INSTRUCTIONS:

- *Use this "TEMPLATE PROTOCOL (HRP-503)" to prepare a study protocol outlining your research plan.*
- *Depending on the nature of your study, some major sections might not be applicable to your research. If so, simply mark as "N/A." For example, a simple survey might have many sections with "N/A." For subsections (e.g., 1.x or 8.x) you can mark as "N/A"if you are certain that the subsection is not applicable.*
- *Once the IRB/HRPP approves your submission, your latest approved version of the protocol will be stored in the IRB Protocol Management online system.*
- *If your research plan changes and you need to modify the protocol, please submit an amendment to Protocol Management with the requested modifications. Download your current protocol from Protocol Management and indicate the changes/revisions using the track changes feature in order to make review of the modifications easier to follow. If you are unable to use track changes, please create a new paragraph wherever you need to make a change, and indicate "Amendment: Date" before making a change to any section. Protocol management will store the older versions of your protocol if the IRB or HRPP staff need to compare them during the review.*

PROTOCOL TITLE:

Include the full protocol title.

Brain Network Modulation and Alcohol Use

PROTOCOL NUMBER:

Include the number assigned in Protocol Management (verify this has been added before submitting protocol to HRPP).

22-016

PRINCIPAL INVESTIGATOR:

Full Name and Degrees: Dr. Stephen LaConte
Department: Fralin Biomedical Research Institute
Telephone Number: 540-526-2008
Email Address: slaconte@vtc.vt.edu

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Funded already or in the proposal phase?: Funded
Is Virginia Tech the primary awardee or the coordinating center of this grant or contract? If not, list the primary institution: Virginia Tech

VERSION NUMBER/DATE:

Include the version number and date of this protocol. Versions should start at 1.0.

Version 1.1

REVISION HISTORY:

Use this table to keep track of changes. Add more rows as needed.

Revision #	Version Date	Brief Summary of Changes (i.e., the different sections)	Consent Change?
1.1	8/4/2022	Title, acronyms, 3.3, 5.1, 6.1, 7.1, 8.1, 8.2, 8.3, 8.4, 12.2, 15.1, 15.2, 15.3, 16.1, 17.1, 17.2	Yes
1.2	10/31/2022	1.0, 8.1, 8.2, 8.3, 11.1, 8.4, 15.5	Yes
1.3	11/16/2022	7.1, 8.1, 8.2, 8.3	No
1.4	12/6/2022	8.1, 8.2	No
1.5	12/17/23	8.1, 8.2	No
1.5	1/17/2023	8.1 and 8.2	No
1.6	3/10/2023	Study population, 3.3, 5.1, 2.2	Yes

Table of Contents

1.0 Study Summary

Study Title	Brain Network Modulation and Alcohol Use
Study Design	This study seeks to investigate brain network modulation in individuals with alcohol use disorder (AUD). Enrolled participants will undergo a real-time fMRI scan and may be asked to complete corresponding questionnaires which will be submitted to the IRB for approval prior to use.
Primary Objective	Directly test the ability to modulate neural activity as a function of AUD severity using real-time fMRI.
Secondary Objective(s)	N/A
Study Population	Individuals who drink alcohol
Sample Size	50 participants
Research Intervention(s)/ Investigational Agent(s)	Data collection will include MRI data, including a real-time modulation task in-scanner, and relevant questionnaires.
Study Duration for Individual Participants	Participants will participate in one rtfMRI session. Prior to their fMRI, they will complete a brief interview to generate cues for use during their scan. We will retain personally identifiable study data for a period of seven years after completion of the study. After the period of 7 years has passed, we will destroy any personally identifiable study data.
Acronyms and Definitions	AUD=Alcohol Use Disorder AUDIT= Alcohol Use Disorders Identification Test fMRI=Functional Magnetic Resonance Imaging rtfMRI=real-time fMRI DMN=Default Mode Network FBRI=Fralin Biomedical Research Institute VTC=Virginia Tech Carilion HNL=Human Neuroimaging Laboratory BAAD = Brief Assessment of Alcohol Demand DD = Delay Discounting

2.0 Objectives

2.1 Describe the purpose, specific aims, or objectives of this study:

This study directly tests the ability to modulate neural activity as a function of AUD severity using real-time fMRI.

2.2 State the hypotheses to be tested:

We hypothesize that individuals with lower AUD severity will have a significantly higher correlation (indicating better modulation ability) than individuals with higher AUD severity.

3.0 Background

3.1 Summarize the relevant prior research on this topic and gaps in current knowledge within the field of study:

rtfMRI Background:
Functional magnetic resonance imaging (fMRI) is a technique that noninvasively measures correlates of neural activity (Ogawa et al., 1992) and allows the identification of cerebral substrates associated with processes that shape human awareness and perception, such as visual, auditory, emotional, somatosensory. Unlike positron emission tomography (PET), fMRI does not require the injection of intravenous tracers or exposure of the subject to any ionizing radiation. Another advantage of fMRI is that multiple scans can be obtained in a single (or multiple) imaging session(s), which allows for acquisition of 1000 scans over a few minutes, while a PET study is limited to 16 scans over 2 hours (Friston et al., 1995; Buckner et al., 1996). Thus, fMRI allows us to capitalize on increased temporal resolution and repetition of conditions capabilities in an effort to study brain function.

Pattern analysis of fMRI is a multivariate, supervised learning approach that is complimentary to univariate analyses – the data acquisition and experimental methods are identical.

As described by Hansen (Hansen et al., 1999), learning problems are generally designated as either supervised or unsupervised. Supervised learning deals with learning from examples, aiming to capture the functional relationships between variables, whereas unsupervised learning captures statistical relationships from the dataset itself. Examples of unsupervised learning applied to fMRI include principal components analysis (Hansen et al., 1999), independent component analysis (McKeown et al., 1998), and clustering techniques (Baumgartner et al., 1998; Hansen et al., 1999; Ngan and Hu, 1999). For brain state analyses, we are interested in multivariate relationships between fMRI images and the corresponding behavior or sensory parameters. Such relationships are usually obtained through the process of supervised learning. Though the majority of fMRI studies use univariate statistical methods, the supervised learning we are focused on generally relies on multivariate approaches. Emphasizing the multivariate aspect of brain state predictive analyses, several reports refer to this as “multi-voxel pattern analysis (MVPA)” (Haxby et al., 2001; Polyn et al., 2005; Norman et al., 2006). Compared with univariate GLM analyses, there are still relatively few multivariate, supervised learning studies, with early neuroimaging (PET and fMRI) work in predictive modeling developed by Strother and Hansen (Lautrup et al., 1994, Hansen et al., 1999, Kjems et al., 2002,

Kustra and Strother, 2001, Morch et al., 1997, Strother et al., 2002, Shaw et al., 2003, LaConte et al., 2003a) and recent explicit testing of distributed brain systems by Haxby et al. (Haxby et al., 2001) and Cox and Savoy (Cox and Savoy, 2003). Continued innovation in methodology and creative experimental designs have since burgeoned (Mitchell et al., 2004; LaConte et al., 2005c; LaConte et al., 2007; Davatzikos et al., 2005; Haynes and Rees, 2005; Pessoa and Padmala, 2005; Kamitani and Tong, 2005; Polyn et al., 2005) It should be noted that the viewpoint that multivariate approaches can lead to new insights and are complementary to univariate analysis has been long and widely echoed (Friston et al., 1995; McIntosh et al., 1996; Moeller and Habeck, 2006). Moreover it is recognized that every method (univariate or multivariate) emphasizes some aspect of the data and cannot capture everything (McIntosh et al., 1996; Moeller and Habeck, 2006; Lange et al., 1999; Strother et al. 2002). To increase our understanding of brain function with fMRI, we must understand the relationships between highly multivariate brain images and categorical quantities describing discrete stimulus or behavioral responses (Victor, 2005). Comparing both, univariate approaches have benefited from much more methodological scrutiny and are highly interpretable and are often more statistically powerful in revealing localized activation. Their primary drawbacks are that they are highly vulnerable to detection limitations imposed by multiple comparisons, and validation of spatial activity is difficult (LaConte et al., 2003a). Multivariate approaches capture distributed relationships and are more powerful at detecting whether a particular stimulus condition is reflected in the data. They have been reported to reveal more information than univariate analyses (Lin et al. 2003; Fletcher et al, 1996). For predictive methods, validation can be performed when the stimulus/behavior of interest can be measured. Though not a specific aim, our general methods section discusses that post processing of all data collected will include comparison of our multivariate brains state models with GLM-based univariate activation patterns. Spatio-temporal properties of BOLD provide feasibility and utility for real-time systems. Blood oxygenation level dependent functional magnetic resonance imaging (BOLD fMRI) relies on changes in cerebral blood flow to indirectly measure neuronal activity (Bandettini et al., 1992; Kwong et al., 1992; Ogawa et al., 1990a; Ogawa et al., 1990b; Turner et al., 1991). The biophysics relating the BOLD signal to the underlying gray matter's neuronal electrical activity has been avidly studied since the introduction of the method. During a task, BOLD signal changes take 6-12 s to reach maximum intensity, where it remains relatively constant for sustained long periods of activity, and 8-20 s to return to baseline values after the task is finished (Chen et al., 1998; Kollias et al., 2000; Noll, 2001). Ultimate limits in timing may be much better than this since early but weak signal changes have been reported to occur roughly 0.5-2 seconds after the onset of neuronal activity (Kollias et al., 2000; Noll, 2001; Yacoub and Hu, 1999). In addition, temporal characteristics vary with spatial region (Chen et al., 1998), and importantly, subjects are capable of modulating strength and spatial extent of local activations, demonstrated by fMRI biofeedback studies (deCharms et al., 2004; deCharms et al., 2005; Yoo and Jolesz, 2002). The field strength of the scanner is also an important factor for real-time feedback studies as field strengths of 3 T or higher have important implications for the BOLD response (Yoo and Jolesz, 2002), namely increased specificity and signal-to-noise ratio (SNR). Recently fMRI, itself, has been evaluated for suitability as a biofeedback signal (deCharms et al., 2004; deCharms et al., 2005; Posse et

al., 2003; Weiskopf et al., 2003; Yoo and Jolesz, 2002). In the investigation by (Yoo and Jolesz, 2002), subjects were trained to interpret activation maps for a simple motor task with the goal of increasing activity in a localized brain region, and the five subjects examined were successful at the task of manipulating the spatial extent of their BOLD response. This result was corroborated and expanded by Weiskopf (Weiskopf et al., 2003) who showed significant changes of local BOLD responses in the anterior cingulate cortex in a subject who was provided with an updated display of level of activity in this area; (Posse et al., 2003) who showed that real-time feedback of amygdala activation in a sad mood task led to increases in both left amygdala activation and self-rated sadness; and DeCharms (deCharms et al., 2004), who directly demonstrated the ability of subjects to learn to exert voluntary control over somatomotor cortex activation using a real-time setup. Recent work of deCharms (deCharms et al., 2005) represents a particularly compelling example of the utility of real-time fMRI for therapeutic applications. This study examined the impact of providing BOLD signal level changes in the rostral anterior cingulate cortex (rACC) as feedback to affect conscious perception of pain. deCharms showed that when subjects increased (decreased) activity in this region, there was a corresponding increase (decrease) in pain perception, for a given pain stimulus. Such training was effective enough to lead chronic pain patients to report decreases in ongoing pain, even after completion of the experiment. Our concept of real-time fMRI provides uniquely different capabilities, and possesses several distinct advantages over existing implementations. The predictive learning framework requires training data, analogous to the functional localizer requirements in the other implementations. Focusing on multivariate relationships in the data, though, brain reading constitutes a distinctly different approach to existing real-time studies, which use time series fluctuations in localized regions as a biofeedback signal (deCharms et al., 2004; deCharms et al., 2005; Posse et al., 2003; Weiskopf et al., 2003; Yoo et al., 2004). By explicitly using distributed brain state patterns, our scientific perspective is that of brain reading rather than that of localized activation. The first advantage of this is that prior assumptions about functional localization and individual performance strategies are not required – it learns these directly from the volunteer. This provides for ultimate flexibility across the spectrum of cognitive domains. The second advantage is that feedback can rely on a direct, intuitive translation of brain state, rather than a display based on increasing or decreasing local activity. A subtle but important methodological consideration from DeCharms (deCharms et al., 2005) was that subjects required cognitive strategy guidelines to be successful. No similar coaching is necessary with our brain state approach – across the cognitive domains subjects were able to intuitively and accurately control cursor movement (LaConte et al., 2007). These advantages are supported by our preliminary results where we demonstrate that i) human-machine training can be accomplished in minutes, ii) near perfect accuracy of brain state is attainable during sustained periods of activation, iii) feedback can respond to changes in brain state much earlier than the time-to-peak of the BOLD response, and iv) great flexibility exists in terms of cognitive domain/psychological task. The shift in emphasis from offline to online analysis and consistent vs. changing behavioral responses raises exciting new challenges. The benefit of real-time feedback derived from brain state models is that it provides the potential for completely new experimental designs. This proposal focuses on dealing with the implications of this to support such experimental flexibility. Although the real-time

system that we have implemented is based on pattern analysis techniques that have been used in numerous studies (LaConte et al., 2003a; Cox and Savoy, 2003; Mitchell et al., 2004; LaConte et al., 2005c; Davatzikos et al., 2005; Haynes and Rees, 2005; Pessoa and Padmala, 2005; Kamitani and Tong, 2005; Polyn et al., 2005), these reports have used post-processing analyses. For offline laboratory analyses, the limitations of the BOLD response are really not that limiting. For example, it is possible to drop transition scans or shift the timing to account for the BOLD delay (LaConte, 2003; LaConte, 2005c, Mitchel, 2004). While these corrections are possible in training runs, in feedback testing runs (where the stimulus is being actively controlled) the BOLD delay can lead to errors or sluggish feedback. An important question is "how fast is fast enough?" Our answer is that this depends on the experiment and the type of cognitive processes being modeled. Rather than developing fMRI techniques that circumvent hemodynamic limitations in the hopes of approaching neuronal time scales, this project proposes characterizations that will enable better experimental designs given the current capabilities and limitations of blood flow-based neuroimaging.

For data acquisition, we use adaptations of standard stimuli for passive sensory perception, memory, etc. (e.g. flashing checkerboard, audio metronome, tactile (touch) stimuli, list of paired associate words/pictures) and internally and sensory cued motor tasks (e.g. foot, hand, or limb movements such as finger opposition, hand clenching, and rapid button pressing). When the scanner is running in real-time mode, we will provide feedback to the volunteer about their internal state (e.g. success of encoding paired associates, attention level, mood, motor performance).

In order to improve the process of data acquisition, we will be developing software additions to the Siemens image reconstruction code to automate data transfer to analysis computers in our lab. These changes in software are isolated from (the code will not have any access to) HIPAA sensitive information. In addition we will not be modifying the sequence itself so the MRI data acquisition and Siemens safety safeguards will not be altered. To summarize, we will be making software changes to streamline our experiments, but safety and privacy risks will not change.

AUD and Default Mode Network (DMN) Background:

Alcohol use disorder (AUD) remains a leading cause of morbidity and mortality in the United States, and most people who attempt to quit drinking relapse within six months. Since treatment efficacy seems in part to be a function of alcohol use severity, existing treatments could benefit from better brain measures that explicitly characterize the severity of AUD. Unfortunately, most imaging studies compare individuals with AUD to healthy controls – or if they do assess severity, only do so in one cognitive domain and in one sample. This research is influenced by the observation that the DMN is altered in AUD and in addiction generally. Although the DMN is typically more prominent in resting-state fMRI, analysis of task-based fMRI has suggested a plausible functional role for DMN activity in addiction.

3.2 Describe any relevant preliminary data:

Preliminary data collected with our rtfMRI apparatus show that healthy participants can control DMN activity bi-directionally. This positions us to examine whether AUD individuals can apply similar control and if this ability is influenced by the severity of their addiction.

3.3 Based on the existing literature, provide the scientific or scholarly rationale for and significance of your research and how will it add to existing knowledge:

Based on these observations, this study directly tests the ability to modulate neural activity as a function of AUD severity using real-time fMRI. The real-time system has been used to demonstrate that healthy participants can successfully learn to gain volitional control over their own DMN activity, and that this ability appears to be impaired in psychiatric conditions. Individuals who drink alcohol, including those with AUD, will be recruited and consented into a real-time study. There are two neuromodulation tasks, which they may complete one or both of. The "DMN" neuromodulation task has them attempt to "focus/wander". The "BAAD" neuromodulation task instructs participants to modulate their brain activity toward a craving for alcohol or orient it toward a future goal. If there is time, and the participant is interested, they will also be given the opportunity to complete the other task to which they weren't initially assigned. In both tasks, participants will see their neural activity and attempt to increase and decrease its level prompted by neurofeedback. We will assess whether this ability is a function of AUD severity by correlating the neural activity with the experimentally-controlled “increase” and “decrease” cues, and then comparing this ability to AUDIT score.

4.0 Study Endpoints

*4.1 Describe the primary and secondary **study** endpoints. See links below for discussion of study endpoints and how they may differ from study objectives. These are most common in clinical trials but are sometimes applicable to other types of biomedical research, as well as social, behavioral, or educational research. See link below for a discussion.*

https://docs.google.com/document/d/1Wocz7K7a0hCQJPPO_khh5l1SQQjhGDDGHzcOPRHR5Tw/edit?usp=sharing

N/A

*4.2 Describe any primary or secondary **safety** endpoints. These should be included for all studies that are greater than minimal risk. (Minimal risk:*

The probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.):

N/A

5.0 Study Design and Statistical Analysis Plan

5.1 Describe the basic study design/approach (e.g., qualitative study using five focus groups of first year students to describe assimilation into the university community; randomized controlled trial of a behavioral change intervention to increase dietary intake of whole grains; pre- post-test evaluation of new pedagogical techniques to improve adult literacy):

50 participants who drink alcohol, including those with AUD, will be recruited and consented into a real-time study intended to assess the relationship between AUDIT score and neural modulation. There are two neuromodulation tasks, which they may complete one or both of. The "DMN" neuromodulation task has them attempt to "focus/wander". The "BAAD" neuromodulation task instructs participants to modulate their brain activity toward a craving for alcohol or orient it toward a future goal. If there is time, and the participant is interested, they will also be given the opportunity to complete the other task to which they weren't initially assigned.

5.2 Describe corresponding data analysis plan/approach (e.g., content analysis of focus group transcripts; descriptive analysis followed by linear regression modeling; nonparametric analysis of pre- and post-test measures):

GLM-based analysis will be performed using AFNI (Cox, 1996). We will perform slice timing correction, motion correction, and spatial smoothing (Gaussian kernel with full-width-at-half-maximum of 2.0 × the voxel size). The stimulus paradigms will be convolved with an ideal hemodynamic response function, and linear regression analysis will be performed to obtain linear regression coefficients (beta-weights) and t-statistic maps. In addition, we will perform support vector machine analysis using the 3dsvm AFNI plugin software we have developed.

6.0 Setting

6.1 Describe the sites or locations where your research team will conduct the research. Consider each of the items listed below:

- *Identify where your research team will identify and recruit potential subjects.*

- *Identify where the team will perform the research procedures.*
- *Describe the composition and involvement of any community advisory board(s).*
- *For research conducted in other locations, describe:*
  - *Site-specific regulations or customs affecting the research at those locations.*
  - *Local scientific and ethical review structure at those locations. Examples include work in other cultures or ethnic groups (within or outside of the U.S.) and work with churches. The HRPP will provide additional guidance for international research.*

Location of Recruitment:
Participants will be recruited from the community via posted flyers, word of mouth, and electronic advertisements (e.g., Craigslist, Facebook). Participants may also be recruited from a pre-existing database of individuals who have given consent to be contacted about studies.

Location of study:
All methods and measures will be conducted using standard operating procedures at the Fralin Biomedical Research Institute at VTC. All staff (including recruitment staff) will be provided with cultural sensitivity training. All participants will enroll on a voluntary basis and sign an IRB-approved consent form prior to study participation.

7.0 Study Intervention(s)/Investigational Agent(s)

7.1 Describe the study interventions (including behavioral interventions) and/or investigational agents (e.g., drugs or devices) to be used in this study. Consider each of the items listed below:

- *Drug/Device Handling: If the research involves drugs or devices, describe your plans to store, handle, and administer the drugs or devices so that they will be used only on subjects, and only by authorized investigators.*
- *Describe whether any of the following will be used: microwaves, X-rays, DEXA scans, general anesthesia, or sedation*
- *If control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference the SOP in this section.*

The primary procedure is an MRI scan. The MRI scanner we will use has a magnetic field of approximately 3.0T. Scanners with a 3.0T field strength have been approved for

clinical use by the FDA and are currently available for routine clinical applications. The MRI session will include a localizer, structural scan, and real-time scans. The localizer and structural scan simply requires the participant to hold still and stay awake. There are two real-time tasks, which they may complete one or both of (depending on time constraints). The "DMN" neuromodulation task starts with a resting-state scan and then has them attempt to "focus/wander". The "BAAD" neuromodulation task instructs participants to modulate their brain activity toward a craving for alcohol or orient it toward a future goal. The BAAD task itself assesses alcohol demand indices using three questions that ask participants about their drinking habits at different price ranges. They will respond to Delay Discounting (DD). During “BAAD” training and neuromodulation, participants will view individualized images of alcohol and positive, goal-oriented life events. Participants will be asked to rate these images (ex: on a scale of 1 to 9) on qualities such as valence, arousal, and craving following their scan. If the staff has reason to be concerned about the quality of a localizer or anatomical scan (for example due to motion in the scanner), the scan will be repeated. If there is additional time, an eye-tracking scan will be included. If a participant decides to discontinue their participation, some parts of the scan will not be completed. Participants will be asked to complete a relevant pre and post-scan questionnaires (see attachment). Any questionnaires used will receive approval from the IRB prior to use with participants.

7.2 List the name of all drugs (including any vitamins, supplements, herbs, or nicotine) to be used in the study. Indicate whether they have FDA approval, and list any limitations for their use:

N/A

7.3 List all devices, how they will be used, their purpose in the study, and if they will be used in a manner consistent with their approved uses. If they will be used in ways that are not yet FDA approved, indicate whether they need an IDE or a determination that they are exempt from the IDE Determination. If a determination of significant risk or non-significant risk is needed for any of the devices, include the researcher’s recommendation for each of those devices:

The primary procedure is an MRI scan. The MRI scanner we will use has a magnetic field of approximately 3.0T. Scanners with a 3.0T field strength have been approved for clinical use by the FDA and are currently available for routine clinical applications.

7.4 If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

- *Identify the holder of the IND/IDE/abbreviated IDE.*
- *Explain procedures followed to comply with sponsor requirements for FDA regulated research for the following:*

	Applicable to:		
FDA Regulation	***IND Studies***	***IDE studies***	***Abbreviated IDE studies***
21 CFR 11	***X***	***X***	
21 CFR 54	***X***	***X***	
21 CFR 210	***X***		
21 CFR 211	***X***		
21 CFR 312	***X***		
21 CFR 812		***X***	***X***
21 CFR 820		***X***	

N/A

8.0 Procedures Involved

8.1 Describe and explain the study design:

The primary procedure is an MRI scan. MRI scans allow the researcher to view brain anatomy and activity relevant to the study question of how AUD interacts with neural modulation. The MRI scanner we will use has a magnetic field of approximately 3.0T. Scanners with a 3.0T field strength have been approved for clinical use by the FDA and are currently available for routine clinical applications. The MRI session will include a localizer, structural scan, and real-time scans. If there is sufficient time, eye-tracking scans will also be completed. The localizer and structural scan simply requires the participant to hold still and stay awake. There are two real-time tasks, which they may complete one or both of (depending on time constraints). The "DMN" neuromodulation task starts with a resting-state scan and then has them attempt to "focus/wander". The "BAAD" neuromodulation task instructs participants to modulate their brain activity toward a craving for alcohol or orient it toward a future goal. The BAAD task itself assesses alcohol demand indices using three questions that ask participants about their drinking habits at different price ranges. They will respond to Delay Discounting (DD) prompts. During “BAAD” training and neuromodulation, participants will view previously-generated individualized images of alcohol and positive, goal-oriented life events. These images will be customized based on a brief phone interview completed prior to their MRI appointment. If the participant is unable to complete these questions over the phone, they will have the option to do so in person. During cue generation, the

participant will be asked to describe the most positive event that could realistically happen at several time points (e.g. 1 week out, 5 years out, etc). For each time point, the participant will be asked to integrate the event and sensory information into concise descriptions to be used in generating images. Participants may also choose to provide images of loved ones involved in these events. Providing images of loved ones is completely optional. Any images of loved ones provided will be kept on secure, password protected servers. The eye-tracking scan has the participant watch a moving dot on the screen for a brief period of time. If the staff has reason to be concerned about the quality of a localizer or anatomical scan (for example due to motion in the scanner), the scan will be repeated. If a participant decides to discontinue their participation, some parts of the scan will not be completed.

Breath Alcohol Concentration (BrAC) will be recorded upon arrival, with a required BrAC less than 0.003 g/dL to begin study procedures. Once their BrAC is cleared, participants will complete an Alcohol Withdrawal Symptoms questionnaire to assess alcohol withdrawal and an out-of-scanner Delay Discounting task (DD). Lastly, prior to scanning participants will complete a series of questionnaires (e.g. Socioeonomic Status (SES), Alcohol Use Disorder Identification Test (AUDIT), Alcohol Reinforcement Questionnaire).

Following the MRI scan, participants will be asked to rate the images from the MRI tasks. They will provide their feedback using a slider (ex: scale of 1-9) on qualities such as valence, arousal, and craving.

Participants will also be asked to complete a relevant post-scan questionnaire asking about their subjective experience during the MRI scan, which would include valuable data such as their effort level, if they were able to stay awake, and their confidence in the task (see attachment). Any questionnaires used will receive approval from the IRB prior to use with participants. Questionnaires used will supplement these findings with relevant information. Prior to study activities, participants will provide consent and review their MRI screening form with the researcher.

8.2 Provide a description of:

- *All research procedures being performed*
- *If the study has more than one procedure, session, and/or subject population, describe each procedure, session, and/or study population separately. For complex studies, you are encouraged to include a figure or chart.*

Participants will be recruited from the community via posted flyers, word of mouth, and electronic advertisements (e.g., Craigslist, Facebook). Participants will be contacted if they have given prior permission (through previous informed consent form) or by completion of a confidential pre-screening questionnaire. Upon contact, participants will

complete an MRI screening form to assess eligibility. At this time participants may be scheduled for their session if they are eligible. Cue questions used for image generation may be asked during this phone call, or at a later time prior to their MRI appointment. During cue generation the participant will be asked to describe the most positive event that could realistically happen at several time points (e.g. 1 week out, 5 years out, etc). For each time point, the participant will be asked to integrate the event and sensory information into concise descriptions to be used in generating images. Participants will also be informed at this time that they may provide images of loved ones if they would like, although this will be in no way a requirement. Any images of loved ones provided will be kept on secure, password protected servers.

Breath Alcohol Concentration (BrAC) will be recorded prior to beginning to study procedures. Participants will be asked to come back another day if they come to their session appointment with a BrAC > 0.003 g/dL. Participants are required to refrain from drinking before beginning assessments in the lab. They will also complete an Alcohol Withdrawal Symptom questionnaire and an initial Delay Discounting (DD) task. DD (a measure of the temporal window) examines the devaluation of monetary rewards as a function of delay to their receipt. These computerized assessments present hypothetical choices between smaller, sooner and larger, later rewards available at a range of delays. Lastly, prior to scanning participants will complete a series of questionnaires (e.g. Socioeonomic Status (SES), Alcohol Use Disorder Identification Test (AUDIT), Alcohol Reinforcement Questionnaire).

At the beginning of this visit, investigators of the study will review safety issues related to MRI with the subject and answer any questions. The primary procedure is an MRI scan. The MRI scanner we will use has a magnetic field of approximately 3.0T. Scanners with a 3.0T field strength have been approved for clinical use by the FDA and are currently available for routine clinical applications.

Prior to entering the scanner participants will be asked to read through instructions for the task with the researcher. Once instructions have been read through, the subjects will lie still in the MR scanner for a total of no more than 90 minutes, and studies will not exceed 2 hours. During the first several minutes acquisition of the structural scans will take place (T1-, T2-, and/or DTI-weighted), which will be followed by acquisition of the functional / real-time images. There are two real-time tasks, which they may complete one or both of (depending on time constraints). The "DMN" neuromodulation task starts with a resting-state scan and then has them attempt to "focus/wander". The "BAAD" neuromodulation task instructs participants to modulate their brain activity toward a craving for alcohol or orient it toward a future goal. The BAAD task itself assesses alcohol demand indices using three questions that ask participants about their drinking habits at different price ranges. They will respond to in-scanner Delay Discounting (DD) prompts. During “BAAD” training and neuromodulation, participants will view their previously-generated individualized images of alcohol and positive, goal-oriented life events. Anatomical scans will be repeated if the staff has reason to be concerned about participant motion which effects image quality. While the subject is inside the scanner, an

investigator will be in constant visual observation of the subject and in between scans will use voice-communication via an intercom to assure the subject remains comfortable. The subject will also have a hand-held squeeze bulb to signal the investigators at any point in the experiment. In the scenario the subject wishes to be withdrawn, the investigator with take the subject out of the scanner immediately. The behavioral tasks that are being proposed do not involve any administration of drugs or placebos or other treatments.

A series of cognitive paradigms will be developed that are based on the presentation of visual, auditory, motor, or somatosensory stimuli to which subjects will give a response covertly or by pressing a button. Images will be generated on a PC interfaced to a long focal length projector or fiber optic, LCD goggles. Attention checks, which require pressing a button when directed, will be acquired with a fiber optic button response box interface to the computer. The fiber optic box allows response acquisition without the generation of electromagnetic noise in the scanner. When the scanner is running in real-time mode, we will provide feedback to the volunteer about their internal state.

Following the MRI scan, participants will be asked to rate the images from the MRI tasks. They will provide their feedback using a slider (ex: scale of 1-9) on qualities such as valence, arousal, and craving.

During the visit, subjects will be asked to complete a post-scan questionnaire related to the task that the subject completed while in the scanner (e.g. "Did you find the tasks easy or difficult?"; "Did you feel like you were able to control the cursor as instructed?"). Any materials given to participants will be submitted to the IRB for approval prior to use.

Eye tracking: If there is adequate time to complete additional procedures, we will collect eye tracking data to allow us to model brain activity related to eye movements, potentially eliminating confounds. Additionally, the eye tracking data will allow us to determine which aspects of the stimulus presentation the subjects attend to. One way to do eyetracking is to use commercially available systems, which rely on infrared light, either through a visual goggle system or an installed tracking system in the scanner suite. While subjects are in the scanner, the position of their eyes will be tracked using an infrared eye-tracking device. For example, the Applied Science Laboratories (ASL), Series 6000 model shines near infrared light (IR-A; wavelengths between 770 and 1400 nanometers) into the scanner bore and then detects the reflection back from the subjects' eyes. This scattering information is used to reconstruct the coordinates of the subjects' eyes. Using the eye tracking information will allow us to model brain activity related to eye movements, potentially eliminating confounds. Additionally, the eye tracking data will allow us to determine which aspects of the stimulus presentation the subjects attend to.

After study procedures are complete, subjects will be removed from the scanner, paid for their participation, and given a CD with images of their brain taken during the structural scan. Participants are compensated $30.00 per hour. If a participant is withdrawn or voluntarily discontinue, their compensation for the study will be pro-rated accordingly.

Procedure for Functional Imaging Scans: The MRI imaging experiments will be performed on a Siemens 3T scanner, and we will only use structural and functional sequences that conform to FDA guidelines for specific absorption rate (SAR) of radio frequency energy. SAR is limited by both hardware and software checs on the MRI scanners. We have three research-dedicated 3T Seimens MRI available for the studies proposed in this project. A standard head coil will be used to collect the MR data. Fast imaging sequences, using echo-planar methods, will be used to enable the high temporal resolution necessary for fMRI. In addition 3-D sequences (MPRAGE or FSPGR) and water diffusion-weighted sequences (DWI or DTI) may be used to acquire structural information (high resolution anatomy and white matter structure), which will allow the subsequent superposition of functional data with its underlying anatomy.

8.3 Describe:

- *Procedures or safeguards intended to reduce the probability and magnitude of risks. (For example: Reducing the risk of injury in a virtual reality study either by having the subjects sit during the study or by providing an obstacle-free space for walking.)*
- *Be sure to describe all drugs and devices used in the research, when they will be administered or used, and their purpose.*
- *Methods used to collect data about subjects. Please upload all data collection forms to Protocol Management. Some common examples are:*
  - *Screening questionnaires*
  - *Survey(s), including online surveys*
  - *Demographic questionnaire(s)*
  - *Interview guide(s), e.g., questions or pool of questions for semi-structured interviews*
  - *Focus group guide(s)*
  - *Other documents used to collect data*

Breath Alcohol Concentration (BrAC) will be recorded prior to beginning to study procedures. Participants will be asked to come back another day if they come to their session appointment with a BrAC > 0.003 g/dL. Participants are required to refrain from drinking before beginning assessments in the lab. They will also complete a Alcohol Withdrawal Symptom questionnaire. A score of >23 on this checklist requires medical oversight for alcohol withdrawal and will trigger the research staff to contact study physician Dr. Anita Kablinger for guidance.

Prior to to scanning participants will complete an out-of-scanner DD task. DD (a measure of the temporal window) examines the devaluation of monetary rewards as a function of delay to their receipt. These computerized assessments present hypothetical choices between smaller, sooner and larger, later rewards available at a range of delays.

The MRI session will include a localizer, structural scan, and real-time scans. If there is sufficient time, eye-tracking scans will be completed as well. The localizer and structural scan simply requires the participant to hold still and stay awake. There are two real-time tasks, which they may complete one or both of (depending on time constraints). The "DMN" neuromodulation task starts with a resting-state scan and then has them attempt to "focus/wander". The "BAAD" neuromodulation task instructs participants to modulate their brain activity toward a craving for alcohol or orient it toward a future goal. The BAAD task itself assesses alcohol demand indices using three questions that ask participants about their drinking habits at different price ranges. They will respond to in-scanner Delay Discounting (DD) prompts. During “BAAD” training and neuromodulation, participants will view their individualized, previously-generated images of alcohol and positive, goal-oriented life events. These images will be customized based on a brief interview completed prior to their MRI appointment. During this, the participant will be asked to describe the most positive event that could realistically happen at several time points (e.g. 1 week out, 5 years out, etc). For each time point, the participant will be asked to integrate the event and sensory information into concise descriptions to be used in generating images. Participants may also choose to provide images of loved ones involved in these events. Providing images of loved ones is completely optional. Any images of loved ones provided will be kept on secure, password protected servers. The eye-tracking scan has the participant watch a moving dot on the screen for a brief period of time. All scans are considered minimal risk. In order to minimize noise from the MRI scanner that can be potentially harmful for the subject, all subjects will be required to wear ear protection while in the scanner. The subject may communicate with the experimenter at any time: 1) before, in between, or after a scan via an intercom device between the scanner and control room, and 2) during a scan via a pneumatic squeeze bulb located in the scanner that triggers an alarm in the control room. Subjects who report discomfort and wish to discontinue their participation will be immediately withdrawn from the scanner. Subjects who are withdrawn from the study will be compensated for their participation to that point.
Following the MRI scan, participants will be asked to rate the images from the MRI tasks. They will provide their feedback using a slider (ex: scale of 1-9) on qualities such as valence, arousal, and craving.

During the visit, subjects will be asked to complete a post-scan questionnaire related to the task that the subject completed while in the scanner (e.g. "Did you find the tasks easy or difficult?"; "Did you feel like you were able to control the cursor as instructed?"). Any materials given to participants will be submitted to the IRB for approval prior to use.

Participants will complete an MRI screening form prior to enrollment which assesses their eligibility and if they are safe to participate in an MRI study. Individuals with MRI contraindications will not participate in the MRI. Any participant-facing documents will

be submitted to the IRB and approved prior to use. All paper documents will be stored in a locked cabinet, in a locked office, accessible only to study staff.

General Safety: Despite our best efforts, we recognize that in rare circumstances participants may experience extreme distress with sudden onset. The PI and study staff are trained to recognize and deescalate such situations. All personnel are instructed to exercise judgment and follow our safety protocol where indicated.

Advanced MR/Operator Training: Required for those persons wishing to conduct research on the HNL MRIs. Training will consist of presentations, observation, and hands-on practice. Topics will include safety and emergency procedures, subject screening and preparation, scanner set-up and operation, and troubleshooting. Each person must also complete at least 4 hours of observation (to include 2 different studies) and at least 16 hours of supervised scanning (to include 4 different studies). Certification will be granted upon completion of the training and passing of a competency exam

In some cases for demonstration, the volunteers will be provided with their own structural brain images to take home on CD, as is done with many of our approved IRB protocols. These images are not diagnostic quality and are provided to subjects routinely after most approved protocols. They are informational only and are not intended to be used as diagnostic tools.

8.4 What data will you collect during the study and how you will obtain them? Please include descriptions of electronic data collection, database matching, and app-based data collection:

During the MRI, we will collect an anatomical scan as well as brain data during the before-mentioned alcohol and modulation tasks, and an eye-tracking task if time permits. Brain images will be collected using an MRI with a magnetic field of approximately 3.0T. Outside of the MRI, participants will complete the before-mentioned Alcohol Withdrawal Questionnaire, DD task, and post-scan questionnaire.

Screening and questionnaire data will be presented on paper which will be stored in a secured location following collection (see 9.0). Cue event data will be collected using Qualtrics, an online survey platform used to develop, administer, and collect participant data in a secure password protected database. Only study personnel will have access to the survey and collected data.

8.5 Who will transcribe or code audio and/or video recordings?:

N/A

8.6 Include a description of any deception to be used in the study. Include justification for the use of deception (why the deception is necessary), describe the debriefing process, and describe how the study meets <u>all</u> the following criteria for alteration of consent (deception is considered an alteration of informed consent):

- *The research involves no more than minimal risk to the subjects*
- *The alteration will not adversely affect the rights and welfare of the subjects*
- *The research could not practicably be carried out without the alteration/deception*
- *(Optional but encouraged in most cases) Subjects will be provided with additional pertinent information after participation (i.e., debriefing for studies involving deception)*

N/A

8.7 If the study involves long-term follow-up (once all research related procedures are complete), describe what data will be collected during the follow up period and when it will occur:

N/A

9.0 Data and Specimen Long Term Storage and Use

9.1 If you will store data or specimens for future use, describe where you will store the data or specimens, how long they will be stored, and how and by whom the data or specimens will be accessed:

Subjects will be assigned a coded description, the key to which will be stored in a locked safe, in a locked room, separate from other study materials. All paper records from the

study, with the exception of the consent form and the MRI screening form, will be identifiable only by this subject number, and all forms will be kept in a locked file cabinet. Electronic data will be accessed via password protected computer and password protected server.

9.2 For specimens, list the data to be stored or associated with each specimen:

All paper records containing participant identity will be stored in locked cabinets and available only to authorized research staff.

9.3 Describe the procedures to release data or specimens outside of the research team, including the process to request a release, approvals required for release, who can obtain data or specimens, and what data will be provided with specimens:

In an effort to foster open neuroscience and reproducible results, anonymized data collected as a part of this study may be made openly available on the internet, in one of the various repositories for housing such data. All data will be de-identified using standards conforming to HIPAA guidelines. For example all high-resolution images will be defaced to avoid the possibility of the subject being identified from the scans. Only subject ages will be released, not subject birthdates, we will not include any subjects whom are old enough to be uniquely identified by age alone. New subject identifiers will be assigned, such that data will not be mappable back to internal subject identifiers. Subjects with rare, and potentially identifying brain abnormalities will not be included in the release.

There are several ways in which openly sharing this data will be beneficial to society. It makes it possible for other researchers to validate any scientific results that we may find. It is a valuable educational resource for new researchers to learn how to analyze these types of data. Also, by allowing other researchers to use (or reuse) the data, we are reducing the amount of time and money required to perform similar scientific research.

9.4 Describe the identifiers to be included with stored data or specimens, as well as any key or code that could be used to make them identifiable. Describe where the code will be stored, who will have access to it, and when it will be destroyed:

Subjects will be assigned a coded description, the key to which will be stored in a locked safe, in a locked room, separate from other study

materials. Codes will not be based on any participant-relevant information. All identifiable data, including the code linking participant name to their study ID, will be destroyed after 7 years.

9.5 Please select the identifiers you will obtain (whether directly from participants or from another source), including but not limited to:

☒	*Name*
☐	*Geographical subdivisions smaller than a state, including street address, city, county, precinct, zip code, and equivalent geocodes (note, the initial three digits of a zip code are not considered identifiable)*
☒	*Elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death, and single year of age over 89 and all elements of dates (including year) indicative of such age (note, such ages and elements may be aggregated into a single category of age 90+)*
☒	*Phone numbers*
☐	*Fax numbers*
☒	*Electronic mail addresses (e-mail)*
☒	*Social Security numbers*
☐	*Medical record numbers*
☐	*Health plan beneficiary numbers*
☐	*Account numbers*
☐	*Certificate/license numbers*
☐	*Vehicle identifiers and serial numbers, including license plate numbers*
☐	*Device identifiers and serial numbers*
☐	*Web Universal Resource Locators (URLs)*
☐	*Internet protocol (IP) address numbers*
☐	*Biometric identifiers, including finger and voice prints (audio recording)*
☐	*Full face photographic images and any comparable images (including video recording)*
☐	*Student record number or identification number*
☐	*User name for online or computer accounts*
☐	*Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)***:** Click here to explain.

10.0 Sharing of Results with Subjects

10.1 Describe whether you will share results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) with subjects or others (e.g., the subject's primary care

physician). If so, describe how you will share the results and include this information as part of the consent document. Upload materials you will use to explain the results to subjects:

We will not share any results with the study participants.

Specific to incidental neuroimaging findings: The Human Neuroimaging Lab at Virginia Tech has a standardized approach to incidental findings across approximately 60 currently active protocols (including scanning over 150 individuals with AUD). Moreover, our process is consistent with the best practices recommendations of the NIMH "MRI Research Safety and Ethics: Points to Consider" whitepaper (https://www.nimh.nih.gov/about/advisory-boards-and-groups/namhc/reports/mri-research-safety-ethics_33826.pdf). Furthermore, our procedures conform with those reported in the literature as appropriate for our research setting. During the consenting process, participants are informed that the scans that will be performed in the study are not the same as those that would be used in a clinical setting, and thus have limited diagnostic value. Further, some of the scans require subsequent data analysis and would never be read by a neuroradiologist. As is common and acceptable in many academic institutions, we do not have a neuroradiologist on staff to read every scan. Our policy (which is communicated to all participants verbally and written in the consent document): "This is not a study for diagnostic purposes and your brain images will not be read by a radiologist. If, by chance, something abnormal is observed, you will be informed of this and counseled as to what clinical referral would be appropriate as we are not qualified to make any diagnosis, nor is this fMRI of diagnostic quality for medical purposes."
We also communicate, however, that we will err on the side of caution in communicating with them if we do observe a possible abnormality.

11.0 Study Timelines

11.1 Describe:

- *The duration of an individual subject's participation in the study (for example, 1 hour, 2-4 weeks, 3-5 years).*
- *The amount of time expected to enroll all study subjects (weeks, months, years, etc.)*
- *The amount of time expected for the investigators to complete this study including primary data analyses.*

Participants will participate in one rtfMRI session. The participants will lie still in the MR scanner for a total of no more than 90 minutes, and MRI sessions will not exceed two hours. The brief cue generation interview, completed prior to the scanning appointment, is expected to take 20 minutes, and will not exceed one hour. We will retain personally identifiable study data for a period of seven years after completion of the study. After the period of 7 years has passed, we will destroy any personally identifiable study data. Recruitment and enrollment

is anticipated to last 18 months. From start to completion, including data analyses, this study is anticipated to last two years.

12.0 Inclusion and Exclusion Criteria

12.1 Describe how you will screen individuals for eligibility. When will screening occur and what procedures will you use? Upload any screening scripts or surveys to Protocol Management:

Potential subjects will be initially screened over the phone or in person. Individuals meeting inclusion/exclusion criteria for the study, as determined by the pre-consent screening form will be enrolled.

12.2 Describe the eligibility criteria that define who will be included and who will be excluded from enrollment for each procedure of your study. Include any geographic criteria (e.g., Virginia Tech undergraduate students, a national sample of adults with engineering degrees, minors aged 8-12 in the New River Valley, university faculty in Virginia and Paris, France):

Inclusion criteria for signing consent will require that participants: (1) drink alcohol (2) be 21 years of age or older,

Exclusion criteria include: (1) meeting moderate to severe DSM-5 criteria for substance-use disorders other than alcohol, nicotine, or marijuana, (2) having a current diagnosis of any psychotic disorder, (3) having a history of seizure disorders or a traumatic brain injury they have not fully recovered from, (4) reporting current pregnancy or lactation.

12.3 Indicate specifically whether you will include or exclude each of the following special populations: (You may not include members of these populations as subjects in your research unless you indicate them in the description of your subject population.)

- *Minors, as defined by state law where the study is performed (infants, children, teenagers)*
- *Pregnant women (can be included in minimal risk studies by mentioning in section 13.1)*
- *Prisoners (including all incarcerated individuals)*
- *Adults not capable to consent on their own behalf*

This project will focus on individuals with alcohol use disorder, aged 21 or over. We will not include individuals under the age of 21 in compliance with Virginia state law. Vulnerable subjects, such as individuals with cognitive impairments, minors, prisoners, and pregnant women will be excluded.

13.0 Vulnerable Populations

13.1 If the research involves individuals who are vulnerable to coercion or undue influence, please describe additional safeguards you will include to protect their rights and welfare. Consider the applicable items listed below:

- *If the research involves Virginia Tech students, indicate whether these are students of any of the investigators. If so, describe whether the activities will take place during class time as part of the curriculum and the steps you will take to reduce the possibility that students feel obliged to participate in order to improve their course grade. The HRPP can provide further guidance as needed. Describe whether you will request access to student records (e.g., SAT, GPA, GRE scores).*
- *If the research involves employees of Virginia Tech or the research sponsor, describe steps you will take to ensure that the employees are freely participating and describe how their data will be protected from inspection by their supervisors.*
- *If the research involves Virginia Tech NCAA athletes, you must obtain approval from the athletic department.*
- *For research involving Montgomery County Public Schools, you must obtain county approval (after obtaining contingent Virginia Tech approval). Other locales have different requirements; please check on these and describe here. Approval is typically granted by the superintendent, principal, and classroom teacher (in that order). Approval by an individual teacher is insufficient. School approval, in the form of a letter or a memorandum should be uploaded as a supporting document.*
- *If the research involves pregnant women, review "CHECKLIST: Pregnant Women (HRP-412)" to ensure that you have provided sufficient information in this protocol.*
- *If the research involves prisoners, review "CHECKLIST: Prisoners (HRP-415)" to ensure that you have provided sufficient information in this protocol.*

- *If the research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research (minors), review the "CHECKLIST: Minors (HRP-416)" to ensure that you have provided sufficient information in this protocol.*
- *If the research involves cognitively impaired adults, review "CHECKLIST: Cognitively Impaired Adults (HRP-417)" to ensure that you have provided sufficient information in this protocol.*

This research study will not include any vulnerable populations.

14.0 Number of Subjects

14.1 Indicate the total number of subjects to be enrolled and how this number was determined (e.g., sample size calculation [show], number of available subjects in a finite pool, number of tests funding award would allow):

G*power (Faul et al., 2007) determined the necessary sample size for this experiment - given a medium expected correlation of 0.4, we would need 42 participants (alpha = 0.01, Power = 0.8). We therefore propose to collect data from 50 participants.

14.2 If this is a multi-site study, indicate the number of subjects to be enrolled at this site and the total to be enrolled from all sites:

N/A

14.3 If applicable, indicate the number of potential subjects you expect to screen for enrollment, and the number of subjects you will need to complete the research procedures:

N/A

14.4 If the study has more than one procedure, indicate the total number of subjects to undergo each procedure separately:

N/A

15.0 Recruitment Methods

15.1 Describe when, where, and how you will recruit potential subjects:

Participants will be recruited from the community via posted flyers, word of mouth, and electronic advertisements (e.g., Craigslist, Facebook). Participants may also be recruited from a pre-existing database of individuals who have given consent to be contacted about studies.

15.2 Describe the source of subjects (for example, clinic patients with specific conditions, students in the library, community members at a gathering, or members of a local gym):

Participants will be recruited from the community via posted flyers, word of mouth, and electronic advertisements (e.g., Craigslist, Facebook). Participants may also be recruited from a pre-existing database of individuals who have given consent to be contacted about studies.

15.3 Describe the methods that you will use to identify potential subjects:

Participants will be recruited from the community via posted flyers, word of mouth, and electronic advertisements (e.g., Craigslist, Facebook). Participants may also be recruited from a pre-existing database of individuals who have given consent to be contacted about studies.

15.4 Describe materials that you will be use to recruit subjects. Attach copies of these documents with this protocol in Protocol Management and be sure to include the IRB protocol number on each document.

- *For flyers, attach the final copy of printed flyers.*
- *For Virginia Tech News, Facebook postings and ads, newspaper ads, websites, MTurk/SONA/online survey systems, etc., attach the final wording and graphics to be used.*
- *For email recruitments, please include the subject line.*
- *For advertisements meant for audio broadcast, please submit the wording of the advertisement prior to taping (to avoid having to re-record with approved language) and submit the final recorded version for IRB review before use.*
- *Describe any compensation to subjects. Separate compensation into appropriate categories, such as: reimbursement for expenses, time and*

effort, and additional incentives for study participation. For each category, specify the amount (including any pro-rated amount), schedule, and method of payment.

Recruitment flyer included in protocol submission.

Participants are compensated $30.00 per hour of distributed via Clincard or approved petty cash accounts. Payments will be submitted the same day as the subject's MRI session. If a participant is withdrawn or voluntarily discontinue, their compensation for the study will be pro-rated accordingly.

16.0 Withdrawal of Subjects

16.1 Describe circumstances under which you anticipate subjects could be withdrawn from the research without their consent:

Participants may be withdrawn from the research without their consent if they become ineligible based on inclusion/exclusion criteria or learning of a contraindication for continuing

If the participant is not complying with FBRI building policies and/or insists on leaving with a BAC >0.08 g/dL, local security will be contacted however, the participant will not be named to avoid breaking confidentiality. They will also complete an Alcohol Withdrawal Symptom questionnaire. A score of >23 on this checklist requires medical oversight for alcohol withdrawal and will trigger the research staff to contact study physician Dr. Anita Kablinger for guidance.

16.2 If applicable, describe any procedures for orderly termination (e.g., discontinuation of a study drug or debriefing after a behavioral intervention):

If a participant is withdrawn from the study, he or she will be informed that we have collected all the data required from their participation. If a participant is withdrawn or voluntarily discontinue, their compensation for the study will be pro-rated accordingly.

16.3 Describe procedures that you will follow when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection (e.g., participant declines to continue with regular blood draws, but continues with periodic behavioral questionnaires):

If a participant is withdrawn or discontinued, they will be withdrawn from the entire study.

17.0 Risks to Subjects

17.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. Include for the IRB's consideration a description of the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, privacy, and economic risks. Do not indicate "No risk" or "N/A." Instead, for studies with very low risk (e.g., anonymous online questionnaire on a mundane topic) indicate "The investigators are not aware of any risks from participation in this study." or "No more than risks than are found in everyday life." The example consent form presents a tabular method for risk information, which you can also use here. Common risk types include:

- *Physical (e.g., potential for pain, discomfort, infection)*
- *Psychological (e.g., potential for stress, discomfort, and/or embarrassment)*
- *Social (e.g., potential for discrimination or stigmatization and disruption of personal and family relationships)*
- *Legal (e.g., potential for disclosure of illegal activity, negligence)*
- *Privacy (e.g., potential for personal information being accessed, used, or disclosed without the subjects' knowledge or consent, breach of confidentiality/security)*
- *Economic (e.g., potential for individuals to lose access to economic services, employment, insurability)*

The risks associated with fMRI are the same as those with conventional MRI. Movement or heating of metallic implants is a potential risk, and so subjects will be screened to exclude people with metallic implants, fragments, or pacemakers. Some individuals experience claustrophobic reactions in the scanner. Any subject experiencing claustrophobia will be removed from the scanner immediately.

The fMRI scanner produces loud noises which could be harmful to the subject. Participants will be required to wear headphones to minimize the noise generated by the scanner.

There is no invasive component to this study, such as IV catheters, and so discomfort, bruising, or infection are not risks. The Siemens 3 T scanner has been approved by the FDA. However, there may be additional risks associated with scanning at 3 T compared to the conventional clinical scanners in the 1.5-2.0 T range. These include:

1. Effect of the static field. There is no conclusive evidence for irreversible or hazardous bioeffects to acute, short-term exposures of humans up to 2.0 T (Shellock and Kanal, 1996). Studies have indicated some side-effects at 4.0 T, namely unusual sensations including nausea, vertigo, and metallic taste (Schenck, 1991). However, there is no evidence that this is either irreversible or harmful. If subjects experience unusual sensations, they will be withdrawn.

2. Effect of the gradient field. MRI operates by rapidly changing small additional fields, called gradients. This will induce small electrical currents in any conductor, and thus could theoretically induce mild peripheral nerve stimulation. However, this is not substantially different at higher magnetic fields since the gradients are separate from the main magnet. There is no evidence that the effect of the gradients is any different at 3 T than at 1.5 T. However, if subjects experience peripheral nerve stimulation, e.g. tingling or twitching, they will be withdrawn.

3. Effect of the RF electromagnetic field. The higher magnetic field strength requires that higher RF frequency pulses are used to excite the protons in the subject's brain. The limits of RF energy that can be safely given to humans has been clearly defined by the FDA: a. The exposure to RF energy below the level of concern is an SAR of 0.4 W/kg or less averaged over the body, and 8.0 W/kg or less spatial peak in any 1 g of tissue, and 3.2 W/kg or less average over the head; or b. The exposure to RF energy that is sufficient to produce a core temperature increase of 1 degree C and localized heating to no greater extent than 38 degrees C in the head, 39 degrees C in the trunk, and 40 degrees C in the extremities, except for patients with impaired systemic blood flow and/or perspiration. We will adhere to the recommendations for the head, which is also monitored by a Siemens built-in monitor.

While in the scanner, subjects will alternate between a resting state and a stimulus-induced state. It is unlikely participant will experience discomfort during these tasks, however, subject comfort will be assessed routinely and subjects will be allowed to discontinue any session at any time.

The subject may communicate with the experimenter at any time: 1) before, in between, or after a scan via an intercom device between the scanner and control room, and 2) during a scan via a pneumatic squeeze bulb located in the scanner that triggers an alarm in the control room. Subjects who report discomfort and wish to discontinue their participation will be immediately withdrawn from the scanner. Subjects who are withdrawn from the study will be compensated for their participation to that point.

Because participants may not participant with a BAC over 0.003, they may experience alcohol withdrawal symptoms.

17.2 Indicate the measures you will use to minimize risks and monitor subjects for safety. (e.g., asking a subject at regular intervals to rate how they are feeling from 1 to 10, or to slowly crouch in order to check their balance.)

General Safety: Despite our best efforts, we recognize that in rare circumstances participants may experience extreme distress with sudden onset. The PI and study staff are trained to recognize and deescalate such situations. All personnel are instructed to exercise judgment and follow our safety protocol where indicated.

Advanced MR/Operator Training: Required for those persons wishing to conduct research on the HNL MRIs. Training will consist of presentations, observation, and hands-on practice. Topics will include safety and emergency procedures, subject screening and preparation, scanner set-up and operation, and troubleshooting. Each person must also complete at least 4 hours of observation (to include 2 different studies) and at least 16 hours of supervised scanning (to include 4 different studies). Certification will be granted upon completion of the training and passing of a competency exam

In some cases for demonstration, the volunteers will be provided with their own structural brain images to take home on CD, as is done with many of our approved IRB protocols. These images are not diagnostic quality and are provided to subjects routinely after most approved protocols. They are informational only and are not intended to be used as diagnostic tools.

Alcohol Withdrawal: In addition, participants who are not drinking alcohol may experience alcohol withdrawal symptoms They will complete the Alcohol Withdrawal Symptom Checklist (AWSC), a validated 17-item checklist of symptoms in which the participant rates their experience from 0 ("Not at all") to 4 ("Extreme"). A score of >23 on this checklist requires medical oversight for alcohol withdrawal and will trigger the research staff to contact Dr. Kablinger. Dr. Kablinger will speak with the participant to determine appropriateness and safety to continue in the study and to provide medical consultation and/or a referral to a clinic/primary care physician. If the participant produces a score of >23 on the checklist, Dr. Kablinger will be contacted to assess the participant's risk and refer as necessary. We have successfully implemented these procedures with Dr. Kablinger in our previous and ongoing studies.

17.3 If applicable, indicate which procedures might have risks to the subjects that are currently unforeseeable. This will be rare, and usually applicable when testing a new drug or device or a new use of an existing drug or device:

N/A

17.4 If applicable, indicate which procedures might have risks to an embryo or fetus should the subject be or become pregnant:

While no data have conclusively determined MR imaging to be unsafe for developing fetuses, it has also not been determined to be safe. Thus, consistent with the guidance document of the American College of Radiology (Kanal et al., 2013), we believe the benefit to the participant does not outweigh potential unknown risks to the developing fetus. Thus, we exclude pregnant women to ensure the safety of participants.

17.5 If applicable, describe risks to others who are not subjects (e.g., collection of sensitive health data that might affect sexual partners if disclosed, mandatory reporting of abuse, DNA testing that might affect family members or relationships):

N/A

18.0 Potential Benefits to Subjects

18.1 Describe the potential benefits that individual subjects might experience from participating in the research. Include the probability, magnitude, and duration of the potential benefits, as this will be useful to the IRB's risk:benefit analysis. Do not include benefits to society or others. Do not list monetary or non-monetary compensation for participation, as this is not a benefit These should be included in section 2 or 3 of this document:

Subjects will receive no direct benefits as a result of study participation, however they may benefit from possible improvement in self-control from these studies, plus education about research participation and fMRI recording methods in the context of research. The project involves minimal risk to confidentiality or other personal rights or to physical or emotional health. Thus, the expected benefits outweighed the very minimal risks to participants.

The knowledge potentially gained about the role of WM training and rtfMRI in repairing self-control of alcohol dependent individuals may inform the neurobiological basis of self-control failure in alcohol dependence, provide novel insights into new treatment approaches, provide new data about the relative efficacy of the two rtfMRI neuro-feedback techniques, and the application of rtfMRI to a complex cognitive task.

18.2 If applicable, specify that there are no anticipated direct benefits for participants:

There are no anticipated direct benefits for participation in this study.

19.0 Data Management and Confidentiality

19.1 Describe procedures that you will use for quality control to ensure validity of collected data:

The PI will oversee monitoring of the data collection procedures. These procedures will be reviewed regularly in a number of settings. For instance, issues pertaining to data validity and integrity will be addressed formally during regularly scheduled meetings.

19.2 Describe any existing data or biospecimens you will obtain as part of this study. Include:

- *Variables or samples to be obtained*
- *Source of the data or specimens*
- *Your authorization to access or receive the data or biospecimens*
- *Whether the data or biospecimens are publicly available*
- *Whether the data or specimens you receive will contain identifiers*

N/A

19.3 Describe the steps that you will take to handle and secure study data during data collection, storage, use, and transmission. Include information about training of study staff, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, separation of identifiers and data, etc.:

Subjects will be assigned a coded description, the key to which will be stored in a locked safe, in a locked room, separate from other study materials. All paper records from the study, with the exception of the consent form and the MRI screening form, will be identifiable only by this subject number, and all forms will be kept in a locked file cabinet. Electronic data will be accessed via password protected computer and password protected server.

19.4 For multi-site studies, describe how data or specimens will be handled and secured for each site (e.g., central or disseminated data storage, data coordinating center):

N/A

19.5 Describe the plan for data disposition following the conclusion of the study (e.g., long term maintenance of data, data destruction methods).

- *What information will be included in the long term storage of data or specimens?*
- *How long will the data or specimens be stored?*
- *Where and how data or specimens will be stored?*
- *Who will have access to the data or specimens during long term storage?*
- *Who is responsible for receipt or transmission of the data or specimens?*
- *How will data or specimens be shared or transported?*
- *When and how will personal identifiers be destroyed?*

We will retain personally identifiable study data for a period of seven years after completion of the study. After the period of 7 years has passed, we will destroy any personally identifiable study data, including the study key, via a secure, locked, shredding service. De-identified will then stay in long term, secure, storage and/or in online data repositories.

20.0 Provisions to Protect the Privacy Interests of Subjects

20.1 Describe the steps that you will take to protect subjects' privacy interests. "Privacy interest" refers to a person's desire to place limits on with whom they interact or to whom they provide personal information (e.g., collecting the minimal amount of private information required to complete the study, protecting the data once it is obtained):

Subjects will be assigned a coded description, the key to which will be stored in a locked safe, in a locked room, separate from other study materials. All paper records from the study, with the exception of the consent form and the MRI screening form, will be identifiable only by this subject number, and all forms will be kept in a locked file cabinet. Electronic data will be accessed via password protected computer and password protected server

20.2 Describe steps that you will take to make subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures (e.g., use of a same gender investigator to place sensors on the torso, a private changing area if clothing must be changed, sensitivity when discussing pregnancy testing with subjects, making it clear on surveys that participants can discontinue at any time, not asking questions about private or sensitive issues unless necessary for the research):

Research staff will check in with participants throughout the session to ensure that participants are informed and understand the study procedures. Their comfort is assessed and in addition to written consent prior to participation, consent is verbally obtained throughout the session. Research staff will check in with participant after the MRI scan to assess emotional and physical states.

20.3 Describe how you plan to access existing sources of information about the subjects (e.g., medical records, grades) and how you will protect participant privacy through the data security plan:

N/A

20.4 Describe any required reporting that might occur as a result of your research questions, study populations, and data collection methods. Examples for Virginia and Virginia Tech include:

- ***Any*** *suspicions (e.g., circumstantial, disclosed) of child abuse (physical, emotional, sexual) and neglect*
- *Sexual discrimination and/or sexual violence that involves a student*
- *Disclosure or signs of intention to harm oneself (i.e., suicidal ideation and/or plan)*
- *Disclosure or signs of desire to harm others (i.e., homicidal ideation and/or plan)*
- *Suspected abuse, neglect or exploitation of vulnerable adults (e.g., individuals with a disability, elderly persons)*

Any mention of current abuse of a child or older person, or intention of a participant to hurt themselves or someone else will be reported in accordance with the Virginia mandated reporting procedures.

21.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

Safety monitoring is required when research involves greater than minimal risk and is sometimes appropriate for other studies.

21.1 Describe:

- *The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe (e.g., periodic reporting to the IRB, establishing a data monitoring committee, reporting data monitoring committee findings to the IRB and the sponsor).*
- *What data you will review, including safety data, unexpected events, and data that show the ability to produce the intended results.*
- *How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with subjects).*
- *The frequency of data collection, including when safety data collection starts.*
- *Who will review the safety data and with what frequency.*
- *The statistical tests for analyzing the safety data to determine whether harm is occurring.*
- *Any conditions that will trigger an immediate suspension of the research (e.g., a serious adverse event).*

N/A

22.0 Compensation for Research Related Injury

22.1 If the research involves more than minimal risk to subjects, describe the available compensation in the event of research-related injury, if any:

N/A

22.2 Provide a copy of contract language, if any, relevant to compensation for research-related injury. At Virginia Tech, this is most common for sponsored research:

N/A

23.0 Economic Burden to Subjects

23.1 Describe any costs that subjects might be responsible for because of participation in the research, including any uncompensated costs for items such as transportation, missed work, and childcare:

There are no costs to participate in this research study. In some cases, additional compensation may be provided for time and travel in order to reduce barriers to participation.

24.0 Consent Process

24.1 Indicate the process by which you will obtain consent for study participation. Please upload all consent, parental permission, and assent forms, documents, and scripts referenced in this section to Protocol Management.

Describe the following:

- *Where the consent process will take place (e.g., clinic waiting area, classroom, online)*
- *The time interval between sharing the consent information with the prospective subject and obtaining consent. For lab, interview, and focus group studies, the Virginia Tech IRB prefers that subjects have at least 24 hours to review the consent form and study information before the appointment where consent will be obtained. For simple online survey studies, you can typically present the consent information immediately before subjects begin participation.*
- *If applicable, processes to ensure ongoing consent or assent (e.g., for multiple sessions; for research in which a minor will turn 18 during the study; for longitudinal research with minors who will later be asked to provide or affirm their assent).*
- *Please review "SOP: Informed Consent Process for Research (HRP-090)" for recommended procedure. Describe your process, being sure to include:*
  - *The name and role of all study personnel who will be trained and certified by the PI to conduct the consent process*
  - *The time that will be devoted to the consent discussion*
  - *Steps that you will take to minimize the possibility of coercion or undue influence*
  - *Steps that you will take to gauge or ensure the subjects' understanding*

The PI, study investigators, and direct members of the research team will oversee the consent process and will ensure that all subjects have been thoroughly briefed on the purpose of the study, potential value of the study to society, the lack of value to the subject personally, and all potential risks to the subjects. It will be the

duty of the PI, study investigators, and research team members to ensure that all subjects are informed that he or she is under no obligation whatsoever to participate, and that if he or she wishes to discontinue their participation in the study at any time during the study, he or she is free to do so without penalty.

Prior, to phone screening, participants will give verbal consent to complete screening questions (see attached). At the scanning session, written informed consent will be obtained as well as the completion of an "evaluation to consent" form to assess proper understanding of the consent form. All subjects will be informed of the purpose of the study, the potential value of the study to society, the lack of value to the subject personally, and all potential risks to the subject. It will be explained to the subject that he or she is under no obligation whatsoever to participate, and that if he or she wishes to discontinue their involvement at any time during the study, he or she is free to do so without penalty. In addition, the researcher will check in with the subject periodically throughout the duration of the study in order to ensure that the subject has a full understanding of the study, to answer any questions that he or she may have, and to address any issues of discomfort or desire to discontinue participation.

Non-English Speaking Subjects

- *Indicate what language(s) other than English are understood by prospective subjects or representatives.*
- *If non-English speakers will be recruited, describe the process you will use to ensure that the oral and/or written consent information provided will be in a language that they understand.*
- *If you translate consent forms and study materials, please provide a certified translation of the form as well as the certification document.*
- *Indicate the spoken language that study personnel obtaining consent will use. Describe how you will assess fluency of personnel obtaining consent to ensure that the translation is accurate.*

N/A

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

- *Review the "CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)" to ensure you have provided sufficient information for the IRB to make these determinations (i.e., that it meets the criteria for a waiver or alteration of the consent process).*

N/A

Subjects who are not yet adults (minors: infants, children, teenagers)

- *Describe the criteria that you will use to determine legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted (e.g., in Virginia, individuals under the age of 18 years).*
  - *For research conducted in Virginia, review "SOP: Legally Authorized Representatives, Minors, and Guardians (HRP-013)" to determine which individuals in the state meet the definition of "minor."*
  - *For research conducted outside of the state, please describe the legal requirements for the definition of "minor."*
- *Describe the process for obtaining parental permission.*
  - *Permission from one parent is acceptable for studies that involve no greater than minimal risk OR involve greater than minimal risk but present the prospect of direct benefit to the minor subject.*
  - *Permission from both parents is required in all other cases (unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the minor).*
- *Describe whether you will obtain permission from individuals other than parents or Legally Authorized Representatives, and if so, who will be allowed to provide permission. Describe the process you will use to determine these individuals' authority to consent to the minor's general medical care.*
- *Indicate whether you will obtain assent from all, some, or none of the minors. If you will obtain assent from some minors, indicate which minors will be required to assent. Consider chronological age and intellectual capacity when determining who will be required to provide assent (e.g., infants are unable to assent. However, teenagers are likely able to read and sign an assent form).*
- *When assent of minors is obtained, describe whether and how you will document it. Will minors sign an assent form or give verbal assent?*
- *Attach parental permission and minor assent forms or scripts in Protocol Management.*

N/A

Adults Unable to Consent

- *Describe the process you will use to determine whether an individual adult is capable of consent.*
- *List the individuals from whom you will obtain permission in order of priority (e.g., durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and non-minor child).*
    - *For research conducted in the Virginia, review "SOP: Legally Authorized Representatives, Minors, and Guardians (HRP-013)" to determine which individuals in the state meet the definition of "legally authorized representative."*
    - *For research conducted outside of Virginia, please describe the legal requirements for obtaining permission from a legally authorized representative in the state where the research will occur.*
- *Describe the process for assent of the subjects.*
    - *Indicate whether you will require assent from all, some, or none of the subjects. If some, indicate which subjects will be required to assent and which will not.*
    - *If you will not obtain assent from some or all subjects, please provide justification for not obtaining assent.*
    - *Describe whether and how you will document assent.*

N/A

25.0 Process to Document Consent in Writing

25.1 Consult "SOP: Written Documentation of Consent (HRP-091)" for recommended procedures, and describe whether and how consent of the subject will be documented in writing:

The participant and person obtaining consent will sign the consent form after the potential participant verbally states that s/he understands the conditions of the study, has no more questions, and chooses to participate.

To enhance understanding, a "evaluation to consent" test will be administered at the end of the consent form. There are no consequences for incorrect answers. The participants' answers will only be used to clarify portions of the procedure and consent that were not understood.

Written consent will include printed name, signature, and date from each of the person obtaining consent (e.g., research coordinator/study staff member), the research

participant, and the PI or study delegate. In addition, a copy of the consent form will be provided to the study participant, if they wish.

25.2 If the research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, you can request that the IRB waive the requirement to obtain written documentation of consent (e.g., consent to participate is indicated by pressing a button for an online questionnaire – after the consent information is presented and before the questionnaire begins):

Participants will provide verbal consent prior to completing the screening questions required to determine eligibility. If eligible and enrolled, written consent will be later be collected at the MRI session.

25.3 If you will document consent in writing, attach a consent document with places for signatures. If you will obtain consent, but not document consent in writing, please attach the consent script or text. Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information. You should use "TEMPLATE CONSENT DOCUMENT (HRP-502)"to create the consent document or script:

Written and phone consent forms attached.

26.0 Resources Available

26.1 Describe the resources available to conduct the research. For example, as appropriate:

- *Describe the PI's availability to supervise the research.*
- *Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?*
- *Describe the time that you will devote to conducting and completing the research.*
- *Describe your facilities.*

- *Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated or unanticipated consequence of participation in the research.*
- *Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions (e.g., training plans, detailed study notebooks).*

Stephen LaConte, the PI on this protocol, will assume full responsibility for all aspects of the project. All staff involved in the conduct and/or monitoring of this study will have completed the VT Human Subject Protection Training and Good Clinical Practice Training. Documentation of training will be maintained.

Participants will be recruited from the community via posted flyers, word of mouth, and electronic advertisements (e.g., Craigslist, Facebook). Participants will be contacted if they have given prior permission (through previous informed consent form) or by completion of a confidential pre-screening questionnaire.

To the extent possible, we will attempt to minimize obstacles to participation. For example, travel barriers will be addressed by providing transportation or parking costs to participants, and scheduling barriers will be minimized by offering a flexible session schedule. All methods and measures will be conducted using standard operating procedures, and all staff (including recruitment staff) will be provided with cultural sensitivity training. We have a history of successful recruitment of drug and alcohol users. All participants will enroll on a voluntary basis and sign an IRB-approved consent form prior to study participation.

All onsite research activities will take place at the Fralin Biomedical Research Institute (FBRI) Virginia Tech Carilion (VTC). The Human Neuroimaging Laboratory (HNL) serves as the primary human imaging facility of the FBRI. The HNL has two 3T Siemens MRI machines (a Trio and a Prisma) within the primary facility. The Fralin Biomedical Research Institute is sited in an approximately 100,000 square feet building, divided among:

32 faculty offices
~ 30,000 sqft of dry-lab space
~ 46,000 sqft of wet-lab space
~ 23,000 sqft of administrative/office space
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30 behavioral testing rooms
2 observation rooms with video/audio recording
4 conference rooms with AV / video conferencing capabilities
1 data center with a 16 rack capacity
3 MRI scanning suites (includes 1 offsite location)
A MuRoom - an ultra-low magnetic field room - equipped with second generation QuSPin optically pumped magnetometer sensors for a lower-cost, less constraining, MEG system

MRI Scanning Resources (FBRI):
FBRI has two research-dedicated Siemens 3T MR scanners (1 Siemens Magnetom TIM Trio, and 1 PRISMA-FIT) available. Each scanner bay is equipped with the following stimulation and response interfaces: behavioral response: two-hand, eight-button optical response pads with USB, serial, and TTL output (Current Designs, Inc.)
video stimulation: rear-projection video display (Hitachi CP-SX635) corrective lenses for use with video stimulation: MR-compatible frames with insertable polycarbonate lenses (prescriptions range from -8.00 to +8.00) (Solo Bambini) stimulus delivery: dedicated computers for experiment presentation (Dell Optiplex 980)
audio delivery: MRI compatible headphones.

27.0 Multi-Site Research

Contact the HRPP for multi-site research (involving multiple institutions) and the details required for this section will be provided. Otherwise, indicate N/A.

N/A