Northeastern University
Human Subject Research Protection
Northeastern University, 560-177
360 Huntington Avenue
Boston, MA 02115-5000
Tel: 617.373.7570; Fax: 617.373.4595

For NU IRB use:

Date Received: _____ *NU IRB No.* _____

Review Category: _____ *Approval Date* _____

APPLICATION FOR APPROVAL FOR USE OF HUMAN PARTICIPANTS IN RESEARCH

Before completing this application, please read the Application Instructions and *Policies and Procedures for Human Research Protections* to understand the responsibilities for which you are accountable as an investigator in conducting research with human participants. The document, *Application Instructions*, provides additional assistance in preparing this submission. ***Incomplete applications will be returned to the investigator. You may complete this application online and save it as a Word document.***

If this research is related to a grant, contract proposal or dissertation, a copy of the full grant/contract proposal/dissertation must accompany this application.

Please carefully edit and proof read before submitting the application. Applications that are not filled out completely and/or have any missing or incorrect information will be returned to the Principal Investigator.

REQUIRED TRAINING FOR RESEARCH INVOLVING HUMAN SUBJECTS

Under the direction of the Office of the Vice Provost for Research, Northeastern University is now requiring completion of the NIH Office of Extramural Research training for all human subject research, regardless of whether or not investigators have received funding to support their project. ***This requirement will be effective as of November 15, 2008 for all new protocols.***

If you have not yet completed some type of human subject protection training, Northeastern University now has an account with CITI for Human Subjects Training, which can be accessed at the following url: **https://www.citiprogram.org.** Once you are on the site, click the "Register" button located on the top right of the page to begin. All NU-affiliates can take the CITI training course at no charge. **Please register using your NU email address and then complete the CITI Social & Behavioral Research Stage 1 Basic Course.**

Principal Investigators, student researchers and key personnel (participants who contribute substantively to the scientific development or execution of a project) must include a copy of their certificate of completion for this web-based tutorial with the protocol submission.

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□ Certificate(s) Attached
□ Certificate(s) submitted previously – on file with the NU's Office of Human Subject Research Protection

A. Investigator Information

Principal Investigator (**PI cannot be a student)** Maiya Geddes MD_____

Investigator is: NU Faculty _____ NU Staff _____ Other Affiliate Associate Professor_____

College: Choose an item.___College of Science_____

Department/Program _____Psychology_____

Address _____Neurosciences, Brigham and Women's Hospital, 60 Fenwood Road, Boston, 02115_____

Office Phone 617-732-8060_____ Email _____mgeddes@bwh.harvard.edu_____

Is this student research? YES _____ NO __*x*_____If yes, please provide the following information:

Student Name _____ Anticipated graduation date _____

Undergrad ____ MA/MS ____ PhD ____ AuD ____ EdD ____ DLP ____ Other Degree Type ____

College: Choose an item. _____

Department/Program _____

Full Mailing Address _____

Telephone _____ Primary Email _____

Cell phone _____ Secondary Email _____

B. Protocol Information

Title: Daily Activity Study of Health (DASH)__

Projected # subjects __80_____
Approx. begin date of project 06/01/2019___ Approx. end date 06/30/2021_____
month, day, year month, day, year

It is the policy of Northeastern University that no activity involving human subjects be undertaken until those activities have been reviewed and approved by the University's Institutional Review Board (IRB).

- **Anticipated funding agency/source for project (or none)** NIH/NIA
- **Has/will this proposal been/be submitted through:**
  - NU's Office of Research Administration and Finance (RAF) x
  - Provost
  - Corp & Foundations
  - Other
- **Grant Title: Changing and understanding motivation to increase physical activity among sedentary older adults**
- **Grant ID:** ePAWS# 10002361

C.

Will Participants Be:	Yes	No
Children (<18)		x
Northeastern University Students?		x
Institutionalized persons?		x
Prisoners?		x
Cognitively Impaired Persons?		x
Non or Limited English Speaking Persons?		x
People Living outside the USA?		x
Pregnant Women/Fetuses?		x
Other? *(Please provide detail)*		

Does the Project Involve:	Yes	No
Blood Removal?		x
Investigational drug/device?		x
Audiotapes/videotapes?		x

Please answer each of the following questions using non-technical language. Missing or incomplete answers will delay your review while we request the information.

D. What are the goals of this research? Please state your research question(s) and related hypotheses.

This multidisciplinary pilot proposal focuses on examining the efficacy of factors that have shown promise in motivating sedentary older adults to become more physically active as well as

to investigate changes in patterns of activation of the neural networks, as indexed by MRI and fMRI, that support these factors and changes in physical activity.

Aim 1: Our primary aim is to assess, in a six-week pilot randomized controlled trial with healthy but sedentary older adults, the efficacy of self-affirmation + gain-framed messaging versus a control group that receives loss-framed messaging only on changes in physical activity. We will also examine whether any differential physical activity engendered in the two groups is maintained at 3 months post-intervention.

Exploratory Aim 2: A secondary exploratory aim will examine the extent to which individual differences in motivation, conscientiousness, growth mindset and other factors moderate the effects of our intervention on physical activity change, for our self-affirmation + gain-framed messaging versus a control group that receives loss-framed messaging only, over the course of the intervention and at 3 months post-intervention.

Exploratory Aim 3: Another exploratory aim will examine the extent to which our intervention influences patterns of activation and connectivity in self-referential brain networks including medial prefrontal cortex and ventral striatum that have been related to self-affirmation of health messages (Falk et al, 2015; Gutchess et al., 2007), as well as other networks associated with aging and physical activity (e.g. resting state executive control, default and salience networks), and whether activation and connectivity within and between these networks is associated with physical activity change both following the intervention and 3 months post-intervention.

We believe that our intervention will provide valuable, novel information about the efficacy of promising factors to enhance physical activity, and in turn cognitive and brain health, in sedentary older adults as well as the functional brain changes and individual differences that support these potential changes in physical activity.

E. Provide a brief summary of the purpose of the research in non-technical language.

Although it is widely known that increased exercise in older age improves cognitive, affective and physical wellbeing, many older Americans are sedentary. Developing and understanding techniques that motivate older adults to engage in physical activity has the potential to impact a spectrum of health-related behaviors and to improve brain health and quality of life. Motivational processes change across the lifespan. Despite a decline in the neurobehavioral influence of motivation on learning, older adults demonstrate relatively preserved reward sensitivity compared to younger adults (Geddes et al., 2018).

Converging evidence has shown that reflection about core values (self-affirmation) before exposure to health messages is associated with positive behavioral change in younger adults (Cohen & Sherman, 2014). This is thought to occur by highlighting the self-relevance of potentially threatening messages (Cascio et al., 2016). Human fMRI studies in younger adults have shown that self-affirmation before exposure to persuasive health messages increases physical activity and is associated with activation of medial prefrontal cortex and ventral striatum, brain systems that support self-referential processing and positive valuation (Cascio et

al., 2016; Falk et al., 2015). There is reason to think that self-affirmation would also be an effective strategy to promote physical activity in older adults: A key node in the brain network underlying self-referential processing, medial prefrontal cortex, is relatively spared in aging (Gutchess et al., 2007; Salat et al., 2004).

We hypothesize that, (1) self-affirmation combined with gain-framed messaging will increase physical activity in older adults, while loss-framed messaging alone will not, (2) the added behavioral benefit from self-affirmation will be associated with increased activity in medial prefrontal cortex and ventral striatum, (3) individual differences in structural and functional frontosubcortical connectivity will predict change in physical activity. The overarching goals of this work are to identify and understand novel strategies to enhance physical activity in sedentary older adults and to characterize individual brain and neuropsychological differences that predict behavioral change. Our ultimate goal is to develop personalized behavioral interventions in older adults that tailor persuasive health-related messaging based on an individual's neurobehavioral profile.

F. Identify study personnel on this project. Include name, credentials, role, and organization affiliation.

Maiya Geddes, M.D., Principal Investigator, Psychology (study design, analysis, reporting). Dr. Geddes is an Affiliate Associate Professor at Northeastern University and a behavioral neurologist and clinician scientist at the Center for Brain/Mind Medicine at the Brigham and Women's Hospital at Harvard Medical School. Dr. Geddes' research focuses on cognitive aging and the influence of motivation on cognitive processes in older adults. Dr. Geddes applies a converging methods approach that combines cutting-edge behavioral and multi-modal neuroimaging techniques. Dr. Geddes will be involved in all aspects of study design and execution.

Professor Susan Whitfield-Gabrieli Ph.D., Psychology (study design, analysis, reporting), Director of the Northeastern University Biomedical Imaging Center (NUBIC). Professor Whitfield-Gabrieli has expertise in healthy aging as well as in amnesic mild cognitive impairment and with cognitive training in mild cognitive impairment. Professor Whitfield-Gabrieli has extensive experience with multimodal neuroimaging analyses and has published papers on topics related to this proposal including, aging and cognition, the self-reference network, temporal discounting as well as brain/behavior changes post interventions. In addition, she has also developed state-of-the art analysis software for quality assurance of functional imaging data (***art***; http://www.nitrc.org/projects/artifact_detect/) as well as for resting state functional connectivity (***conn***; http://www.nitrc.org/projects/conn/) [32] both of which are particularly useful for the proposed research.

Professor Arthur Kramer Ph.D., Faculty Advisor, Psychology (study design, analysis, reporting). Professor Kramer has spent over twenty-five years conducting exercise intervention research with participants across the lifespan, but primarily with older adults. His main focus in these studies was the assessment of changes in cognition and brain structure/function using multimodal imaging technologies including MRI, fMRI, fNIRS, EEG and ERPs. His role in the

current project will be to assist Dr. Whitfield Gabrieli with the development and execution of all aspects of the projects as well as the analysis and interpretation of the data.

Professor Charles Hillman Ph.D., Psychology (study design, analysis, reporting). Professor Hillman has over 18 years of experience as a PI of exercise and physical activity projects that examine effects on cognition and brain function. Professor Hillman is the Co-Director of the Center for Cognitive and Brain Health at Northeastern University. He will be involved in the design and analyses of the physical activity data and its association with cognitive and psychosocial measures.

Katherine McDonald, B.A., Doctoral Student, Psychology (data collection, analysis)

Lauren Raine, Ph.D., Post-Doctoral Associate (data collection, analysis, consulting)

Dinesh John, Ph.D., Department of Health Sciences, Associate Professor (data collection, analysis, consulting).

Frank D'Agostino, Undergraduate Student, Harvard College (study design, data collection, analysis)

Aida Elizabeth Quiñonez Flores, B.S., Research Technician, Psychology (study design, data collection, analysis)

Cora Ordway, B.S., Research Technician, Psychology (study design, recruitment, data collection, analysis)

Meishan Ai, B.S., Doctoral Student, Psychology (study design, data collection, analysis)

Dominika Pindus, Ph.D., Assistant Professor, University of Illinois at Urbana-Champaign (study design, analysis, consulting)

Timothy Morris, Ph.D., Post-Doctoral Associate (study design, data collection, analysis)

Adrián Noriega de la Colina, M.D., Ph.D., Post-Doctoral Associate, McGill University (study design, analysis)

Farah Makram, Undergraduate, Northeastern University (recruitment, data collection, analysis)

Ana Escobedo, Undergraduate, Northeastern University (recruitment, data collection, analysis)

Lauren Voso, Undergraduate Co-Op, Northeastern University (recruitment, data collection, analysis)

Calvin Tobias, Undergraduate Co-Op, Northeastern University (recruitment, data collection, analysis)

Emily Melsky, Research Technician, Northeastern University (recruitment, data collection, analysis)

Naga Thovinakere, B.S., Master student, McGill University (recruitment, data collection, analysis)

Madhura Lotlikar, B.S., Doctoral student, McGill University (recruitment, data collection, analysis)

Zeynep Yalcin, Undergraduate student, McGill University (recruitment, data collection, analysis)

G. Identify other organizations or institutions that are involved. Attach current Institutional Review Board (IRB) approvals or letters of permission as necessary.

N/A

H. Recruitment Procedures

Describe the participants you intend to recruit. Provide all inclusion and exclusion criteria. Include age range, number of subjects, gender, ethnicity/race, socio-economic level, literacy level and health (as applicable) and reasons for exempting any groups. Describe how/when/by whom inclusion/exclusion criteria will be determined.

Participants will not be excluded based on sex, race, or ethnicity. If a participant is excluded for any reason, they will be immediately informed that they have not met all criteria and their participation will be discontinued. All interested participants will be selected to participate until the desired number (n = 80 older adults) is reached. We recognize that women in this age group are over-represented relative to men and are also more likely to volunteer for health-related studies. However, we will do our best to recruit 50% women and 50% men in our sample. Participants will be randomly assigned to one of the two study conditions. Children will not be included since the study is focused on older adults. Potential participants will be screened over the phone for cognitive function and will be assessed by the Telephone Interview of Cognitive Status (TICS) to ensure normal level of cognitive function. Any participant not passing the TICS as 'normal' will be ineligible for further consideration in the study. Participants with implanted devices that are likely to be adversely influenced by MRI will be marked as "MRI-ineligible" but may be able to participate in the remote/behavioral version of the study.

Inclusion Criteria:
• Men and women of all ethnicities/races and socio-economic status, 55-95 years

• Normal or corrected-to-normal vision based on the minimal 20/20 standard in order to complete the cognitive tasks
•
• Able to speak, read, and write English
• Ambulatory without significant increase in pain or the assistance of walking devices
• No diagnosis of a neurological disease
• No contraindications to MRI imaging (if opting into MRI)
• Exercising less than 150 minutes per week (half of the recommended 150 minutes per week) AND sitting down more than 8 hours per day
• Regular access to a computer with internet
• Reliable transportation to the Northeastern University campus for 2 visits (if opting into MRI)
• Right-handed (if opting into MRI)
• Weight under 275 pounds (if opting into MRI)

Exclusion Criteria:
• Current or previous formal diagnosis of a DSM-V Axis I or II disorder including Major Depression (not including post-partum depression or anxiety)
• History of major psychiatric illness including schizophrenia
• Current treatment for cancer – except non-melanoma skin
• Neurological condition (MS, Parkinson's, Dementia, MCI) or brain injury (traumatic or Stroke)
• Type I Diabetes
• Type II Diabetes if unstable or controlled by insulin
• Current alcohol or substance abuse
• Current treatment for congestive heart failure, angina, uncontrolled arrhythmia, DVT or other cardiovascular condition
• A blood clot in the legs in the last 2 years
• Myocardial infarction, coronary artery bypass grafting, angioplasty or other cardiac event in the past year
•
• Regular use of an assisted walking device or significant increase in pain when walking
• Claustrophobia (if opting into MRI)
• Not passing the Telephone Interview of Cognitive Status (TICS) as normal
• Use of any anti-psychotic, anti-depressant, anti-anxiety, and ADD/ADHD medications.
• Not fluent in English
• Contraindications to MRI (if opting into MRI)• No regular access to a computer with internet
• Involvement in conflicting research studies currently or recently

Screening Procedures:
Screening procedures will involve verbally screening potential participants over the phone. A staff member doing the screening will begin with an overview of the DASH project. The screener will then obtain verbal consent (see telephone script). The telephone script will ask questions regarding potential participants' demographic information such as age and gender along with medical history questions in relation to inclusion and exclusion criteria. The total

time to administer all screening questions is approximately 30 minutes. The telephone screen will also assess level of physical activity via self-reported physical activity. If eligibility is verified, a date and time will be scheduled for a virtual meeting between the participant and a researcher where the formal study consent will be signed. Those individuals that are deemed ineligible from the screening call will have their forms kept in a separate file on REDCap. This information will be used to quantify how many were ineligible from the screening call and reasons for ineligibility.

The criteria will be assessed by one of the listed study personnel. No special expertise is required to evaluate screening responses. If a participant requires exclusion due to information received during a visit, they will be contacted via telephone or email and informed that they have been excluded from further study. The reason provided for their exclusion will be brief, and will include a statement such as, "Based on the data collected in your last session, we will not require any further testing. As indicated in the beginning, participation depends on a number of factors and not all participants qualify for the entire study."

Describe the procedures that you will use to recruit these participants. Be specific. How will potential subjects be identified? Who will ask for participation? If you intend to recruit using letters, posters, fliers, ads, website, email, PsyLink description, HIT, etc., copies must be included as attachments for stamped approval. Include scripts for intended telephone recruitment.

Older adult participants will be recruited through the local media (television, radio, newspapers), promotional flyers and targeted postcard mailings, announcements to local aging and senior citizen agencies, bus advertisements, online sites (e.g., Craig's list and Facebook), university registries, and announcements through local religious places of worship. All of the above recruitment strategies will use the same language as attached flyer and social media ads.

What remuneration, if any, is offered?

Remuneration will be offered as follows:

VISIT	**Approx. Hours**	**Approx. Pay**
T1	4	$80
T2	3	$60
T3	3	$60
T4	2	$40
Accelerometry Completion	N/A	$100
TOTALS	*12 hours*	*$240 without accelerometry completion, $340 with. Less if*

		the participant opts out of MRIs.

Participants will be paid $20/hour for study activities including cognitive and behavioral assessments, physical assessments, and MRIs. The time they spend on each activity may be slightly variable due to whether they opt into MRIs, their speed completing tasks and other, everyday factors, so individuals may spend about 12-18 hours on the study and will be paid accordingly. They will be paid after each of the four main study visits through a check that will be sent to them through the mail, but exceptions will be made in payment schedule for those who request it (in order to alleviate any concerns with Social Security interference). Participants will fill out a W-9 tax form at the time of consent to allow for their payment. If they finish the study and complete all parts, including wearing the physical activity monitoring devices consistently, responding to daily messages, and returning the devices at the end of the study, they will be able to earn an extra $100.

If the participant attempts but is unable to complete the scan (e.g., scanner issue, claustrophobia, etc.), they will be compensated in full for that particular scan.

I. Consent Process

Describe the process of obtaining informed consent*. Be specific. How will the project and the participants' role be presented to potential participants? By whom? When? Where? Having the participant read and sign a consent statement is done only after the researcher provides a detailed oral explanation and answers all questions. Please attach a copy of informed consent statements that you intend to use, if applicable. **Click here for consent form templates.**

If your study population includes non-English speaking people, translations of consent information are necessary. Describe how information will be translated and by whom. You may wait until the consent is approved in English before having it translated.

Participants' consent will be obtained remotely before they begin participating in research activities. The consent process will be administered by experimenters (i.e., research personnel described above). Individuals who agree to participate after the phone screen will receive a copy of the consent document in advance and will schedule a time to speak with an experimenter over the phone. They will be asked to read, but not sign, the consent document before the phone call, and the experimenter will coordinate with the participant so they have enough time to read the document before the call. During the call, the experimenter will explain the study and answer any questions the participant has. If the participant wants to continue with the study, they will then sign the consent document electronically in REDCap. Participants will be made aware that their participation is completely voluntary and they may quit the experiment at any time.

If your population includes children, prisoners, people with limited mental capacity, language barriers, problems with reading or understanding, or other issues that may make them vulnerable or limit their ability to understand and provide consent, describe special procedures that you will institute to obtain consent appropriately. If participants are potentially decisionally impaired, how will you determine competency?

N/A

*If incomplete disclosure during the initial consent process is essential to carrying out the proposed research, please provide a detailed description of the debriefing process. Be specific. When will full disclosure of the research goals be presented to subjects (e.g., immediately after the subject has completed the research task(s) or held off until the completion of the study's data collection)? By whom? Please attach a copy of the written debriefing statement that will be given to subjects.

Complete disclosure will be provided during the consent process.

J. Study Procedures

Provide a detailed description of all activities the participant will be asked to do and what will be done to the participants. Include the location, number of sessions, time for each session, and total time period anticipated for each participant, including long term follow up.

PARTICIPANTS:
In 80 sedentary and cognitively asymptomatic older adults (60 – 95 years) we will test whether a behavioral intervention combining self-affirmations and gain-framed health messages decreases the amount of time participants are sedentary, as measured by accelerometry. Participants completing MRIs will be in the "MRI group," while those who do not will be in the "behavioral group." We will use stratified randomization to be sure that half of the participants in each group will be randomized to the self-affirmation + gain-framed health messaging condition (intervention) and the other half will be randomized to a loss-framed health messaging only condition (control). Participants will not be explicitly told to exercise as part of the study, but during the experiment they will receive messages that encourage walking or decreasing sedentary time. The primary measure of interest is decrease in sedentary behavior. All participants will be recruited and screened remotely by researchers affiliated with the Center for Cognitive & Brain Health in the Interdisciplinary Science and Engineering Complex under the direction of Drs. Geddes, Kramer and Hillman.

In addition to these 80 participants, we will recruit up to 20 pilot participants who will complete smaller portions of the study and whose data will only be used to improve design.

PERSONNEL:
All staff and personnel associated with screening, collecting data, and analyzing data will have been trained in their laboratory and will have undergone all necessary research modules for safety and research ethics. Dr. Geddes will meet with all staff on a regular basis to ensure that they are conducting research protocols appropriately. In addition, all staff who interact with participants will be certified in AED and CPR. All staff who administer remote study visits will be familiar with an emergency protocol (including calling emergency services) to prepare for the unlikely event that a participant has a medical emergency during a video or phone appointment. MRI data will be collected by licensed MR technicians and staff trained to analyze MRI scans.

RESEARCH ACTIVITIES:

Overview:
There will be a total of --- visits, with each visit split into multiple sessions. Participants will complete neuropsychological and behavioral inventories, cognitive tests, writing tasks, and computer tasks at these visits. There will also be 2 visits, one before intervention and one after dedicated to physical assessments. Additionally, participants opting into the MRIs will come in-person before and after intervention for the MRI. Outside of the sessions, participants will wear two accelerometry devices for 4 separate weeks in the study and receive and respond to daily messages as part of the intervention. Each of these aspects and what they entail is detailed below.

Surveys:
During the first visit, known as "Consent Visit 1", participants will sign the consent form, complete the W-9 form and complete surveys. Participants will complete screening measures for anxiety, depression, and cognitive impairment. If they pass these screenings, they will be randomized into the intervention (self-affirmation + gain-framed messaging) or control group (loss-framed messaging only). In this visit and the next (Consent Visit 2) they will also complete neuropsychological and behavioral inventories. We expect testing to take about 3 hours total over the 2 sessions and will administer the assessments with breaks every ~40 minutes to reduce fatigue. They will complete behavioral inventories that capture individual differences in traits potentially predicting responsiveness to the intervention. These measures (listed in the attached spreadsheet) include validated questionnaires to assess factors like motivation for physical activity, self-efficacy for exercise, self-efficacy for walking, barriers to exercise, mood, conscientiousness and grit, growth mindset, loneliness, future time perspective, and purpose in life. Participants' educational attainment and total personal income levels will also be collected to create a measure of socioeconomic status, as described by Hartanto et al. (2019). These questionnaires will be administered through REDCap, a "secure, HIPAA-compliant, web-based application… housed in a secure local data center, behind the Tufts Medical Center firewall, and all web-based information is encrypted" (tuftsctsi.org/research-services/informatics/redcap-research-electronic-data-capture/).

Cognitive Tests:
Throughout the visits, participants will also complete a cognitive battery (also listed in the attached spreadsheet) that examines important cognitive constructs that have been associated with changes in physical activity and aging including general cognitive function (BTACT), verbal fluency (MoCA phonemic fluency), executive function (Trail Making Test A and B), . Additional paradigms are described below:

The *Intrinsic Motivation Effort Expenditure for Rewards Task* (EEfRT), captures the construct of Reward Valuation and Effort. This multi-trial computerized task presents participants with a (variable) level of reward and a (variable) amount of work (effort) to win that reward. For each trial, the participant must accept or reject the proposal based on whether they think the reward is worth the effort. If they accept the trial, they have a 1/3 chance of then being asked to perform that work. The "work" is fast key presses on the left and right arrow keys, using the right-hand index and middle fingers. The amount of work is communicated using a vertical rectangle with a horizontal line through it at different heights; the higher the line, the more key presses are required. Participants are given visual feedback during the trial as the line is moved to the bottom and is progressively raised with each button press, with the goal of raising the line up to its original height for that trial. Rewards come from three domains: monetary rewards (hypothetical money), social rewards (hypothetical time with loved ones), and intrinsic rewards from curiosity (the answers to trivia questions). There are 6 "levels" of reward in each of the three domains, and 5 levels of work.

We will use a common paradigm for *optimistic bias* (Sharot et al., 2011, 2012), which was previously approved for our lab by MIT Couhes (protocol #1901648694 "How risk is considered"). In the first session, participants will be presented with 40 adverse life events. On each trial, participants will be asked to estimate how likely the event is to happen to them in the future, and will next be presented with the base rate of the event in a demographically similar population. In a second session, immediately after the first, participants will be asked again to provide estimates of their likelihood of encountering the same events. Biased learning will be calculated using participants' updates of their initial estimates in response to the information presented. Participants will rate all stimuli on vividness, familiarity, prior experience, arousal, controllability, and negativity, and will be tested for memory of the information presented. The "optimistic bias" reflects a human tendency to discard undesirable information and integrate desirable information, mostly in the form of health and non-health-related estimated risks. This is evident in a selective error-processing mechanism, in which learning from errors which contain good news ("my risk is lower than I estimated") is faster than learning from bad-news errors, generating a biased learning mechanism.

The *Option Generation Task* (Hartmann et al., 2015) measures participants' fluency and ability to generate options for future behavior. In each trial, the experimenter will present the participant with a hypothetical "open" (e.g., It's a rainy and cold Sunday. What could you do?) or "problem solving" situation (e.g., You are in a foreign city and you are totally lost. What could you do?). The participant will be given 2 minutes to generate options for action. They will be encouraged to describe each option briefly, mainly using keywords.

The *Progressive Ratio Task* (Wolf et al., 2014) includes 7 sets of trials at each of 3 monetary reward levels ($0.50, $0.25, and $0.10). For each individual task trial, participants will view 2 numbers on the screen and identify the larger one by pressing one of two keys on a standard keyboard. Numbers will be randomly selected between 0 and 1000. The effort (i.e., number of correct responses) required to achieve a reward will increase with each successive trial set within a given reward level. Before each set, the number of trials required and the monetary value of the set will be presented and the subject will choose whether to perform the set or not; they could also choose to quit a set at any point. When a subject chooses not to complete a set, the higher

effort sets at that monetary value will not be presented and the next set to be offered will be the lowest effort set at the next (lower) monetary value.

The *Delay Discounting Task* is a measure of temporal discounting; the tendency for people to prefer smaller, immediate monetary rewards over larger, delayed rewards. Participants will respond to a series of 27 questions that ask them to choose between a smaller, immediate reward (e.g., $25 today) versus a larger, later reward (e.g., $35 in 25 days). The 27 items are divided into three groups according to the size of the larger amount (small, medium, or large). Modeling techniques are used to fit the function that relates time to discounting. The main dependent measure of interest is the steepness of the discounting curve such that a more steeply declining curve represents a tendency to devalue rewards as they become more temporally remote (Science of Behavior Change, Columbia University).

The *Future Time Perspective Task* (Wallace, 1956; Fellows and Farah, 2005) assesses the length of individuals' views of the future, where more limited views of the future have been linked with pathological impulsive behavior like drug use. Participants will be asked to generate a list of five future life events and respond orally, without a time limit. After the events are generated, the experimenter will ask the participant to estimate how far into the future each event might occur. The two dependent measures for this task are the 'extension', which is the maximum length of time generated by each subject, and the mean future time period for all five items.

The *N-Back Task* is a behavioral measure of working memory within the larger domain of executive function. It assesses the cognitive ability to store and control information on a short-term basis. In this computer task, a sequential stream of visual stimuli (typically letters) are presented one at a time. Participants' task is to identify whether a current stimulus (e.g., the letter B) is the same as a stimulus that appeared N trials previously, where N has a variable value that changes at times during the task to alter the level of demand on participants' cognitive resources. Each stimulus is typically presented very briefly (e.g., 0.5 seconds) with a substantial delay between each one (e.g., 2 seconds) to ensure that working memory is sufficiently taxed. A typical block of the task includes 12 sequentially presented stimuli. In recent versions of the task participants are instructed to ignore the case of the letter (e.g., B is the same as b) in order to reduce the confound of perceptual familiarity. As an example, in a 2-back condition within this task, the correct answers for the final three stimuli in the sequence D b v d V would be the following: no, no, yes. In contrast, in a 3-back condition for the same sequence, the correct answers for the final two letters would be the following: yes, no. In the adaptive version, task complexity (i.e., n-back level) is adjusted according to each participant's performance. The dependent measures are accuracy and response time for each level of task complexity (i.e., each n-back level) (Science of Behavior Change, Columbia University).

In the *simple reaction time task*, the participant will be presented with a blank white screen and asked to press a button as quickly as possible each time a large, black "X" appears. The "X" will always appear in the same spot in the center of the screen. This measures the participant's reaction times.

In summary, in order to understand the variability in participants' responses to persuasive messaging, we will gather a rich dataset of individual differences across behavioral traits and

cognitive, structural, and functional brain measures. Some of these tests will be administered verbally by adapting in-person, pen and paper versions to phone calls or videoconferencing formats. Certain phone-based tasks require researchers to collect audio recordings of participant responses for timing and other scoring purposes. Online replacement tests will be administered using TestMyBrain.org and Pavlovia.org.

TestMyBrain was developed by Dr. Laura Germine and colleagues in 2008 and is updated continuously. TMB provides online alternatives to classic pen and paper neuropsychological assessment tools and has normative data from thousands of online test subjects aged 12 to 90. TMB only provides tests that have been validated online and shown to be comparable to hard copy versions. The TMB Neuropsychology Toolkit follows HIPAA regulations and does not collect personal identifiable data or demographic information. They retain test performance data for quality assurance and temporarily store access information (IP address, access URL, timestamp, and user agent) for 14 days to help prevent or identify security breaches or other fraudulent behavior.

Pavlovia was created by John Pierce and colleagues at the University of Nottingham and is now run by Open Science Tools LTD. It is fully GDPR, or General Data Protection Regulation, compliant. The GDPR concerns data protection and privacy in the European Union and the European Economic Area. Source: https://pavlovia.org/docs/home/ethics

Accelerometry:

Participants will be fitted with two accelerometers and have their cardiorespiratory status estimated. The estimation uses a regression equation that includes age, sex, body mass index, and resting heart rate. We will obtain a non-exercise CRF estimation before and after the six-week intervention. To perform the CRF estimation, which will be remote, we will ask participants to report their supine resting heart rate (i.e., the average of all R-R intervals over ten seconds) after they have rested quietly for ten minutes. Participants will also complete a physical assessment focused on their basic walking speed, their ability to transition repeatedly from sitting to standing, and their balance.

Accelerometers, chargers, and related materials will be sent to participants through the mail after the consent meeting and will be returned after the 3-month follow-up session. Accelerometry data will be recorded during wakefulness and sleep, with the exception of bathing or swimming, for the week between the Red and Orange visits (before the intervention begins; i.e., baseline), for two separate weeks during the 6-week intervention (with additional days during this timeframe for any participant who does not wear the devices consistently during the original period), and for a week after the 3-month follow-up visit. This will characterize change in physical activity from baseline and maintenance. It will be assessed using two accelerometers worn simultaneously. The first is a wrist-worn tri-axial accelerometer (ActiGraph GT3X Link, Pensacola, FL). This accelerometry data will be downloaded in 60-second epochs (ActiLife software, ActiGraph, Pensacola, FL) and will be screened for wear time using standard methods (Choi et al., 2011). The second device is a tri-axial accelerometer and inclinometer (activPAL) and will be worn on the thigh using an adhesive.

Physical activity will be measured with an ActiGraph accelerometer model GT9X Link (ActiGraph LLC, Pensacola, FL). The ActiGraph GT9X Link is a small (3.5 x 3.5 x 1 cm) and light (14 g) device that measures acceleration in three planes: vertical, anteroposterior and mediolateral. Participants will wear the device on their wrist 24 hours a day to improve compliance. The 24-hour protocol has resulted in greater compliance over waking time wear protocol (Tudor-Locke et al., 2015). Participants will be instructed to take the device off for swimming, showering and bathing. Data from this device will be synced with the CentrePoint app (HIPAA compliant, also through ActiGraph) on the participant's phone or computer. Raw data will be reduced and processed using ActiLife software (http://www.actigraphcorp.com). Participants will fill in sleep and activity logs.

Sedentary behavior will be assessed with an activPAL, thigh-worn tri-axial accelerometer and inclinometer. ActivePAL provides a noninvasive, valid measure of posture (sitting and standing) and transitions between these postures. Participants will be asked to attach the device with an adhesive patch to the front of the thigh, roughly half of the way between hip and knee. They will wear the device 24 hours a day. A waterproof covering and adhesive patches will be provided for the attachment of the device, and participants will be provided with the additional sets of adhesive patches should they need to change the dressing (e.g. taking off the device for swimming). Participants will be provided with instructions on how to mount the device and change the adhesive dressing. Data will be reduced using activPAL software (PAL Technologies). The activPAL shows perfect and near perfect (r=.99) correlations with direct observation in the assessment of time spent sitting/lying, standing, and walking in simulated free-living activities, and transitions from sit-to-stand and stand-to-sit (Aminian and Hinckson, 2012).

Physical Assessments:
The physical assessment will be administered at Orange Visit 1 and Indigo Visit 3. Participants will report their supine heart rate (i.e., the average of all R-R intervals over ten seconds) after resting for 10 minutes. After completing some warm-up exercises and stretches to reduce possible risks of overexertion, they will perform 5 physical assessments: a 6-minute walk test, a balance test, a gait speed 4-meter course, a chair stand test, and an 8-foot up and go test. Before and after the 6-minute walk test, the participant will report their blood pressure and heart rate. They will also rate their perceived level of exertion (RPE) before and after this test.

Neuroimaging:
At Yellow Visit 2, participants will either undergo neuroimaging (i.e., task fMRI, resting-state MRI, structural MRI, DWI) or complete replacement tasks at home. For the self-affirmation intervention, all participants will be shown a series of eight core values (i.e., money, creativity, religion, politics, family & friends, sense of humor, independence, spontaneity) and will be asked to choose the values they think are most and least important to them as per Cascio et al. (2016). They will proceed to fill out a simple activity sheet of questions about the value they chose (both intervention and control group versions attached). The questions will be designed to help them practice the thorough reflection required for the scanner self-affirmation task. Each participant's vision will be assessed using a Snellen chart so they can be fitted with appropriate, MRI-safe

corrective eyewear if necessary. The randomization scheme will be prepared by the Harvard Catalyst Biostatistical Group using a permuted block method with random blocks. The randomization ratio will be 1:1. Sealed envelopes will be provided to the investigator and stored at the designated site. All participants will perform an fMRI task with a block design containing a self-affirmation manipulation followed by either gain- or loss-framed persuasive messaging about physical activity. Participants in the intervention group will be asked to think about situations that allow them to reflect on their highest ranked value before being presented with gain-framed health messaging, whereas participants in the control group will reflect on their lowest ranked value before receiving loss-framed health messages. During the self-affirmation block, participants will be presented with prompts about value-relevant topics to allow them to elaborate upon and connect with situations that are pertinent to their core value (e.g., if religion was the highest ranked value, an example self-affirmation statement would be, 'Think of a time in the future when you would be inspired by religion' or 'Think of a time in the future when you would feel grateful for religion'). All statements will focus on the self rather than relying on factual knowledge to ensure that topic importance rather than topic knowledge differentiates high- and low-ranked values. As a within-subject control condition, participants in both groups will also be shown prompts about value-neutral statements (e.g., 'Think of a time in the future when you would check the weather'). For a detailed description of the self-affirmation manipulation see Cascio et al. (2016) and Falk et al. (2015). Next, participants will undergo exposure to a block of gain-framed persuasive health messages that encourage physical activity, as in Notthoff et al. (2014), or a block of comparably constructed loss-framed persuasive health messages that similarly encourage physical activity. The set of health messages primarily consists of wellness information taken from the Physical Activity Guidelines for Americans published by the U.S. Department of Health and Human Services. The method of balancing gain- and loss-framed messages was inspired by Notthoff et al. (2014). In older adults, gain-framed messages (e.g., 'Walking has important cardiovascular health benefits') have previously been shown to be more effective at encouraging exercise compared to loss-framed messages (e.g., 'Not walking enough can lead to increased risk for cardiovascular disease') (Notthoff et al., 2014).

Previous fMRI studies in younger adults have used an anatomically defined medial prefrontal cortex region-of-interest (ROI) in the analysis of self-affirmation manipulations (Cascio et al., 2016; Falk et al., 2015). To improve upon this, we will apply a functionally defined ROI by gathering a monetary incentive delay task (Knutson et al., 2001) shown to localize the valuation brain networks including ventromedial prefrontal cortex and striatum. Two runs of the monetary incentive delay task will take approximately 12 minutes total.

The monetary incentive delay (MID) task follows the NIMH RDoC construct of Reward Anticipation and Responsiveness: In each trial, participants are cued with arrows indicating the reward value of a button press during the upcoming target (a white star). Cues signal potential reward (up arrow), potential punishment (down arrow) or no monetary outcome (sideways arrow). The amounts at stake are 0, 1 or 5 dollars (participants will have been informed that we will not be paying them actual money at the end. This task has been shown to be effective and recruit the same brain structures even without real monetary incentives. Ten trials from each condition (reward, punishment or neutral) are presented in a pseudo-randomized order in each run yielding a total of 20 trials for each condition for each participant. The cue (1 s) and

feedback (2 s) appear after a temporally jittered delay (3 – 5 s). Difficulty is titrated by performance to a 67% hit rate by adjusting the reaction time window for allowed responses. After target presentation, a feedback screen displays the reward (for hits) or penalty (for misses) and the cumulative total. There is evidence that the MID task activates the reward network including ventral striatum, dACC, vmPFC and cerebellum.

Daily Messaging:
Over a period of six weeks, all participants will receive daily prompts about their highest- (intervention group) or lowest- (control group) ranked value, followed by gain-framed (intervention group) or loss-framed (control group) messaging about physical activity. The daily self-affirmation and health messages will be a combination of the same 21 messages the participants had seen in the fMRI scanner task mixed with 21 new messages. We expect that only the participants in the self-affirmation + gain-framed messaging group will increase their physical activity from baseline. All participants will also answer questions about their memory of the messages (whether they are old or new), affect, self-efficacy, and implementation intention. This will be delivered via email or text using oTree (Robinson & Lachman, 2016; Lachman et al., 2018; Chen et al., 2015).

We will use the oTree library to distribute survey questions via email or text to participants during the 6-week intervention. oTree is licensed under the MIT open source license and offers use of several libraries and capabilities for psychological research. It was designed specifically for "controlled behavioral experiments in economics, psychology, and related fields" (www.otree.org). The messaging system runs on a Heroku server, which is a Cloud application program that allows websites to be hosted online. The messaging system sends out participant-specific, hash-encrypted links. This safety measure prevents participants from guessing other links and accessing other participants' survey pages. Links will be sent to participants individually through email; however, survey responses will be identified solely by the Participant ID that oTree randomly generates, and will not be connected to names, emails, or any other identifying information. Further, links cannot be used to figure out the email address of the respondent. Only the necessary research staff will have access to the information connecting participants to the links they were sent.

The data are stored on a Heroku server. Heroku's privacy policy states that, "We take steps to protect the privacy of our customers and protect data stored within the platform. Some of the protections… include authentication, access controls, data transport encryption, HTTPS support for customer applications, and the ability for customers to encrypt stored data." Further, answers to survey questions are stored in number form corresponding to the multiple-choice option selected, without a key to the meaning of the choice or the question itself. There is a mandatory Administrator login, requiring a username and password, to gain access to this data. Only necessary research personnel will have the login information.

We will use the Remind app to deliver links to the oTree survey via text to participants every day. Remind is a texting service primarily used by educators, students, and parents that is compliant with federal privacy laws protecting students. It has been awarded the ISO 27001:2013 certification, which is an international standard for information security

management and governance (https://www.remind.com/blog/iso-27001-certification). Participants will not discuss personal and/or health information through Remind, and the links sent to them will not contain private information.

Follow-up measures:

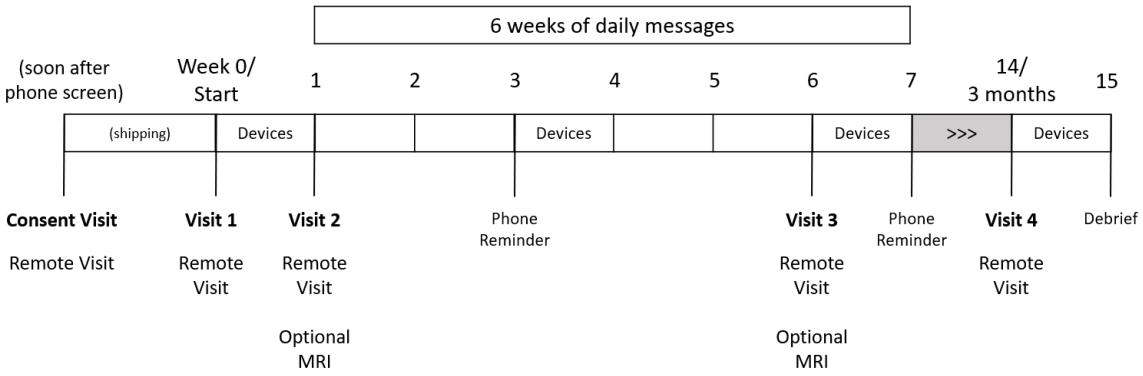
After the intervention, participants opting into the MRIs will undergo repeat neuroimaging (i.e., resting state MRI, structural MRI, task fMRI, DWI), physical assessment session, and specified cognitive tests. Additionally, in an attempt to determine the extent of benefits following the end of the formal intervention, participants will be assessed again at 3 months post-intervention, with 7 days of accelerometry recording to determine physical activity, and bevavioral and psychosocial measures to assess continued cognitive benefits.

Outcome measures outside of the neuropsychological assessment battery are as follows:

Outcome measure	Type	Timeframe	Brief description
Total step count (average steps/day)	**Primary**	Week 0 (baseline); Week 3; Week 6; 3 Months	This metric quantifies the change in the average number of steps taken each day, from the baseline, Week 2, Week 6, and 3-month periods. It is a marker of change in habitual ambulatory activity.
Sedentary behavior (average min/day)	**Primary**	Week 0 (baseline); Week 3; Week 6; 3 Months	This metric quantifies the change in the average amount of time spent sedentary each day, from the baseline, Week 2, Week 6, and 3-month periods. It is a marker of time spent inactive.
Moderate-vigorous activity (average min/day)	Secondary	Week 0 (baseline); Week 3; Week 6; 3 Months	This metric quantifies the change in the average amount of time spent engaged in moderate-to-vigorous physical activity each day,

			from the baseline, Week 2, Week 6, and 3-month periods. It is a marker of physical activity.
Walking Cadence	Secondary	Week 0 (baseline); Week 3; Week 6; 3 Months	This metric reflects the participant's average steps per minute. We will examine change from baseline over the course of the intervention and follow-up.
Walking Bouts	Secondary	Week 0 (baseline); Week 3; Week 6; 3 Months	This measures the number of 'bouts' of physical activity (in our case, steps). We will have two counts: the number of 5+ minute bouts and the number of 10+ minute bouts of walking. We will examine change from baseline over the course of the intervention and follow-up.

A spreadsheet holding the list of neuropsychological assessments to be used, with brief descriptions, is attached. They will be administered at T1 (Week 0), T2 (Week 1), T3 (Week 6), and/or T4 (3 Months).



Who will conduct the experimental procedures, questionnaires, etc.? Where will this be done? *Attach copies of all questionnaires, interview questions, tests, survey instruments, links to online surveys, etc.*

Most research activities are remote and will be completed by participants in their homes. Optional MRIs occur in the Center for Cognitive & Brain Health in the ISEC on the Northeastern University Boston campus. As indicated above, all experimental procedures will be implemented and monitored by trained staff in the Lab. All questionnaires, surveys, etc. are attached.

K. Risks

Identify possible risks to the participant as a result of the research. Consider possible psychological harm, loss of confidentiality, financial, social, or legal damages as well as physical risks. What is the seriousness of these risks and what is the likelihood that they may occur?

The procedures, techniques, equipment, and measures to be used in the proposed study are commonly used in educational and research settings involving human subjects, and are not new, untested, or of questionable safety. Experimenters are aware of the potential for serious adverse events to occur with any type of moderate intensity exercise, but such risks are considered minimal in this population. In addition, the primary focus of this study is decrease in sedentary behavior and increase in walking rather than moderate to vigorous exercise. There is a risk of physical injury during exercise, particularly if participants have little to no previous experience. Fatigue and muscle soreness may also occur in participants who do not normally engage in physical activity. Exercise is associated with a very small risk of serious medical complications including heart attack and sudden death, although this risk is particularly small in healthy older adults. Lastly, protocols currently exist to respond to any adverse events by contacting emergency response personnel and facilitating their arrival to the correct rooms (if the event occurs at the Center).

<u>Access to private health information</u>

There is a potential risk of breach of confidentiality that is inherent in all research protocols. There is a possibility that if research data were to become generally known, this knowledge could potentially impact a subject's future insurability, employability, or reproduction plans, or have a negative impact on family relationships, and/or in paternity suits or stigmatization.

Exercise

There are several common risks associated with exercise participation including injury to muscles or joints, especially when initiating an exercise program after a period of being sedentary. Further, there is a minor risk of dehydration or heat exhaustion. More commonly, there is a risk of falling. Based on our considerable experience in walking and balance-based research assessments and interventions in adults, many of whom are much older than the cohort anticipated for enrollment into this study, we are confident that this risk is rare, meaning that it will occur in less than .001% (less than 1 out of 100000) of people in the otherwise healthy adults targeted for this study. This risk will be minimized as we are focusing on walking and reductions in sedentary behavior rather than exercise training. Adverse or unstable cardiovascular or pulmonary response to exercise, including disorders of heart rhythm, heart attack, stroke, or sudden death will be minimized, because assessment of vital signs and history of heart disease are included in our screening procedures, and only those adults with satisfactory results as detailed in our eligibility criteria will be allowed to participate in experimental procedures for this study. As such, we anticipate that this risk is rare. According to American College of Sports Medicine (ACSM) guidelines published in 2000, the risk of myocardial infarction (MI) in symptomatic (categorized with males and females having ventricular arrhythmias) and asymptomatic (without any signs or symptoms indicative of ischemic heart disease) individuals during exercise is less than 0.04%. The risk of death in the same population is less than or equal to 0.01%, and the risk of needing hospitalization (including acute heart attack and/or serious arrhythmia) is less than or equal to 0.2%. The risk of cardiovascular complications occurring during exercise is rare (occurs in less than 1% of people). A retrospective survey by the YMCA revealed 1 death and 1 cardiac arrest per 2,897,057 and 2,253,267 person-hours. To minimize the risk, we are using a *non-exercise estimation of cardiorespiratory fitness* that requires BMI and heart rate measurement only.

Cognitive assessment and questionnaires

Some inconvenience and/or anxiety may occur due to time required to complete formal rating scales and questionnaires. The cognitive assessments impose some risk of emotional discomfort. Fatigue is associated with performing the cognitive tasks. The Geriatric Depression Scale, the Geriatric Anxiety Inventory, and the Montreal Cognitive Assessment may warrant a follow-up if the subject receives a clinically significant score on any of these items (e.g., >5 on the GDS). These items will be scored immediately after completion by the subject.

ActiGraph physical activity monitor

Participants may experience red skin or discomfort from wearing the device around the wrist too tightly or for an extended period of time.

ActivPAL physical activity monitor

Participants may experience skin irritation from the adhesive worn on the thigh. There is also a small risk of injury from shaving a portion of the right thigh at home in preparation for the study.

MRI

It is possible that during the completion of the MRI scan, participants may become frustrated or fatigued. Some subjects experience discomfort associated with confinement and remaining stationary for a long period of time. Since the MRI is very noisy, there is minimal risk of hearing impairment. There is also the risk of injury related to metal attraction, since the MRI machine is a magnet. Some participants may become claustrophobic or anxious during a scan. Anxiety may continue even after the scan. Sometimes people feel lightheaded when they sit up after a scan. A clinically significant, unexpected disease or condition might be identified during the MRI scan. Additionally, there is a risk of unknown ferrous materials. The magnet of the MR system has a very strong magnetic field that is dangerous to a person entering the magnet room if they have certain metallic, electronic, magnetic, or mechanical implants, devices, or objects.

Describe in detail the safeguards that will be implemented to minimize risks. What follow-up procedures are in place if harm occurs? What special precautions will be instituted for vulnerable populations?

PERSONNEL:

All staff and personnel associated with screening, collecting data, and analyzing data will have been trained in their laboratory and will have undergone all necessary research modules for safety and research ethics. Dr. Geddes will meet with all staff on a regular basis to ensure that they are conducting research protocols appropriately. MRI data will be collected by licensed MR technicians and staff trained to analyze MRI scans. There will be regularly scheduled meetings in which study staff will review each participant with regards to the progression through the baseline sessions. During these meetings, staff will have the opportunity to discuss any participants who have safety concerns along with any questionnaire answers that may raise a red flag to certain behaviors.

Regarding use of the physical activity monitoring devices, participants will be guided through the use of the devices at the Red Visit and will be reminded repeatedly throughout the study. We will help participants through the fitting process of the device and alert them to the sound the device will make when it is properly adjusted and ready to collect data. We will ensure that participants understand how the device works and how to correctly wear it so as to avoid any discomfort or incorrect usage. We will also instruct participants to notify us if any discomfort occurs. If any discomfort does arise as a result of wearing either of the physical activity monitoring devices, we will instruct participants to discontinue use of the device.

MRI scans: To alleviate fatigue, frustration, and anxiety that might occur during the MRI scan, participants will be asked how they are feeling and will be offered breaks between cognitive tests. Participants will be able to squeeze a ‘panic ball’ if they become claustrophobic during the MRI scan. Doing so will stop the scan so that the participant can exit the scanner. Participants who experience claustrophobia during the scan will be withdrawn from the study. Care will be taken to minimize distress by thoroughly training all project staff who come in contact with participants, to ensure that they are sensitive to their distress and will be capable of dealing with them in a courteous manner. If a clinically significant, unexpected disease or condition is

identified during the MRI scan, we will inform the participant that they should follow-up with their personal physician for further testing, diagnosis, and prognosis information.

To address the risk of unknown ferrous materials, a standard screening instrument will be used prior to any individual entering the magnet room. This form is attached.

The MRI technologist and researchers will be able to view images of the participants' brain during the scanning session and there is a slight possibility that they incidentally detect something unusual on the MRI scans. An incidental finding is defined as a finding concerning an individual research participant that has potential health importance and is discovered in the course of conducting research but is incidental or unrelated to the study intervention or procedures. If the research team discovers an incident or abnormality (e.g., tumor) as a part of the MRI scan, it is important for the study subject to be informed (a) that these scans were not designed for clinical purposes and so a clear diagnosis and prognosis cannot be made, but (b) that if an incidental finding or abnormality is found in the scan that Dr. Geddes, a board certified neurologist, will assess the scan and provide feedback to the participant. If feedback to the participant is necessary, this may include the recommendation that the participant inform their personal physician about the abnormality and request follow-up procedures that are outside the purview of the research study.

MRI scans will be flagged in one of two methods:

1) The MR technician performing the scan at Northeastern notices a clear abnormality in the scans being collected. If the MRI technician sees something that is abnormal, they will advise Dr. Geddes and other relevant staff (e.g., project coordinators), notifying them of an incidental finding. The scan will still be completed for this participant and the MR technician will refrain from informing the study participant about the possible incidental finding. The project coordinator will then start the incidental finding process. This includes:
    i. Informing the Principal Investigator, Dr. Geddes, with the study ID and date of the scan.
    ii. The imaging director at Northeastern will alert the study neuro-radiologist that a scan has been flagged and needs to be examined. All data sent to the neuro-radiologist will be de-identified.
    iii. An Adverse Event form will be completed.
2) Staff notice an incidental finding while checking quality control of the data. If an incidental finding is found in this way the data manager will contact the PI (Dr. Geddes), the imaging director at Northeastern (Co-I Professor Susan Whitfield-Gabrieli) and the project coordinator who will then start the incidental finding process described above.

After examining the MRI scans, the neuro-radiologist will categorize the incidental finding into one of three categories:

1. **SERIOUS**: The participant should be notified immediately by the site PI and told to follow-up with their PCP (exclude from study).
2. **BENIGN**: The participant is informed that we found something but it is likely benign and doesn't need an immediate follow-up with their PCP

3. **NO CONSEQUENCE**: No need to evoke anxiety in the participant so there is no reason to tell them.

Cognitive assessments: In order to alleviate any fatigue that may occur, participants are offered breaks during testing periods. They will also be provided with a referral for psychiatric consultation upon request or if their scores on the GDS, GAI, or MoCA are clinically significant, according to each evaluation's scoring guide. Any person scoring highly on the depression, anxiety, or cognitive impairment items will be referred back to their PCP for consultation.

L. Confidentiality

Describe *in detail* the procedures that will be used to maintain anonymity or confidentiality during collection and entry of data. Who will have access to data? How will the data be used, now and in the future?

To reduce the risk of breach of confidentiality we will separate all information obtained during the screening period from identifying documents. All research data will be de-identified. These documents will be stored in a separate location from the data and the screening information on REDCap, in a project file to which only lab personnel have access. Data that is saved electronically (computer system) is protected by the Northeastern University and Tufts Medical School (REDCap) firewalls. Only the researcher acting as the Project Coordinator (Elizabeth Quiñonez) will have access to the key pairing participants' complete names and participant ID numbers. Remaining research staff will have access to participant ID numbers only. During data collection from participants, staff will converse with participants and have knowledge of names, but will be encouraged to maintain a first name basis whenever possible. All data will be blinded and only used in aggregate to understand physical activity effects on brain and cognition.

How and where will data be stored? How will electronic data be encrypted? When will data, including audiotapes and videotapes, be destroyed? If data is to be retained, explain why. Will identifiers or links to identification be destroyed? When? Signed consent documents must be retained for 3 years following the end of the study. Where and how will they be maintained?

We will ensure participant confidentiality by coding all participants' data according to a numbering system and separating it from the informed consent. All informed consent documents and data files pertaining to subject data information will be kept in encrypted, password-protected files on an encrypted, password-protected flash drive that only researchers involved in the project will have access to. Multiple levels of password protection (e.g., record, file, directory, server, and computer levels) are employed to ensure data security. All personnel involved in the study will be approved through the IRB and agree to protect the security and confidentiality of identifiable information. All data pertaining to the individual will be stripped of all identifying information. Paper copies of data will be destroyed 7 years from the data of study completion.

M. If your research is HIPAA-protected, please complete the following; Individual Access to PHI

Describe the procedure that will be used for allowing individuals to access their PHI or, alternatively, advising them that they must wait until the end of the study to review their PHI.

N/A

N. Benefits

What benefits can the participant reasonably expect from his/her involvement in the research? If none, state that. What are potential benefits to others?

There is the potential for direct benefit to participants randomized to the self-affirmation + gain-framed health messaging arm of the study. Participants may experience direct benefits from participation such as improved cognition, mood, quality of life, physical fitness or decreased sedentary behavior as a result of participating in the behavioral intervention over a 3-month period. There may be a reduction in central adiposity and cardiovascular benefits. In addition, we are hoping that participants will maintain reductions in sedentary behavior beyond the completion of the study. The findings of this study provide information regarding the effect of simple and cost-effective behavioral intervention in reducing sedentary behavior and improving brain health in a population at risk for cognitive decay. As such, dissemination of this information stands to improve public health.

O. Attachments

Identify attachments that have been included and those that are not applicable (n/a).

x	Copy of fliers, ads, posters, emails, web pages, letters for recruitment *
x	Scripts of intended telephone conversations*
	Copies of IRB approvals or letters of permission from other sites
x	Informed Consent Form(s)* (see our templates for examples)
	Debriefing Statement*
x	Copies of all instruments, surveys, focus group or interview questions, tests, etc.
x	Signed Assurance of Principal Investigator Form ***(required)***
x	Human Subject Training Certificate(s) ***(required if not already on file at HSRP)***

(Approved forms must be stamped by the IRB before use)

P. Health Care Provision During Study

Please check the applicable line:

____x__ I have read the description of HIPAA "health care" within Section 4 of the Policies & Procedures for Human Research Protection. I am not a HIPAA-

covered health care provider and no health care will be provided in connection with this study.

_____ I am a HIPAA-covered health care provider or I will provide health care in connection with this study as described in Section 4 of the Policies & Procedures for Human Research Protection. This health care is described above under "Study Procedures," and the Informed Consent and Health Information Use and Disclosure Authorization form will be used with all prospective study participants.

If you have any questions about whether you are a HIPAA-covered health care provider, please contact Nan C. Regina, Director, Human Subject Research Protection at n.regina@neu.edu or (617) 373-4588.

Completed applications should be submitted to Nan C. Regina, Director, Human Subject Research Protection *with the exception of applications from faculty and students of the College of Professional Studies, which should be submitted to Kate Skophammer, IRB Coordinator for CPS.*

Nan C. Regina, Director Northeastern Univ., Human Subject Research Protection 360 Huntington Ave., Mailstop: 560-177 Boston, MA 02115-5000 Phone: 617.373.4588; Fax: 617.373.4595 n.regina@northeastern.edu	**CPS applications only** Kate Skophammer, IRB Coordinator Northeastern Univ., College of Professional Studies Phone: 617.390.3450; k.skophammer@northeastern.edu

The application and accompanying materials may be sent as email attachments or in hard copy. A signed Assurance of Principal Investigator Form may be sent as a scan, via fax or in hard copy.