Human Subjects Protocol (HSP)

Form Version: February 1, 2017

- You are applying for IRB review of the research described in this form.
- To avoid delay, respond to all items in order and include all required approvals and documents. For more tips, see the UAB IRB website.
- To complete the form, click the underlined areas and type or paste in your text; double-click checkboxes to check/uncheck.
- All responses should be Times New Roman, Bold, and Underlined.
- Submit all materials to AB 470, 701 20th Street South, Birmingham, AL 35294-0104.

Indicate the type of review you are applying for:

☒ Convened (Full) IRB ***-OR-***

☐ Expedited - See the Expedited Category Review Sheet, and indicate the category(ies) here:

☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7

1. IRB Protocol Title: Neuroimaging the expectancy versus pharmacotherapy effect of Adderall on cognitive performance

2. Investigator and Contact Person

a. Name of Principal Investigator: **Karen Cropsey, PsyD**

Degree(s)/Title: **PsyD, Professor** BlazerID: **kcropsey**

Dept/Div: **Psychiatry/Behavioral Neurobiology** Mailing Address: **1001 Sparks** UAB ZIP: **35294-0017**

Phone: **5-4204** Fax: **5-4482** E-mail: **kcropsey@uabmc.edu**

b. Name of Contact Person: **Roberta May** Title: **Associate Professor** Phone: **5-2605**

E-mail: **rmay@uabmc.edu** Fax: **5-4462**

INVESTIGATOR ASSURANCE STATEMENT & SIGNATURE

By my signature as Principal Investigator, I acknowledge my responsibilities for this Human Subjects Protocol, including:

- Certifying that I and all key personnel comply with reporting requirements of the UAB Conflict of Interest Review Board;
- Certifying that the information, data, and/or specimens collected for the research will be used, disclosed and maintained in accordance with this protocol and UAB policies;
- Following this protocol without modification unless (a) the IRB has approved changes prior to implementation or (b) it is necessary to eliminate an apparent, immediate hazard to a participant(s);
- Verifying that all key personnel listed on the protocol have completed initial IRB training and will complete continuing IRB training as required;
- Verifying that all personnel are licensed/credentialed for the procedures they will be performing, if applicable;
- Certifying that I and all key personnel have read the *UAB Policy/Procedure to Ensure Prompt Reporting of Unanticipated Problems Involving Risks to Subjects or Others to the IRB, Institutional Officials, and Regulatory Agencies* and understand the procedures for reporting;
- Applying for continuing review of the protocol at least annually unless directed by the IRB to apply more frequently;
- Conducting the protocol as represented here and in compliance with IRB determinations and all applicable local, state, and federal law and regulations; providing the IRB with all information necessary to review the protocol; refraining from protocol activities until receipt of initial and continuing formal IRB approval.

Signature of Investigator: Karen Cropsey PsyD **Date:** 7-12-18

3. Protocol Personnel

Including the PI, list all key personnel (each individual involved in the design and conduct of this protocol). See the Key Personnel Flowchart.

Complete the UAB (3.a.) and non-UAB (3.b) tables, as applicable. Use the checkboxes to show each individual's role, whether the individual has financial interests as defined by the UAB CIRB, and briefly describe the individual's protocol responsibilities and qualifications to perform those responsibilities. **Insert additional rows as needed.**

FDA: For studies involving investigational drugs, list all investigators who will be listed on FDA Form 1572 and include a copy of the 1572. Send the IRB a copy of Form 1572 any time you update the form with the FDA.

a. UAB Personnel (includes UAB affiliates and Children's of Alabama personnel)

Name, Degree, and Dept.	Blazer ID	Role	Financial Interest?*	Protocol Responsibilities and Qualifications (indicate if this person obtains consent)
Name: **Karen Cropsey** Degree: **PsyD** Department: **Psychiatry**	**kcropsey**	Principal Investigator	☒No ☐Yes	**Oversight of the conduct of this study, assure scientific integrity, responsible for data quality and compliance with all regulatory requirements. Investigator on multiple studies with this population.**
Name: **Roberta May** Degree: **MA** Department: **Psychiatry**	**bmay**	☐Sub-Investigator ☒Other	☒No ☐Yes	**Preparation of regulatory documents; experienced clinical researcher.**
Name: **Rachel Fargason** Degree: **MD** Department: **Psychiatry**	**rfarg**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Oversight of medical aspects of the study: Experienced psychiatrist and psychiatric researcher**
Name: **Jarred Younger** Degree: **PhD** Department: **Psychology**	**younger**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Oversight of Neuroimaging, Experienced Psychologist**
Name: **Badari Birur** Degree: **MD** Department: **Psychiatry**	**bbirur**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Oversight of medical aspects of the study: Experienced psychiatrist and psychiatric researcher**
Name: **Michelle Sisson** Degree: **MA** Department: **Psychology**	**msisson2**	☐Sub-Investigator ☒Other	☒No ☐Yes	**Will recruit participants Graduate Student**
Name: **Joanne Lin** Degree: **PhD** Department: **Psychology**	**jclin**	☒Sub-Investigator ☐Other	☒No ☐Yes	**Responsible for neuroimaging including, recruitment, screening, scanning/data collection, analysis/interpretation of results: Postdoctoral student**
Name: **Samantha Schiavon** Degree: **MA** Department: **Psychology**	**schiavon**	☐Sub-Investigator ☒Other	☒No ☐Yes	**Will recruit participants Graduate Student**
Name: **Stephanie Mueller** Degree: **MS** Department: **Psychology**	**cm1**	☒Sub-Investigator ☒Other	☒No ☐Yes	**Will recruit participants and assist neuroimaging team Graduate Student**
Name: **Janaki Kher** Degree: Department: **Psychology**	**jrrajput**	☐Sub-Investigator ☒Other	☒No ☐Yes	**Will recruit participants and assist neuroimaging team Undergraduate Student**
Name: **Micheah Hugley** Degree: Department: **Psychology**	**Mickeah1**	☐Sub-Investigator ☒Other	☒No ☐Yes	**Will recruit participants and assist neuroimaging team Undergraduate Student**

b. Non-UAB Personnel Relying on UAB IRB - If you are requesting that the UAB IRB serve as the IRB of record for anyone not affiliated with UAB, list these individuals below.

Name and Degree	From Institution with or without own IRB?	Financial Interest?*	Protocol Responsibilities and Qualifications (indicate if this person obtains consent)
Name: _____ Degree: _____ Institution: _____ Email: _____	☐Has own IRB but requests that UAB IRB serve as IRB of record?***-OR-*** ☐Does not have own IRB and needs to rely on UAB IRB.	☐No ☐Yes	_____

***Financial Interest** – for each individual listed above, answer **Yes** or **No** as to whether the individual or an immediate family member has any of the following:

- An ownership interest, stock options, or other equity interest related to the investigator's institutional responsibilities of any value.
- Compensation greater than $5,000 in the previous two years when aggregated for the immediate family
- Proprietary interest including, but not limited to, a patent, trademark, copyright, or licensing agreement.
- Board of executive relationship, regardless of compensation.
- Any other Financial Interest as defined by the UAB CIRB.

UAB Personnel: If the individual or his/her spouse or dependent child has a Financial Interest, a disclosure has to be made to the UAB CIRB. A completed CIRB evaluation has to be available before the IRB can complete its review.

Non-UAB Personnel: If the individual has a Financial Interest, ***include a copy of the report from his/her own institution's conflict of interest review with this submission to the UAB IRB.***

c. Do the investigators listed above include any students using this research for their thesis or dissertation?

☒ No, continue with Item 3.d.
☐ Yes, complete the following

Student Name	Thesis/Dissertation Title
_____	_____

d. Is the principal investigator a student, fellow, or resident? ☐Yes ☒No

If Yes, complete items below and obtain signature of faculty advisor or supervisor:

Supervisor's Name: _____
Degree(s) / Job Title: _____
Additional Qualifications pertinent to the protocol: _____
Telephone: _____
E-Mail: _____
Signature: _____

e. Describe the principal investigator's activities related to this protocol and provisions made by the PI to devote sufficient time to conduct the protocol: **Dr. Cropsey will oversee all aspects of the protocol including supervision of the research team. She will ensure that the data are maintained appropriately and will communicate with the UAB IRB in a timely manner.**

f. Is medical supervision required for this research? ☒Yes ☐No

If Yes, who will provide the medical supervision?

☐ PI will provide ***-OR-***
☒ Other:
Name: **Rachel Fargason, MD** Telephone: _____
If other than PI, obtain signature of person providing medical supervision:
Signature _____

g. Describe your process for ensuring all key personnel are adequately informed about the protocol and their research-related duties and functions: **The research team have all obtained IRB certification. In addition, prior to study initiation, a meeting will be held with all co-investigators and research staff to review the protocol procedures for obtaining informed consent, procedures that ensure**

accurate and reliable data collection, and roles and responsibilities of each person. Weekly meetings will be held to discuss issues which arise during the course of the study.

4. Funding

Is this protocol funded? ☐Yes ☒No

If No, specify that costs of the protocol will be covered by funds from the UAB department or other source named: **The costs of the study will be funded by the Department of Psychiatry**

If Yes, attach one copy of completed application or request for funding sent to sponsor, and complete a-d.

a. Title of Grant, Contract, or Agreement: _____

b. UAB PI of Grant, Contract, or Agreement: _____

c. Office of Sponsored Programs (OSP) Assigned Number: _____
(If not yet available, enter "Pending" and provide upon receipt from OSP.)

d. Sponsor, Funding Route:
(Check and describe all that apply)
(If subaward, list both the funding source and the institution receiving the direct award)

☐ Gov't Agency or Agencies—Agency name(s): _____
- ☐ Department of Defense (DoD): Identify DoD component: _____
- ☐ Department of Energy (DOE)
- ☐ Department of Justice (DOJ)
- ☐ Department of Education

☐ NIH Cooperative Group Trial - Group name: _____
☐ Private Nonprofit (e.g., Foundation) - Name: _____
☐ Industry, investigator-initiated - Name: _____
Describe the funding arrangement: _____
NOTE: The UAB IRB typically only reviews industry-sponsored protocols that are investigator initiated or when the protocol qualifies for expedited review or involves gene therapy.
☐ UAB Departmental/Division Funds—Specify: _____

5. Locations Involved

a. Indicate all performance sites that will provide space, services, or facilities for the conduct of this protocol.

☐ UAB Hospital
☒ UAB Hospital - Highlands
☐ The Kirklin Clinic of UAB Hospital
☐ The Kirklin Clinic at Acton Road
☐ UAB Callahan Eye Hospital
☐ UAB Clinical Research Unit
☐ Children's of Alabama
☐ Birmingham Veterans Affairs Medical Center
☐ Jefferson County Department of Health
☒ Other (i.e., any performance site not listed above, including those covered by subawards related to this protocol) - Describe: **Sparks Center**
NOTE: Documentation of IRB approvals from sites receiving subawards must be received by the UAB OIRB before funding will be released for that subaward.

b. Describe the space, service, or facilities available for the conduct of the research in the performance sites listed in Item 5.a (For research on UAB campus, include building names): **Sparks Center, 10th floor; Civitan International Neuroimaging Laboratory (CINL) at UAB Highlands Hospital**

c. Is this protocol a clinical trial requiring clinical services at one of the performance sites listed in Item 5.a above? ☐Yes ☒No

If Yes, will any of the services be billed to either participants/their insurance or to the study account through the Hospital Billing Office (PFS) or the HSF Billing Office (MSO)? ☐Yes ☐No

If Yes, submit a Full Fiscal Approval Process (FAP)-designated unit submission to s complete a FAP submission and send to fap@uab.edu. For more on the UAB FAP requirements, go to FAP - SiteMinder Processes.

d. Is this a field study? ☐Yes ☒No

If Yes, describe the community and include information about how the community will be involved in the design, implementation and analysis of the research. This would include focus groups, training local facilitators/community health advisors: _____

e. Has this protocol been rejected or disapproved by another review board (another IRB, similar review board, or departmental review committee(s)) that authorizes the use of its patient populations? ☐Yes ☒No

If Yes, provide name(s) of the review board(s) and reason(s) not approved: _____
Attach copies of the disapprovals.
NOTE: If this protocol is subsequently rejected or disapproved by another review board, promptly notify UAB IRB.

f. Will the protocol be conducted at or recruit participants from the Birmingham Veterans Affairs Medical Center (BVAMC)? ☐Yes ☒No

If Yes, describe the involvement of the BVAMC: _____
Attach the VA IRB approval and VA IRB-stamped consent form(s), if applicable.
NOTE: See the BVAMC section of the IRB Guidebook for more information.

g. Will the protocol be conducted at or recruit participants from the Jefferson County Department of Health (JCDH)? ☐Yes ☒No

If Yes, describe the involvement of the JCDH and list the JCDH clinics being used: _____
Attach the JCDH Research Review Panel approval, if applicable.
NOTE: Human subjects research conducted at certain JCDH clinics requires review by the JCDH Research Review Panel. See the JCDH section of the IRB Guidebook for more information.

6. Clinical Trial

Does this protocol meet the following definition of a clinical trial? ☒Yes ☐No

**A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. For more information, see the full definition of clinical trial here.*

If Yes, you will need to fulfill the following requirements (regardless of funding):

a. All key personnel must complete the Good Clinical Practices (GCP) training. For information on this requirement, visit the IRB website here.

b. This protocol must be registered on ClinicalTrials.gov. Provide the National Clinical Trial (NCT) identifier number: **NCT03530631**
If you have any questions regarding registering a study on ClinicalTrials.gov, email the UAB Center for Clinical and Translational Science at ccts@uab.edu.

7. Multi-Site Studies

a. Is this a multi-site study with the UAB investigator as the lead investigator? ☐Yes ☒No

b. Is this a multi-site study with UAB as a coordinating site? ☐Yes ☒No

c. If Yes to a or b, describe the management of information obtained in multi-site research that might be relevant to the protection of participants. Include, at a minimum, how the following items are managed:

- IRB approvals from other sites
- Unanticipated problems involving risks to participants or others. (For example, if there is an unanticipated problem involving risks to participants or others, which site is responsible for reporting it?)
- Interim results
- Protocol modifications

8. Drugs

Will any drugs or supplements be *used or studied* in this protocol? ☒Yes ☐No

If Yes, attach the completed Drug Review Sheet.

9. Devices

a. Will any devices be *studied* in this protocol? ☐Yes ☒No

b. Will any *not FDA-approved* devices be *used or studied* in this protocol? ☐Yes ☒No

If Yes to a or b, attach the completed Device Review Sheet.

10. Special Approvals

a. Does this protocol involve the use of radioisotopes? ☐Yes ☒No

If Yes, attach documentation of approval from the Radiation Safety Division.

b. Does this protocol include patients with contagious infections (e.g., mumps, measles, chickenpox, TB, meningitis)? ☐Yes ☒No

If Yes, attach documentation of approval from the Infection Control Committee of the appropriate facilities.

c. Does this protocol involve obtaining remnant biopsy or surgical material from the Department of Pathology or any other source? ☐Yes ☒No

If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Anatomic Pathology Release of Pathologic Materials).

d. Does this protocol require obtaining any remnant clinical laboratory specimens, body fluids, or microbiological isolates from the Department of Pathology or any other source? ☐Yes ☒No

If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Laboratory Medicine Release of Pathologic Materials).

e. Does this protocol use stored (existing) specimens from a repository? ☐Yes ☒No

If Yes, attach documentation of approval for use of specimens, and describe how existing specimens are labeled: _____

11. Use of Specimens

Does this protocol involve the collection of specimens? ☒Yes ☐No

If Yes, complete 11.a-11.h.

If No, skip to Item 12.

a. How will specimens be obtained, processed, distributed, and stored? **A urine drug screen and pregnancy test for females will be obtained during the screen visit. If positive, participants will be screen failures and will not be enrolled in the study. Specimens will not be distributed or stored.**

b. How will specimens be labeled (e.g., unique identifier, medical record number, Social Security number, name, date of birth)? **They will be labeled with a unique study identifier, but will not be stored.**

c. How will clinical data associated with the specimens be collected and stored? **There will be no clinical data associated with the specimens. They are used only to establish eligibility for the study.**

d. What participant-identifying information will be collected and linked to the specimens? **No**

e. What steps will be taken to maximize the confidentiality of linked identifiers? For example, procedures could include using a password-protected computer database to link identifiers, with limited personnel knowledgeable of the password, or coded identifiers released without the ability to link to clinical data (also called "stripped" or "anonymized" specimens). **NA**

f. Is genetic testing planned as part of this protocol? ☐Yes ☒No
If Yes, describe the planned genetic testing here. _____

g. Will specimens be stored for future use? ☐Yes ☒No
If Yes, indicate whether they will be used for the disease under study in this protocol or research on other diseases. _____

h. Will specimens be shared with other investigators in the future? ☐Yes ☒No
If Yes, answer i. and ii.
i. What identifiers, clinical information and demographic information will be shared; or will the specimens be stripped of identifiers (i.e., anonymized)? _____
ii. Outline your procedure for assuring IRB approval for release and use prior to release of specimens.

_____

NOTE: Investigators who receive and/or use these specimens must document approval from the appropriate IRB(s) before the specimens may be released.

12. Gene Therapy

Does this protocol involve gene therapy or administering recombinant materials to humans? ☐Yes ☒No
If Yes, submit the Gene Therapy Project Review Panel Report ***-OR-*** the Protocol Oversight Review Form For Clinical Vaccine Trials, as applicable.

13. HIPAA Privacy and Security

Will the PI or others obtain, review, or make other use of participants' "protected health information" (i.e., information, whether oral or recorded in any form or medium that (a) is created or received by a health care provider and (b) relates to past, present, or future physical or mental health or condition of an individual; or provision of health care; or payment for provision of heath care)? ☒Yes ☐No
If Yes, complete Items 13.a-13.f.
If No, skip to 14.

a. Will the data/information be stored or managed electronically (on a computer)?
☒Yes ☐No

b. Is the principal investigator requesting that the UAB IRB waive patient HIPAA authorization from another institution or entity (e.g., insurance company, collaborating institution)? ☐Yes ☒No
If Yes, attach copies of the privacy notices from each institution/entity, and provide the name of each institution/entity: _____

c. Indicate which of the entities would provide health information for this protocol, maintain health information as it was collected for this protocol, and/or store health information after it has been collected for this protocol.
☒ UAB Hospital or UAB Hospital - Highlands
☐ The Kirklin Clinic of UAB Hospital or Acton Road (and/or associated clinics)

☐ UAB Callahan Eye Hospital
☐ Children's of Alabama
☐ Jefferson County Department of Health
☐ School of Dentistry
☐ School of Health Professions
☒ School of Medicine
☐ School of Nursing
☐ School of Optometry
☐ University of Alabama Health Services Foundation
☐ UAB Health Centers
☐ Viva Health
☐ Ophthalmology Services Foundation
☐ Valley Foundation
☐ Medical West - UAB Health System Affiliate
☐ None - **If None, skip to Item 14.**

d. Indicate any information systems that will be the sources of information used for the protocol.

☐ A system maintained centrally by UAB Health System (these include the following: HealthQuest for registration, billing, and patient administration; PowerInsight (clinical data warehouse); Cerner IMPACT for PowerNotes for meds, Lab, Radiology, UED, Surgery

NOTE: If a researcher needs information in a specified format or a specified time, the researcher must confirm with the unit who can supply the information/service that the request can be met before writing the information/service into the research protocol. In addition, the researcher must be aware that these services may have a cost attached that should be considered in the research budget.

To request access to clinical systems for research purposes, visit https://www.oneuabmedicine.org/web/hsis/technical-support, click "Accounts Request" and complete the form indicating access for research purposed.

☐ Another system on a UAB server - Describe: _____

e. Indicate which of the listed identifiers will be accessed, associated and/or linked with the protected health information (PHI) used for this protocol.

☒ Names
☒ Geographic subdivisions smaller than a state
☒ Elements of dates (except year) related to an individual
☒ Telephone numbers
☐ Fax numbers
☒ Email addresses
☐ Social security numbers
☐ Medical record numbers
☐ Health plan beneficiary numbers
☐ Account numbers
☐ Certificate/license numbers
☐ Vehicle identifiers and serial numbers
☐ Device identifiers and serial numbers
☐ Biometric identifiers
☐ Web universal resource locators (URLs)
☐ Internet protocol address numbers

☐ Full-face photographic images
☐ Any other unique identifying number - Describe: _____
NOTE: Codes are not identifying as long as the researcher cannot link the data to an individual
☐ None - **If None, skip to Item 14.**

f. Choose one plan to describe your use of the personal health information:
☐ The data collected meet the specifications for a "limited data set" (LDS)
-If the LDS will leave the covered entity or will be received from another covered entity you will need a Data Use Agreement

☒ Research staff will obtain authorization from each participant to use the information
-Include the HIPAA Authorization form, complete except for participant name and IRB protocol number, as the final page of the consent form

☐ PI requests waiver of authorization to use the information
-Attach Waiver of Authorization and Informed Consent form

PROPOSED RESEARCH

- The IRB will not accept grant applications and/or sponsor's protocols in lieu of the items as outlined below.
- Do not separate responses from items. Instead, insert your response to each item below the item, keeping the information in the order of this form.

14. Purpose - in nontechnical, lay language

a. Summarize the purpose and objectives of this protocol in one short paragraph.

The purpose of this study is to pilot a study designed to further explore the current evidence that stimulant medications are not cognitive enhancers despite this rampant belief in young adults. Participants' performance on neurocognitive tasks will be compared across different groups varying in medication administered, and which medication participants are told they have been administered. For example, participants will either be given stimulant medication or placebo, and will either be accurately told or inaccurately told they received stimulant medication or placebo. Neuroimaging will be utilized to investigate whether participants' expectations regarding the benefits of stimulant medication affects their performance on neurocognitive tasks. The hypothesis of the study is that participants' expectations regarding stimulant medication will affect their performance on neurocognitive tasks, rather than the actual effect of the medication. While the lack of cognitive enhancement from stimulant medication has been documented in prior research, this study will be the first to utilize neuroimaging technology to examine brain regions activated during neurocognitive tasks when participants believe they have been administered stimulant medication or placebo.

b. Describe how outcomes will be measured for this protocol.

Outcomes will be measured with neurocognitive tasks and magnetic resonance imaging (MRI) scanning.

15. Background - in nontechnical, lay language

Summarize in 2-3 paragraphs past experimental and/or clinical findings leading to the design of this protocol. Include any relevant past or current research by the PI. For drug and device studies, summarize the previous results (i.e., Phase I/II or III studies).

The conceptualization of prescription stimulant medications as cognitive enhancers is weakly supported by science. Nonmedical use of prescription stimulants for the purpose of academic enhancement is rampant in institutes of higher learning with potent negative public health implications. A recent series of recent military studies of healthy subjects comparing prescription stimulants to the ubiquitous caffeine and less abuse-prone modafinil demonstrated equivalent benefits between stimulants in sustaining alertness and attention during fatigue states. No improvement in higher order thinking skills (aka.

cognitive enhancement) was noted for any stimulant. Nevertheless, 44% of healthy college students see prescription stimulants as superior to caffeine for cognitive enhancement (Franke, 2012). Evidence for prescription stimulants as cognitive enhances is lacking: two studies found dextroamphetamine improved a single measure of verbal memory, however, a number of studies have demonstrated that a 60-90 minute nap resulted in consolidation of memory on multiple measures.

Young adults have misconceptions about prescription stimulants. The majority of undergraduate students overestimated the prevalence of non-medical use of prescription stimulants (70.2%) among peers on their campus. Additionally, opinions about the use of illegally acquired substances were partly based on evidence based medical facts, but were also strongly influenced by their individual preferences of substances used for cognitive enhancement (Frank 2012). Among college students, actual self-reported non-medical use of prescription stimulants rates range from 1.5% to 31% between survey studies (Mcabe, 2008) with the majority reporting that the primary reason for use was to improve academic performance. (Bogle, 2009) In one survey, 11.3% of students in health care professional schools admitted to nonmedical prescription stimulants use for the purpose of: enhancing alertness/energy (65.9%), to improve academic performance (56.7%), to experiment (18.2%), and to use recreationally/get high (4.5%) (Bossier, 2013). The lifetime prevalence of prescription stimulant use in a sample of 144 medical students was 20%, with 15% using during medical school. 83% reported using them specifically for cognitive performance enhancement such as studying more effectively and staying awake longer. (Webb, 2013) (Arria). Substance abuse in late adolescence is more dependent on peer exposure to drug-abusing peers than intrinsic factors. (NIH, National Institute on Drug Abuse Website www.drugabuse.org)(Gerstein and Green 1993;Dishion et al. 1999). Accurate differentiated empiric data about the true benefit/risk ratio of prescription stimulants to caffeine and in healthy subjects vs. ADHD subjects could reduce nonmedical use resulting from peer-peer misinformation (Hawkins et al. 2002) (Frank, 2012).

The cognitive effect of prescription stimulants on normal healthy adults has not been characterized definitively. No studies have shown that cognitive gains from prescription stimulants exceed the benefits from caffeine, a less risky and legal product. Since caffeine is well known to enhance attention and vigilance during fatigue states, subjects desirous of cognitive enhancement are presumably seeking to enhance high order thinking such as learning and memory. In a double blind placebo-controlled crossover study, 19 healthy young male volunteers were tested after a single dose of placebo or methylphenidate. Declarative memory consolidation was significantly improved relative to placebo for the 20 and 40 mg methylphenidate states as measured by a word-learning test, but not on spatial working memory or a planning task. (Linnsen, 2012). Another double-blind, cross-over placebo controlled study assessed healthy controls on 13 measures of cognitive abilities and found no cognitive enhancement from stimulant medication. However, subjects in this study believed their performance was enhanced by the stimulant medication (Illieva, Boland, & Farah, 2013).

A previous study conducted by the principal investigator and one of the co-investigators of this proposed study involved the administration of a neurocognitive battery to healthy controls after receiving either stimulant medication or placebo. Participants were either accurately or inaccurately informed whether they received medication or placebo. Out of 31 subtests, participants only showed improvement on two of the subtests during active medication. Expecting stimulant medication was associated with improved cognitive performance and expecting placebo was associated with worse cognitive performance, regardless of the type of medication given. The results of this study demonstrated that individuals' expectancies influenced cognitive performance while the use of stimulant medication did not (Cropsey et al. 2017).

16. Participants (Screening and Selection)

a. How many participants are to be enrolled at UAB (if other sites relying on UAB IRB, list the number for each site)? **10**

If multi-site study, total number at all sites/institutions: _____

b. Describe the characteristics of anticipated or planned participants (if multiple groups, repeat list for each group).
Sex: **Male and Female**
Race/Ethnicity: **all**
Age: **18-24 years of age**
Health status: **In good health**

c. From what population(s) will the participants be derived? **Participants will be derived from the UAB campus.**

Describe your ability to obtain access to the proposed population that will allow recruitment of the necessary number of participants: **UAB has a large student population and we should easily be able to recruit 10 students.**

d. Describe the inclusion/exclusion criteria

Inclusion Criteria:

- **Age (18-24)**
- **College student with at least Average IQ**
- **Willingness to standardize caffeine intake to 100mg on day of study**

Exclusion Criteria:

- **ADHD**
- **First degree relative with ADHD**
- **Unwillingness to comply with caffeine specifications**
- **Regular use of Adderall**
- **Pregnant/breastfeeding**
- **History of substance use disorders**
- **Illicit stimulant use within the last year**
- **Contraindications to stimulants (i.e., tics, Tourette's, cardiac disease, hypertension)**
- **Uncontrolled medical illness**
- **Active contagious infection**

e. If participants will comprise more than one group or stratification, describe each group (e.g., treatment/intervention, placebo, controls, sham treatment) **and** provide the number of participants anticipated in each group.

This is a within subjects 2 x 2 design and all 10 participants will experience all four conditions during four sequential weeks. For example, for the expectancy condition, participants will be told either accurately or inaccurately that they are receiving mixed amphetamine salts (MAS). In the medication condition, participants will either receive MAS or placebo medication. This creates four conditions that will be delivered over four weeks (see table below). The presentation of these conditions will be counter-balanced across the four weeks for each of the participants such that they will not always receive the same ordering of conditions.

	Week 1	**Week 2**	**Week 3**	**Week 4**
Expecting	MAS	MAS	Placebo	Placebo
Medication	MAS	Placebo	Placebo	MAS

***MAS = Mixed amphetamine salts (Stimulant medication)**

(Expecting refers to whether participants are told that they are taking stimulant medication or a placebo pill. Medication refers to the pill that participants are actually receiving.)

f. Indicate which, if any, of the special populations listed below will be involved in the protocol. Include the Special Populations Review Form (SPRF) if indicated.

☐ Pregnant Women: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
☐ Fetuses: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
☐ Neonates/Nonviable Neonates: SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
☐ Prisoners: Attach SPRF—Prisoners
☐ Minors (<18 years old): Attach SPRF—Minors
☒ Employees or students at institution where research conducted
☐ Persons who are temporarily decisionally impaired
☐ Persons who are permanently decisionally impaired
☐ Non-English Speakers

For each box checked, describe why the group is included **and** the additional protections provided to protect the rights and welfare of these participants who are vulnerable to coercion:

Employees and students at the institution where research is conducted (UAB) may be included in the study. Students will be informed they may withdraw from the study at any time, for any reason, before it is completed. They will be informed their participation will not affect their class standing or grades at UAB. They will not be offered or receive any special consideration if they take part in the research. Employees will be informed that taking part in the research is not part of their UAB duties and refusing to be a part of the study will not affect their job or relationship with UAB. They will not be offered or receive any special job-related consideration if they take part in this research.

g. List any persons other than those directly involved in the protocol who will be at risk. If none, enter "None": **None**

h. Describe the recruitment process (e.g., medical record review, referrals, letter of invitation, existing patients) that will be used to seek potential participants (e.g., individuals, records, specimens). Research recruitment by non-treating physicians/staff may require completion of Partial Waiver of Authorization for Recruitment/Screening.

Advertisements posted around campus will include tear-off slips of paper with contact information. The study investigators have been able to recruit healthy controls in this age group in previous studies of a similar nature without going to TV or radio advertisements. A telephone pre-screen interview will be designed to capture the most obvious exclusion criteria so that potential screen failures can be eliminated prior to an office visit.

i. If you will use recruitment materials (e.g., advertisements, flyers, letters) to reach potential participants, attach a copy of each item. If not, identify the source (e.g., IRB Protocol Number for approved databases) from which you will recruit participants. **Flyers are attached.**

j. Describe the screening process/procedures for potential participants.

Self-referred potential subjects will have a pre-screen telephone interview. If self-referred potential subjects meet criteria from this pre-screen telephone interview, a screening appointment will be scheduled.

Screening Appointment (1-2 hours): During the consent process, the purpose of the study, its risks and benefits, the rights of the participants, and what will be required of participants will be discussed. The participants will be given time to ask questions and have their questions answered by trained research staff. A pregnancy test will be obtained in all non-sterile female participants and a urine drug screen will be obtained in all participants at the screening interview. Positive results on either will result in

immediate termination. Results will be read prior to giving any medication to a subject. These procedures will not be repeated during the study unless considered clinically necessary based on history or signs and symptoms at the discretion of the study physicians. Participants will review the MRI safety questionnaire to ensure that it is safe for them to be scanned. Participants will then fill out a demographics sheet, MRI Safety Questionnaire, Prescription Stimulant Expectancies Questionnaire (PSEQ-II), and an ADHD screener, the Adult Self-Report Scale (ASRS) Symptom Checklist. Medical and psychiatric history will be reviewed. The absence of an ADHD diagnosis will be confirmed by a physician investigator at the beginning of the study session.

If the participant is eligible based on screening criteria, the study appointment will then be scheduled for 9:00 a.m. on a week day for neuroimaging and testing. They will be expected to show up to this study appointment having consumed the minimum amount of caffeine necessary to prevent withdrawal according to the following schedule: light users (<100 mg/day of caffeine) - no caffeine consumption that day, as cognitive effects from caffeine withdrawal is not expected; medium users (100-200 mg/day) and heavy users (>200 mg/day) - (1)(2)1 MG/KG or 75 mg /day to prevent withdrawal, as this dose has been shown adequate to reverse withdrawal related cognition problems without bringing about a cognitive advantage in caffeine deprivation situations in moderate to heavy users. Participants will also be instructed that on the day of the testing they should consume a lowfat breakfast with less than 9 grams of fat and avoid acidic food and drinks such as cranberry juice or Vitamin C fortified food items. Participants should consume caffeine and/or breakfast a minimum of one hour before testing.

Caffeine Consumption

Drink	Mg of Caffeine
8 oz coffee	100 mg (approximately depending on type of coffee)
12 oz can of Coke	34 mg (ranges from 25-50 across different types of sodas)
8 oz cup of green tea	15-30 mg (depending on steeping time)

Examples of low-fat breakfasts

Menu	Fat (g)
1. ½ cup steel cut oats, 2 tablespoons raisins, ¼ cup skim milk	6.5 g
2. Fruit and chia smoothie made form: 1 cup skim milk, ½ banana, ½ tsp cinnamon, 1 cup frozen berries, 2 tablespoons unsweetened cocoa powder, Stevia to taste	8.5 g
3. Green smoothie made from: 1 cup spinach, 1 cup romaine lettuce, 1 banana, 1 apple, ½ cup fat-free yogurt	1.5 g
4. ½ cup low-fat granola, 1 cup blueberries, 12oz acai juice	5 g
5. Breakfast sandwich made with: 1 turkey sausage breakfast patty, 1 whole wheat English muffin, 3 scrambled egg whites, 1 slice tomato, 1 slice fat-free cheese, 1 pear, 8 oz apple juice	6.5 g

17. Protocol Procedures, Methods, and Duration - in nontechnical, lay language

a. Describe the procedures for all aspects of your protocol. Tell us what you are doing.

Study Appointment (2-3 hours): Pulse and blood pressure will be measured before medication is administered. A potential side effect checklist (attached) will also be reviewed. The MRI safety questionnaire will be reviewed and signed at each scanning visit. This questionnaire will be filed at the

CINL. Any abnormal findings will be discussed with physician investigator who will determine if the subject is fit to participate in the study.

The participant will be given either a placebo or stimulant medication depending on randomization. Each participant (N = 10) will either be told that he/she is receiving stimulant medication or not receiving stimulant medication. The subject will have already formally consented during the screening session to receive varying doses of stimulant medication. The participant will either receive medication or placebo as they are informed, not receive medication when they believe they are receiving medication, or will receive medication when they believe they are not receiving medication. This will allow for measurement of expectancy, which is a core measure for this study. This study design makes the comparison of cognitive performance based on actual versus perceived benefit possible. Participants will be assigned to one of the following:

	Week 1	**Week 2**	**Week 3**	**Week 4**
Expecting	MAS	MAS	Placebo	Placebo
Medication	MAS	Placebo	Placebo	MAS

***MAS = Mixed amphetamine salts (Stimulant medication)**
(*Expecting refers to whether participants are told that they are taking stimulant medication or a placebo pill. Medication refers to the pill that participants are actually receiving.)*

Before the medication is administered and after the MRI scan, participants will complete the POMS (Profile of Mood States) to measure mood and euphoria (attached). Participants will also self-report on their perceived mental acuity pre-dose and after each cognitive task (described below) performed in the scanner on a scale of 0-100with 100 indicating " more sharp than normal.".

Cognitive testing will be timed to begin 45 minutes after medication or placebo is given.

Participants will then start the magnetic resonance spectroscopy scanning portion of the session, which will take one hour. The MRI scan will not include the use of a contrast agent. A 3 Tesla Siemens Prisma scanner and 20-channel head coil will be used. Scan sequences are listed below –

- **Auto-align scout (1 min): to determine brain orientation and slice prescription. Will use 260mm field of view (FOV), 160 x 160 matrix, 3.15ms repetition time (TR), 1.37ms echo time (TE), 1.6mm slice thickness, no gap. The scout data are not used in post-scan analyses, so processing and analysis steps are not described.**
- **T1-weighted magnetization prepared rapid gradient echo (MPRAGE) high-resolution scan (10 min): for anatomical localization and to achieve standard space for group analyses. Will use 230mm FOV, 256 x 256matrix, 2000ms TR, 2.51ms TE, 0.9mm slice thickness, and no gap, yielding 0.9x0.9x0.9mm voxels.**
- **Functional MRI (60 min): Axial T2*-weighted images will be acquired using an echo-planar sequence – 220x220 FOV, 64x64 matrix, 2000ms TR, 28ms TE, 3mm slices, yielding 3x3x3 mm voxels. Heart rate and respirations will be measured continuously in the scanner.**
  - **Participants will complete a "resting state" scan in which they are instructed to close their eyes and rest.**
  - **While undergoing fMRI scans, participants will complete three different cognitive tasks measuring aspects of sustained attention, new learning, and working memory. Participants will receive a short explanation of each task, as well as sample items, prior to entering the scanner, and will be able to have their questions answered. Specific task instructions will also be presented on screen inside the scanner prior to each task.**
  - **The first task will utilize a paced serial addition paradigm. Participants will be presented with a string of single digits (0-9), one every three seconds, for approximately 12 minutes. The digits**

will be presented in auditory form via headphones. Participants will be asked to add the two most recently presented digits in their mind, and will respond with a button press each time the two digits add up to 10. The task does not require participants to maintain a running total of all digits, meaning that participants can resume the task at any point in case of set loss. We will measure the accuracy of participants' responses.

During the second task, a sustained attention task, A row of 5 left- or right-pointing arrows will be presented on each trial. The participant will be required to indicate the direction of the central arrow (left or right) by pressing one of two buttons. The target arrow in the center of the row will be flanked by two non-target stimuli on either side, which point either in the same direction as the target, the opposite direction, or will be circles. The row of arrows will be presented in rapid succession and the participant is to indicate their response as quickly as possible on each trial by pressing the button. The task will last no longer than 15 minutes.

- **During the final task, a visual version of a paired associates learning task, participants will be presented with 50 word pairs on screen, and will be asked to memorize both words in each pair. The pairs will be presented individually, at a rate of one word pair per three seconds. The 50 word pairs will be presented three times in the same order, for a total of 7 minutes and 30 seconds. Words in each pair will be everyday objects of neutral emotional valence, and will be limited to 8th grade reading level (e.g. rose – bag; elephant – glass). fMRI scans will be acquired during the learning phase of this task, although no response is required from participants during this time. Immediately following completion of the learning phase, participants will be presented with the first word from each pair on screen, and will be asked to name the second word in the pair. No brain scans will be acquired during the recall phase, but the accuracy of participants' responses will be recorded by a member of the research team.**
- **Each task will take no longer than 15 minutes to complete, and participants will be given short periods of rest between tasks, as needed. Participants will not receive feedback about the accuracy of their performance.**

After the MRI portion of the session is complete, an additional neuropsychological battery will be administered to participants:

Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): Measures various domains including immediate and delayed memory, visuospatial/constructional, language, and attention

Debriefing (10 minutes): After all four weeks of the protocol, a research assistant will conduct the debriefing portion of the session to inform participants about the deception aspect of the study and disclose whether they received stimulant medication or placebo. The research assistant will discuss the participants' feelings about the deception, use this as a chance to educate them about cognitive enhancers, and more fully explain the reasons for doing the study. Participants will be given as much time as deemed clinically appropriate to answer all questions and concerns or address any feeling of betrayal in an accepting way.

Prior to leaving, the side effect checklist will be completed a final time and blood pressure and pulse rechecked by trained study staff. Stable subjects will be allowed to leave. Any subjects experiencing side effects will be observed longer, or in the rare event of more moderate to severe adverse events (most commonly hypertension < 160/110), will be referred to the ER at the discretion of the physician and PI. Orange juice will be kept on site for use in subjects experiencing negative symptoms as acidifying urine increases amphetamine excretion. The side effect checklist includes simple questions asked the participant to assess tolerance to medication (or placebo). A study physician will be available at all times.

Participants will be discouraged from using any of the following over the counter products containing stimulants during the course of the study:

Caffeinated beverages such as coffee, green tea, tea, soft drinks (cola, root beer, crème soda), energy drinks such as "5 hour energy" and Red Bull.
Caffeine medications such as No Doz and pain relievers such as Goody's Powder and Midol
Herbal supplements such as salvia, nutmeg and Herbal Ectacy (ephedra)
Dietary supplements/ weight loss pills particularly those containing ma huang (ephedra)
Cough and/or cold medications containing dextromethorphan, chlorpheniramine, and/or pseudoephedrine such as Robitussin, NyQuil and Coricidin

b. What is the probable length of time required for the entire protocol (i.e., recruitment through data analysis to study closure)? **One year**

c. What is the total amount of time each participant will be involved? **9 hours over a 5 week period.**

d. If different phases are involved, what is the duration of each phase in which the participants will be involved? If no phases are involved, enter "None." **There will be a screening appointment , which will take approximately one hour, and 4 weekly study appointments, which will take approximately two hours each.**

e. List the procedures, the length of time the procedure takes, the total # of times the procedure is performed, and indicate whether each is performed solely for research or would already be performed for treatment or diagnostic purposes (routine care) for the population.
-Insert additional table rows as needed.
-If procedure is sometimes research and sometimes routine care, include on separate lines with number of times as each.

Procedure	Length of Time Required of Participants	Total # of Times the Procedure is Performed	Research (Res) –OR- Routine Care
Consent	**20 minutes**	**1**	☐Res ☐Routine
Urine drug screen	**1 minute**	**1**	☒Res ☐Routine
Pregnancy test (if applicable)	**1 minute**	**1**	☒Res ☐Routine
Demographic Questionnaire	**2 minutes**	**1**	☒Res ☐Routine
MRI Safety Questionnaire	**5 minutes**	**1**	☒Res ☐Routine
ADHD screener	**10 minutes**	**1**	☒Res ☐Routine
Medical history	**10 minutes**	**1**	☒Res ☐Routine
Side effect checklist	**1 minutes**		☒Res ☐Routine
Pulse and blood pressure	**3 minutes**	**4**	☒Res ☐Routine
Study drug administration	**1 minute**	**4**	☒Res ☐Routine
PSEQ-II	**5 minutes**	**4**	☒Res ☐Routine
POMS	**5 minutes**	**4**	☒Res ☐Routine
MRI scan with 3 cognitive tasks	**60 minutes**	**4**	☒Res ☐Routine
Mental acuity scale	**1 minutes**	**16**	☒Res ☐Routine

RBANS	**20 minutes**	**4**	☒Res ☐Routine
Heart rate and respirations	**Continuously while in the scanner**	**4**	☒Res ☐Routine
Debriefing	**10 minutes**	**1**	☒Res ☐Routine

f. Will an interview script or questionnaire be used? ☒Yes ☐No
If Yes, attach a copy.

g. Will participants incur any costs as a result of their participation? ☐Yes ☒No
If Yes, describe the reason for and amount of each foreseeable cost. _____

h. Will participants be compensated? ☒Yes ☐No
If Yes, complete i-v.
i. Type: (e.g., cash, check, gift card, merchandise): **Check**
ii. Amount or Value: **$ 50 for screen visit and $100 for the 4 scanning visits. If the participant does not complete the study, payments will be prorated to pay them for the visits they did complete.**
iii. Method (e.g., mail, at visit): **by mail**
iv. Timing of Payments: (e.g., every visit, each month): **Payments will be processed after participant completes the study.**
v. Maximum Amount of Compensation per Participant: **$450**

18. Benefits
Describe the potential benefits of the research.
Participation in this study might increase participants' awareness of their own mistaken expectations vis-à-vis cognitive enhancement and the relative lack of benefit from cognitive enhancers.

Participation in this study potentially advances the larger goal of reducing prescription stimulant abuse through definitive studies disproving cognitive enhancing effects of these medications. Stimulant prescription abuse is a large public health issue; a study definitively disproving the cognitive enhancing qualities of these medications could have broad implications in saving lives and reducing morbidity from abuse and misuse of these medications.

19. Risks - in nontechnical, lay language
a. List the known risks for participants as a result of participation in the research. This should not include the minimal risk of loss of confidentiality. However, it should include any physical, psychological, social, economic, and/or legal risks. If there is a greater than minimal risk of loss of confidentiality describe why this is so. Do not list risks associated with the standard-of-care procedures.
NOTE: Risks included here should be included in the consent form or information sheet, as applicable.
The risks from this study are the risk of two doses of 10 mg of Mixed amphetamine salts(Adderall) and the risk of MRI. This dose is the routine starting dose for patients receiving this medication and these are healthy patients lacking health risks and screened specifically for contraindications for medications. Hence the risks at this standard dose are the standard risks of side effects and toxicity at therapeutic doses any patient experiences in routine care. This includes:
The following warnings are listed on the FDA website about Adderall (http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4202b1_07_fda-tab07.pdf) and the NIH website (www.nlm.nih.gov/medlineplus/druginfo/meds/a682188.html). :
Amphetamines have a high potential for abuse: however the subject receives only one starting dose (not high enough to produce euphoria and given with the expectation of improved focus not euphoria, which is shown in studies to alter the likelihood of stimulating reward pathways that lead to addiction) on two separate occasions. Hence the risk for two doses at therapeutic, not "high" inducing doses at least a week apart, creating an addiction is extremely low.

Participants will be monitored for these more common potential symptoms especially if they are severe or last for longer than a few hours:

- **o nervousness**
- **o difficulty falling asleep or staying asleep**
- **o dizziness**
- **o nausea**
- **o vomiting**
- **o loss of appetite**
- **o stomach pain**
- **o diarrhea**
- **o heartburn**
- **o dry mouth**
- **o headache**
- **o muscle tightness**
- **o drowsiness**
- **o uncontrollable movement of a part of the body**
- **o restlessness**
- **o numbness, burning, or tingling in the hands or feet**
- **o decreased sexual desire**

The following are rarer but more serious side effects. Participants will be asked to inform us immediately if any of the following occur. Medical attention will be given immediately with possible transfer to the ER per investigator physician discretion. Acidification of the urine to increase amphetamine excretion through use of orange juice will be applied for any of the following symptoms :

- **o fast, pounding, irregular heartbeat**
- **o chest pain**
- **o shortness of breath**
- **o excessive tiredness**
- **o slow or difficult speech**
- **o fainting**
- **o weakness or numbness of an arm or leg**
- **o seizures**
- **o changes in vision or blurred vision**
- **o agitation**
- **o believing things that are not true**
- **o feeling unusually suspicious of others**
- **o hallucinating (seeing or hearing voices that do not exist)**
- **o motor tics or verbal tics**
- **o depression**
- **o abnormally excited mood**
- **o mood changes**
- **o erection that lasts longer than 4 hours(sexual activity will be discouraged until evening time when medications should be largely excreted)**
- **o numbness, pain, or sensitivity to temperature in the fingers or toes**
- **o skin color change from pale to blue to red in the fingers or toes**
- **o unexplained wounds on the fingers or toes**
- **o fever**
- **o hives**
- **o rash**
- **o blistering or peeling skin**
- **o itching**
- **o swelling of the eyes, face, lips, mouth, tongue, or throat**
- **o hoarseness**

- **difficulty breathing or swallowing**

Risks of MRI

MRI Scanning: Minimal. MRI is non-invasive and does not use ionizing radiation. The screening protocol will exclude those who have conditions for which it would be unsafe for them to undergo imaging. If ferromagnetic objects are brought close to the bore of the magnet, they could be pulled in and injure the person in the magnet, but this possibility is avoided by having the magnet room closed when the participant is in the magnet, and having the access hallway to the magnet closed and under keypad control access. It is possible that individuals with tattoos could experience first degree burns during scanning because some inks contain high levels of iron oxide; however, iron oxide is less commonly found in tattoos from the United States. Tattoos are generally not a contraindication for having an MRI scan; however, we mitigate the risk of burns by warning participants of the risk of burns and instructing them to inform us if they notice warming in the area of the tattoo.

b. Estimate the frequency, severity, and reversibility of each risk listed.

All neurologic, gastrointenstinal and psychiatric symptoms are reversible with termination of medication use. Anaphlactic reactions, which can occur due to any medication, are potentially fatal but generally can be managed with an epipen, which will be on site, or emergency room management. Cardiac side effects which cause no permanent damage are more likely on stimulants but cardiac events are not. Large population studies show that adults and children taking stimulants at therapeutic doses are not more likely to have cardiac events than those not on medication. In the very rare event of a myocardial infarction at 10 mg MAS, cardiac damage could persist, though rapid transfer to the ER to prevent this would occur.

The following percentages were obtained from MedTV.com (http://adhd.emedtv.com/adderall-xr/adderall-xr-side-effects.html)

Loss of appetite -- in up to 36 percent of people
Dry mouth -- up to 35 percent
Difficulty sleeping (insomnia) -- up to 27 percent
Headaches -- up to 26 percent
Abdominal pain (stomach pain) -- up to 14 percent
Temporary increase in blood pressure -- up to 11 percent
Weight loss -- up to 11 percent (see Adderall and Weight Loss)
Emotional changes -- up to 9 percent
Nausea, upset stomach, or vomiting -- up to 8 percent
Dizziness -- up to 7 percent
Diarrhea -- up to 6 percent
Feeling of weakness (asthenia) -- up to 6 percent
Increased heart rate (tachycardia) -- up to 6 percent
Other side effects are considered extremely rare

The risks of MRI scanning are minimal: MRI is non-invasive and does not use ionizing radiation. The screening protocol will exclude those who have conditions for which it would be unsafe for them to undergo imaging. If ferromagnetic objects are brought close to the bore of the magnet, they could be pulled in and injure the person in the magnet, but this possibility is avoided by having the magnet room closed when the participant is in the magnet, and having the access hallway to the magnet closed and under keypad control access. It is possible that individuals with tattoos could experience first degree burns during scanning because some inks contain high levels of iron oxide; however, iron oxide is less commonly found in tattoos from the United States. Tattoos are generally not a contraindication for having an MRI scan; however, we mitigate the risk of burns by warning participants of the risk of burns and instructing them to inform us if they notice warming in the area of the tattoo.

c. Is this a therapeutic study or intervention? ☒Yes ☐No

If Yes, complete i.-iii.

i. Describe the standard of care in the setting where the research will be conducted: **10 mg is a standard starting dose for individuals who are prescribed Adderall for therapeutic purposes.**

ii. Describe any other alternative treatments or interventions:

The main alternative for study applicants is to not participate in this study. There are several non-prescription methods for improving cognitive function, including healthy diet and sleep patterns, daily physical activity, acquirement of new skills, exposure to new experiences, exposure to sunlight, use of creative thinking, social engagement, brain-training games, and relaxation exercises. Non-prescription substances thought to improve mental alertness include caffeine, green tea extract, alpha lipoic acid, NAC N-acetyl cycteine, Acetyl-L-Carnitine, COQ10, IGF-1, vitamin B12, Curcumin Turmeric Extract, Alpha-GPC, and Astaxanthin (www.biosynergy.com).

Other methods for treating ADHD symptoms include: Methylphenidate (Ritalin) and lisdexamfetamine (Vyvanse) are other stimulants commonly prescribed to ADHD patients. Non-stimulant medications include atomoxetine (Strattera), guanfacine (Intuniv), and clonidine (Kapvay). Therapy sessions targeted at reduction of impulsive behavior and improved time management and organizational skills are also effective in improving focus. (www.fda.gov/drugs/resourcesforyou/specialfeatures/ucm289089.htm

iii. Describe any withholding of, delay in, or washout period for standard of care or alternative treatment that participants may be currently using: **This is not a treatment study so no care is withheld or delayed.**

d. Do you foresee that participants might need additional medical or psychological resources as a result of the research procedures/interventions? ☐Yes ☒No

If Yes, describe the provisions that have been made to make these resources available. _____

e. Do the benefits or knowledge to be gained outweigh the risks to participants?

☒Yes ☐No

If No, provide justification for performing the research: _____

20. Precautions/Minimization of Risks

a. Describe precautions that will be taken to avoid risks and the means for monitoring to detect risks.

Participants will be chosen from a relatively young age group and thoroughly screened for contraindications to stimulant medications or use of medications which could interact with the Adderall . This includes screening for psychotic tendencies, mania, tics, Tourette's syndrome, cardiac diseases, vascular diseases, hypertension, and use of other medications with stimulant properties. Individuals who are pregnant and females of childbearing age who cannot commit to abstinence or a reliable form of birth control during the study period will also be excluded to prevent potential birth abnormalities that can occur when a pregnant woman is exposed to stimulants. Finally, to avoid the risk of participants becoming ill with other diseases, people who have an active, contagious infections (e.g., mumps, measles, chickenpox, TB, meningitis) will be asked to delay their participation in the study to a time at which they are no longer contagious. Participants will be administered small, therapeutic doses of Adderall in controlled environments, where their symptoms can be observed and overuse is not possible. Participants will receive a total of two 10 mg doses with a separation of at least one week between doses. According to pharmacologic literature, this is not considered enough exposure to form an addiction. Participants who have a self-reported history of substance abuse or use of illegal substances will not be allowed to participate in the study, and participants may contact the research team at any time to request the contact information of addiction specialists. A doctor will observe for one hour

after medication administration until the patient is cleared to release home according to the exhaustive symptom checklist and a BP and pulse in the acceptable range. Risks of MRI

If the protocol involves drugs or devices skip Items 20.b. and 20.c. and go to Item 21. Instead include this information in the Drug Review Sheet or Device Review Sheet, as applicable.

b. If hazards occur to an individual participant, describe (i) the criteria that will be used to decide whether that participant should be removed from the protocol; (ii) the procedure for removing such participants when necessary to protect their rights and welfare; and (iii) any special procedures, precautions, or follow-up that will be used to ensure the safety of other currently enrolled participants.

c. If hazards occur that might make the risks of participation outweigh the benefits for all participants, describe (i) the criteria that will be used to stop or end the entire protocol and (ii) any special procedures, precautions, or follow-up that will be used to ensure the safety of currently enrolled participants.

21. Informed Consent

a. Do you plan to obtain informed consent for this protocol? ☒Yes ☐No
If Yes, complete the items below.
If No, complete and include the Waiver of Informed Consent or Waiver of Authorization and Informed Consent, as applicable.

b. Do you plan to document informed consent (obtain signatures) for this protocol? ☒Yes ☐No
If Yes, complete the items below.
If No, complete the items below **and** include the Waiver of Informed Consent Documentation.

c. How will consent be obtained? **During the consent process, the purpose of the study, its risks and benefits, the rights of the participants, and what will be required of participants will be discussed. The participants will be given time to ask questions and have their questions answered by trained research staff. After the informed consent has been signed, study procedures will begin.**

d. Who will conduct the consent interview? **The investigator and/or research staff**

e. Who are the persons who will provide consent, permission, and/or assent? **The participants themselves**

f. What steps will be taken to minimize the possibility of coercion or undue influence? **It will be made clear to the participants in a neutral manner that they are not obligated to participate and their grades, employment or general clinical care will not be altered as a result of either participating or not participating in the study.**

g. What language will the prospective participant and the legally authorized representative understand? **English**

h. What language will be used to obtain consent? **English**

i. If any potential participants will be, or will have been, in a stressful, painful, or drugged condition before or during the consent process, describe the precautions proposed to overcome the effect of the condition on the consent process. If not, enter "None." **None**

j. If any protocol-specific instruments will be used in the consenting process, such as supplemental handouts, videos, or websites, describe these here and provide a copy of each. If not, enter "None." **None**

k. How long will participants have between the time they are told about the protocol and the time they must decide whether to enroll? If not 24 hours or more, describe the proposed time interval and why the 24-hour minimum is neither feasible nor practical. **If a person calls in about the study, a pre-**

screen telephone interview will take place to determine possible eligibility. If the caller appears to be potentially eligible, a description of the study will be given over the phone. There will be a minimum of 24 hours between the pre-screen telephone call and the time the participant comes in for a screening visit at which time the formal consent process will begin.

22. Procedures to Protect Privacy

Describe how you will protect the privacy interest of the participants. Include how you will make sure others cannot overhear your conversation with potential participants and that individuals will not be publicly identified or embarrassed. **Every precaution will be taken to protect privacy. Participants will be seen in private clinic offices behind closed doors. Their cases will not be discussed in public places (hallways or elevators) and they will not be publicly identified or embarrassed.**

23. Procedures to Maintain Confidentiality

a. Describe how you will store research data to maintain confidentiality (both paper records and electronic data), including how access is limited. If data will be stored electronically anywhere other than a server maintained centrally by UAB, identify the department and all computer systems used to store protocol-related data. **The study records will be kept confidential to the extent provided by Federal, State, and local law. The records will be kept in a locked file by the research staff in offices maintained by the Department of Psychiatry and Behavioral Neurobiology. When a participant is enrolled in the study protocol, they are given a unique identification number that is used to identify all data associated with that person. All identifiers will be stored locally in secure areas of a computerized file system, with several levels of access security built in, thus assuring confidentiality. Unique identifiers can be linked to personal identifiers only by key study personnel with access to the personal identifier database protected by password.**

b. Will any data from this protocol be given to any person, including the subject, or any group, including coordinating centers and sponsors? ☐Yes ☒No

If Yes, complete i-iii.

i. Who will receive the data? **ii.** What data will be shared?

iii. How will the data be identified, coded, etc.?

24. Genomic Data Sharing (GDS)

Researchers who collect genomic data as part of a NIH grant funded after January 25, 2008 may be required to submit those data to a NIH database for broad scientific sharing. See Genomic Data Sharing in the IRB Guidebook for more information.

a. Does this protocol involve the proposed submission of genetic data into genomic repositories created to share genetic information for research purposes? ☐Yes ☒No

b. Will UAB be uploading the final genomic data to the central repository (e.g., dbGaP)? ☐Yes ☒No

If Yes to both a and b, submit a Detailed Data Sharing Plan to the IRB for review. This plan should include any known data use limitations and indicate whether aggregate-level data are appropriate for general research use. For guidance see the NIH Genomic Data Sharing Policy.

c. Submit a copy of the NIH Institutional Certification Form.

To determine which certification form to include, answer i-ii.

i. Was this protocol funded prior to January 25, 2015? ☐Yes ☒No

- **If yes,** and consent will be obtained, submit the Extramural Institutional Certification - Before January 25 - With Consent.
- **If yes,** and consent will not be obtained, submit the Extramural Institutional Certification - Before January 25 - Without Consent.

ii. Was this protocol funded after January 25, 2015? ☐Yes ☒No

- **If yes,** submit the Extramural Institutional Certification - After January 25.

25. Additional Information

In the space below, provide any additional information that you believe may help the IRB review the proposed research, or enter "None." **None**