Investigating Gains in Neurocognition in an Intervention Trial of Exercise (IGNITE)

NCT02875301

12-01-2022

University of Pittsburgh

Consent to Act as a Participant in a Research Study

Study Name:	Investigating Gains in Neurocognition in an Intervention Trial of Exercise
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Why is this research being done?
The purpose of this research study is to learn whether a 12-month moderate intensity exercise program in older adults can improve cognitive function and brain health (the ability to maintain attention and remember things). This research study will also obtain information on whether the exercise enlarges certain areas of the brain and what changes in blood biomarkers bring about the improvements.

Who is being asked to take part in this study?
You are being asked to participate in this study because you are between the ages of 65 – 80 years of age. Up to 213 men and women of all races are being asked to participate. The study is being conducted by the Department of Psychology at the University of Pittsburgh. This is a multi-site trial that includes two other locations. A total of 639 study participants will be enrolled (213 at each location).

What procedures will be performed for research purposes?
If you decide to take part in this research study, you can expect to undergo the following study procedures:

Baseline assessment
Before being randomly assigned into one of the three study groups, you will be asked to complete a six-part baseline assessment to learn about your level of physical fitness, cognitive function (the ability to maintain attention and remember things), body composition, and brain imaging. *Random assignment is like "drawing of straws" providing a one in three chances of being placed into one of the three groups.* At the time of your enrollment, you will meet with a member of the research staff and complete the six-part assessment. All aspects of the six assessment visits must be completed in full in order to be randomized to this research project. Each of these is described below.

Cognitive Assessment:
The cognitive assessment will be the first two sessions and each session will last approximately 2 hours. These assessments will take place in Dr. Erickson's lab (Brain Aging and Cognitive Health Lab) located at 210 South Bouquet Street (Sennott Square Building) on the University of Pittsburgh campus. Parking will be provided at this location. These sessions will be conducted by staff of Dr. Erickson's lab. These staff members have been involved in many federally funded research projects and have vast knowledge in administering the tasks. During the cognitive assessment portion, you will be asked to complete measures of cognitive function and quality of life (general well-being) and symptoms. Some of these tests will be completed using pencil and paper and some will be done on a computer. You do not need to have any computer experience to complete these tests. In these tasks, you will be responding to either letters, symbols, words, or faces presented on the display by pressing buttons as rapidly and accurately as you can on a standard keyboard. For some of the stimuli, you may be asked to recall the items at a later time in the session. During this session, there will be break periods at regular intervals for you to rest your fingers and eyes, and several practice trials for you to gain experience on the task before beginning. This assessment will be repeated at 6-month midpoint and after the 12-month intervention. After you complete the first cognitive session, you will be given a packet of

questionnaires to complete on your own time at home and return these questionnaires at the second cognitive session. It is expected to take approximately 60 minutes to complete the questionnaires.

Fitness Assessment:
The physical fitness assessment (Session 3) will also take place in Dr. Erickson's lab located at Sennott Square and will be conducted by an exercise physiologist with experience in exercise testing and coaching. This session should take no longer than 90 minutes to complete. A physician will also be present during this test. Your fitness level will be assessed using a maximal VO_2 fitness test, which will be completed on a motor driven treadmill. VO2 is your body's maximum rate of oxygen uptake during the exercise test with increasing intensity. During this exercise test, you will be asked to steadily increase your intensity until you reach your maximal effort. You stop the test whenever you are unable to continue due to fatigue or any discomfort. The exercise physiologist or physician may stop the test before you reach max effort if they observe any values of heart rate and blood pressure or EKG changes that would put you at risk if you were to continue. They may also stop the test if any other signs of distress are observed such as difficulty with walking, impaired performance, difficulty in awareness or any other physical observation that would signal excessive distress on your part. The increase in intensity is accomplished by increasing the level of incline while asking you to maintain a constant speed. During the test, you will wear a mouthpiece that collects all the air that you breathe out. To collect all the air you breathe out, you will also wear nose clips; therefore, all your breathing during the exercise test will be done through your mouth. The mouthpiece is attached to a hose, which allows the air to travel to a chamber. In this chamber, the air will be used to measure your fitness level. Also, during this test, you will have electrodes placed on the chest area for a 12 lead EKG for the physician to view while the test is being performed. Throughout the test your blood pressure will be obtained along with how hard you perceive yourself as working. This test typically takes about 15 – 30 minutes to complete. During this visit, you will also complete 2 paper and pencil questionnaires related to exercise barriers and motivation. These questionnaires will take 5 minutes to complete. If you are prescribed a beta blocker after your original exercise test, we may need you to come back and repeat your exercise test. This test will be scheduled after 14 days of beginning the new beta block medication. The test will follow the same speed and intensity of the original exercise test with no repeat of questionnaires or additional ActiGraph wear required.

Prior to completing the exercise test, you will be asked to walk for 45 seconds in a long hallway at your own normal walking pace along with walking trials while counting. During these walking trials, you will have a smart phone placed in your pocket or worn on a belt clip. You will be given a break between walking trials. This task is expected to last 10 minutes.

You may also be fitted with a (FDA approved) small physical activity monitoring device, (Actigraph Link), to be worn around your wrist that will energy expenditure, number of steps, physical activity duration and intensity of the physical activity along with sleep duration and sleep efficiency. This is a safe device used to assess a person's activity habits.
You will be provided with detailed instructions regarding the device, (including the option to remove the device if it becomes a problem). We will ask you to wear the device for approximately 1 week to obtain activity information outside of the laboratory environment. We will collect the device after the one-week time period and download the information. While wearing this device, you will not be able to view any of the data. You will not be able to keep the device as it will need to be used by other subjects throughout this research project. The

physical activity monitoring will be repeated every other month for a total of 7 wear time periods.

After this session, you may be asked to complete at home the Diet History Questionnaire (supported by NCI) which asks about the past month food intake and portion sizes, this questionnaire is also completed post 12-month exercise intervention.

MRI Imaging:
Imaging (MRI Scan)
You may be asked to complete a (Magnetic Resonance Imaging) MRI scan at the fourth session and completion of the 12-month intervention. This session takes approximately 2 hours to complete. The MRI will take place at the University of Pittsburgh Magnetic Resonance Research Center (MRRC) located at Presbyterian University Hospital or the Neuroscience Imaging Center (NIC) location on the Pitt campus once the new location in the Learning Research and Development Center is fully operational. An MRI scan produces images like x-rays, except that is does not use any radiation. MRI uses a large magnet in a tunnel-like machine. You will lie on a table that will move you into the tunnel for one hour. During this hour, the movement of your head will be limited so that the machine can record images of your brain and how it is functioning. You will be able to talk to, and hear the replies of, the researchers performing the tests.

Prior to the scan, you will practice the tasks you will complete in the scanner. You will also complete a brief questionnaire. Then you will undergo a series of scans in the MRI machine.

You will be asked to lie still in the MRI machine for one hour without moving. During parts of the hour you will be asked to think of nothing in particular. At other times, you will be asked to look at a screen positioned in front of you and to complete tasks that use the parts of your brain involved in attention, memory, and mood. You will perform a number of tasks examining brain responses during which you will be asked to look at a range of different types of images on a screen and press a button in response to certain images. These images may include pictures of people's faces, shapes, letters, and/or words.

The MRI scans that we will acquire in this study are research scans designed to answer research questions, and not designed to detect brain abnormalities. The research scans that we will collect are not the type of scans that reveal medical conditions. Nevertheless, there is a remote possibility that an abnormality may be detected in one of the scans. All scans will be read by a neuroradiologist at the coordinating center of the project (University of Pittsburgh Medical Center). If anything abnormal is found on the MRI that is of clinical significance, the PI will review the findings with you, and you may be told to follow-up with your personal physician. Any recommended follow-up is your responsibility to be completed on your own time and cost. Serious MRI incidental finding may exclude you from the trial. You will not have access to the MR images unless they are determined to contain an abnormal finding.

Blood Draw and Pulse Wave Velocity:
This is the fifth session as part of the baseline assessment. This series of procedures will take place at Dr. Erickson's lab (Brain Aging and Cognitive Health Lab) located at 210 South Bouquet Street (Sennott Square Building) on the University of Pittsburgh campus. .

Pulse Wave Velocity (30 minutes to complete): You will undergo a procedure to measure the hardness and stiffness of your blood vessels (arteries). This test uses something called "pulse-wave velocity techniques." For this test, you will be asked to lie quietly while sensors (small disc shaped handheld sensors) that are able to measure change in pressure are placed on the right side of your neck and your groin. These sensors can measure the time it takes for the pulse waveform generated by each heartbeat to travel from the heart to the arterial sites being measured; in this case, the artery in your neck and the artery in your groin. The less time it takes for the pulse wave to travel from your heart to the blood vessels in your body, the stiffer your arteries are. This test will take about 30 minutes and there is no discomfort involved. This testing will be performed by trained vascular technologists at the Brain Aging and Cognitive Health Lab at the University of Pittsburgh. We will also perform automated blood pressure measurement before and after the test while you are lying quietly.

During this session, you will also be asked to provide a sample of blood (approximately 11 teaspoons). This will require you to be fasting for 10 hours (water only). After the blood draw is complete, you will be offered a light snack and refreshment. Blood will be collected and stored at the University of Pittsburgh Behavioral Immunology Laboratory for future testing of biomarkers, genes and gene products related to this study. We cannot, at this time, tell you exactly which biomarkers, genes or gene products will be tested. Blood draw will be repeated at 6 month (midpoint) and 12 months (end point) of the study. The risk of doing genetic studies includes the potential for a breach of confidentiality, which means someone could see your genetic testing results who is not authorized. The information could be used to affect what insurance or jobs you may be able to get. Or it could affect your decision to have children. It could also cause stress and conflict in your family relationships, as it can confirm who is a child's father, identify a risk for a certain disease, or cause you or other people to have negative feelings if the results show you may be more likely to get certain diseases. As part of this session, you will complete a few questionnaires while having the light snack and refreshment after blood draw is complete. Along with the blood draw, you will be asked to provide a small sample of hair.
Hair strands will be collected with fine scissors as close as possible to the scalp from a posterior vertex position, which means hair from the upper part of the back of the head or the crown of the head. We will measure the level of cortisol in your hair, in at least 50 mg of hair (~40 strands) in the 2-cm segment closest to the scalp. Cortisol is a hormone released in response to stress."

This session will finish with a short physical function assessment of balance, walking speed, flexibility, and strength if these were not completed prior at the VO2 session.

DXA SCAN:
This standalone visit will be completed at Endocrinology Clinical Research Core located in Montefiore hospital. DXA (Dual-Energy X-ray absorptiometry) will be completed to measure body composition. It provides a measure of lean mass, fat mass, and bone density. Body composition will be measured using Dual X-ray Absorptiometry (DXA). This scan is done like an x-ray, but it gives more information. You will lie flat on your back on the DXA scanning table in a private room for approximately 20 minutes. There are no injections, IVs or bloods samples, and the test is painless. You may feel slightly uncomfortable lying on the hard surface of the scanning table. This procedure involves lying on your back on an exam table as a scanner moves from the head down to the feet. Prior to the DXA scan you will have waist circumference

measured.

PET Imaging:
PET imaging scan is the 6th and final assessment and it may or may not be completed by each subject. This session will take 2.5 hours and is completed at on the ninth floor of the B-wing at Presbyterian-University Hospital, University of Pittsburgh Medical Center (UPMC) Health System. This procedure measures the amount of Amyloid in the brain. You will be asked to fast for at least one hour prior to your scheduled PET scan. You will be asked to avoid all caffeinated beverages (coffee, tea, soft drinks, etc.) the day of the PET scanning. You will be asked to avoid all alcoholic beverages for 48 hours before the PET scanning. You may take your prescribed medications at their usual times.

For this procedure, an IV catheter is placed in one arm by an experienced nurse or certified nuclear medicine technician. A FDA approved radiotracer called Neuraceq (Florbetaben F18) is injected through the IV catheter. A radiotracer is a very small amount of a drug that contains a radioactive substance that will be injected into the vein in your arm or hand and will be detected in your brain by a special camera in the PET scanner. You will receive 8 milliCuries (mCi) of the radiotracer Neuraceq. A "mCi" is a unit of radioactivity dosage explained more in the risks section below. The Neuraceq radiotracer will be injected while you sit or recline comfortably about 75 minutes before you are positioned in the scanner. As part of the PET scanning session, you will be asked to lie on your back on a padded table and remain very still. Your head will be strapped to the table for support during the scan to help you to keep your head still. After you are positioned on the table as comfortably as possible, a low-dose CT scan will be completed using a very small amount of external radiation to adjust the PET scanner. This will take a few minutes. Following the low-dose CT scan, the PET camera will take images to determine if there are amyloid deposits in your brain. This scan will take about 20-30 minutes. After you leave the PET scanner, you will be observed in a comfortable room for at least 30 minutes. You also will be offered something to eat while you wait. You will be asked to drink fluids and empty your bladder before you leave.

Randomization:
A Computer will randomly assign (like flipping a coin) you to one of the three exercise groups. Each group will meet for supervised exercise sessions 3 times per week for 12 months. The three groups are: a) 150 minute per week exercise group, b) 225 minutes per week exercise group, or c) light intensity stretching and toning group.

EXERCISE INTERVENTION GROUPS:
At your first exercise session (all three of the exercise intervention groups), a functional fitness assessment of your walking speed, balance, leg strength, mobility flexibility and endurance will be completed. Each group will also complete exercise diaries for exercise performed outside of the supervised exercise sessions. Subjects will receive feedback on these logs. Home exercise may be completed at a community center, local fitness facility or at home.

Aerobic Exercise program
If you are assigned to either of the two aerobic exercise groups (150 minutes / week or 225 minutes / week), you will be asked to complete a 12-month aerobic exercise program where you report for 3 supervised exercise sessions per week and complete two home-based exercise sessions. All sessions will be conducted in the Physical Activity and Weight Management

Research Center near the campus of the University of Pittsburgh or the BACH exercise lab at Sennott Square on the campus of the University of Pittsburgh. This location has state of the art exercise equipment, AED, first-aid kit, and emergency procedures. A member of the study team will supervise each exercise session. This staff member is trained and has experience in exercise prescription. We will use brisk walking on a motor-driven treadmill as the main mode of exercise, however, you may choose other types of exercise such as an elliptical trainer, recumbent bike, etc. Participants will begin with a 5-minute warm-up, brisk walk in an intensity range of 50 % – 60% of maximal heart rate for the first six weeks and then and 60% - 75% of maximal heart rate for remainder of the program. Each session with a cool-down period. The exercise duration will begin at 10 – 15 minutes per session during the first two weeks of the program and gradually increase to 30 minutes per session for the 150-minute group and remain there for duration of the intervention. This group will be instructed to do two 30-minute sessions at home during the intervention each week. The duration will be increased to 45 minutes by the sixth week for the 225-minute group and remain there for duration of the intervention. This group will be instructed to complete two 45-minutes at home each week. At each session, your heart rate and perceived exertion will be continuously monitored to ensure that the exercise intensities are performed at the prescribed intensity level along with safety reasons. Heart rate will be monitored by wearing a heart rate monitor around your wrist. Blood pressure will also be measured and recorded before and after exercise. Blood pressure reading will be obtained with the use of manual auscultatory technique mechanical aneroid sphygmomanometer. During all exercise sessions, subjects will have access to water cooler, sweat and shower towels, fans that can be placed in various locations to keep subjects cool. For those participants that struggle to complete their randomized aerobic based group time goal, exercise staff will provide options (supervised and home based) within and possibly beyond the three supervised sessions per week.

Stretch and Tone Program

If you are assigned to the stretch and tone group, you will be asked to attend 3 sessions per week during the 12-month intervention. Each session is 30 minutes in length and the location is the Physical Activity and Weight Management Research Center near the campus of the University of Pittsburgh or the BACH exercise lab at Sennott Square on the campus of the University of Pittsburgh. Blood pressure and heart rate will be monitored in the same method as the aerobic exercise group. This program will focus on improving balance, flexibility, and strength. It will use devices such as resistance bands, balance disks, yoga blocks and exercise mats. These exercises are progressive in nature and can be modified to accommodate any injury or physical difficulty. Every week, new activities will be introduced. For participants who are having difficulty attending the Stretch and Tone sessions in person, they will have option of doing session live via zoom under the direction of one of the study exercise trainers.

Mid-point assessment

All participants, regardless of group assignment, will be asked to repeat the cognitive sessions and blood draw (described above) approximately 6 months after the baseline assessment.

Follow-up assessment

All participants, regardless of group assignment, will be asked to complete a final follow-up assessment about 12 months after enrolling in the study. The follow-up assessment will be the same as the baseline assessment in collecting data with the Cognitive assessment, fitness assessment, MRI imaging, DXA, Pulse wave velocity, blood draw and PET imaging.

What is the length of Study Participation?

Study participation is estimated to be 14 – 16 months. This includes the 12-month exercise intervention along with approximately 4 – 8 weeks prior to the intervention to complete all baseline measurements and 4 – 8 weeks after the intervention to complete post study measurements.

What are the possible risks, side effects, and discomforts of this research study?
The possible risks of this research study are described below:

Risks of blood draw
Bruising, bleeding, soreness, or rarely, fainting or infection may occur as a result of the needle sticks to obtain blood from your vein. This risk is minimized by having qualified individuals draw your blood, only collecting as much as is required for the study and making sure you are okay after your blood is drawn and before you leave the lab. Due to having to fast for 10 hours prior to the blood draw, there is a risk of dehydration, fainting, dizziness, and weakness. This risk in minimized by being reminded to drink plenty of water prior and up to the blood draw time. At this session, the blood draw will be the first thing completed.

Genomic information
A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information that we get from this research when making decisions regarding your eligibility or premium.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment

Be aware that this new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it provide you against genetic discrimination by all employers. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Risks of aerobic exercise intervention and gait analysis
There is a possibility that during or after participation in aerobic exercise, you may have an injury to joint or muscle, or have muscle soreness or fatigue. This risk is minimized by starting the exercise session at low level and increasing the level as you tolerate. Other infrequent risks include equipment malfunction, dehydration, and heat exhaustion. These risks are minimized by having the room temperature at a comfortable level and fans located throughout the exercise facility. Falling is another infrequent risk involved in doing exercise, although this risk will be lessened by the close monitoring of exercise sessions by an experienced exercise physiologist. Physical activity may be related to serious cardiac events in less than 1 per 20,000 exercising adults, but this appears to be minimized when participation is directed by knowledgeable and experienced professionals and when progressed in a moderate and appropriate manner. Since assessment of vital signs and history of heart disease are included in the screening procedures, we anticipate that this risk is rare.

Risks of Exercise Testing

As with all exercise, there is possibility of having an injury or soreness to a muscle or joint. This is minimized by doing a warm up at a lower intensity. During the exercise test, you will be continuously monitored by ECG and vital signs (blood pressure and heart rate). It is possible that you may have abnormal blood pressure and / or ECG responses to the intensity of the exercise test. There is minimal risk of major complication (death or hospitalization) from exercise testing. All exercise test documents and ECG tracings are reviewed by study cardiologist. In the event of abnormal finding, the PI will review the findings with you, and you may be told to follow-up with your personal physician before proceeding in the trial. It is also possible that you may have dry mouth from the facemask worn during test, water is provided and advised for consumption prior to test to help prevent mouth from becoming dry. There is a small chance that you may become nauseous or lightheaded during the exercise test.

Risks of cognitive measures

It is possible that during the completion of some of the cognitive function and quality of life measures you may become bored, frustrated, or tired. There is also a rare risk of slight eye strain. In order to prevent these risks, you are offered breaks during testing periods. You do not have to complete questions that you choose not to answer. Any person scoring highly on the depression or anxiety items will be directly referred by the study team to mental health specialist.

Risks of MRI scan

The risks associated with having an MRI brain scan are minimal. The scanner magnet makes loud, banging sounds, so we will provide ear protection for you to wear.

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. To minimize risks, you will be asked questions about any metallic or electrical objects in your body and preexisting medical conditions prior to entering the magnet room.

Because you must lie with your head and neck inside the narrow scanner tube, you might experience claustrophobic feelings (fear of enclosed spaces) while in the scanner. You may also become frustrated, fatigued, or anxious during the scan. If you experience claustrophobia or for any reason feel that you cannot remain in the scanner, we will stop the scan and withdraw you from the study. We will ask how you are feeling and offer breaks between each test in the scan. You will be given a squeeze ball so that you can stop the scan if you become uncomfortable at any time. Sometimes people feel anxious even after the scan is stopped, so the researcher will help you to calm down. You may feel lightheaded when you sit up after the scan, but this should go away quickly. The researcher will help you exit the scanner and relax before you leave.

Radiation Risks associated with DXA and PET Scans

Participation in this research study will involve exposure to radiation associated with the two DXA scans, two low dose CT scan, and two Neuraceq PET scans. The total, whole body radiation dose that you will receive from these procedures is about 1.16 rems (a "rem" is a unit of radiation dose). For comparison, this radiation dose is about 24% ($1/4^{th}$) of the maximum, annual, whole body radiation dose (5 rems) permitted by radiation workers by Federal regulation. There is no minimum amount of radiation exposure that is recognized as being totally free of the risk causing genetic mutations or cancer. However, the risk associated with the radiation dose that you will receive from participation in this research study is considered to be

low in comparison to everyday risks. Post intervention PET imaging will be completed at a date greater than 1 year from the baseline scan.

Risks of PET Imaging

Since an IV catheter is used, you have the same risks of a blood draw in bruising, bleeding, soreness, or rarely, fainting or infection. This risk is minimized by having qualified individuals insert the IV line. There is a common risk that you may experience muscle aches and fatigue from lying still for the PET scan. Risks of being immobile are minimized by keeping the time of immobility as brief as possible and allowing breaks out of the scanner. A radioactive tracer is injected into the IV. Participation in this research study involves exposure to radiation from the PET transmission / low-dose CT scan and from the injected radiotracer, Neuraceq. Neuraceq is approved by the United States Food and Drug Administration (FDA) to estimate amyloid levels in adult patients with memory problems who are being evaluated for AD and other causes of cognitive decline. Neuraceq is an imaging agent that uses a small amount of radioactivity to produce an image.

To date, Neuraceq has been tested in over 872 subjects with1090 administrations.
In completed studies involving these subjects, the most common side effect (<4%) was pain at the injection site. Also, reported (<2%) were the reddening and irritation of skin at the injection site. You may also experience side effects that are not listed above.

If you become claustrophobic or for any reason, feel that you cannot remain in the scanner, we will stop the scan and withdraw you from the study. We will ask how you are feeling and offer breaks between each test in the scan. You will be able to communicate with the technician at all times during the scan. Because the investigators assume that this study represents the only research exposure to radiation that you will be exposed to this year, it is important that you inform the investigators of your participation in any other research studies during the past year. If you have participated in a previous PET imaging brain scan or brain scan research study, we will ask you to wait 1 year after the scan to participate in this study.

Risks of Physical Activity monitoring device

Although the physical activity monitoring device has been designed to be comfortable and easy to wear, you are in no way obliged to continue wearing it if it is uncomfortable, or in any way bothers you. If you have any discomfort or skin irritation with the device, we would like to be informed as soon as possible.

Risks of Obtaining hair sample

We will obtain hair segments from your hair from a posterior vertex position, which means hair from the upper part of the back of the head or the crown of the head. The amount of hair obtained is likely not to be noticeable. There is a risk of injury while collecting hair samples using fine scissors. Hair sampling will be conducted by a trained nurse or interviewer to minimize this risk. If you are uncomfortable, hair sampling may be conducted at a later time.

Risks of DXA Scan

There is a risk that you would become uncomfortable lying on the exam table with no movement during the scan.

Risks of Pulse Wave Velocity

Pulse-wave velocity is measured using noninvasive techniques and involves no significant risk to study participants. The pressure measuring sensors or the blood pressure cuff may occasionally cause some skin redness from the pressure. This is an infrequent adverse event. This redness may last up to 48 hours. Severe pain may be experienced while the blood pressure cuff is inflated. This is a rare adverse event.

Risks of email correspondence

Throughout the IGNITE study, you may receive email communication from the IGNITE study team. These could include but not limited to quarterly newsletter and study updates. We will make reasonable efforts to protect the privacy of your information on social media. Each platform has their own privacy policies and terms of use that may change at any time. The University of Pittsburgh cannot guarantee the privacy and confidentiality of information shared on social media in this research study. You should never expect your information to remain private. Remember to regularly visit the site privacy policies and update your own privacy settings. Social media retains information shared across accounts for an unknown length of time and it may be shared with others including targeted advertisers.

Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study."

Risks of privacy and breach of confidentiality

There is a possibility that your study research data could become generally known, however, all data (including blood samples) will be identified by a code and will not contain identifying information (e.g., name, birthdate). All documents will be stored in a separate location from the data and the screening information in locked filing cabinets in a locked and secure room that only lab personnel have access to. All data collected will be forwarded to the coordinating center at the University of Pittsburgh. The transfer of data 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 not be transferred to any of the other locations as part of the IGNITE trial. 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 will sign a statement agreeing to protect the security and confidentiality of identifiable information. All data pertaining to the individual will be stripped of all identifying information. All data transferred to coordinating center will be via REDCap or XNAT. REDCap and XNAT are secure web applications that are recommended by NI for building and managing online surveys and databases and imaging data. Only authorized users are allowed to connect to the network, and the security of the network is actively monitored. Representatives from Harvard Medical School (gait testing) and the National Cancer Institute (food record) will have access to de-identified data. These data do not contain anything that identifies you.

What are possible benefits from taking part in this study?

Participants in each of the exercise groups may experience improvements in mood, sleep, cognitive function, and physical functioning. There may be a reduction in central adiposity and cardiovascular benefits. In addition, we are hoping that by engaging people in physical activity they will learn how to engage in physical activity on their own time after the completion of the intervention.

What treatments or procedures are available if I decide not to take part in this research study?

Because this study does not involve any type of medical treatment, there are no treatments or procedures available if you decide not to take part in this research study. However, you are free to seek out and participate in exercise opportunities throughout the study period. In addition, the National Institute of Aging (NIA) has information about exercises for older adults (https://go4life.nia.nih.gov/exercises).

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?

You will be promptly informed if, during the conduct of this research study, any new information develops which may cause you to change your mind about continuing to participate.

Will my insurance provider or I be charged for the costs of any procedures performed as part of this research study?

Neither you, nor your insurance provider, will be charged for the costs of any of the procedures (i.e., fitness testing, cognitive testing, blood draws, MRI, or PET Scan) performed for the purpose of this research study. You will be charged, in the standard manner, for any procedures performed for your routine medical care.

Your insurance may be charged for a visit to your physician if they require you to come in for a visit before signing clearance for you to participate in this research project. All subjects are required to have PCP medical clearance to participate in this project.

If you require medical care outside of the study, you will be billed in the standard manner for any procedures performed for your routine medical care, including any applicable co-pays, coinsurances, and deductibles. If you are referred to treatment outside of the study, and you decide to pursue this treatment (such as private practitioner or to your PCP), you will be responsible for the costs of such treatment. You are responsible for paying the costs of transportation to and from intervention sessions

Who will pay if I am injured as a result of taking part in this study?

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be

responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You waive no legal rights by signing this consent.

Will I be paid if I take part in this research study?

You will be paid for each procedure that you elect to participate and fully complete. Payment is made through a reloadable debit card. The payment table is listed; if you would need to repeat the VO2 exercise test, you will be compensated an additional $35.

MEASURE	BASELINE	MIDPOINT 6 MONTHS	POST	DURING INTERVENTION	TOTAL
Cognitive (Both Sessions)	$50	$50	$50	NA	**$150**
VO2 / Gait	$35	NA	$35	NA	**$70**
Accelerometer	$5	$5	$5	$20	**$35**
MRI	$100	NA	$100	NA	**$200**
Blood / Hair	$10	$10	$10	NA	**$30**
DXA	$10	NA	$10	NA	**$20**
PWV	$10	NA	$10	NA	**$20**
Amyloid	$100	NA	$100	NA	**$200**
Take Home Questionnaire	$20	NA	NA	NA	**$20**
Diet Questionnaire	$10	NA	$10	NA	**$20**
TOTAL	**$350**	**$65**	**$330**	**$20**	**$765**

Parking is provided free of charge for all sessions of the research study.

Please note: payment received as compensation for participation in research is considered taxable income for a research subject. IF payments are more than $600 in any one calendar year, University of Pittsburgh is required to report this information to the Internal Revenue Service (IRS). Research subject payment exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the research subject and a copy will be sent to the IRS

Who will know about my participation in this research study?

Although every reasonable effort has been taken to de-identify your research information, confidentiality cannot be guaranteed, and it is possible that re-identification of research / data samples may occur. Any information about you obtained from this research will be kept as confidential (private) as possible. All records related to your involvement in this research study will be stored in a locked file cabinet. Your identity on these records will be indicated by a case number rather than by your name, and the information linking these case numbers with your identity will be kept separate from the research records. You will not be identified by name in any publication of the research results unless you sign a separate consent form giving your permission (release).

Will this research study involve the use or disclosure of my identifiable medical information?

This research study will not involve the recording of current and/or future identifiable medical information from your hospital and/or other (e.g., physician office) records. The information

that will be recorded will be limited to information concerning your demographics (such as age, date of birth, education, occupation, marital status, race, and health history), your name and social security number. In addition, we will record information about your physical health and results from your cognitive tests and other procedure

Who will have access to identifiable information related to my participation in this research study?

In addition to the investigators listed on the first pages of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study:

1. Authorized representatives of the FDA, the University Of Pittsburgh Human Use Sub-committee (HUSC) of the Radiation Safety Committee, the University of Pittsburgh's Office of Research Protections, the National Institute of Aging, and other groups or organizations that have a role in the study will have access to and may inspect and/or copy research records due to your participation in this study. This access is necessary to ensure the accuracy of the findings and your safety and welfare. If any publication or presentations result from this study, you will not be identified by name. Results will be reported in a summarized manner such that you cannot be identified.

2. Payment received as compensation for participation in research is considered taxable income for a research subject. If payments are more than $600 in any one calendar year, the University of Pittsburgh is required to report this information to the Internal Revenue Service (IRS). Research subject payments exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the research subject and a copy will be sent to the IRS

3. In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical information) related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

4. Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as

explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally-funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Data Sharing:
This is a multi-site study in collaboration with the University of Kansas, Northeastern University, University of Illinois and Carnegie Mellon University. Data collection will occur at the University of Pittsburgh, University of Kansas and Northeastern University. Thus, investigators at the other collection sites of the University of Kansas and Northeastern University will have access to data. Thus, investigators all 3 sites will share de-identified data. It will be used for analysis, publication and future research purposes.
We plan to make the data from this study available to outside investigators under a data-sharing agreement. The data-sharing agreement provides for: (1) a commitment to using the data only for research purposes and not to identify any individual human participant; (2) a commitment to securing the data using appropriate computer technology; and (3) a commitment to destroying or returning the data after analyses are completed. An oversight committee made up of the Principal and Co-Investigators will monitor, approve, and distribute the data. The oversight Committee will also monitor data analysis plans and development of manuscripts. Protecting the rights and confidentiality of your data will be our first priority. All data will be de-identified before sharing; that means no data that we share will have anything that personally identifies you.

For how long will the investigators be permitted to use and disclose identifiable information related to my participation in this research study?
The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your demographics such as age, date of birth, education, occupation, marital status, race, and health history), your name and social security number related to your participation in this research study for a minimum of seven years after final reporting or publication of a project.

May I have access to my medical information that results from my participation in this research study?
You will not be permitted access to information (including information resulting from your participation in this research study) contained within study records. However, if any abnormal unanticipated findings are seen, you will be notified by the study principal investigator. You will be notified if any of your cognitive scores (first two sessions of the study) are below normal for your age. These are tasks that are completed using paper and pencil and look at things such as memory, attention, concentration and thinking.

Where will my blood sample be stored?
Samples will be maintained in a freezer in the University of Pittsburgh Physical Activity and

Weight Management Center under the control of the principal investigators of this research project and will be maintained indefinitely. In the event that we need to send samples to a different facility for analysis and possible genetic analysis in the future, no identifying information will accompany the sample. Your blood sample will be stored indefinitely. We may share de-identified samples with other researchers in the future.

Is my participation in this research study voluntary?

Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your identifiable information for the purposes described above, you will not be allowed, in general, to participate in the research study.) Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

Can I participate in another research study while enrolled in the IGNITE trial?

Your participation in anther intervention (Exercise, Balance, Nutritional, Pharmacologic, healthy behaviors) is not recommended as they could influence the various measures of the IGNITE study. By signing this consent form, you agree to refrain from enrolling in another intervention trial. The IGNITE study does understand that some study participants may be involved in a long-term trial that asks them to complete various tests on an annual basis. You may continue to complete these testing sessions but will be asked at 6 months and 12 months if you completed any testing for another trial and type of testing.

May I withdraw, at a future date, my consent for participation in this research study?

You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. (Note, however, that if you withdraw your consent for the use and disclosure of your identifiable information for the purposes described above, you will also be withdrawn, in general, from further participation in this research study.) Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw your consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

Your decision to withdraw your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Your decision to withdraw your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

If I agree to take part in this research study, can I be removed from the study without

my consent?
You may be removed from the study if you are not able to complete the study procedures, or if the research staff determine that it is in your best interest to stop participating. For instance, if the subject experiences an injury, illness or other condition at any time during the course of this study, his or her participation may be suspended (e.g. after temporary illness, such as a cold) or terminated by researchers to ensure safety and well-being.

Might I be contacted after I have completed my participation in this study?
We may contact you after you have completed this study if we need more information from you for this study, or if we have other studies in which you may be interested in participating.

New discoveries or commercialization.
Your stored blood samples used in this research study may contribute to a new discovery or treatment for cognitive performance and brain health. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may realize.

Clinical Trials website: A description of this clinical trial will be available on www.clinicaltrials.gov, as required by US 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.

VOLUNTARY CONSENT

I understand that I have the right to request that my questions, concerns, or complaints be addressed by other investigators in the consent form. My initials below indicate how I used this right:

_____ I request that a physician-investigator speak with me and sign this consent before I give my consent for participation in this study.

_____ I believe that all my questions, concerns and complaints were addressed by the non- physician-investigator. Although I have given my consent without talking to a physician-investigator, I understand that I still have the right to ask to speak to a physician-investigator at any time during the study

Any questions which I have about my rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668).
By signing this form, I consent to participate in this research. A copy of this consent form will be given to me.

_____ _____

Participant's Signature Date

_____
Participant's Printed Name

CERTIFICATION of INFORMED CONSENT
I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise."

I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____
Printed Name of Person Obtaining Consent Role in Research Study

_____ _____
Signature of Person Obtaining Consent Date

_____ _____
Printed Name of Physician Obtaining Consent Role in Research Study

_____ _____
Signature of Physician Obtaining Consent Date