and whether or not they will be able to discuss the study with family/friends before deciding on participation.***
Subjects will be provided with an overview of the study procedures via phone, typically within 1 week before the study visit, which should provide them ample time to discuss their participation with family/friends before participating. Also, subjects will be provided with a study contact name and number to call to discuss any study procedures prior to study visit.

VII.D.28 ***How long after the subject agrees to participate do study procedures begin?***
1 to 2 weeks depending on study schedule

VII.D.29 ***Provide a description of the enrollment and consent process for adult subjects***

- ***Describe each study population separately including control population***
- ***Include when recruitment and consent materials are used***
- ***Use 3rd person active voice "The Principal Investigator will identify subjects. For example, the principal investigator will identify potential subjects, the study coordinator will discuss the study with subjects over the telephone and schedule the first study visit, etc..."***
- ***Describe the steps that will be taken by the research team to minimize the possibility of coercion or undue influence during the consent process***

This study does not involve a control group. The study population consists of healthy men and women ages 18-40, gender balanced, and meet the study inclusion/exclusion criteria.

Prospective subjects will be identified using the NADS participant database and outreach to underrepresented populations. An approved email will be sent to eligible subjects or contacted via telephone. Potential subjects will have access to websites that can be used to show their interest: www.drivingstudies.com and www.nads-sc.uiowa.edu. Both sites will have approved website script located on website. The approved email will be sent to UI faculty and staff and students if other measures do not meet study requirements. Additionally, fliers will be distributed to help increase minority enrollment.

Once subjects have expressed interest in participating, they will be recruited via phone and, we, the study staff, will inform the subject of the study procedures and time commitment. Then, we the study staff, will determine if the potential subject meets initial study criteria by asking the inclusion/exclusion criteria questions over the phone. These questions ask potential subjects about their driving qualifications, health history, current health status, medications used (MSD_Screening Procedures). Answers from the Screening Procedures will not be recorded except the question asking the potential subject about their susceptibility to motion sickness which could exclude them from participating in the study. If subject meets the inclusion/exclusion criteria, we, the staff will appoint subject for study visit. A copy of the approved Informed Consent document will be available to subjects if requested prior to first study visit when consent will be obtained.

We, the study staff, will consent subjects at The National Advanced Driving Simulator, located on the UI Research Park. We, the study staff, will verbally explain the purpose and procedures involved in the study and answer questions subjects may have about their participation. Following verbal review of the informed consent, the subject will be asked to thoroughly read the informed consent document and we, the study staff, will answer any further questions about the subject's participation in the study. Ample time will be allowed for subjects to ask questions to us, the study staff, about the study and their participation. The subject will be considered enrolled into the study once they have signed the Informed Consent Document. A copy of the signed informed consent document will be provided to each subject and the original will be maintained by NADS.

VII.D.37 ***Does the study include any form of deception (e.g., providing participants with false information, misleading information, or withholding information about certain study procedures)?***

Examples:

- ***Procedure includes a cover story that provides a plausible but inaccurate account of the purposes of the research.***
- ***Participants will be provided with false information regarding the particular behaviors of interest in the research.***
- ***Procedures include a confederate pretending to be another participant in the study.***
- ***Participants will be told that the research includes completion of a particular task, when in fact, that task will not be administered.***
- ***Study is designed to introduce a new procedure (or task) that participants are not initially told about.***
- ***If yes, a waiver of informed consent must be requested under question IV.3.***

No

VII.E. Project Description (E)

VII.E.1 ***Will subjects be randomized?***
Yes

VII.E.1.a ***Will any subjects be blinded to which study arm they have been assigned?***
Yes

VII.E.1.b ***Does the protocol permit telling subjects their treatment assignment at the end of the entire study?***
Yes

VII.E.1.c ***Describe the circumstances under which subjects will be told what study arm they have been assigned.***
Subjects can be told what conditions they were assigned to after the blinding has been broken after analysis.

VII.E.2 ***Describe randomization scheme/assignment including ratio such as 1:1, 2:1 etc.***
All subjects will complete a "sober" session where they receive the placebo and a "dosed" session where they receive the adderall. Half of the population will be randomly assigned to each of the following orders:
* First visit: sober, Second visit: dosed
* First visit: dosed, Second visit: sober

Randomization will occur after the screening visit.

VII.E.3 ***Will any questionnaires, surveys, or written assessments be used to obtain data directly from subjects in this study?***
Yes

VII.E.4 ***List all questionnaires, surveys, written assessments and ATTACH each one to the application. (NOTE: You are NOT prohibited from attaching copyrighted materials to this application)***
MSD_DrivingSurvey - A questionnaire that asks questions about demographic information, driving record, driving behavior, and driving history

MSD_Wellness - Asks questions how subject is feeling

MSD_Realism-Asks questions about how realistic the subject viewed the simulator and simulation.

MSD_SSS - Stanford Sleepiness Scale - survey about current sleepiness level

MSD_SFI - Sleep and Food Intake - a questionnaire about sleep and food intake over the last 24 hours

MSD_PhoneScreening_Adderall - A screening instrument that will be used to identify those with potential sleep apnea that would be excluded.

VII.E.5 ***Does this project involve creating any audiotapes, videotapes, or photographs?***
Yes

VII.E.6 ***Provide a detailed description in sequential order of the study procedures following the consent process - DO NOT cut and paste from the Consent Document.***

Describe study populations separately if they will be participating in different procedures - include CONTROL population if applicable.

DESCRIBE:

- ***What subjects will be asked to do/what happens in the study (in sequential order)***
- ***The time period over which procedures will occur***
- ***The time commitment for the subject for individual visits/procedures***
- ***Long-term followup and how it occurs***

Subjects will be asked to complete 3 study visits, one screening visit of approximately 2 hours in length, two daytime study drive visit approximately 5 to 6 hours in length starting at 8:00 am.

Screening Visit

Subjects will first complete a screening visit. They will be asked to provide a urine sample and a urine drug screen test will be performed. Female subjects' urine specimen will additionally be tested and screened to determine if they are pregnant. Results from the drug screen, and for females, pregnancy test will remain confidential and their eligibility status will be documented as either a yes or no. Subject participation will end if their drug screen test is positive, and if female, they test positive for pregnancy. Subjects height and weight will be recorded. A questionnaire that asks questions about demographic information, their driving record, driving behavior, and driving history (MSD_DrivingSurvey) will be completed. Subjects who fail to meet study criteria, will be paid for their time and effort. If subject meet criteria,

subjects will watch an overview presentation of the simulator cab and staff will train them on an in-vehicle tasks. Subjects will drive the simulator for about 5-8 minutes. This drive allows the subjects a chance to become comfortable with driving the simulator. After the practice drive, subjects will fill out a questionnaire about how they feel(MSD_Wellness). If the MSD_Wellness indicates a high propensity for simulator sickness, subjects will be excluded from continuing in the study and paid for their time and effort. If they can continue, subjects will have the B-ALERT® EEG Wireless Sensor Headset(MSD_B-alert X-10.pdf)that wirelessly records brain activity for nine channels, and ECG from leads placed on the lower left chest and right collarbone. They will then complete a 45 minute Mobile Alertness Memory Profiler (M-AMP) Assessment, which involves three tests. The first is a multiple choice vigilance task that requires the subject to identify a predetermined target from amongst three objects. The second is task is divided into and eyes open task and an eyes closed task. The eyes open task requires the subject to press a button each time an image appears on the screen. They eyes closed task requires the subject to press a button each time you hear an auditory tone. The third task is an image recognition task in which the subject will be presented a set of images and then asked to indicate whether images from another set were in the original set they were shown. Then staff will confirm the next two study visits and ask subjects to arrange for third party transportation to and from NADS on both study visit days. In the event that the subject cannot arrange for third party transportation, taxi transportation or transportation by NADS staff will be arranged by study staff at no cost to the participant.

Study Visits:

On arrival, staff will first collect a urine sample to test for illicit drug use and pregnancy. Subjects will then complete a sleep and food intake questionnaire (MSD_SFI) and will also complete a questionnaire about their current sleepiness level (MSD_SSS). If subject meets study criteria (had 7-9 hours of sleep) a baseline 4mL blood sample will be obtained by a medical professional using an individual needle poke. Subjects will then be fitted with the B-ALERT® EEG Wireless Sensor Headset. This device is a non-intrusive wireless recording device that is worn on subjects' head. After being escorted to the prep room, the subject will be administered a 30mg dose of Adderall or a placebo, and rest for 30 minutes before completing the M-AMP assessment. A medical professional will obtain a second blood sample of 4 ml by individual needle stick. The subject will be asked to complete the Stanford Sleepiness Scale (MSD_SSS) questionnaire again about their current sleepiness level. The subject will be escorted to the simulator where any questions will again be answered. The subject will complete a 35 minute drive. The study drive consists of 3 segments, each 10 minutes in length which includes urban, freeway, and rural roadways. After the drive subjects complete questionnaires about how they feel (MSD_Wellness) and about the simulator(MSD_Realism). A third and final blood sample of 4 ml will be obtained by the medical professional via individual needle poke. The blood samples will later be analyzed to assess the pharmacokinetics of the drugs relative to each participant. If this is the second visit, the date for the final visit will be confirmed. If it is the third visit, payment will be finalized.

No follow-up for this study.

The driving trials will be recorded using a digital video tapes/camera that will record the driver and the drivers interaction with the simulator. The video will play a role in verifying reduced simulator data. The video will not be destroyed but will be stored in locked archive room along with other data.

VII.E.7 ***Will you attempt to recontact subjects who are lost to follow-up?***
No - followup is not required in this study

VII.E.9 ***Will subjects be provided any compensation for participating in this study?***
Yes

VII.E.10 ***Cash***
No

VII.E.11 ***Gift Card***
No

VII.E.12 ***Check***
Yes

VII.E.13 ***Who will be providing the research compensation check to the subject?***
Accounting Services directly via the e-Voucher system

VII.E.16 ***Other***
No

VII.E.19 ***Describe the compensation plan including***

- ***Compensation amount and type per visit***
- ***Total compensation***
- ***Pro-rating for early withdrawal from study***

Screening visit: $25

1st dosing visit: $115

2nd dosing visit: $135

If participants are unable to complete procedures at a visit they will be paid for any past visits as well as be compensated $10 for every half hour with a $10 minimum.

VIII. Risks

VIII.1 ***What are the risks to subjects including***
- emotional or psychological
- financial
- legal or social
- physical?
The risk involved driving the simulator is possible discomfort associated with simulator disorientation. Previous studies with similar driving intensities and simulator setups have produced few disorientation effects. When effects were reported, they are usually mild to moderate and consisted of slight uneasiness, warmth, or eyestrain for a small number of subjects. These effects are believed to last for only a short time, usually 10-15 minutes, after leaving the simulator. Subjects may quit driving at any time if they are experiencing any discomfort.

Side effects associated with the study medications may include:

Adderall: Cardiovascular problems such as heart attack, stroke, high blood pressure, hypertension and arrhythmia. Symptoms of psychosis may occur, such as aggression, psychosis and mania, or hallucinations. Given that the study only administers one 30mg pill, and subjects will be screened for contra-indications, these symptoms are not likely to occur.

Blood Draws: The risk of blood sampling is pain, tenderness, bruising, or bleeding at the needle puncture site, and transient lightheadedness or dizziness.

Some people may find the use of the EEG gel unpleasant as it needs to be washed out of the hair after the procedure is complete.

Loss of confidentiality is always a risk.

VIII.2 ***What have you done to minimize the risks?***

- ***If applicable to this study ALSO include:***
  - ***How you (members of your research team at Iowa) will monitor the safety of individual subjects.***
  - ***Include a description of the availability of medical or psychological resources that subjects might require as a consequence of participating in this research and how referral will occur if necessary (e.g. availability of emergency medical care, psychological counseling, etc.)***

If a subject asks to quit driving as a result of discomfort, they will be allowed to quit at once. If a subject does quit driving due to discomfort, they will be escorted to a room, asked to sit and rest, and offered a beverage and snack. A trained staff member will determine if and when the subject will be allowed to leave. If the subjects shows few or no signs of discomfort, they will be transported home. If the subject experiences anything other than slight effects, a follow-up call will be made 24 hours later to ensure the subject is not feeling ill effects.

Female subjects who participate in the study will be required to provide urine for a pregnancy test and at phone screening it will be suggested to all females that if it is possible that they may be pregnant they should not enroll into this study.

To protect confidentiality, subjects will be consented in a private room and study procedures will occur in private. Additionally, the investigators have requested a certificate of confidentiality from the Department of Health and Human Services.

For the medications, dosage is consistent with general use and staff and subjects will be monitored for side effects during their visits.

VIII.3 ***Does this study have a plan to have an individual or committee review combined data from all subjects on a periodic basis (such as summary or aggregate safety and/or efficacy data)?***
No

IX. Benefits

IX.1 ***What are the direct benefits to the subject (do not include compensation or hypothesized results)?***
A subject may not benefit personally from being in this study. However, many subjects find driving the simulator of this type to be an exciting and unique experience.

IX.2 ***What are the potential benefits to society in terms of knowledge to be gained as a result of this project?***
It is hoped that in the future, other people might benefit from this study because the information gathered in this research study might benefit society from obtaining a better understanding of how to detect drugs being used by drivers. This may allow the development and refinement of new technologies that could minimize drugged driving related crashes in the future.

X. Privacy & Confidentiality

X.1 ***What are you doing to protect the privacy interests of the subjects?***
Subjects will be escorted into a private room for the consent process. All study procedures prior to and after completing simulator drive(s) will take place in a private room. All research staff involved in data collection have received certification in the human subjects protection education program. The researchers will only ask questions related to the study and will collect minimum private information needed to answer the research questions.

X.2 ***Are you collecting the Social Security Number of any subjects for any purpose?***
Yes

X.3 ***Provide the intended usage of SSN:***

- To provide compensation to subjects

X.4 ***How will information/data be collected and stored for this study (check all that apply):***

- Paper/hard copy records (hard copy surveys, questionnaires, case report forms, pictures, etc.) - Participants will be assigned a research number that staff will use during data collection, analysis, and reporting. Data, paper and biological samples wil use the participant's research number. Study documents identifying the participants to their research number will be kept in a locked cabinet within a secure building that can only be entered by personnel with a marlock key during data collection and analysis. After completion of analysis, all hard copies except the Informed Consent Documents will be scanned, placed on a CD and placed into the NADS archival room that has limited access by designated archival personnel. The original Informed Consent Documents will be stored in the NADS archival room that has limited access by designated archival personnel.
- Electronic records (computer files, electronic databases, etc.) - Electronic study data is collected and recorded onto data storage media and will be password protected and can only be accessed by investigator, study personnel, or system administrator. All videotapes and questionnaires will be locked in filing cabinets during the data analysis phase and will only be accessible by study personnel. Data will be transferred to a permanent data storage area at the end of the project where it will only be available to the funding agency, principal investigator, or research team members. Simulator data is captured and initially stored on a mirrored RAID system located within a limited access area of the NADS facility. This data is behind a hardline firewall. Access to study data is controlled through validated user login, authentication protocols and access permissions established on a per-study basis. Data backups are maintained as dual copies on physical hard drive devices. One drive is stored within a secured location on-site, and the other is stored off-site under the auspices of The University of Iowa Information Technology Services. All backup drives are inventoried and access to study data requires a request for access and authorization from a designated authority. Some surveys are designed and data collected on-line via Qualtrics. The information is saved in a password protected account on their website. Data is downloaded by UI project staff and saved on the password protected computer located at NADS. Access to our account is password protected and only the team (or Qualtrics staff only at our request) can access the survey to view or export the data. Once the survey has closed, all subject identifiers will be removed before the data is exported. The exported survey data will be stored in a separate file than the subject key. Only the members of the research team will have access to the locally stored subject key which will be saved in a password protected directory.
    - Name - Steve Cable
    - Title - Systems Administrator
    - University/VA Job Classification - Senior Systems Administrator
- Biologic samples (blood draws, check swabs, saliva samples, tissue samples, etc.) - Biologic samples (blood draws, check swabs, saliva samples, tissue samples, etc.) - Urine specimens will be collected using a sterile lidded container. After specimen has been screened, the extra urine will be discarded in toilet and sample container will be resealed and disposed into a leak proof plastic waste bag in a covered biological waste container and trained staff will dispose daily. Safe biohazardous material transport through a public area is required to prevent spills and accidental exposure. Biological specimens include, blood, plasma, serum, urine, sputum, other body fluids, biopsy tissue etc. Listed below is how this will be accomplished. Specimen to be transported must be identified by study with a label. It should be signed out by the transporter from the point of origin. 1. Place specimen in a primary container (blood tubes or conical tubes, for example) secured with a tight-fitting cap, Parafilm, or tape. 2. The primary container should be labeled with its contents. If the primary container is not labeled, documentation of the contents should be taped to the outside of the secondary container or placed inside of it. 3. Place the primary container in a secondary container with an absorbent paper towel or wipe to cushion the primary container and to absorb liquids in the event of a leak or spill. Acceptable secondary containers include plastic containers or sealable (zip lock) bags. The bag containing the primary container should be clearly marked “biohazard.” 4. The secondary container (containing the primary container) should be placed in an external carrier container. The external carrier must be labeled with a biohazard symbol and the labs contact information. The external carrier container should have an additional absorbent paper towel or wipe to cushion the secondary container and to absorb liquids in the event of a leak or spill. Upon receipt of sample it should be signed in and stored properly documenting its location within the lab.
    - Name - Kayla Smith
    - Title - Research Assistant

- University/VA Job Classification - Temp/Misc

X.5 ***Do the confidentiality protections indicated above allow only members of the research team to access the data/specimens?***
No

X.6 ***Describe***
Data will be shared with the sponsor. This data will include a full deidentified data set including the raw data files from EEG data. Reduced simulator data in an Excel spreadsheet will be shared along with coded survey data. No identifiable information linking the subject to the data will be shared with the sponsor. Data transfer will occur through the NADS password protected file exchange system.

XI. Data Analysis

XI.1 ***Describe the analysis methods you will use, including, if applicable, the variables you will analyze***
A variety of driving performance measures including speed, lane keeping, time to collision, and gap acceptance will be analyzed using the SAS general linear models procedure to verify differences in driving performance between the treatments. The planned method will be to calculate difference scores between the dosed and baseline drive for each day and to then compare changes in performance associated with the study drugs.

Driving data will also be correlated with data from the M-AMP (including reaction time and accuracy) and Stanford Sleepiness Scale.

Peripheral venous whole blood is collected from participants for analysis on three occasions on each visit –before dosing, before driving, and after driving. Blood levels for the drugs in question will be quantified.

A 3 (Drug) X 2 (Clean vs. Drug) ANOVA will also be conducted on variables found in the step-wise regressions within each study.

Finally, step-wise discriminant function and other algorithm development approaches will be explored to delineate between stimulant, depressant, and normal baseline state.

XI.2 ***Provide the rationale or power analysis to support the number of subjects proposed to complete this study.***
This study has a within subject design so that control vs drug driving performance can be compared. Based on prior research, we expect driving performance as measured by Standard Deviation of Lane Position to be 1.015 ft. We would hope to detect a 10% change in this measure. In review of the data, we expect the variability in the difference across subjects to be 0.1269. A sample of 20 would provide a power of 0.92 for a two-side paired t-test.

XII. Future Research

XII.1 ***Do you wish to keep any information about subjects involved with this research project so that members of the current research team may contact them in the future for your own research projects?***
Yes

XII.2 ***Do you wish to keep any information about subjects involved with this research project so that other researchers may contact them for future research?***
No

XII.3 ***List the data or information you will keep:***
Members of the current research team may contact subjects for future studies. Subjects that are not currently in our database will be asked to either sign up online or research staff will ask their demographic information, contact numbers, birthdate, annual mileage driven per year, whether they are a student or not, if they are a current resident, do they have a current driver's license, what is their occupation, what year did they first received their driver's license, do they drive a manual or standard transmission, use of cell phone while driving and frequency, if they drink alcoholic beverages, do they wear corrective lenses while driving and if they have any susceptibility to motion sickness. For subjects that are currently in the database but not interested in participating in the study, research staff will verify their contact numbers if they wish to be contacted for future studies.

Only Research conducted at the NADS facility as access to NADS database.

XII.4 ***Does this project involve storing any data, tissues or specimens for future research?***

Yes – contribution for future use is mandatory for participation in the study