U.S. Army Aeromedical Research Laboratory

CONSENT TO PARTICIPATE IN RESEARCH

Title of Protocol: Enhancing Operational Performance in Healthy Rested Soldiers with Pharmacological Stimulants

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Associate Investigators (AIs): Katie Feltman, Ph.D., Mike Wilson, Ph.D.

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INTRODUCTION

You are being asked to participate in this research study because you are a healthy Soldier. Your participation in this research is voluntary.

This study involves two medications: modafinil (Provigil) and a mixture of amphetamine and dextroamphetamine (Adderall [or generic substitute]). These two medications have been used in sleep-deprived (Provigil) individuals or individuals with attentional difficulties (Adderall [and generic substitute]). They are FDA-approved; however, we are using them in an investigational manner, outside of how the FDA approved the drugs. We are examining whether these medications can improve performance abilities on a variety of cognitive (memory, attention) and military tasks (marksmanship) in healthy, well-rested soldiers who do not have attention problems.

This is a double blind study, which means that neither you nor the research team will know whether you are getting the study medications or a placebo. A placebo is an inactive, harmless substance, like a sugar pill and it will look like the other study medications. You will be given all 3 medications (Provigil, Adderall [or generic substitute], placebo), but the order will be randomized through a computer program.

*** The Drug Enforcement Agency lists Adderall** (and generic substitute) **and Provigil as controlled substances with potential for abuse. If you have a history of drug abuse, you are not eligible for participation in this study.**

*** Adderall** (and generic substitute) **is an amphetamine and may be detected in a urine drug screen. If you choose to participate in this study, we will give you an SF-600 and memorandum for record to file in your medical record. It is very important that you promptly file these documents in the event of a urine drug screen.**

***The only alternative to participation is NOT to participate.**

WHY IS THIS RESEARCH BEING DONE?

This research will help us determine whether these types of medications can be used to improve the Warfighter's battlefield performance. We plan to have up to 40 individuals participate in this study.

WHAT WILL HAPPEN DURING THIS RESEARCH?

Before each test day, you will need to:

- Have 6 hours of sleep the night before each test session
- Refrain from taking over-the counter-medications which may cause drowsiness (e.g., some allergy medications, Benadryl, sleep aids, Tylenol PM or Advil PM) for a minimum of 16 hours before each test day
- Refrain from nicotine consumption for a minimum of 8 hours before each test day
- Refrain from using any stimulants including caffeine (e.g., coffee, soda), energy drinks (e.g., Monster, Red Bull), supplements (e.g., creatine, Omega-3 fatty acids, amino acids), over-the-counter nootropics (e.g., Alpha Brain) for a minimum of 16 hours before each test day.
- Refrain from alcohol consumption for a minimum of 16 hours before each test day

***It is very important that you refrain from the substances listed prior to test sessions and to tell us if you consumed any of the substances for your own safety and to protect the integrity of our research results. The study physician or medical practitioner will review a full list of substances with you prior to participation.**

If you agree to participate in this research, you will be asked to do the following things:

Session 1: (total time for this day = approximately 1 hour)

- Once you have agreed to participate and signed a copy of this consent form, you will complete a medical history and screening questionnaire then meet with the study physician. If eligible, you will be enrolled in the study.

- Next, you will be given an Actiwatch, similar to a Fitbit, to wear throughout your participation in the study, which will monitor your sleep.

- Next you will schedule 4 days for testing. 1 baseline test day and 3 experimental test days.

Session 2: (total time for this day = approximately 1.5 hours)

- Baseline testing: you will complete five questionnaires about attention disorders, sleep habits, depression symptoms, mental tasks and risk taking.

- Next you will complete six mental tasks on a computer that will look at your attention, memory, and decision making.

- You will complete a virtual reality scenario depicting a first-person patrol in Afghanistan while reporting observed improvised explosive device (IED) markers. During this task, you will use an exercise step to simulate patrol duties and elevate your heart rate. Note that your heart rate will be closely monitored during the task so as not to exceed 85% of your age-predicted maximum rate.

- Finally, you will complete a shooting task on the Engagement Skills Trainer 2000 (EST 2000), the Army's small arms training device.

Sessions 3-5: (total time for each day = approximately 8 hours)

- Experimental testing. 3 days will be scheduled with one day off in between visits (2 days off and 3 test days for a total of 5 days).

- During each of these 3 test days you will be given a typical dose of Provigil (200mg) or Adderall [or generic substitute] (10mg), or a placebo in capsule form.

- After taking the medication, you will have recreational time while it takes effect (2 hours). You will not be allowed to have any caffeine or use tobacco during this time.

- After the 2 hours rec. time, you will complete the same tasks as in Session 2 (with the exception of the survey about depression).
  For safety purposes, you will be required to stay at USAARL for 8 hours (including testing) after taking the medication for safety purposes. Once the 8 hours have passed, a study physician will meet with you to confirm that it is safe for you to be released.

It will take under two weeks to complete all sessions.

WHAT ARE THE POTENTIAL RISKS AND DISCOMFORTS FROM BEING IN THIS RESEARCH?

1. **Side effects from the medications**: There are a number of side effects possible from taking these medications. They typically occur with regular dosage over some weeks. In this study, you will be administered a single dose of each drug. For Provigil, the typical dose prescribed for adults is 200-400 mg per day and you will receive 200 mg one time. For Adderall [or generic substitute], the typical dose prescribed for adults is 20 mg/day and you will receive 10 mg. The side effects and the likelihood of occurrence for both drugs are summarized below:

Provigil and Adderall [or generic substitute] **Adverse Reactions in Placebo-Controlled Trials**

Reaction or Symptom	Frequency of occurrence
Headache, nausea, dry mouth, loss of appetite, insomnia, weight loss, nervousness	Common (10-30%)
Stuffy nose, back pain, diarrhea, anxiety, dizziness, indigestion, sore throat, chest pain, increased or decreased blood pressure, jaundice, constipation, depression, palpitation, skin tingling or numbness, sleepiness, rapid heart rate, low energy, agitation, urinary tract infection	Infrequent (>1% and <10%)
Abnormal or blurred vision, asthma, chills, confusion, fidgeting, swelling, mood changes or uncontrollable laughter/crying, inflammation, nose bleed, gas, muscle twitches or stiffness, mouth ulceration, sweating, taste perversion, thirst, vertigo, abnormal heart rhythm, hives, hallucination, painful erection, heart attack, stroke, addiction, suicidal thoughts, hepatitis, psychosis, seizure, chest pain, hair loss, kidney dysfunction, or severe skin reaction	Rare (≤1%)

- **Precautions:** While we cannot protect you from the occurrence of side effects, we can be prepared for them. One or more research technicians will be with you throughout the study. A study physician will administer the medication and will be present in the laboratory until the time you are released to go home. Investigators and technicians are certified in administering CPR (cardiopulmonary resuscitation). In the event that you need medical assistance beyond what the study physician can provide, 911 will be called.

2. **Discomfort with questionnaires**: An additional risk is that you may feel uncomfortable answering some of the questions in the questionnaire packet.

- **Precautions:** The questionnaires will ask questions related to depression and anxiety symptoms as well as substance use. You are allowed to skip any questions you do not wish to answer. If you are feeling distressed or hopeless, thinking about death or wanting to die, or, if you are concerned about someone who may be suicidal, please contact Suicide Prevention Lifeline at 1-800-273-TALK (8255). If you feel concerned about your alcohol or substance use, please contact the Army Substance Abuse Program at Fort Rucker at (334) 255-7905.

Additional safeguards: You will be given a SF-600, chronological record of medical care, documenting the dates of participation and medications administered. You can take this to Lyster and have it placed in your medical record if you choose. If applicable, you will also receive a memorandum for record signed by the PI and a study physician documenting your participation in the study, drugs administered, and the date that flight status can be reinstated.

WHAT ARE THE POSSIBLE BENEFITS FROM BEING IN THIS RESEARCH?

Your participation will contribute to the medical knowledge and scientific investigation of possible uses for these medications in a military operational setting.

WILL I HAVE TO PAY FOR ANYTHING IF I TAKE PART IN THIS RESEARCH?

You will be responsible for your own transportation to and from USAARL. You will be provided drinks, snacks, and lunch throughout the study. You may bring your own drinks, snacks, and lunch, if you would prefer, however, you will not be allowed any caffeine until after the testing session is complete.

WILL I BE PAID TO TAKE PART IN THIS RESEARCH?

You must be on approved annual leave and must show your approved leave slip to be compensated for participation in this study. You will be compensated $400 for each 8-hour experimental testing day ($1200 for all three days). It is important for you to note that you will need to report this compensation as personal income on your next income tax return.

You will receive your compensation in the form of a check that you can pick up or have mailed to you at an address you provide. Checks will be available approximately six to eight weeks following participation. A member of the research team will call you when it is ready for pick-up.

WHAT HAPPENS IF I AM INJURED AS A RESULT OF TAKING PART IN THIS RESEARCH?

If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active duty in the military, military spouse or dependent, retiree), you are entitled to medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary.

If you are injured because of your participation in this research and you are not a DoD healthcare beneficiary, you are entitled to medical care for your injury at an Army hospital or clinic; medical care charges for care at an Army hospital or clinic will be waived for your research-related injury. You are also entitled to care for your injury at other DoD (non-Army) hospitals, but such care for your injury at other DoD (non-Army) hospitals or clinics may be time-limited, and your insurance may be billed. It cannot be determined in advance which Army or DoD hospital or clinic will provide care. If you obtain care for research-related injuries outside of an Army or DoD hospital or clinic, you or your insurance will be responsible for medical expenses.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided. No reimbursement is available if you incur medical expenses to treat research-related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights. If you believe you have sustained a research-related injury, please contact the Principal Investigator (PI). If you have any questions, please contact the PI, Dr. Amanda Kelley (334-498-2456).

HOW WILL YOU PROTECT MY PRIVACY AND THE CONFIDENTIALITY OF RECORDS ABOUT ME?

The PI will keep records of your participation in the research. To protect your privacy questionnaire responses, medical screening, and performance on the mental and shooting tasks, will be labeled or “coded” with an assigned number and kept in a locked filing cabinet in a locked office. This number will not include your name or social security number. The PI will keep the link between your participant number and your research records in a locked office on a password-protected computer. The principal and associate investigators are the only people who will be able to match your research participant number with any of your personal identifying information. In the event of a medical emergency or adverse reaction, the study physician will be able to identify which medication you received.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity to others.

Authorized representatives of the following groups may need to review your research and/or medical records as part of their responsibilities to protect research participants:

- U.S. Food and Drug Administration
- U.S. Army Medical Research & Materiel Command Institutional Review Board
- U.S. Army Human Research Protections Office and other DOD offices charged with oversight of human research
- U.S. Army Aeromedical Research Laboratory Regulatory Compliance Office

Complete confidentiality cannot be promised for military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities. For example, if you indicate that you are a danger to yourself or others, you will be withdrawn from the study and escorted to the Lyster Army Health Clinic's Behavioral Health Clinic. Your chain of command would be notified in such an event.

It is the policy of the U.S. Army Medical Research and Materiel Command that data sheets are to be completed on all volunteers participating in research for entry into this Command's Volunteer Registry Data Base. The information entered into this confidential data base includes your name, address, Social Security number, study name and dates. The intent of the data base is two-fold: first, to readily answer questions concerning an individual's participation in research conducted within the USAMRMC; and second, to ensure that the USAMRMC can exercise its obligation to ensure research volunteers are adequately warned (duty to warn) of risks and to provide new information as it becomes available. The information will be stored at USAMRMC for a minimum of 75 years.

WHAT IF I DECIDE NOT TO PARTICIPATE IN THIS RESEARCH?

Your participation in this research is voluntary. You may decline to participate now or stop taking part in this research at any time without any penalty or loss of benefits to which you are entitled. Deciding not to participate now or withdrawing at a later time does not harm, or in any way affect, your future relationships with USAARL or Lyster Army Health Clinic

If you withdraw from the study, you may also choose to request your data be removed from the study. If you request your data to be removed, all hardcopies of your data will be destroyed and computer files will be deleted. If you decide to withdraw from the study following administration of a medication, you will be required to first consult with the study physician prior to being released, for your own health and safety.

WHAT COULD END MY INVOLVEMENT IN THE RESEARCH?

The investigator or study sponsor may withdraw you from participating in this research if circumstances arise which warrant doing so. These circumstances may include: you are unable to complete the tasks, or it is determined that it is in your best interest to stop your participation in the study, or if questionnaire data suggests that your answers are not reliable (this is determined after your participation). The investigator will make the decision and let you know if it is not possible for you to continue.

WHO SHOULD I CALL IF I HAVE QUESTIONS OR CONCERNS ABOUT THIS RESEARCH?

If you have questions about the research at any time, you should contact Dr. Katie Feltman 334-255-6803, or email Dr. Amanda Kelley at amanda.m.kelley.civ@mail.mil.

If you have questions regarding your rights as a research participant, you may contact the USAARL Regulatory Compliance Office at (334) 255-6940 or (334) 255-6992, or you may

contact the HQ USAMRMC IRB Office at 301-619-6240 or by email to usarmy.detrick.medcom-usamrmc.other.irb-office@mail.mil.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

I agree to be contacted in the future about other research studies.

_____Yes _____No *(Initial your choice)*

Phone Number for future contact: _____

Email Address for future contact: _____

SIGNATURE OF RESEARCH PARTICIPANT

I have read the information provided above. I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF PERSON OBTAINING CONSENT

My signature certifies that the participant signed this consent form in my presence as his/her voluntary act and deed.

_____
Printed Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date