RUNNING HEAD: HIIT TO BREAK PROLONGED SITTING FOR BRAIN HEALTH

Breaking prolonged sitting with high-intensity interval training to improve cognitive and brain health in older adults: a protocol for the pilot feasibility HIIT2SITLess trial

Dominika M. Pindus[1,2,3], Scott Paluska[1,4,5], Joseph So[1,6], Miroslaw Wyczesany[7], Tomasz S. Ligeza[7], Jesus Sarol[8], Jin Kuang[1], Flor B. Quiroz[1,9], Ramiya Shanmugam[1,10], Maciej Kos[11], Naiman A. Khan[1,2,3,12], Charles H. Hillman[11,13,14] & Arthur F. Kramer[2,11,13]

[1]Department of Health and Kinesiology, University of Illinois Urbana-Champaign, email: pindus@illinois.edu, sojoseph@uic.edu, paluska@illinois.edu, nakhan2@illinois.edu

[2]Neuroscience Program, University of Illinois Urbana-Champaign, Urbana, IL, USA

[3]Beckman Institute for Advanced Science and Technology, University of Illinois Urbana-Champaign, Urbana, IL, USA

[4]University of Vermont College of Medicine, Burlington, VT, USA

[5]Evergreen Sports Medicine, Williston, VT, USA

[6]Hospital Medicine Department and Urgent Care VA, Danville, IL, USA

[7]Insitute of Psychology, Jagiellonian University, Krakow, Poland; email: m.wyczesany@uj.edu.pl, tomasz.ligeza@uj.edu.pl

[8]Interdisciplinary Health Sciences Institute, University of Illinois Urbana-Champaign, Urbana, IL, USA; email: jsaroljr@illinois.edu

[9]Department of Psychology, University of Illinois at Urbana-Champaign, IL, USA; email: fquir3@illinois.edu

[10]The School of Cellular and Molecular Biology, University of Illinois Urbana-Champaign, Urbana, IL; email: ramiyas2@illinois.edu

[11]Center for Cognitive & Brain Health, Northeastern University, Boston, MA, USA; email: mkos@ccs.neu.edu, a.kramer@northeastern.edu, c.hillman@northeastern.edu

[12]Division of Nutritional Sciences, University of Illinois at Urbana- Champaign, Urbana, IL, USA

[13] Department of Psychology, Northeastern University, Boston, MA, USA

[14]Department of Physical Therapy, Movement, & Rehabilitation Sciences, Northeastern University, Boston, MA, USA

RUNNING HEAD: HIIT TO BREAK PROLONGED SITTING FOR BRAIN HEALTH

Corresponding Author: Dominika Pindus, Department of Kinesiology and Community Health, University of Illinois at Urbana-Champaign, 305 Louise Freer Hall, 906 S. Goodwin Avenue, Urbana, IL 61801, Email: pindus@illinois.edu

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Supplementary Material 1. Screening Consent

Consent and Authorization Document

Consent to Screening Procedures

Principal Investigator Name and Title: Dominika M. Pindus, Assistant Professor

Department and Institution: Kinesiology and Community Health, UIUC

Contact Information: 217-300-7317; pindus@illinois.edu

Sponsor: National Institutes of Health (specifically, National Institute on Aging), pending.

KEY INFORMATION ABOUT HIIT2SITLess TRIAL

You have indicated an interest in participating in a research study conducted by Dr. Dominika M. Pindus at the University of Illinois Urbana-Champaign. The main goal of this research is to gain knowledge about the utility of short physical activity breaks to sitting to reduce sitting and enhance cognitive and brain function in the short term (over several hours). This is a short-term study. If you qualify, you will be asked to visit our laboratory three times over approximately five to seven weeks and wear activity monitors for two weeks between visits.

KEY INFORMATION ABOUT THE SCREENING PROCESS

The screening procedures aim to assess your eligibility for the study. Today, a researcher will ask you questions about your age, physical activity, physical function, sitting habits, smoking, history of stroke or a transient ischemic attack, long COVID-19, your vision and hearing. The researcher will ask you questions and give you small tasks to measure how you think and how well you remember things. You will also complete a questionnaire about your general medical history, and questionnaires about your physical activity and how you feel. If you qualify based on this phone call, you will complete a medical clearance release form allowing the research team to contact your physician to determine if you can participate in high-intensity exercise. Today's call will last approximately 1 hour 15 minutes. We will also invite you to an in-person screening visit. During the screening visit, we will measure your height and weight, blood pressure, and heart rate. You will also complete several cognitive tests, a health and demographics questionnaire, and cycle at a maximal intensity on a stationary bike. The total screening time commitment for this visit is about **2.5 hrs**.

Risks of screening: Cycling on a stationary bike has been shown to be a safe mode of exercise in older adults. However, the risks include a chance of incurring a minor injury and some discomfort due to intensified use of major muscle groups that have not received a great deal of use. However, no major injuries are anticipated. There is also a very slim chance of serious cardiac events while exercising. This is very rare, and the benefits of exercise are known to outweigh the risks. As preventive measures, all participants need a medical clearance from their physician to participate in this research. Furthermore, our study physician will monitor you during a maximal exercise test and all our research staff are CPR and First Aid certified. The physician will observe the electric activity of your heart using an electrocardiogram. He will also measure your blood pressure throughout exercise. If you are taking beta-blocker medication, we will ask for your consent to discontinue the medication for 24 hours upon

your physician's clearance to do so, before the exercise test to ensure that the test can accurately assess your heart responses to the test. **Benefits of screening:** There are no direct benefits to you that come from screening. However, if you are eligible and agree to take part in this study, there may or may not be a transient health benefit to you. Specifically, breaking long sitting with short exercise breaks has been shown to improve sugar metabolism over several hours. We do anticipate that participation in this research may also result in transient (over several hours) benefit to cognitive and brain function.

BACKGROUND

You are being asked to take part in a research study. Before you decide, it is important for you to understand why the screening for this research is being done and what it will involve. Please take time to read the following information carefully. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you want to volunteer to take part in this screening process.

This screening process is being done to evaluate your eligibility to participate in research. The research study will evaluate brief high-intensity exercise breaks as a means to reduce a long bout of sitting. Such long bouts of sitting may negatively affect brain function and cognition. However, we do not know if interrupting long bouts of sitting with short exercise breaks could improve these functions and if exercise intensity matters. The screening is designed to evaluate if high-intensity exercise is safe for you and whether you meet our inclusion criteria based on your health history and cognitive tests.

SCREENING PROCEDURE

Your participation in this screening for a research study will include today's visit to the Physical Activity and Neurocognitive Health (PNC) laboratory. You may also need to see your primary care physician to ensure that high-intensity exercise is safe for you. If you are eligible, you will return to the laboratory for four study visits.

You have been asked to participate in this screening process because you indicated an interest in this research.

Scheduled Assessments

You will not be compensated for the screening procedures. However, if you qualify and participate in the study, you will be compensated up to $250 if you complete the entire study.

Screening Phone Call

During the phone call the researcher will ask you questions about your age, English language fluency, physical function, physical activity, sitting habits, and how you feel. S/he will also ask whether you can engage in vigorous exercise. To ensure that your participation in the study is safe, s/he will also ask questions about your health. For example, whether you had a stroke or a transient ischemic attack or a long COVID-19, and if you smoke. Next, s/he will ask you questions that let us know how you think, pay attention, know a few common facts, and remember words. If you qualify based on these questions, you will also complete a general health history questionnaire. You will answer questions about your cardiovascular history, including a history of heart disease and common signs and symptoms of cardiovascular disease. The questionnaire will ask about other health conditions that may increase

cardiovascular risk such as type 2 diabetes or increase the risks of high-intensity exercise such as pulmonary disease (e.g., COPD). Other conditions will include condition that may affect how you think such as epilepsy (i.e., having seizures) or a traumatic brain injury. Next, you will complete a Physical Activity Readiness Questionnaire. If you qualify based on these procedures, a researcher will ask if you agree for our research staff to contact your physician to ask for medical clearance for you to participate in a maximal exercise test on a stationary bicycle and high-intensity exercise during the intervention. If you are taking beta-blockers, s/he will also ask if you consent for the research staff to ask for your doctor's consent for you to discontinue your beta-blocker medication for 24 hours before the exercise test to ensure that the test accurately represents your heart responses to the maximal exercise test. If you do, you will sign the release of information form, which indicates that you are happy for us to contact your physician and include information that we collected about your heath history to help your physician decide if it is safe for you to engage in exercise test and high-intensity exercise in our study. It will also indicate that you are happy for your doctor to indicate their consent for you to discontinue beta-blockers for 24 hours before the exercise test. Your physician will be asked to confirm that you do not have type 1 or type 2 diabetes and that you did not have type 1 or 2 diabetes in the past. S/he will also confirm that your fasting glucose levels are below the threshold for diabetes in the last 12 months, and that your cholesterol levels are within normal range. If your physician is not able to confirm your blood sugar levels in the last 12 months but you otherwise qualify for an in-person screening visit based on the information provided to us today and by your physician, the research staff will measure your fasting glucose levels in the laboratory during your screening visit. Your physician will also confirm whether you are receiving or have received in the past cancer treatment, if your treatment included chemotherapy, and whether you have been cancer free for more than 12 months. If your physician clears you for participation in the maximal exercise test and study participation, we will invite you to an in-person screening visit at the PNC laboratory at Freer Hall in Urbana.

Today's phone call will last approximately **1 hour and 15 minutes**.

In-person Screening Visit 1 at the PNC Laboratory

Once we receive medical clearance from your physician, a researcher will contact you to confirm the time and date of your in-person screening visit. At the beginning of the visit, you will receive a heart rate monitor to wear around your chest. This is a strap with a single sensor that goes over your sternum and is attached snugly with an elastic belt. If your physician could not confirm your blood glucose levels in the last 12 months, a trained researcher will collect a blood sample from your fingertip to measure fasting capillary blood glucose. Next, the researchers will measure your height and weight. Then, you will rest for 5 minutes, and a researcher will take your blood pressure three time and your heart rate. You will also complete a questionnaire about your hand preference, about how you feel, and demographics questionnaire. Next, a trained researcher will ask you questions to measure your attention, memory, and language. You will complete patterns based on pictures, solve riddles, and tell the researcher the meaning of specific words. You will then complete two questionnaires about your exercise levels and activities you like to engage in. Then, a researcher will place electrocardiogram electrodes around your chest and on the side of your waist. They will collect electrocardiogram data while you rest for 10 s while lying down and standing. Next, you will cycle on a stationary bike for about 8 to 15 minutes until you cannot cycle any longer so that we can measure your aerobic fitness. The study physician will monitor the electrocardiogram during exercise to observe your heart's responses to exercise. He will also measure your blood pressure regularly during the test. This test will take place at Freer Hall on the University of Illinois campus. The amount of time you will cycle on the cycle ergometer will vary but most people cycle approximately 8-15 minutes. If you discontinued your beta-blockers for 24

hours before the test, a researcher will remind you to take your medication after the test. Total time commitment for this appointment is approximately 2 hours and 30 minutes.

Assessments and Screening Requirements

Phone Screening

You will answer questions about your health, physical activity, sitting and complete a short test measuring your attention and memory.

- ***General Health History*** –You will also complete a questionnaire asking about your general health history. These questions will be kept confidential and will only be used to determine whether or not it is safe for you to participate in our study. For example, we will ask about your cardiovascular health, recent medical events (e.g., hospitalization), current medication, and lifestyle habits. All information you provide to us is strictly confidential. If you qualify for the study, we will keep this information as part of your confidential record. We will also ask about food allergies, your vision, hearing, and your medications.
- ***Questionnaires*** – You will complete a questionnaire that asks about your lifestyle and a physical activity readiness questionnaire. You will also complete questionnaires about how you feel and which hand you use for most daily tasks such as writing, brushing your teeth, etc.
- ***Physician's Release and Medical Clearance*** – To qualify for the study, you will be required to provide documentation from a physician regarding the exercise and research testing. The HIIT-2-SITLess research staff will ask for your permission to contact and send information to your primary care physician regarding your participation in this research. The physician must be willing to provide documentation indicating that you are cleared to participate in high-intensity exercise. If your physician determines that a physical examination is necessary or that you need to be seen by your oncologist (if you had the history of cancer) before clearing you for participation, then you or your insurance company will be responsible for all costs associated with such an exam or a visit to the oncologist.
- If you are taking beta-blockers we will ask for your permission to ask your physician to determine if it is safe for you to discontinue the medication for 24 hours before the exercise test.
- We will ask for your permission to share your medical history information with your primary care physician to help them determine your eligibility to participate in this research. However, you can opt out from sharing your medical history with your primary care physician. You will still need medical clearance from your primary care physician to participate in the study.

In-person Screening Visit at the PNC Laboratory

- ***Height, weight, and waist circumference***
  - A researcher will measure your height, weight, and waist circumference three times.
  - We will measure your waist in three points: the natural waist (the narrowest point), the umbilical (just above your navel), and around your hips.
- ***A finger prick***
  - A trained researcher will collect a blood sample from your fingertip to measure fasting capillary blood glucose using a point-of-care glucometer.

- ***Blood pressure and heart rate at rest***
    - You will wear a heart rate monitor around your chest. After a 5 min rest, a researcher will measure your blood pressure and heart rate 3 times.
- ***Questionnaires*** – You will complete a demographic questionnaire. We will also ask questions about cognitive activities that you like to better understand your sitting habits, and about which hand you prefer to use for different activities to determine your hand preference.
- ***Cognitive and Neuropsychological Tests*** – You will complete a short cognitive test and a longer neuropsychological test where you will be asked about the meaning of words, you will choose patterns that best fit a picture, and solve some riddles.
- ***Graded Exercise Test*** - At this appointment, you will cycle on a stationary bike to measure your aerobic fitness. We will do that by measuring the air you exhale while you are cycling on a stationary bike. You will pedal at a constant speed while the researcher periodically increases the workload until you feel as if you cannot cycle any longer. You will be monitored by a physician and several exercise specialists certified in CPR and First Aid. We will measure oxygen through a mask that will collect your exhaled air. Your heart rate will be measured regularly through a 10-lead electrocardiogram chest monitor and your blood pressure will be taken several times throughout the test. The test including resting state electrocardiogram measures and preparation time will last about an hour. However, you will only cycle for about 8 to 15 minutes.

RISKS

Risks for blood collection: The blood sample collection is very common and involves minimal risk. There is a one in five chance of bruising in the area of sampling. This is generally not serious and will completely disappear within a few days. As with all invasive procedures, there is a slight risk of inflammation and infection. There is also risk of callus formation. This risk will be minimized by the use of sterile procedures and equipment at all times. Risk will also be minimized because a trained researcher will draw all blood samples.

Risks of exercise testing: As indicated in the introduction, it is necessary to inform you that when individuals who have been inactive engage in exercise, there is a chance of incurring minor injury, and most certainly some discomfort due to the increased use of major muscle groups that have not received a great deal of use. Although the maximal exercise test on the cycle ergometer is age appropriate, it is possible that you could be injured or experience discomfort as a result of engaging in the exercise test. However, no major injuries are anticipated. Should you become injured as the result of these activities, we encourage you to let the exercise leader in attendance know and to consult your physician if necessary. The University of Illinois does not provide medical or hospitalization insurance coverage for participants in this research study nor will the University of Illinois provide compensation for any injury sustained as a result of participation in this research study, except as required by law. There is also a very slim chance that sudden death or cardiac irregularities can occur while exercising. As noted, this is very rare, and the benefits of exercise are known to outweigh the risks. As preventative measure, during all on-site physical assessments all staff members are First Aid and CPR certified. In addition, the maximal exercise test is supervised by a physician trained in supervising maximal exercise tests using the electrocardiogram, blood pressure readings, heart rate and observing how participants respond to the test.

Confidentiality: Although we will use all reasonable efforts to keep your personal information confidential, we cannot guarantee absolute confidentiality. We describe efforts taken to protect your information in the section “How will the researchers protect my information”.

BENEFITS

Participating in the screening process is unlikely to have a direct benefit to you. We also cannot promise any direct benefit for taking part in this study if you qualify. However, previous research has shown that interrupting continuous sitting with short bouts of exercise can transiently improve sugar metabolism in adults (over several hours). We do anticipate that participation in this research may also result in a transient (over several hours) benefit to cognitive and brain function. We also hope the information we get from this study may help develop a greater understanding of how interrupting sitting with exercise can enhance cognitive and brain function in older adults and if the intensity of exercise matters. The study will also help us understand if older adults are likely to use short, high-intensity exercise breaks to reduce sitting.

ALTERNATIVE PROCEDURES

If you do not want to participate in the screening procedures for HIIT2SITLess study, the alternative is not to participate.

HOW WILL THE RESEARCHERS PROTECT MY INFORMATION?

Confidentiality is assured for all participants with regard to any responses and information you provide. The blood samples will be used only to determine the levels of fasting glucose as an inclusion criterion for the study. This identifying information will not be available to anyone outside of our research group. All data collected will be numerically coded so that no individual data will be identifiable. We will use all reasonable efforts to keep your personal information confidential, but we cannot guarantee absolute confidentiality. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. Your personal information may be given out only if required by law.

Organizations that may look at and/or copy your information and responses for research, quality assurance, and data analysis include:

- Government representatives, when required by law;
- University of Illinois Urbana-Champaign Institutional Review Board;
- National Institute on Aging – the funder for this research;
- Your primary care physician, if the research staff, in the course of the project, learn of a medical condition that needs immediate attention;
- Your primary care physician; with your consent, we will send a health history questionnaire to your primary care physician to assist them with medical clearance.

Participation in this screening process is voluntary, and you are free to withdraw your participation without penalty at any time.

Certificate of Confidentiality:

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

Identifiable information that could still be disclosed beyond the research team: The Certificate does not stop reporting that federal, state, or local laws require. Some examples are laws that require reporting

of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate cannot be used to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate does not stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also does not prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers, or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

WHO WILL HAVE ACCESS TO THE INFORMATION COLLECTED DURING THIS RESEARCH STUDY?

Efforts will be made to limit the use and disclosure of your personal information, including research study records, to people who have a need to review this information. We cannot promise complete secrecy.

There are reasons why information about you may be used or screened by other people beyond the research team during or after this study. Examples include:

- ***University officials, government officials, study funders, auditors, and the Institutional Review Board may need access to the study information to make sure the study is done in a safe and appropriate manner.***
- ***Collaborating researchers at other institutions who are involved with this study.***

Most tests done in research studies are only for research and have no clear meaning for health care. If the research results have meaning for your health, the researchers will contact you to let you know what they have found.

We will destroy the blood sample after we know your eligibility for the study. If you qualify and consent to participate in the study, we will retain all other data collected during screening. However, if you withdraw early from the screening process or choose not to participate in the study before you enroll, your data will be securely destroyed. To ensure confidentiality and anonymity during the screening, you will be assigned a numeric code and identified by this number only. We will keep the master list on the hard drive of a password-protected microcomputer. We will destroy this list when the study is completed.

All data will be kept on the local server at the University of Illinois. A duplicate copy of the de-identified data (only numeric codes, not your name will be used) will be stored in a cloud using the University of Illinois Box account. In addition, data will be stored on a local computer and backed up to an external hard drive or SSD drive. Your consent form and most questionnaire data will be held in a secure web-based system Illinois REDCap compliant with the Health Insurance Portability and Accountability Act of 1996. Only the research team will have access to person-identifiable data. If the data is used for future research or training (see below), only de-identified data will be made available to other researchers, students, or trainees. De-identified data will be stored indefinitely.

HOW MIGHT THE INFORMATION COLLECTED IN THIS STUDY BE SHARED IN THE FUTURE?

If you qualify and consent to participate in the study, we will keep the information we collect about you during this screening for record keeping and for potential use in future research projects and training of junior researchers. As a research participant in this study, you consent to the use of your data for this study and future research by others. We will keep private information about you confidential to the extent allowed by laws and university policies. When researchers publicly discuss or publish the results of this research, they will not tell anyone that you were in the study. However, government or university officials who are responsible for monitoring this study and journal staff who review the research results for accuracy may see information that identifies you, including your signed consent form. If you give us your permission, we will use de-identified data from this study for use in future research studies. We will not ask for your additional informed consent for these studies. Your name and other information that can directly identify you will be stored securely and separately from the rest of the research information we collect from you. De-identified data from this study may also be shared with the research community, with journals in which study results are published, and with databases and data repositories used for research. We will remove or code any personal information that could directly identify you before the study data are shared. This means that a number will be assigned to your record. Therefore, if any data collected about you is shared for use in future research or training, researchers or students will only see a number and not your name. Despite these measures, we cannot guarantee the anonymity of your personal data. If you do not qualify or you do not consent to be enrolled in the study, we will destroy the information we collect about you during screening.

With your consent, the PI would like to retain your contact information to contact you for future research participation. This information will not be shared with other researchers but will only be retained for potential interest in research with this PI. We will ask for your consent to do so at the end of this form.

PERSON TO CONTACT

If you have questions, complaints, or concerns about this screening process for the HIIT-2-SITLess study, you can contact Dr. Dominika M. Pindus at 217-300-7317 or email: pindus@illinois.edu. If you feel you have been harmed as a result of participation, please call Dr. Dominika M. Pindus at 217-300-7317, who may be reached from Mondays to Fridays, 8 am to 5 pm.

Institutional Review Board: If you have any questions about your rights as a research subject, including concerns, complaints, or to offer input, you may call the Office for the Protection of Research Subjects (OPRS) at 217-333-2670 or email OPRS at irb@illinois.edu. If you would like to complete a brief survey to provide OPRS feedback about your experiences as a research participant, please follow the link here or through a link on the OPRS website: https://oprs.research.illinois.edu/. You will have the option to provide feedback or concerns anonymously, or you may provide your name and contact information for follow-up purposes.

VOLUNTARY PARTICIPATION

If you decide to participate in this screening, you are free to withdraw your consent and discontinue participation at any time. You can start the screening process and then choose to stop the screening later. This will not affect your relationship with the investigators. The researchers also have the right to stop your participation in this screening without your consent if they believe you do not qualify for the study, it is in your best interest, and/or if you were to object to any future changes that may be made in the screening and study plan.

COSTS AND COMPENSATION TO PARTICIPANTS

Participation in this screening process is free. However, you or your health care plan or insurance company may need to pay for costs associated with obtaining medical clearance if your physician asks for a physical examination or a visit to an oncologist (if you had the history of cancer) in order to clear you for participation. Some health plans will not pay these costs for people taking part in research studies. Check with your health care plan or insurance company to find out what coverage they will provide. You will not be paid for taking part in this screening.

The University of Illinois does not provide medical or hospitalization insurance coverage for participants in this research study, nor will the University of Illinois provide compensation for any injury sustained as a result of participation in this research study, except as required by law.

If you qualify based on the screening phone call and Screening Visit 1, you will receive $30 compensation for your exercise test and information about your current levels of aerobic fitness.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION

Signing this document means you allow us, the researchers in this study, and others working with us to use some information about your health for this research study.

This is the information we will use and include in our research records:

- Demographic and identifying information like name, address telephone number, and email address
- Related medical information about you like your medical history disclosed on the General Health History questionnaire during screening, including your family history of cardiovascular disease, current and past medications or therapies, and information from physical examinations, such as blood pressure reading, heart rate, graded maximal exercise test, and lab results, fasting glucose levels determined during screening.
- All tests and procedures that will be done in the study

How we will protect and share your information:

- We will do everything we can to keep your information private but we cannot guarantee this. Study information will be kept in a secured manner and electronic records will be password protected. Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this

information as part of the regular treatment, payment, and health care operations of the hospital. We may also need to disclose information if required by law.

- This research is covered by a Certificate of Confidentiality from the National Institutes of Health as described in the section on How Will the Researchers Protect My Information. Please refer to this section for details.
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.
- In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:
    - Members of the research team at the University of Illinois Urbana-Champaign
    - The University of Illinois Urbana-Champaign Institutional Review Board (IRB), which reviews research involving people to make sure the study protects your rights;
    - Other academic research centers we are working with: Prof. Charles Hillman and Arthur Kramer at Northeastern University, who are co-investigators on the study.
    - The study sponsor: National Institute on Aging
    - Limited information may also be shared with first responders from Emergency Medical Systems (EMS) to assist them with medical treatment; this information may include your name, address, emergency contact, your physician's contact details, age, information about your cardiovascular risk history, current medications, and description of the event;
- If we share your information with groups outside of the University of Illinois Urbana-Champaign, for example with Northeastern University, we will not share your name or identifying information. We will label your information with a code number, so they will not know your identity.
- If you do not want us to use information about your health, you should not be part of this research. If you choose not to participate, you can still receive health care services at Carle Health, OSF Healthcare, Christie Clinic or other local healthcare providers.

What if I decide to Not Participate after I sign the Consent and Authorization Form?

You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

WOULD YOU LIKE TO BE CONTACTED ABOUT FUTURE RESEARCH OPPORTUNITIES?

❑ Yes, please include your email _____ and/or

phone number _____

❑ No

You can be in this current research study without agreeing to future research use of your identifiable information.

CONSENT

By signing this consent form, I confirm I have read the information in this consent form and have had the opportunity to ask questions. I will be given a signed copy of this consent form. I voluntarily agree to take part in this screening process for the HIIT-2-SITLess trial.

Optional

I consent for my General Health History questionnaire to be shared with my primary care physician to assist them with medical clearance for the study.

❑ Yes ❑ No

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

Supplementary Material 2. Study Consent

Consent and Authorization Document

Principal Investigator Name and Title: Dominika M. Pindus, Assistant Professor

Department and Institution: Kinesiology and Community Health, UIUC

Contact Information: 217-300-7317; pindus@illinois.edu

Sponsor: National Institutes of Health (specifically, National Institute on Aging), pending.

KEY INFORMATION ABOUT HIIT-2-SITLess Trial

You have indicated an interest in participating in research study conducted by Dr. Dominika M. Pindus at the University of Illinois Urbana-Champaign. The main goal of this research is to gain knowledge about the feasibility and utility of short exercise bouts to reduce long sitting over several hours. This is a short-term study where you will be asked to visit the PNC laboratory three times over approximately five to seven weeks. You will also wear activity monitors for two weeks in between visits. *The risks* of this study include a chance of incurring a minor injury and some discomfort due to intensified use of major muscle groups that have not received a great deal of use. However, no major injuries are anticipated. Cycling on a stationary bike has been shown to be a safe mode of exercise in older adults. There is also a very slim chance of serious cardiac events while exercising. This is very rare, and the benefits of exercise outweigh the risks. As preventive measures, you will need a medical clearance from your physician to participate in this research. Based on your responses to the maximal exercise test which was monitored by a study physician, you were considered to be at a lower risk of such events. Our research staff will also monitor your heart rate and physical responses to exercise (such as how hard you are working out and if you experience any unusual pain, fatigue etc.) during and after exercise. All our research staff are CPR and First Aid certified. If you agree to take part in this study, there may or may not be transient health benefit to you. Specifically, *breaking long sitting with short bouts of exercise has been shown to improve sugar metabolism* over several hours. We do anticipate that participation in this research may also result in a transient (over several hours) benefit to cognitive and brain function.

BACKGROUND: THE HIIT-2-SITLESS TRIAL

This research is funded by the National Institute on Aging. You are being asked to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you want to volunteer to take part in this study.

This research is being done to evaluate brief high-intensity exercise breaks to sitting. Although long bouts of sitting may attenuate brain function, we do not know if breaking long sitting with short bouts of exercise could improve brain function and if exercise intensity matters. The HIIT-2-SITLess trial will assess if short high-intensity exercise breaks to sitting are acceptable, and practical to older adults as means of reducing long periods of sitting. The trial will also compare changes in brain function and cognition after three and half hours of sitting interrupted with 6-min of high-intensity exercise breaks relative to 6-min of light-intensity exercise.

You have been asked to participate in this research because you are 40-75 years old and met inclusion criteria, we reviewed over the phone and during your screening visit, such as being right-handed, not exercising regularly, planning to be in the Urbana-Champaign area for the duration of the study, etc. Approximately 54 participants will be involved in this study at the University of Illinois.

STUDY PROCEDURE

Your participation in this study will last about eight weeks. You will come to the laboratory on four occasions and wear activity monitors for the total of two weeks between study visits.

Study Logistics

Scheduled Assessments

You will be compensated for these scheduled assessments and the compensation amounts are stated later in this document.

1. **Baseline Visit: Cognitive Tasks, HIIT, and LIIT Breaks Practice and Questionnaires**
   - ***Blood pressure and heart rate.*** Researchers will give you a heart rate monitor to wear around your chest. The monitor has a small flat electrocardiogram electrode inside a plastic casing attached to an elastic strap that goes around your chest. The monitor will sit in the center of your chest, and researchers will place electroconductive gel on the strap to enhance the connection between the electrode and the electrical signal from your heart. Researchers will also measure your resting blood pressure three times to monitor for high blood pressure that could prevent you from exercising.
   - ***HIIE and LIIE Practice Session***. During this visit, you will also practice high-intensity and low-intensity interval training breaks supervised by our research staff. This ensures that you feel comfortable with exercise and that we know the cadence (speed) and workload that can elicit your target heart rate during exercise. You will also fill in questionnaires (described below).
   - ***Questionnaires.*** To help us better understand your responses to high-intensity exercise, we will ask you to complete a set of questionnaires about your physical activity, enjoyment of physical activity, physical function, sleep, and sitting behaviors.
   - ***Cognitive tasks practice.*** To help you get used to cognitive tasks, you will practice two tasks on a computer for 12 minutes each. You will complete two tasks by pressing buttons on a response pad based on task instructions. You will see asterisks and letters come up on the computer screen one by one. You will need to look away from an asterisk to "catch" which letter just appeared. You will also see arrows on the screen and will have to press a button, which corresponds to the direction of a middle arrow. You will practice tasks in between physical exercise breaks.
   - Total time commitment for this appointment is approx. **2 hrs.**

2. ***High-Intensity Exercise Intervention***
   You will be asked to participate in a half-day intervention designed to minimize long bouts of sitting by cycling on a stationary bike at a high intensity every 30 min. You will

come to the laboratory in the morning fasted. This means not eating or drinking (plain water is ok) for 8-10 hours before your visit. Trained researchers will measure your resting blood pressure and heart rate. You will also wear a chest strap with a heart rate monitor and two activity monitors to measure your sitting and physical activity. You will then complete a 24-h dietary recalls, and questionnaires about sleepiness. Next, you will eat a light breakfast, which is nut free oats and seeds bar. You will then complete the same neurocognitive tests as during your EEG visit. You will start the intervention after these neurocognitive assessments. You will sit for three hours and a half hours while you complete light administrative tasks and read popular science articles. For example, you will plan a family vacation and read articles about how snowflakes form or how whales help cool the earth. You will answer brief questions about how engaging and difficult these activities are. You will also answer questions about your energy levels, and fatigue. Every 30 min, the researchers will measure your blood pressure and heart rate before and after you complete a 6-minute high-intensity exercise (HIIE) break. You will also complete a shorter neurocognitive assessment twice during sitting: 15 min after the first and the third HIIE break. You will sit in a wheelchair while a researcher will push the wheelchair to the cycle ergometer. The neurocognitive assessment will last 15 min. You will then complete another HIIE break. You will complete five HIEE breaks in total. During each break, researchers will ask you questions about the levels of physical effort, and about how you feel. Researchers will monitor your blood pressure and heart rate after each break. After the last break, a researcher will transport you back to the EEG equipment and fill in the electrodes with gel while you sit and eat the second light meal (a similar oats and seeds bar). You will then complete the same set of cognitive tests as before the intervention while researchers record EEG signal. If this is your first intervention visit, you will receive two activity monitors to take home. If it is your last visit, you will complete a questionnaire about your experience in the study, and your participation will be complete. Total time commitment: **approx. 6 hours.**

EEG. You will be asked to visit Freer Hall where you will undergo neurocognitive assessments. You will wear an electroencephalography (EEG) cap that looks like a swim cap with small electrodes located throughout the cap. The researchers will fill in the electrodes with electroconductive gel so that we can measure tiny electric currents produced by your brain while you rest and complete cognitive tasks. We will first record your brain activity while you rest with your eyes open and closed for six minutes. You will then perform various cognitive tests on a computer that assess attention, executive function, and memory. For example, for one of the tests you will see pictures of common objects. Next, you will see more pictures. For each picture you will have to indicate if you saw it before or not. You will complete assessments again after the intervention is finished. In addition, you will complete one of the tasks twice during the intervention.

Cognitive Tasks. In addition to the two tasks that you practiced during the baseline visit, you will also complete a task where you will see pictures of objects. You will make judgments about pictures, such as determining if they represent an indoor or an outdoor object.

High-Intensity Interval Exercise Break: First, you will cycle at the same speed as during the maximal exercise test with progressively increased resistance for 1 min to warm up. Next, we will increase resistance on the bike to the same level at which your heart rate increased to 90% of its maximum during exercise test. These short bouts are designed to be very hard and you will cycle at this speed and resistance for 2 minutes. Then, you will rest while sitting still on the bike for 1 minute. Next, you will cycle again for 2 minutes at the same high intensity. At least two CPR and First Aid certified researchers will assist you and monitor your heart rate throughout exercise and ask you to rate how tired your body feels due to exercise and how you feel overall during each HIIE break. Finally, you will sit again and continue with either administrative activities or reading. You will complete **5** HIEE **breaks** lasting **6 min each** for **a total of 30 min** of exercise.

3. Low-Intensity Interval Exercise Intervention

You will complete all the same procedures and tests as during the HIIE intervention day except for high-intensity exercise breaks. Instead, you will complete 6-min low intensity interval exercise breaks (LIIE).

Light-Intensity Interval Exercise Break. You will first warm up by pedaling for 1 min with minimal workload at an intensity of about 50% of your maximum heart rate. Next, you will pedal at a higher speed and workload chosen to elicit light intensity or about 57-60% of your maximum heart rate which is considered very light to fairly light intensity. You will then rest and remain stationary on the cycle ergometer for 1 minute, followed by another 2 minutes pedaling at the speed and workload to elicit the same heart rate. Total time commitment: **approx. 6 hours.**

Randomization

We will assign the order of two exercise interventions randomly at baseline. This means that the order in which you will complete HIIE and LIIE interventions, will be chosen by chance, like flipping a coin. Neither you nor the study team will choose which intervention you will complete first. The study team will let you know which exercise intervention you will complete first on the day of your first intervention visit. All participants will be asked to participate in all testing procedures.

Additional Assessments and Study Requirements

1. ***Questionnaires*** – You will be asked to complete one packet of questionnaires related to your physical abilities, physical activity, sedentary activities, sleep, diet, attitudes, thoughts, and feelings. The packet should take approximately 45-60 minutes and you will be able to complete it during the Baseline visit while you practice HIIE and LIIE breaks. At the end of the second intervention visit, you will also fill in a brief questionnaire about your experiences of the intervention.
2. ***Accelerometers*** – You will be asked to wear two activity monitors for seven days on two occasions, a week before each intervention visit. The first device is about the size of a pocket watch, similar to a pedometer. It is worn around your waist during waking hours and sleep except for bathing and showering. You will wear a second device on your thigh. The device is called activPAL. It is small and flat, similar to a flat piece of a domino. This device will measure how much you sit and stand. It is attached to your thigh with transparent film

dressing. You can wear this device while bathing or showering. You will also fill out an activity and sleep log to indicate hours of the day you wore the devices, when you went to sleep, and when you woke up. The devices do not track GPS or geographic data. They will only record the movement and sitting.

3. ***Health and Demographics Questionnaire*** – You already completed this questionnaire during screening. It has become part of your research record.
4. ***General Health History*** - You also provided information about your health history during screening call, which has become the part of your research record.
5. **Physician's Release and Medical Clearance** – Before qualifying, you provided documentation from a physician regarding the exercise and research testing, which is also part of your research record.

Additionally, the investigators may contact you in the future regarding other research at this institution.

You may opt out of these communications and opportunities at any time.

RISKS

Risks of high-intensity exercise participation: As indicated in the introduction, it is necessary to inform you that when individuals who have been inactive engage in exercise, there is a chance of incurring minor injury, and most certainly some discomfort due to the increased use of major muscle groups that have not received a great deal of use. Although the exercise breaks have been designed to offer activities that are safe and age appropriate, it is possible that you could be injured or experience discomfort as a result of engaging in these activities. However, no major injuries are anticipated. Should you become injured as the result of these activities, we encourage you to let the exercise leader in attendance know and to consult your physician if necessary. The University of Illinois does not provide medical or hospitalization insurance coverage for participants in this research study nor will the University of Illinois provide compensation for any injury sustained as a result of participation in this research study, except as required by law. There is also a very slim chance that sudden death or cardiac irregularities can occur while exercising. As noted, this is very rare, and the benefits of exercise are known to outweigh the risks. As preventative measure, during all on-site physical assessments all staff members are First Aid and CPR certified.

Risk of EEG: In rare instances, some individuals have reported some discomfort from the EEG cap. If this occurs, we will take the cap off and re-schedule the visit.

Confidentiality: Although we will use all reasonable efforts to keep your personal information confidential, we cannot guarantee absolute confidentiality. We describe efforts taken to protect your information in the section "How will the researchers protect my information".

BENEFITS

We cannot promise any direct benefit for taking part in this study. However, previous research has shown that interrupting long sitting with short bouts of exercise can improve sugar metabolism in adults over several hours. We do anticipate that participation in this research may also result in a transient (over several hours) benefit to cognitive and brain function. We also hope the information we get from

this study may help develop a greater understanding of how breaking long sitting with exercise can enhance cognitive and brain function in older adults and if the intensity of exercise matters. The study will help us understand if older adults are likely to use short high-intensity exercise breaks to reduce sitting.

ALTERNATIVE PROCEDURES

If you do not want to participate in the study, the alternative is not to participate.

HOW WILL THE RESEARCHERS PROTECT MY INFORMATION?

Confidentiality is assured for all participants with regard to any responses and information you provide. You understand that the blood samples will be used only to determine the levels of fasting glucose as the inclusion criterion for the study. Information that could identify you will not be available to anyone outside of our research group. All data collected will be numerically coded so that no individual data will be identifiable. We will use all reasonable efforts to keep your personal information confidential, but we cannot guarantee absolute confidentiality. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. Your personal information may be given out only if required by law.

Organizations that may look at and/or copy your information and responses for research, quality assurance, and data analysis include:

- Government representatives, when required by law;
- University of Illinois Urbana-Champaign Institutional Review Board;
- National Institute on Aging – the funder for this research;
- Primary care physician if the research staff, in the course of the project, learn of a medical condition that needs immediate attention;
- Primary care physician (PCP) with participant's consent we will send health history questionnaire to PCP to assist them with medical clearance;

Participation in this project is voluntary and you are free to withdraw your participation without penalty at any time.

Certificate of Confidentiality:

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

Identifiable information that could still be disclosed beyond the research team: The Certificate does not stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate cannot be used to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate does not stop disclosures required by the

federal Food and Drug Administration (FDA). The Certificate also does not prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

WHO WILL HAVE ACCESS TO THE INFORMATION COLLECTED DURING THIS RESEARCH STUDY?

Efforts will be made to limit the use and disclosure of your personal information, including research study records, to people who have a need to review this information. We cannot promise complete secrecy.

There are reasons why information about you may be used or seen by other people beyond the research team during or after this study. Examples include:

- ***University officials, government officials, study funders, auditors, and the Institutional Review Board may need access to the study information to make sure the study is done in a safe and appropriate manner.***
- ***Collaborating researchers at other institutions who are involved with this study.***

Most tests done in research studies are only for research and have no clear meaning for health care. If the research results have meaning for your health, such as your fasting glucose levels, the researchers will contact you to let you know what they have found.

We will destroy the blood sample collected during screening after we know your eligibility for the study. We will retain all other data collected in the course of the study. For example, if you withdraw early from the study, your data will be retained for the analyses. To ensure confidentiality and anonymity during the study, you will be assigned a numeric code, and identified by this number only. We will keep the master list on the hard drive (or SSD) of a password protected microcomputer. We will destroy this list when the study is completed.

All data will be kept on the local server at the University of Illinois. A duplicate copy of the de-identified data (only numeric codes not your name will be used) will be stored in a cloud using the University of Illinois Box account. In addition, data will be stored on a local computer and backed up to an external hard drive or SSD drive. Your consent form and most questionnaire data will be held in a secure web-based system Illinois REDCap, which is compliant with Health Insurance Portability and Accountability Act of 1996. Only research team will have access to person-identifiable data. If the data is used for future research or training (see below), only de-identified data will be made available to other researchers, students or trainees. De-identified data will be stored indefinitely.

HOW MIGHT THE INFORMATION COLLECTED IN THIS STUDY BE SHARED IN THE FUTURE?

We will keep the information we collect about you during this research study for record keeping and for potential use in future research projects and training of junior researchers. Your name and other information that can directly identify you will be stored securely and separately from the rest of the research information we collect from you. De-identified data from this study may also be shared with the research community, with journals in which study results are published, and with databases and data repositories used for research. We will remove or code any personal information that could directly identify you before the study data are shared. This means that a number will be assigned to your record. Therefore, if any data collected about you is shared for use in future research or training, researchers or students will only see a number and not your name. Despite these measures, we cannot guarantee the anonymity of your personal data.

The PI would like to retain your contact information to contact you for future research participation. This information will not be shared with other researchers but will only be retained for potential interest in research with this PI. We will ask for your consent to do so at the end of this form.

PERSON TO CONTACT

Example: If you have questions, complaints, or concerns about this study, you can contact Dr. Dominika M. Pindus at 217-300-7317 or email: pindus@illinois.edu. If you feel you have been harmed as a result of participation, please call Dr. Dominika M. Pindus at 217-300-7317, who may be reached during Mondays to Fridays 8 am to 5 pm.

Institutional Review Board: If you have any questions about your rights as a research subject, including concerns, complaints, or to offer input, you may call the Office for the Protection of Research Subjects (OPRS) at 217-333-2670 or e-mail OPRS at irb@illinois.edu. If you would like to complete a brief survey to provide OPRS feedback about your experiences as a research participant, please follow the link here or through a link on the OPRS website: https://oprs.research.illinois.edu/. You will have the option to provide feedback or concerns anonymously or you may provide your name and contact information for follow-up purposes.

VOLUNTARY PARTICIPATION

If you decide to participate, you are free to withdraw your consent and discontinue participation at any time. You can start the study and then choose to stop the study later. This will not affect your relationship with the investigator. The researchers also have the right to stop your participation in this study without your consent if they believe it is in your best interests, you were to object to any future changes that may be made in the study plan.

COSTS AND COMPENSATION TO PARTICIPANTS

Participation in the study is free. However, you or your health care plan or insurance company may need to pay for costs associated with obtaining medical clearance if your physician asks for a physical examination in order to clear you for participation. Some health plans will not pay these costs for people taking part in research studies. Check with your health care plan or insurance company to find out what coverage they will provide. You will be paid for taking part in the ***scheduled*** appointments described above. As an incentive, and appreciation for contributing your time to this study, you will be paid a

stipend as indicated in the table below. Thus, you will receive up to *$250* if you complete all the study assessments. The total time commitment for these scheduled appointments is approximately 16.5 hours.

Appointment	**Time**	**Stipend**	**Location**
Neurocognitive tests + HIIE + LIIE Practice	2 hrs.	$50	Freer Hall
HIEE Intervention	6 hrs.	$100	Freer Hall
LIIE Intervention	6 hrs.	$100	Freer Hall

If you live more than 10 miles away from the study site, we will reimburse the cost of your travel in the amount of $0.625 per mile.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION

Signing this document means you allow us, the researchers in this study, and others working with us to use some information about your health for this research study.

This is the information we will use and include in our research records:

- Demographic and identifying information like name, address telephone number, and email address
- Related medical information about you like your medical history disclosed on the General Health History questionnaire during screening, including your family history of cardiovascular disease, current and past medications or therapies, and information from physical examinations, such as blood pressure reading, heart rate, graded maximal exercise test, and lab results, fasting glucose levels determined during screening.
- All tests and procedures that will be done in the study

How we will protect and share your information:

- We will do everything we can to keep your information private but we cannot guarantee this. Study information will be kept in a secured manner and electronic records will be password protected. Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this information as part of the regular treatment, payment, and health care operations of the hospital. We may also need to disclose information if required by law.

- This research is covered by a Certificate of Confidentiality from the National Institutes of Health as described in the section on How Will the Researchers Protect My Information. Please refer to this section for details.
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.
- In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:
    - Members of the research team at the University of Illinois Urbana-Champaign
    - The University of Illinois Urbana-Champaign Institutional Review Board (IRB), which reviews research involving people to make sure the study protects your rights;
    - Other academic research centers we are working with: Prof. Charles Hillman and Arthur Kramer at Northeastern University, who are co-investigators on the study.
    - The study sponsor: National Institute on Aging
- If we share your information with groups outside of the University of Illinois Urbana-Champaign, for example with collaborators at Northeastern University, we will not share your name or identifying information. We will label your information with a code number, so they will not know your identity.
- If you do not want us to use information about your health, you should not be part of this research. If you choose not to participate, you can still receive health care services at Carle Health, OSF Healthcare, Christie Clinic or other local healthcare providers.

What if I decide to Not Participate after I sign the Consent and Authorization Form?

You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

WOULD YOU LIKE TO BE CONTACTED ABOUT FUTURE RESEARCH OPPORTUNITIES?

❑ Yes, please include your email _____ or

phone number _____

❑ No

You can be in this current research study without agreeing to future research use of your identifiable information.

CONSENT

By signing this consent form, I confirm I have read the information in this consent form and have had the opportunity to ask questions. I will be given a signed copy of this consent form. I voluntarily agree to take part in this study.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

RUNNING HEAD: HIIT TO BREAK PROLONGED SITTING FOR BRAIN HEALTH

Supplementary Table 1. Name and contact information for the trial sponsor

Trial Sponsors:	University of Illinois Urbana-Champaign Sponsor's Reference: 1376000511A6 Federal Employment Identification Number Contact Name: Paul N. Ellinger, Comptroller Address: 1901 S. First Street, Suite A Telephone: 217-333-2187 Email: spa@illinois.edu

Supplementary Table 2. Trial registration data

Data Category	**Information**
Primary registry and trial identifying number	ClinicalTrials.gov No. NCT06243016
Date of registration in primary registry	2024-02-05
Secondary identifying numbers	IRB24-0010, 1R21AG080411-01A1
Source(s) of monetary or material support	National Institute on Aging
Primary sponsor	University of Illinois Urbana-Champaign
Secondary sponsor(s)	Northeastern University, National Institute on Aging
Contact for public queries	Dominika M Pindus, Ph.D.
Contact for scientific queries	Dominika M Pindus, Ph.D.
Public title	Breaking Sitting With High-intensity Interval Training for Brain Health (HIIT2SITLess)
Scientific title	Breaking prolonged sitting with high-intensity interval training to improve cognitive and brain health in older adults – a pilot feasibility trial
Countries of recruitment	USA
Health condition(s) or problem(s) studied	Prolonged sitting, high-intensity interval training bouts, frontoparietal function, inhibitory control and episodic memory
Intervention(s)	*Active comparator*: 6-minute high-intensity interval training (every 30 minutes over 3.5 hours of sitting) *Passive comparator*: 6-minute low-intensity interval training (every 30 minutes over 3.5 hours of sitting)
Key inclusion and exclusion criteria	Age 40-70 years, BMI < 40 kg/m^2, sedentary (≥ 6 hours of sitting per day), low to moderately physically active (based on IPAQ Short Form), capable to engage in vigorous exercise (PARQ+), medical clearance from primary care physician, normotensive, IQ ≥85, fasting plasma glucose < 126 mg/dL, good or corrected vision and hearing, no significant abnormalities on the ECG during a maximal exercise test, no signs or symptoms suggesting of underlying cardiovascular disease as recorded during maximal exercise test, no indications to prematurely stop the maximal exercise test as per ACSM's Guidelines for Exercise Testing and Prescription.
Study type	Interventional
Date of first enrolment	February 2024
Target sample size	54
Recruitment status	Recruiting
Primary outcome(s)	Change in task-evoked brain activity (P3b component)
Key secondary outcomes	Change in cognitive functions, change in resting state and task evoked brain activity

Notes. ECG: electrocardiogram, IPAQ Short Form: International Physical Activity Questionnaire Short Form, PARQ+: Physical Activity Readiness Questionnaire for Everyone, IQ: intelligence quotient.

HIIT TO BREAK PROLONGED SITTING FOR BRAIN HEALTH IN AGING - PROTOCOL

Supplementary Table 3. Schedule of study assessments

Assessment	**Screening Phone Call (Day -37 to Day -7)**	**Screening visit (Day-23 to Day -4)**	**Baseline (Day 0) – Pre-allocation**	**Intervention Visit 1 Day 8-21 (±2 Days)**	**Intervention Visit 2 Day 16-36 (±2 Days)**	**Follow Up Day 17-43 (± 2 Days)**
	ENROLMENT		**ALLOCATION (post-baseline)**	**INTERVENTION**		**FOLLOW-UP**
TIME POINT	**-t2**	**-t1**	**t0**	**t1**	**t2**	
ELIGIBILITY SCREEN						
Screening Informed Consent Form	**x**					
Screening Questionnaire	**x**					
Health & Demographics Questionnaire	**x**					
General Health History Questionnaire incl. current medications	**x**					
PASB-Q	**x**					
PARQ+	**x**					
Hospital Anxiety and Depression Scale	**x**					
Medical Clearance	**x**					
Blood Sample Fasting Glucose Analysis		**x**				
Anthropometric Assessments		**x**	**x**			
Resting Heart Rate and Blood Pressure		**x**	**x**	**x**	**x**	
Montreal Cognitive Assessment		**x**				

HIIT TO BREAK PROLONGED SITTING FOR BRAIN HEALTH IN AGING - PROTOCOL

Ohio State TBI Identification Interview Form		**x**				
Geriatric Depression Scale		**x**				
Beck Depression Inventory-2						
Florida Cognitive Activity Scale		**x**				
KBIT-2		**x**				
Inclusion/Exclusion Criteria	**x**	**x**				
Graded Maximal Exercise Test (GxT)		**x**				
Informed Study Consent Form			**x**			
ENROLLMENT			**x**			
Cognitive Tasks			**x**			
HIIT and LIIT Breaks Practice			**x**			
Borg Rating of Perceived Exertion Scale			**x**	**x**	**x**	
Feeling Scale			**x**	**x**	**x**	
Pittsburgh Sleep Quality Index (PSQI)			**x**			
Godin-Shephard Leisure Time Physical Activity Questionnaire			**x**			
Preference for Tolerance of the Intensity of Exercise Questionnaire			**x**			
FDI DIS Abbreviated FDI-Disability			**x**			
FDI FxN Abbreviated FxN- Function			**x**			
FxNSE Function Self Efficacy without a device			**x**			
Gait Efficacy Scale (GES)			**x**			

HIIT TO BREAK PROLONGED SITTING FOR BRAIN HEALTH IN AGING - PROTOCOL

Sedentary Behavior Questionnaire (SBQ)			**x**			
SEQUENCE ALLOCATION			**x**			
INTERVENTIONS						
HIIT Breaks*				**x**		
LIIT Breaks*					**x**	
INTERVENTION ASSESSMENTS						
Physical Activity & Sitting Time Monitoring in Free-Living (7 d each)			**x**	**x**		
Heart rate Monitoring (during visits)			**x**	**x**	**x**	
Physical Activity Monitoring (during visits – ActiGraph GT9x Link)				**x**	**x**	
Sitting Time Monitoring (activPAL) (during visits)				**x**	**x**	
Epworth Sleeping Scale (ESS)				**x**	**x**	
ACT24 Physical Activity Recall				**x**	**x**	
Mental Effort Scale				**x**	**x**	
Task Engagement Scale				**x**	**x**	
Vigor and Fatigue Scale				**x**	**x**	
Cognitive Tasks				**x**	**x**	
EEG Recordings				**x**	**x**	
HIIT Breaks Surveys					**x**	
HIIT2SITLess Study Survey					**x**	
AEs		**x**	**x**	**x**	**x**	**x**

HIIT TO BREAK PROLONGED SITTING FOR BRAIN HEALTH IN AGING - PROTOCOL

FOLLOW-UP						
Phone call						**x**

Note. ACT24: Activities Completed over Time in 24 Hours; AE: adverse event; HIIT: high-intensity interval training; KBIT-2: Kaufman Brief Intelligence Test 2; LIIT: low-intensity interval training; PARQ+: Physical Activity Readiness Questionnaire for Everyone; The Canadian Society for Exercise Physiology (CSEP) Physical Activity and Sedentary Behaviour Questionnaire (PASB-Q); *The order of the interventions is randomized across participants.

HIIT TO BREAK PROLONGED SITTING FOR BRAIN HEALTH IN AGING - PROTOCOL

Supplementary Table 4. Version history

Item	**Item Details**
Original IRB Protocol Number:	IRB24-0010
Original IRB Approval Issue Date:	02/20/2024
Protocol amendment number:	3
Protocol amendment approval date:	
Authors:	*DMP, RJS*
Revisions chronology	
Amendment 1 Approval Date:	04/20/2024
Amendment 1 changes:	Use of point-of-care glucose monitor instead of a venous blood sample and research-grade glucose reader.
Amendment 2 Approval Date:	05/28/2024
Amendment 2 Changes:	Expanding research staff who can perform a finger prick to collect a blood sample
Amendment 3 Approval Date:	09/13/2024
Amendment 3 Changes:	Age range change from 60-75 to 40-75 years. Amendment to inclusion criteria; shorter screening and baseline protocol.