# Applying Novel Technologies and Methods to Self-Regulation: Behavior Change Tools for Smoking and Binge Eating

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## 1. PURPOSE OF THE STUDY

### a. Brief Summary

This study aims to examine targets of self-regulatory function among two exemplar populations for which behavior plays a critical role in health outcomes: smokers and individuals who binge eat (BED). This is the fourth phase of a study (first phase is IRB #34926) that aims to identify putative mechanisms of behavior change to develop an overarching "ontology" of self-regulatory processes. This phase features a mobile interaction period to engage targets in these samples with self-regulation assessment and behavior change tools.

### b. Objectives

**This study aims to improve our understanding of self-regulation by integrating a diverse literature under one ontology. An ontology systematizes our knowledge, and provides a common language to discuss relationships between putative control processes. Additionally, health risk behavior characterized by self-control deficits (e.g. non-adherence to medical regimens, poor impulse control) are destructive to persons and societies, making self-control a fruitful target for intervention. A systematic ontology of self-regulation will better define the 'nodes' and 'relationships' that interventions should act upon, thus increasing their efficacy. This fourth phase of this ongoing project attempts to intervene and improve self-regulation based upon a cell-phone based intervention.**

### c. Rationale for Research in Humans

**This is a study of human brain function and behavior, and thus it is essential to use human subjects for the project.**

## 2. STUDY PROCEDURES

### a. Procedures

**Study participation will include timely completion of the eligibility process, completion of an introductory session for signing a consent form and completing baseline surveys (see below), completion of 1 MRI session, completion of a 4-week mobile interaction period, and completion of 1 additional follow-up MRI session.**

**Participants will be compensated in full at the end of the study period.**

**Eligibility Process:**

**The eligibility process consists of an online eligibility questionnaire, which is housed on the Stanford Research Electronic Data Capture (REDCAP) website.**

**The questionnaire will have branching criteria that aligns with the inclusion and exclusion criteria. Potential participants are assigned a study identification number upon beginning the questionnaire. This number is not associated with any protected health information.**

**A Waiver of Documentation is being requested because participants will be consenting on the online eligibility questionnaire without signing the consent form (only selecting yes/no options). In addition, a Waiver of Authorization for Recruitment is being collected due to the collection of personal health information on the online eligibility questionnaire (See Attachments for Waiver of Documentation and Waiver of Authorization for Recruitment).**

**If eligible and willing to participate after completing the online eligibility questionnaire, potential participants will then be invited to participate in a study session at the CNI (Center for Cognitive and Neurobiological Imaging) at Stanford.**

**Prior to the MRI session, subjects will be invited to attend Session 1 in person, lasting 30-60 minutes. This session is aimed at improving retention efforts for subjects planning on arriving to the MRI session, by developing an initial point of in-person contact. At this session, participants will first see a copy of a HIPAA embedded informed Consent form including project title, PI's contact information, brief descriptions about the study, a description on the risks and benefits, payment information and privacy/confidentiality. The researcher will verbally confirm that the participant has read through and understood the entirety of the consent form.**

**During this session, participants may also be asked to show proof of vaccination for COVID-19. Proof of vaccination will not be retained by the study team.**

**Participants will also fill out the screening questionnaire provided by CNI to check for contraindications (attached in attachments as CNI screening form). Two different researchers will look through and check the responses to the screening form.**

**Prospective participants will have an option to decline or to take part in the study. The subject will be informed explicitly that they may opt out of participation of the experiment at any point without penalty.**

**After signing the consent form, subjects will be asked to complete certain questionnaire items.**

**These include:**

**Alcohol, Smoking and Drug Questionnaire: Subjects are presented with a questionnaire assessing smoking, drinking, marijuana and other drug habits. The questions for marijuana are taken from Cannabis Use Identification Test.**

**The questions for other drugs are taken from the DAST-10.**

**Reward-based Eating Drive-13 Scale Questionnaire: Subjects are presented with questions from the RED-13 scale prior to scan in order to capture individual differences in the severity of feeling and behaviors related to binge eating.**

**This Questionnaire also includes questions about physical activity, drawn from the LCAT-2.2 scale.**

**In addition to completion of tasks and questionnaires, subjects will be asked to fill out a demographic form prompting them for age, sex, weight, height, race, ethnicity, education level, relationship status, divorce count, years in a relationship, number of relationships, number of children, household income, debt, retirement account, whether they own or rent a house, traffic tickets, traffic accidents, past or current problems with gambling, caffeine intake, and legal troubles. These "real-world" questions will be related the constructs measured in the above tasks and questionnaires.**

**Please see attachment [Baseline & Follow-Up Questions (Stanford IRB)_date] for full suite of questions asked to subjects, including their source.**
**These items from questionnaires relate to personality and self-control, and any questions not answered during session 1 will be completed during the MRI session.**

**This will conclude the Session 1.**

**Subjects will then participate in 1 MRI session (1.5 hours of MRI scanning plus 1.25 hours of practice and setup time) at the CNI in Jordan Hall.**
**This may be on a separate date from the Session 1.**

**Subjects will complete 5 tasks (see below) in the scanner.**

**Prospective participants will have an option to decline or to take part in the study. The subject will be informed explicitly that they may opt out of participation of the experiment at any point without penalty.**

**MRI SESSIONS**

**Subjects will participate in MRI sessions in the CNI in Jordan Hall, where they will complete the tasks described below.**

**Participants may practice the experimental tasks they will be performing in the scanner on a desktop or laptop computer in the observation room.**

**They will also complete the battery of Participants will be informed that they may leave if at any time they feel uncomfortable or realize they no longer wish to participate.**

**Subject in our smoking subject group will be asked to abstain from smoking for 3 hours before the start of the session (4 hours before the start of the scan and totaling 5.75 hours of abstaining from smoking per scan session).**

**b.** **Subjects in our Binge Eating group will be asked to fast for 3 hours before the start of the session (4 hours before the start of the scan and totaling 5.75 hours of fasting per scan session). All subjects will be asked to weigh themselves on a body weight scale at the CNI prior to entry.**

**After entering the magnet room, participants will be given earplugs and/or headphones to wear. They will be instructed to lie on a table. They will be provided with foam padding and blankets for comfort while in the scanner. The table will then be slid into the scanner so that the head and upper body are inside the magnet tube.**

**Anatomical Imaging: Conventional anatomical scans (images that show us the structures of the brain) will be taken during the MRI sessions.**

**Functional Imaging: After that, high-speed functional MRI images will be obtained while the subjects complete a set of tasks (see 'TASKS' below) or lie at "rest" while performing no explicit task or watching a movie clip that may include images of smoking or palatable food stimuli.**

**Participants will be in the MRI scanner for approximately 90 minutes and at all times will have access to a means with which they can immediately indicate their desire to terminate the session. They will be encouraged to terminate the session if they become uncomfortable.**

**The study will use the 3T UHP system at CNI. The UHP shares a common software and hardware architecture to GE's FDA-approved Premier system but uses a higher-performance gradient coil and is not FDA approved for diagnostic use and is subject to the 21 CFR 812 investigational device(IDE) regulations as well as 21 CFR 50 and 56. The system has been tested by GE according to UL606001-1 and also for compliance with IEC 60601-2-33 (ed 3.1) --meeting limits and guidelines for peripheral nerve stimulation, patient thermal, SAR limit, acoustic noise, flammability rating UL94-5VA for safety covers, hydrostatic pressure, electrical hazards, dielectric strength and pinch point. The MRI scans in this study will also utilize operational parameters within FDA guidelines for Nonsignificant Risk thus an Investigational Device Exemption (IDE) from FDA should not be necessary.**

**TASKS**

**Stop Signal Task: Subjects are presented with 4 "go" shapes (circle, triangle, diamond, square) and are instructed to respond to two shapes with one key press and the other two shapes with another key press. On each trial, subjects make a speeded choice response to the "go" stimulus, except on a subset of trials when an**

**additional "stop signal" occurs after the "go" stimulus. This instructs the subject to try to withhold responding on that trial.**

**Conditional Motor Selective Stop Signal Task: Similar to the Stop Signal task except subjects stop to the stop signal only if they were going to make one go response on that trial (e.g., right hand response) but not if they were going to make the other response (e.g., left hand response).**

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**c.** **Delay Discounting Titration Task: Subjects must choose between sooner but smaller rewards versus larger but later rewards. The smaller reward will not always be immediate and the reward amounts will be chosen randomly from a uniform distribution of a given interval. This allows for the estimation of a subjects' discount rate and for the comparison of different model fits of discounting behavior.**

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**Regulation/Manipulation task: One each trial, subjects will be presented either a "now" cue or a "later" cue, then will see a stimulus from one of three classes, then rate the stimulus on their degree of craving. On "now" cue trials, subjects are directed to think about the immediate feelings associated with consuming that stimulus. On the "later" cue trials, subjects are directed to think about the long-term consequences associated with consuming that stimulus. The following are the three classes of stimuli: smoking-related (presented only to the smoking group), palatable food (presented only to the binge eating sample), or neutral stimuli (presented to both groups). Finally, on each trial, subject rate the stimulus for their current degree of craving.**

**Movie Watching "task": Subjects will watch a small set of movie clips with embedded smoking and food stimuli.**

**• Physiological Monitoring and Recording: Subjects may be asked to allow non-invasive physiological measurements during other tasks. Eye movements may be tracked using a small camera. Physiological data including respiration, heart rate, and galvanic skin response may be monitored using the Biopac monitoring system. If tasks require spoken responses, the responses may be recorded using a microphone in the scanner.**

**• Other Information: For subjects who have previously participated in studies in the Poldrack lab, information from other tasks will be available.**
**This information may be added to the study record for this study. This information may include:**

**o Questionnaires for screening**
**o Physiological data including spontaneous eye blink rate**
**o Imaging data from structural and functional MRI sessions**

**MOBILE INTERACTION PERIOD:**

**Participants will be asked to complete items in response to queries using mobile ecological momentary assessment (EMA); i.e., questions/questionnaires asked at a given time point outside of a laboratory setting via a mobile device. We will assess antecedent conditions prior to health risk behavior: smoking or binge eating among**

**our smoking and binge eating samples, respectively. These antecedent conditions include mood, companionship, location, and temptation. We will offer the resources of Laddr? (a science-based behavior change intervention delivered via an interactive, self-directed mobile platform) to individuals and assess the effect of this mobile intervention system on putative targets of self-regulatory function. Laddr will also be used to deliver the EMAs to participants.**
**Participants will use their own smartphones.**

**We will ask participants to respond to EMAs and to engage with the mobile intervention for 28 consecutive days. We will prompt them four times daily to inquire about health risk behavior and ask them to complete measures of self-regulation and potentially important contexts. Please see the attachment [EMA Questions] for the list of actual questions asked.**

**We will send the four prompts at random times within time windows (e.g., 8–**
**11:30 AM, 11:30 AM–3 PM, 3–6:30 PM, 6:30–10 PM). The time windows may vary based on participants' waking hours, and we will program through the software at least an hour between prompts (e.g., if a participant receives a prompt at 11 AM, he/she cannot receive another prompt until 12 PM). We will ask them to use Laddr daily to, at a minimum, update progress toward goals and complete various activities on the application that we expect will improve their self-regulation.**
**Participants will be recommended priority therapy guides (binge eating for the binge eating sample; smoking for the smoking sample) and can also choose to engage with other guides, such as depression, anxiety, and substance use.**

**Participants will also be asked to use devices that allow for objective measuring of behaviors of interest. We will ask participants in the smoking sample to provide carbon monoxide (CO) samples via a breath CO meter (iCO? Smokerlyzer?, Bedfont? Scientific Ltd.). The monitor measures breath CO in parts per million (ppm) based on the conversion of CO to CO2 over a catalytically active electrode. We will ask smoking participants to provide one CO sample in the same time window each day. Smoking participants will have a goal of smoking abstinence by the end of the study, as evidenced by a CO reading of less than 4 ppm. We will ask participants in the binge eating sample to wear a physical activity tracking device (Fitbit Flex 2?), which tracks steps, distance, calories burned, active minutes, hourly activity, stationary time, and sleep.**
**Objective measures of eating are in a nascent phase, and all participants in the binge eating sample are overweight or obese, making physical activity a suitable behavior to measure. We will ask binge eating participants to wear the activity tracker for at least 12 hours per day. We will encourage participants to use a changing criterion design to set stepped goals, in which participants set a 7-day activity criterion goal and are encouraged to increase their criterion goals in each subsequent 7-day block if they achieve the goal on at least 4 of**

**the 7 days. We will ask Binge eaters to also self-report their activity for the day in Laddr.**

**Please see the attachments [Fitbit Flex 2] and [ICO Smokerlyser] for a description of each of the devices used in measuring our behaviors of interest.**

**Participants in the smoking sample may use nicotine replacement medications, and we will track which participants use these medications. Potential participants taking medications for psychiatric reasons will be excluded from both samples.**

**After completion of the 4-week mobile interaction period, participants will return for a 2.75 hour follow-up neuroimaging session, consisting of around 1.25 hour of practice, setup and assessments outside the scanner, and around 1.5 hours of scanning. Participants will be compensated in full at the completion of this session.**

**d. Procedure Risks**

**None of the proposed procedures involve more than minimal risk.**

**e. Use of Deception in the Study**

**Deception will not be used.**

**f. Use of Audio and Video Recordings**

**Video recording may be used to record eye movements and pupil diameter, but only traces of these measures will be saved; no raw video will be saved.**

**g. Alternative Procedures or Courses of Treatment**

N/A

**h. Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?**

N/A

**i. Study Endpoint(s)**

N/A

## 3. BACKGROUND

**a. Past Experimental and/or Clinical Findings**

**Health risk behavior, including poor diet, physical inactivity, tobacco and other substance use, causes as much as 40% of the illness, suffering, and early death related to chronic diseases. Non-adherence to medical regimens is an important exemplar of the challenges in changing health risk behavior -- and is common, costly (due to increased utilization of healthcare services), and associated with poor**

**patient outcomes. This may be particularly evident among older adults who experience a disproportionate amount of the chronic disease burden in the U.S. Although an**
**array of interventions have been shown to be effective in promoting health behavior change, much of this work has been "siloed" (focused on one disorder at a time).**

**Additionally, interventions are typically intended to engage multiple mechanisms of behavior change, but the mechanisms by which they actually work are infrequently systematically examined. Because the need to alter health-related behavior is ubiquitous across medicine, understanding the extent to which the principles of effective health behavior change, and the mechanisms by which they work, are similar or differ across health conditions and settings is a critically important area of scientific inquiry.**

**One promising domain of putative behavior change targets is that of self-control -- a person's ability to manage cognitive, motivational and emotional resources to act in accordance with his/her long-term goals. A systematic ontology of self-control will better define the 'nodes' and 'relationships' interventions should act upon, thus increasing their efficacy.**

**b. Findings from Past Animal Experiments**

**Because this work is focused on self-regulation in humans, there are no animal studies that are directly relevant.**

## 4. RADIOISOTOPES OR RADIATION MACHINES

**a. Standard of Care (SOC) Procedures**

| Identify Week/Month of Study | Name of Exam | Identify if SOC or Research |
|---|---|---|
| N/A | N/A | N/A |

**b. Radioisotopes**

i. Radionuclide(s) and chemical form(s)

N/A

ii. Total number of times the radioisotope and activity will be administered (mCi) and the route of administration for a typical study participant

N/A

iii. If not FDA approved: dosimetry information and source documents (package insert, Medical Internal Radiation Dose [MIRD] calculation, and peer reviewed literature)

N/A

**c. Radiation Machines – Diagnostic Procedures**

i. Examination description (well-established procedures)

N/A

ii. Total number of times each procedure will be performed (typical study participant)

N/A

iii. Setup and techniques to support dose modeling

N/A

iv. FDA status of the machine and information on dose modeling (if procedure is not well-established)

N/A

### d. Radiation Machines – Therapeutic Procedures

i. Area treated, dose per fraction/number of fractions, performed as part of normal clinical management or due to research participation (well-established procedures)

N/A

ii. FDA status of the machine, basis for dosimetry, area treated, dose per fraction and number of fractions (if procedure is not well-established)

N/A

## 5. DEVICES USED IN THE STUDY

### a. Investigational Devices (Including Commercial Devices Used Off-Label)

| **Investigational Device 1** | |
|---|---|
| Name: | Laddr Mobile Application |
| Description: | Laddr is a mobile phone-based behavioral tool addressing self-regulatory function in individuals via self-management tools and skills training modules. |
| Significant Risk? (Y/N) | N |
| Rationale for Non-Significant Risk | The device does not meet the definition of a significant risk device. The device is not intended as an implant, does not support or sustain human life, is not being used for the purposes of diagnosing, curing, mitigating, treating disease or preventing impairment of health, cannot cause significant harm to any subjects, does not appear on any FDA list of significant risk devices, and cannot cause any harm to subjects which could be life threatening, cause permanent impairment of body function, cause permanent damage to body structure, or necessitate medical or surgical intervention to preclude permanent impairment of a body function or preclude permanent damage to body structure. |
| **Investigational Device 2** | |
| Name: | 3T-UHP |
| Description: | The 3T Ultra-High Performance (UHP) MRI scanner from GE is an upgrade to the 3T MR750 which was a commercial FDA- approved system. The UHP system utilizes many components from GE's 3T Signa Premier, including gradient drivers, power supply, transmit and receive system electronics, but uses a higher-performance gradient coil. |
| Significant Risk? (Y/N) | N |

| | |
|---|---|
| Rationale for Non-Significant Risk | The 3T Ultra-High Performance (UHP) MRI scanner from GE is an upgrade to the 3T MR750 which was a commercial FDA-approved system. The UHP system utilizes many components from GE's 3T Signa Premier, including gradient drivers, power supply, transmit and receive system electronics, but uses a higher-performance gradient coil. The 3T UHP system is not FDA approved, and is subject to the 21 CFR 812 investigational device(IDE) regulations as well as 21 CFR 50 and 56. The system has been tested by GE according to UL606001-1 and also for compliance with IEC 60601-2-33 (ed 3.1) -- meeting limits and guidelines for peripheral nerve stimulation, patient thermal, SAR limit, acoustic noise, flammability rating UL94-5VA for safety covers, hydrostatic pressure, electrical hazards, dielectric strength and pinch point. The MRI scans in this study will also utilize operational parameters within FDA guidelines for Nonsignificant Risk thus an Investigational Device Exemption (IDE) from FDA should not be necessary. In addition, the MR research being conducted requires highly specialized software that does not exist in the clinical MR market so it is designed and implemented by researchers at the CNI. Any such software will be considered investigational, will function as a non-significant risk device, and is subject to the 21 CFR 812 investigational device(IDE) regulations as well as 21 CFR 50 and 56. The investigational image acquisition software will conform to FDA guidelines for MR safety related to heating (SAR), peripheral nerve stimulation (dB/dt), and acoustic noise. |

### b. IDE-Exempt Devices

| **IND-Exempt Device 1** | |
|---|---|
| Name: | Fitbit Flex 2 |
| Description: | The device is a fitness tracker meant to be worn around the wrist, and capable of tracking steps, distance, calories burned, and sleep. |
| **IND-Exempt Device 2** | |
| Name: | iCO Smokerlyzer |
| Description: | The device is a breath carbon monoxide (CO) monitor connected to a personal mobile device, allowing testing of CO levels in participants. |

## 6. DRUGS, BIOLOGICS, REAGENTS, OR CHEMICALS USED IN THE STUDY

### a. Investigational Drugs, Biologics, Reagents, or Chemicals

| **Investigational Product 1** | |
|---|---|
| Name: | N/A |

### b. Commercial Drugs, Biologics, Reagents, or Chemicals

| **Commercial Product 1** | |
|---|---|
| Name: | N/A |

## 7. DISINFECTION PROCEDURES FOR MEDICAL EQUIPMENT USED ON BOTH HUMANS AND ANIMALS

The bed/table and accessories that are used for the animals is different than the table humans use. Physiologic monitoring equipment is cleaned with a commercial disinfectant such as Roccal, Conflick,Sani-Wipes, or a 10% Bleach solution. All RF coils and positioning accessories are wrapped in plastic wrap or plastic bags for use with animals. Everything, even if it is animal use

only, is cleaned with the above disinfectants after every use even if they are wrapped in plastic. The Lucas Center is checked yearly by several groups at Stanford who approve animal research in human systems: Stanford Health & Safety. We are reviewed by: Stanford APLAC panel; USDA; NIH; and Aaalac."

## 8. PARTICIPANT POPULATION

### a. Planned Enrollment

We plan to recruit a local sample of 100 subjects; because of attrition, we may need to recruit up to 125-154 individuals in order to obtain 100 complete subjects. Sample will consist of 50 smokers and 50 individuals who binge eat (BED). These are two exemplar populations that putatively involve self-regulatory dysfunction.

### b. Age, Gender, and Ethnic Background

Our experiments will not restrict participants based upon gender, racial, or ethnic background. We will restrict participants to an age range of 18-50 years.

### c. Vulnerable Populations

Students may be enrolled in the proposed study, though they are not targeted specifically for recruitment.
The rationale for including students is that they comprise a significant proportion of the local population and fall within the stated age range for our study. To protect these individuals, participation will not be made mandatory as a part of any academic work, and the PI will not recruit students from his own classes as subjects.

### d. Rationale for Exclusion of Certain Populations

The present research will include women and minorities, though the research is not specifically targeting these groups. Children are excluded because their brains are still developing and thus including them would introduce unwanted variability in the study.

### e. Stanford Populations

Volunteers will be recruited from Stanford campus and surrounding areas. Although enrollment will not be restricted to Stanford community members, based on past experience of other labs we anticipate that the participants will come from the Stanford community, including students and university personnel. All participants will provide informed consent and will receive equivalent compensation. No participants will be associated with the lab.

### f. Healthy Volunteers

All participants will be healthy volunteers, with the rationale being that we aim to understand the brain bases cognitive and self-regulatory processes in the human brain.

Subjects are specifically being recruited for either meeting DSM criteria for Binge Eating Disorder, or falling under classification as heavy smokers (5+ cigarettes/day), and all recruitment language is written in a neutral but explicit way relevant to the goals of the study (please see attached language for recruitment).
It is possible that, based on information gained during this study, the investigators may be required to report information to the appropriate authorities.
The Protocol director and study research staff will monitor participant safety throughout the duration of the study, and follow all procedures outlined in the Stanford CNI's recommendations for incidental findings outlined here:
https://cni.stanford.edu/wiki/Operations#Incidental_Findings.
Subjects will be screened for lifetime history of major depression using the Stanford PHQ-8 scale, but will not be excluded on this basis.
Standard MRI procedures are associated with no more than minimal risk to participants.

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**g. Recruitment Details**

Subjects will be recruited from the local community utilizing several methods of recruitment.
First, we will advertise our studies through approved paper flyers around the Stanford campus (see Attachments for Study Flyers). Minor editing changes may be made to recruitment materials to enhance clarity.
These flyers may include the web address for the department-wide recruitment website.
We will use the same language in our flyers in some of the following recruitment methods:
The study will be posted on Sona, the online recruitment system used by the psychology department.
We may advertise our studies in local newspapers (specifically, the Palo Alto Daily and the Palo Alto Weekly).
Phone scripts may be used by personnel Sunjae Shim and/or Jaime Rios in order to contact potential subjects drawn from Dr. Bohon's prior studies, who have indicated they wanted to be contacted about future studies.
We may advertise on our lab web site (www.poldracklab.org).
We may advertise using online resources such as Craigslist.
Additional recruitment methods include online ads that display our study logo and link on newsfeeds of individuals who meet our demographic and/or inclusion criteria; online postings (e.g., Craiglist, NextDoor); existing e-mail distribution lists (e.g., KMGZ sports station, Stanford Staffers, corporate wellness programs, local support groups); advertisements through Reddit and Google Adwords; email invitations to individuals from Dr. Bohon's prior studies who indicated they wanted to be contacted about future studies; email invitations sent by other Stanford PIs to individuals who indicated they wanted to learn more about future studies (other PIs would forward our recruitment materials on our behalf).
We have also created a Facebook business page for our study, through which we have posted the language from the attached 'onlineadvertisements_aim4' files. Facebook does not allow advertisers to disable comments or likes on advertising posts, a potential avenue for participants to share the study. One of the potential risks of this is that patients may inadvertently post about their health conditions as relevant to the smoking or binge

eating studies. In order to avoid this, we will implement the solution detailed here (https://www.pcsteps.com/2273-disable-comments-on-a-facebook-page/), in order to automate our comment disabling. This approach entails listing commonly used words (such as 'to') as 'forbidden' through the 'page moderation' available on Facebook. Any comments not captured by this approach will be deleted manually by our account admin (Amy Chieng on our protocol) within no more than 24 hours of their submission.
These methods also include posting and circulating recruitment flyers and posters at community and corporate organizations (e.g., Paint the Bay, Palo Alto Medical Foundation, Stanford Multicultural Fest, Be Well Fair, Apple events).
Additional subjects will also be identified from records of subjects identified by local collaborators at Stanford (Dr. Bohon and Dr. Prochaska), as particularly suitable for our desired subject populations. (Please see Attachment for Recruiting from Existing Databases).
We will use email contact as a potential method of recruitment, iso that we might contact lists of interested participants, such as the psych-subjects list maintained by the department.
Individuals who are interested in participating in psych studies self-subscribe to the department's email list, and are free to unsubscribe at any time. Only registered experimenters in the department are permitted to post to the list, and it is carefully monitored by the department. This recruitment method is widely used in the department.

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**h. Eligibility Criteria**

i. Inclusion Criteria

Selection of participants will involve screening for suitability for fMRI, along with general health questionnaire. Screening survey [See Appendix item 'Screening Eligibility V(x) '] will also be administered online in order to determine eligibility for study.

Follow-up questionnaire will be administered immediately before the scan session. Upon arrival for the scan session, if participants do not meet selection criteria (detailed below) they will be paid at a rate of $20/hour for their time but will discontinue participation in the study. If subjects do meet selection criteria they will then participate in the fMRI session.

All potential subjects will also need to successfully complete the screening forms at the Stanford Center for Cognitive and Neurobiological Imaging (CNI). Those subjects who present no contraindications to being scanned will be allowed to participate.

All participants must meet the following criteria:

Inclusion criteria:
- Age 18–50 years
- Understand English sufficiently to provide informed consent
- Use a smartphone operating system compatible with Laddr
- Have received a COVID-19 vaccine, and completed the vaccine-specific waiting period for full immunity

Additional inclusion criteria for binge eating sample:
- 27 ≤ BMI ≤ 40 kg/m2
- Have binge eating disorder according to DSM-5 criteria

- Non-smoking (defined as no cigarettes in past 12 months—this includes former and never smokers) - Confirmed interest in a physical activity intervention
- Use a smartphone compatible with Fitbit

Additional inclusion criteria for smoking sample:
- Smoke 5 or more tobacco cigarettes/day for past year
- 17 ≤ BMI < 27 kg/m2
- Confirmed interest in a smoking quit attempt
- Use a smartphone compatible with the iCO Smokerlyzer

ii. Exclusion Criteria

MRI specific exclusion criteria:

- Volunteers will be excluded for any contraindications to MRI as identified on the CNI screening form:
https://cni.stanford.edu/cniwiki/images/5/59/CNI_Screening_form.pdf

Significant medical illness (both samples):
Have had heart attack (MI), stroke, coronary heart disease, congestive heart failure, or angina

Have had coronary artery bypass surgery or cardiac catheterization such as percutaneous transluminal coronary angioplasty (PTCA), cath or stent placement

Have moderate to severe asthma, or chronic obstructive pulmonary disorder (also called emphysema or chronic bronchitis)

Had cancer within the past 5 years (except non-melanoma skin cancer)

Currently under medical care for digestive issues, gastrointestinal distress, abdominal pain, or diarrhea

Had an organ transplant

Have an immunodeficiency disorder

NOTE: Ask about but don't exclude on diabetes

Any current substance use disorder

Will not exclude based on use of substances, but need to be sure they aren't intoxicated in scanner

History of head trauma with loss of consciousness, cerebrovascular accident, seizures, neurosurgical intervention, or brain tumor

History of mental disorder due to a medical condition

Lifetime history of major psychotic disorders (including schizophrenia and bipolar disorder)

Current use of medication for psychiatric reasons (excluding for anxiety and depression)

Current use of prescription pain medications (e.g., Vicodin, oxycodone)

Current use of any medication for smoking (Exceptions: short-acting NRT (e.g., gum, lozenge, nasal spray, inhaler)) - (will screen out for Wellbutrin or varenicline)

Current use of any medication for weight loss

Have undergone weight-loss surgery (e.g., gastric bypass, lap band)

Current nighttime shift work or obstructive sleep apnea

Additional exclusion criteria for Binge Eating Sample:

Compensatory behavior (e.g., purging, excessive exercise, fasting) as determined through Q14-19 of QEWP-5 (Please see appendix item 'Screening Survey')

Lost weight in recent past (>10 pounds in past 6 months)

Currently in a weight-loss program (e.g., Weight Watchers, Jenny Craig)

Currently on a special diet for a serious health condition

Additional Exclusion Criteria for Smoking Sample:

Binge eating behavior according to QEWP-5 ("yes" to Qs 8 and 9 and for Q10, at least one episode per week for three months). (Please see appendix item 'Screening Survey')

- Compensatory behavior (e.g., purging, excessive exercise, fasting)
- Already excluded as part of the DSM-5 binge eating disorder criteria

- Lost weight in recent past (>10 pounds in past 6 months)

- Undergoing current treatment for binge eating with a clinician

- Currently in a weight-loss program (e.g., Weight Watchers, Jenny Craig)

- Will ask about, but won't exclude on, online/mobile app weight-loss programs as part of the screener

- Currently on a special diet for a serious health condition

-Nickel allergy (because the Fitbit includes nickel)

Additional exclusion criteria for smoking sample:

- Binge eating behavior according to QEWP-5 ("yes" to Qs 8 and 9 and for Q10, at least one episode per week for three months).

- QEWP-5 #8: During the past three months, did you ever eat in a short period of time (for example, a two-hour period) what most people would think was an unusually large amount of food? [yes or no]

- QEWP-5 #9: During the times when you ate an unusually large amount of food, did you ever feel you could not stop eating or control what or how much you were eating? [yes or no]

- QEWP-5 #10: During the past three months, how often, on average, did you have episodes like this? That is, eating large amounts of food plus the feeling that your eating was out of control? (There may have been some weeks when this did not happen. Just average those in.) [less than one episode per week, five response options for 1 or more episodes per week]

**i. Screening Procedures**

**Interested potential participants will receive descriptions of the studies as well as a list of requirements for participation. Potential participants will be asked to confirm that they understand the requirements. Screening will be done primarily through an online screener via RedCap, please see attachment [Eligibilty Screening Questions V(x)] for list of screening questions.**

**Subjects may also be contacted for screening via phone scripts. Scripts for these forms of contact are included as appendices. (See attachment Scripts for Phone Contact)**

**Please note that participants will not provide PHI until after consent.**
**Waiver of Authorization for Recruitment and Waiver of Documentation are attached.**

**j. Participation in Multiple Protocols**

**Subjects will be asked whether they have participated in additional protocols. In addition, we will check our database of subjects (stored in Redcap) to ensure that subjects are not run multiple times in the same protocol.**

**k. Payments to Participants**

**Up for $ 350 per participant for all baseline tasks, surveys, and neuroimaging (required to complete full battery of tasks, surveys, and neuroimaging to receive $ 350). This full compensation schedule breaks down as follows:**

**$20 for completion of a 30-minute introductory session with baseline surveys and consent form signing $61 for completion of the first neuroimaging session**
**Up to $230 (see below for detail) for completion of the four-week EMA period:**
**$.50 per EMA * 4 EMAs per day * 28 days = up to $56**

**$10 bonus per week for completing minimum of 25 EMAS (~90% of 28 total EMAs in the seven-day period) * 4 weeks = up to $40**

**$2 per day for Laddr activities (at least 5 minutes of engagement) * 28 days = up to $56**

**$2 per day for wearing the wrist sensor for a minimum of 12 hours per day and inputting activity data into Laddr (binge eating sample) or using the CO monitor daily and inputting CO reading into Laddr (smoking sample) * 28 days = up to $56**

**$61 for completion of the second neuroimaging session**

**Participants will be compensated after completion of the session. Participants will not be compensated for any time spent completing the online screening.**

**This payment rate is commensurate with the compensation other fMRI labs in the department provide.**

**Smoking only**
**Participants may keep the carbon monoxide monitor, which is intended for use by a single person. The research team may deduct up to $10 from a participant's compensation for failure to return, or for damage to, the lightning-to-headphone jack adapter if they borrowed one. The research team may withhold all payment until the adapter has been returned.**

**Binge eating only**
**The research team may deduct up to $55 from a participant's compensation for failure to return, or for damage to, the wrist sensor and band, charging cable, or charging adapter. The research team may withhold all payment until the wrist sensor and band, charging cable, and charging adapter have been returned.**

**The opportunity for compensation expires six months after the end of the participant's study period. Each participant who is unable to be reached (e.g., after three tries) for compensation will be notified of this expiration date. This expiration is implemented to account for the end of study funding from the National Institutes of Health.**

**Finally, subjects may be compensated for travel expenses, up to $50, and offered the option of receiving a parking pass provided by the Stanford CNI for the Q parking locations.**

**l. Costs to Participants**

**No costs will be charged to the participant.**

**m. Planned Duration of the Study**

**This arm of the study will last from September, 2018 to August 2022. Each subject's participation will take around 5.5 hours and 28 days. Screening will take up to 30 minutes. Each Session 1 will take approximately 30-60 minutes. Each MRI session will be approximately 90 minutes, plus 1-1.25 hour(s) of practice/setup time. The mobile interaction period will last for 28 days.**

## 9. RISKS

**a. Potential Risks**

i. Investigational devices

N/A

ii. Investigational drugs

N/A

iii. Commercially available drugs, biologics, reagents or chemicals

N/A

iv. Procedures

There are no known physical, psychological, social, or legal risks associated with the proposed studies, as we are excluding subjects with contraindications for MR studies (e.g., metallic implants such as pacemakers, surgical aneurysm clips, or known metal fragments embedded in the body). We do not anticipate any significant risks associated with performing the simple cognitive tasks also involved with these experiments.

v. Radioisotopes/radiation-producing machines

N/A

vi. Physical well-being

Risks from mobile sensing of physical activity (binge eating participants only): This project does not involve any risks beyond those ordinarily encountered in daily life or the performance of routine tests. Participants may experience slight initial discomfort while wearing the wrist sensors, such as minor skin irritations. As with any electrical device, the sensors can theoretically cause electric shocks. Electrical shocks can be a health concern with certain health conditions (e.g., heart conditions that require a pacemaker). Additionally, participants could have privacy concerns regarding mobile sensing.

Risks from carbon monoxide monitor (smoking participants only): The carbon monoxide (CO) monitor requires participants to hold their breath for approximately 15 seconds and then to exhale for 15–20 seconds, which may cause slight discomfort for some participants. Additionally, the CO monitor carries the risk of spreading illnesses.

Risks from physical activity intervention (binge eating participants only): There may be physical health risks associated with increases in physical activity.

vii. Psychological well-being

Risks from smoking quit attempts (smoking participants only): There may be psychological discomfort experienced as a result of making a smoking quit attempt.

viii. Economic well-being

There are no known economic risks associated with the proposed studies.

ix. Social well-being

There are no known social risks associated with the proposed studies.

x. Overall evaluation of risk

Low - innocuous procedures such as phlebotomy, urine or stool collection, no therapeutic agent, or safe therapeutic agent such as the use of an FDA approved drug or device.

**b. International Research Risk Procedures**

N/A

**c. Procedures to Minimize Risk**

**Standard MR safety procedures are in place at the Stanford Center for Cognitive and Neurobiological Imaging (CNI). All study personnel will receive extensive training in MR safety guidelines. These MRI procedures have been associated with no known adverse effects since initiating fMRI investigation in 1994. In addition, all subjects will complete the CNI screening form prior to the scan and will not undergo the scan if there is the potential for any risk.**

**Any incidence of complications, whether or not related to these procedures, will be reported immediately.**

**Risks to students as potentially vulnerable individuals will be minimized by not requiring participation as a part of any academic requirements, and not recruiting directly from the investigator's courses.**

**Please review our attached Data Sharing SOPs for a discussion of steps to minimize risks to confidentiality of identifiable information.**

**d. Protection against risks from mobile sensing (binge eating participants only):**
**Previous studies with wristband sensors have indicated that after a brief adjustment period, the majority of the participants adjusted to wearing the bands and did not find them to be intrusive or restraining. Although slight discomfort is possible from wearing the wrist sensors, Fitbit sensors have been used in over 600 studies. Therefore, we assess the severity of the discomfort and irritation of wearing the wrist sensors to be minimal. If irritation persists to a point where the participant no longer wishes to participate, any irritation is entirely reversible once the participant removes the wrist sensors.**

**While electrical devices do introduce the risk of electric shocks, the probability of a participant experiencing even minor electrical shocks is negligible. High impedance circuitry is used to limit current flow, even in the case of external events (e.g., through physical breaking of the sensor board or shorting of the battery leads). All sensors in the wristbands are commonly used in mobile phones and other activity monitors and pose minimal risk to participants. We expect that the wrist sensors, which have precedent of prior use in a research study or have otherwise been designed for everyday wear, will elicit similar acceptability among the participants in this study.**

**Regarding privacy concerns, participants' contact information will be linked to their study data via a code. The key to this code will be available only to the research staff at Stanford, and will be secured separately from the rest of the study data that is transmitted to Fitabase. Participants will be informed of their rights to terminate their participation in the study at any time. Participants will also be informed of their rights to remove the wrist sensors if they so choose, if they do not wish to be tracked. Participants will be given a summary of the incentive structure, and will be informed how their participation will affect their final incentive payment.**

**All personnel that will be present for the research activities will be essential personnel in the conduct of this research. All personnel who will interact with participants at Stanford are trained in human participants research. Moreover, all staff at Small Steps Labs LLC, which owns and operates Fitabase, will receive only coded data. No directly identifiable data will be provided to Small Steps Labs LLC staff, and the key linking participant codes to identifiers will not be shared under any circumstances.**

**Study participants will be informed that this research is conducted with the use of Fitabase and that coded data, which will not directly identify them, will be maintained in a database owned and operated by Small Steps Labs LLC.**

**Protection against risks from physical activity intervention (binge eating participants only): Participants will be encouraged to set physical activity goals in line with their current health and fitness status. Participants who have concerns about increasing their physical activity will be encouraged to contact a medical professional.**

**Protection against risks from smoking quit attempts (smoking participants only): While participants may experience psychological discomfort from making a smoking quit attempt, this discomfort is not beyond what participants would ordinarily encounter in daily life (e.g., cravings, disappointment from a lack of success). Laddr is designed to support participants through a smoking quit attempt. Participants experiencing psychological discomfort beyond that encountered in ordinary life will be withdrawn from the study and referred to the appropriate resources.**

**e. Study Conclusion**

**Subjects are given a squeeze-ball that they can use to signal at any time to the experimenter to stop the MRI scan. If an individual asks to terminate the study during a scan, they will be removed from the scanner immediately. If they do not wish to re-enter the scanner to continue the study, then the study will be ended and they will be paid for their time.**

**f. Data Safety Monitoring Plan (DSMC)**

i. Data and/or events subject to review

N/A

ii. Person(s) responsible for Data and Safety Monitoring

N/A

iii. Frequency of DSMB meetings

N/A

iv. Specific triggers or stopping rules

N/A

v. DSMB Reporting

N/A

vi. Will the Protocol Director be the only monitoring entity? (Y/N)

Y

vii. Will a board, committee, or safety monitor be responsible for study monitoring? (Y/N)

N

**g. Risks to Special Populations**

N/A

## 10. BENEFITS

Participants may learn self-regulation skills through the Laddr mobile application, which may have a positive impact on their smoking (in the smoking sample) or binge eating behavior (in the binge eating sample). Additionally, the information to be gained from their participation may benefit others in the future. Knowledge of brain function may have implications for our understanding of the diagnosis or treatment of CNS disease in the future.

## 11. PRIVACY AND CONFIDENTIALITY

All participant information and specimens are handled in compliance with the Health Insurance Portability and Accountability Act (HIPAA) and privacy policies of Stanford University, Stanford Health Care, and Stanford Children's Health.