UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: A video game to enhance cognitive health in older adults, children, and adolescents

This is a research study about the brain mechanisms that underlie memory, attention and perceptual processes. The study researcher Adam Gazzaley, M.D., Ph.D. from the UCSF Department of Neurology, Physiology and Psychiatry, or a member of his laboratory, will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study researcher.

You are being asked to take part in this study as a healthy volunteer.

Why is this study being done?

The purpose of this study is to find out whether our ability to remember and pay attention can be improved through practice on different kinds of tasks. This study is also being performed to understand if these abilities can be improved through training by practicing on different tasks.

How many people will take part in this study?

Approximately 180 people will take part in this study. Individuals will be healthy adults.

What will happen if I take part in this research study?

If you agree, the following procedures will occur:

First, you will participate in a prescreening where we will evaluate your attention and memory in order to determine your eligibility for the main part of the study. If the screening exam shows that you are eligible and you choose to continue, then you will be asked to participate in some or all of the procedures described below. By writing your initials, it means that you have been invited to participate in the corresponding part(s) of our research study.

Study Procedures

Phase I: In lab testing at UCSF (~ 3 week period)

Initials ☐ Behavioral Assessment: You will take part in a cognitive testing session at the Gazzaley Laboratory at UCSF. These behavioral testing measures will assess your attention, working memory, perceptive and motor abilities. An entire session should last no more than four hours, and may be divided across 2 visits.

Initials EEG Cognitive Testing: You will take part in a cognitive assessment at the Gazzaley Laboratory at UCSF, during which electrical activity from your scalp will be recorded through electroencephalography (EEG). You will perform computer tasks while we record electrical activity from your scalp with EEG equipment. Upon arriving at the laboratory, we will train you on the tests first. You will be presented with images on a computer monitor and/or sounds through headphones and instructed how to engage in the task. You will be asked to press a button in response to certain stimuli. Following this training, you will perform these same cognitive tests while wearing a cap that contains multiple EEG electrodes applied to your scalp with a removable gel, or perform the cognitive tests without the EEG electrodes. The EEG measures electrical activity produced by your brain. An entire session should last no more than four hours. There is also a possibility that you may wear an alternative "dry" electrode cap without any gel.

Initials fMRI Cognitive Testing: You will take part in a cognitive testing session at the Neuroimaging Center (NIC) at UCSF. Upon arriving at the NIC, we will train you on a memory or attention test. Depending on the individual study, you will be presented with either pictures or words on a computer monitor or sounds through headphones. You will be asked to pay attention to and remember the different pictures, words, or sounds. You will be asked to press a button in response to certain stimuli. In the fMRI study, we will use a magnet to measure blood flow to your brain. We use the fMRI to study which parts of your brain are most active while you do different cognitive tasks. You will be asked to lie down on a platform that can be slid into the middle of a magnet. A plastic MRI imaging coil will be placed around your head. You will not come into contact with the coil during the experiment. Foam pads will be placed around your head to limit head movement during the experiment. We will then slide you into the magnet. At different points during the experiment, you will be asked to do the same tasks you did in the training session. It will take about 60 to 90 minutes. The entire session should last no more than three and one-half hours.

Initials Simultaneous EEG-fMRI Cognitive Testing: Simultaneous EEG-fMRI testing will occur at the Neuroscience Imaging Center (NIC) at the UCSF Parnassus campus in San Francisco. Upon arriving at the NIC, you will first be trained to perform the task. You will be presented with images on a computer monitor and/or sounds through headphones and instructed how to engage in the task. You will be asked to press a button in response to certain stimuli. Following this training, you will perform these same cognitive tests while inside the magnet (i.e., fMRI scanner), or perform the cognitive tests outside of the magnet. The magnet records hemodynamic (i.e., blood flow) activity produced by your brain. Before entering the magnet, you will be fit with an MR-safe EEG cap that contains multiple EEG electrodes applied to your scalp with a removable gel. The EEG measures electrical activity produced by your brain. fMRI uses a magnet to measure blood flow to your brain. We use the fMRI to study which parts of your brain are most active while you do different cognitive tasks. You will be asked to lie down on a platform that can be slid into the middle of the magnet. A plastic MRI imaging coil will be placed around your head. You will not come into contact with the coil during the experiment. Foam pads will

be placed around your head to limit head movement during the experiment. We will then slide you into the magnet where you will perform computer tasks while we record your neural activity. Once you are wearing the EEG cap and you are inside the scanner, EEG and fMRI data can be recorded simultaneously. An entire session should last no more than four hours.

Initials

Saliva Sample Collection for Genetic Testing:
You will be asked to spit into a small container until we have collected 1 tablespoon of specimen. Alternatively, we may perform a buccal cell sample collection. In which we will rub the inside of your cheek with an abrasive cotton swap, the abrasiveness of the swap might cause slight and brief discomfort. This part of the experiment will take less than one minute. The saliva sample will be used to conduct genetic testing. These results will not be shared with the participants. The samples will be banked at the UCSF DNA Genomics Core Bank for a minimum of 1 year and will be reassessed on a monthly basis thereafter. The DNA can be banked for up to 20 years maximum.

Initials

Saliva Sample Collection for Biological Markers of Stress:
You will be asked to run a swab through the inside of your mouth, which will collect a small amount of saliva. The saliva samples will be used to look at biological markers of stress, like cortisol and alpha-amylase. Your samples will be sent to Universitaet Trier for analysis, and will be destroyed after testing.

Initials

Skin conductance level and heart rate:
Skin conductance level (also known as Galvanic Skin Response) and heart rate will be monitored via non-invasive sensors on a watch-like device, in contact with the inner wrist of one hand. Skin conductance level and heart rate will be recorded while you complete a cognitive task; these measures are used to look at psychological or physiological arousal.

Initials

Physical Assessment
You will be asked to perform a series of physical assessments, demanding various cardiovascular and aerobic exercise activities. The assessment duration will not exceed a total of 4-hours, and all participants will be offered breaks, water and snacks throughout the duration of the assessment.

Initials

Fasting Blood Draw (venipuncture)

You will be asked to participate in a blood draw. We will be drawing 200ml of blood total. Because we are measuring hormones related to metabolism, such as insulin, we must draw blood before you have eaten breakfast. Therefore, for each visit, you will be asked to not eat or drink anything (except water) after midnight before you come in for the blood draw. This blood will be analyzed for indices of stress, aging, vascular health, and metabolism (stress and metabolic hormones, markers related to immunology, and potential genetic markers for aging, stress, and depression).

Based on standard assays from the blood draw, if diabetes or any other clinically significant condition is detected, you will be informed after your visit, and advised to consult your doctor, and you will no longer be eligible to continue in the study.

☐ Initials Blood Bank

If you consent by checking the above box, we will bank extra blood for future assays, as new hypotheses are developed. Blood would be banked for 10 years. For example, we would assay for any new important genetic markers of vulnerability to stress or aging. All samples will be identified by ID only, and participants will not be told any results, given that we are only looking at experimental questions that have no diagnostic significance.

Phase II: At-Home or in-lab Training (~ 4 week period)

At-home and in-lab training only differ in the way data is collected. At-home training will involve being sent home and asked to complete training from home. In-lab training will involve coming into the UCSF Gazzaley lab for each day of your training.

☐ Initials Visuomotor Training: You will be provided with a laptop or mobile device (i.e. iPhone, iPad, computer tablet, smart phone, etc.) and/or controller to play a video game developed in our lab. You may also be given a wireless, dry-electrode, electroencephalography (EEG) cap so that neural data can be recorded at home while you are playing the game. In the in-lab version, you may be alternatively set-up with a wired, wet-electrode EEG cap. Members of the Gazzaley Lab may visit your home to assist you in the initial set up of the equipment. Equipment set-up will be done by qualified research staff in the in-lab training version. Telephone and email support will be provided to you throughout your involvement. You will also receive regular email reminders and check-in phone calls as reminders to your at-home or in-lab training sessions.

During at-home game play (and only when the game is in play), a video of your face will be recorded with a camera located in front of the laptop. The camera will automatically turn on when the game begins and turn off when it ends. You will always know when the camera is on because this will be indicated by a green light on the front of the laptop. A member of the Gazzaley lab will show you this function during the initial set-up. This data will be used to evaluate compliance with the instructions, which will aid us in interpreting performance and EEG recordings. For example, we will evaluate your eye position, to insure that fixation on the crosshair is maintained.

Additionally, we ask that you play only the specified number of sessions of the game and no more.

☐ Initials Audiovisual Training: You will be given a hands-on tutorial by the lab staff to guide you how to access the computer audio-visual game from the internet. You will then be able to access the game from your home computer. Telephone and email support will be

provided to you throughout your involvement. An optional at-home visit for initial set-up assistance by research personnel will be available if necessary. You will also receive regular email reminders and check-in phone calls. You may also be given a wireless, dry-electrode, electroencephalography (EEG) cap so that neural data can be recorded at home while you are playing the game.

Initials

Saliva Sample Collection for Biological Markers of Stress:
You will be asked to run a swab through the inside of your mouth, which will collect a small amount of saliva. The saliva samples will be used to look at biological markers of stress, like cortisol and alpha-amylase. Your samples will be sent to Universitaet Trier for analysis, and will be destroyed after testing.

Initials

Skin conductance level and heart rate:
Skin conductance level (also known as Galvanic Skin Response) and heart rate will be monitored via non-invasive sensors on a watch-like device, in contact with the inner wrist of one hand. Skin conductance level and heart rate will be recorded while you complete a cognitive task; these measures are used to look at psychological or physiological arousal.

Initials

Physical Training:

The physical training program will require in-lab participation. You will be asked to come into lab for 3 days a week for up to 8 weeks for 90-120 minutes physical training sessions. This training will involve simultaneous heart rate monitoring, and use of an in-lab motion captures system. You will respond to the task using physical movements. Responses will be in the form of reaching either up and down or left and right, jogging in place, kicking laterally or vertically, and other various aerobic movements. The assessments are portioned into maximal 5-minute blocks, and participants will perform no more than 9 blocks in a given training session. Stretching and warm-up exercises will be mandated prior to and following the tasks.

Once you consent to participating in this study, we ask that you do not change your interaction with technology (i.e., do not spend more time on your computer or expand the number/type of activities you use the computer for, upgrade your cellular phone to a smart phone, begin playing other video games, etc.) until you are no longer enrolled in this study. If any changes of this nature do occur, we ask that you let us know.

Phase III: In lab testing at UCSF (~ 3 week period)

Initials Behavioral Assessment: You will take part in a post-training cognitive testing session at the Gazzaley Laboratory at UCSF. These behavioral testing measures will assess your attention, working memory, perceptive and motor abilities. An entire session should last no more than four hours, and may be divided across 2 visits.

Initials Survey Questionnaires: You will take part in completing post-training surveys online through a secure web interface. Paper versions of these surveys will be available upon request. These surveys will assess your multimedia use, mood, daily habits and routines to better characterize individual differences following the training protocol. The entire session should last no more than two hours.

Initials EEG Cognitive Testing: You will take part in a post-training cognitive assessment at the Gazzaley Laboratory at UCSF, during which electrical activity from your scalp will be recorded through electroencephalography (EEG). An entire session should last no more than four hours.

Initials fMRI Cognitive Testing: You will take part in a post-training cognitive testing session at the Neuroimaging Center (NIC) at UCSF. The entire session should last no more than three and one-half hours.

Initials Simultaneous EEG-fMRI Cognitive Testing: You will take part in a post-training EEG-fMRI memory assessment at the Neuroscience Imaging Center (NIC) at UCSF. An entire session should last no more than four hours.

Initials Saliva Sample Collection for Genetic Testing: You will be asked to spit into a small container until we have collected 1 tablespoon of specimen. Alternatively, we may perform a buccal cell sample collection. In which we will rub the inside of your cheek with an abrasive cotton swap, the abrasiveness of the swap might cause slight and brief discomfort. This part of the experiment will take less than one minute. The saliva sample will be used to conduct genetic testing. These results will not be shared with the participants. The samples will be banked at the UCSF DNA Genomics Core Bank for a minimum of 1 year and will be reassessed on a monthly basis thereafter. The DNA can be banked for up to 20 years maximum.

Initials Saliva Sample Collection for Biological Markers of Stress:
You will be asked to run a swab through the inside of your mouth, which will collect a small amount of saliva. The saliva samples will be used to look at biological markers of stress, like cortisol and alpha-amylase. Your samples will be sent to Universitaet Trier for analysis, and will be destroyed after testing.

Initials Physical Assessment
You will be asked to perform a series of physical assessments, demanding various cardiovascular and aerobic exercise activities. The assessment duration will not exceed a total of 4-hours, and all participants will be offered breaks, water and snacks throughout the duration of the assessment.

☐ Fasting Blood Draw (venipuncture)
Initials

You will be asked to participate in a blood draw. We will be drawing 200ml of blood total. Because we are measuring hormones related to metabolism, such as insulin, we must draw blood before you have eaten breakfast. Therefore, for each visit, you will be asked to not eat or drink anything (except water) after midnight before you come in for the blood draw. This blood will be analyzed for indices of stress, aging, vascular health, and metabolism (stress and metabolic hormones, markers related to immunology, and potential genetic markers for aging, stress, and depression).

☐ Blood Bank
Initials

If you consent by checking the above box, we will bank extra blood for future assays, as new hypotheses are developed. Blood would be banked for 10 years. For example, we would assay for any new important genetic markers of vulnerability to stress or aging. All samples will be identified by ID only, and participants will not be told any results, given that we are only looking at experimental questions that have no diagnostic significance.

Based on standard assays from the blood draw, if diabetes or any other clinically significant condition is detected, you will be informed after your visit, and advised to consult your doctor, and you will no longer be eligible to continue in the study.

Saliva Sample Collection – Genetic Testing:

Types of specimen kept, and where:

Saliva samples will be collected from each participant for genetic testing. These will be housed at the UCSF DNA Genome Bank in Rock Hall at the Mission Bay Campus. This is a core facility of UCSF and accepts the clinical samples from projects that have been approved by the Committee on Human Research (CHR). Genomic DNA isolation is performed utilizing standardized and quality controlled Gentra Systems' PureGene DNA isolation system or Qiagen Kits.

Types of research the specimens can be used for and duration of specimen retention:

The specimen will be used for genetic testing for genes associated with cognitive enhancement or decline in healthy aging and Alzheimer's disease. The samples will be banked at the UCSF DNA Genomics Core Bank for a minimum of 1 year and will be reassessed on a monthly basis thereafter.

Types of data/medical information collected with the specimens and how long the information will be collected:

The information that will be collected with the specimen includes demographics, testing

performance, and measures of brain activity. The information will be collected during a single visit or over a series of visits based on the project goals. The specimen will be collected during a single visit.

Who will have access to specimens and data:

UCSF researchers or collaborators will have access to the specimen and data

Protection of subject privacy and data confidentiality:

The samples and results will be protected using a de-identified code that is distinct from the database participant code. The link between codes will be kept in a password-protected spreadsheet.

The specimen will not be used to develop commercial products. The participants are compensated $15/hour for completing specimen visits.

The genetic testing results will not be disclosed to the participants or any non-affiliated UCSF researchers/collaborators; therefore, there will not be any direct consequences to the participant.

Saliva Sample Collection – Biological Stress Testing:

Types of specimen kept, and where:

Saliva samples (salivette with synthetic roll) will be collected from each participant for evaluation of biological markers of stress. These will be sent to the Biochemistry Laboratory at Universitaet Trier for analysis of cortisol and alpha-amylase.

Types of research the specimens can be used for and duration of specimen retention:

The specimen will be used for testing of biological markers of stress, including cortisol and alpha-amylase. Specimen will be destroyed after testing is complete.

Types of data/medical information collected with the specimens and how long the information will be collected:

The information that will be collected with the specimen includes demographics, testing performance, and measures of brain activity. The information will be collected during a single visit or over a series of visits based on the project goals. The specimen will be collected during a single visit.

Who will have access to specimens and data:

UCSF researchers or collaborators will have access to the specimen and data. The

Biochemistry Laboratory at Universitaet Trier will receive de-identified saliva samples.

Protection of subject privacy and data confidentiality:

The samples and results will be protected using a de-identified code that is distinct from the database participant code. The link between codes will be kept in a password-protected spreadsheet.

The specimen will not be used to develop commercial products. The participants are compensated $15/hour for completing specimen visits.

The saliva testing results will not be disclosed to the participants or any non-affiliated UCSF researchers/collaborators; therefore, there will not be any direct consequences to the participant.

How long will I be in the study?

Phase I will be completed in lab across 1-3 sessions and take place prior to Phase II. Each session will not exceed 4 hours, and the total amount of time for this phase will not exceed 12 hours.

Phase II will take two to eight weeks of at-home or in lab training. There will be no more than 5 training sessions per week, with a per session training maximum of one and a half hours of at-home or two hours in-lab. The number of sessions will vary between 10 over 2 weeks and up to 40 over 8 weeks of training. Total at home training time will vary between 10-20 hours over 2 weeks up to a maximum of 60 hours over 8 weeks of training. In lab training will require between 10 visits over 2 weeks up to 40 visits over 8 weeks. Time for the in lab training sessions will vary from 10-20 hours over 2 weeks up to a maximum of 80 hours over 8 weeks.

Phase III will be completed in lab across 1-3 sessions and take place following the completion of Phase II. Each session will not exceed 4 hours, and the total amount of time for this phase will not exceed 12 hours.

Can I stop being in the study?

Yes. You can decide to stop at any time. Just tell the study researcher or staff person right away if you wish to stop being in the study.

Also, the study researcher may stop you from taking part in this study at any time if he or she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

• **Cognitive Tasks:** Depending on the nature of the cognitive tasks, mental fatigue or boredom are minor risks.

• **EEG:** All of the EEG procedures have been used extensively in previous research. We try to remove all of the electrode paste from your scalp, but some may remain. You can easily remove this extra paste by shampooing. The pictures/sounds used in the studies are presented at a comfortable lighting/hearing level. The button presses require minimal effort.

• **fMRI:** The levels of energy used to make fMRI measurements are far less than are used in a single X-ray, and many patients have been safely studied using MRI techniques. While there are no significant risks from fMRI as it is to be performed, the fMRI procedures can be risky for people with pacemakers or metal in their bodies. We will not ask you to participate in the fMRI if you have a pacemaker or any metal in your body that cannot be easily removed. Some people get claustrophobic in the MRI scanner. If you have a history of claustrophobia, we will not ask you to participate in the fMRI study. Because the fMRI scan makes loud noises, we will give you ear plugs to dampen the sound. You may also experience peripheral stimulation, which will feel like a gentle tap or sensation of mild electric shock. If you do not like being in the scanner for any reason, we will immediately stop the experiment.

• We do not know if the fMRI procedure is associated with risks to an unborn fetus. We ask that all women of child-bearing age take a pregnancy test before participating. This is an "over-the-counter" pregnancy test that identifies pregnancy through a urine sample. We will give you the test kit for you to take by yourself, in private, in the bathroom. If you are pregnant, please tell the experimenter that you cannot participate in the fMRI scan.

• **Saliva Sample Collection-Genetic Testing:** No adverse effects are associated with spitting into a container; however, some people might find it embarrassing to do so. Buccal cell sample collection might cause slight and transient discomfort due to the abrasiveness of the swab.

• **Saliva Sample Collection-Biological Stress Testing:** Swab sample collection might cause slight and transient discomfort due to the abrasiveness of the swab.

• **Physical Testing:** The physical testing and training will be physically demanding, and there is a risk that you will perspire, feel exhausted, feel out of breath, and potentially feel dizzy. At any point in the testing if you begin experiencing any physical effect that exceeds your comfort level, you will be asked to please let us know immediately and testing will be either paused or discontinued, which will be at the participant's discretion.

- **Blood Draw:** The risks of drawing blood and catheter insertion include temporary discomfort from the needle stick, localized bleeding and bruising, lightheadedness, and rarely, fainting or localized infection. A registered nurse or phlebotomist will do the blood draw in a sterile manner. Up to 200 mls of blood will be collected per visit, which amounts to around 14 tablespoons. To give you a sense of how much blood this is, it is a lot less than a typical blood donation, which is around 31 tablespoons.

- For more information about potential risks and side effects, ask one of the researchers.

Are there benefits to taking part in the study?

There will be no direct benefit to you from participating in this study. If you are currently undergoing medical treatment, these procedures will not benefit or adversely affect you. The test(s) we will perform on the saliva sample will not be shared with you, or anyone else, without exception.

At the end of the experiments, we will explain what we expect to learn from the study (with the exception of the saliva sample collection). We hope that this knowledge will be useful in the future diagnosis and treatment of neurological patients.

What other choices do I have if I do not take part in this study?

You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you.

Will information about me be kept private?

We will do our best to make sure that the personal information gathered for this study is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

The results of the genetic testing will remain confidential and will not be released to the participant. The samples and results will be protected using a de-identified code that is distinct from the database participant code. The link between codes will be kept in a password-protected spreadsheet.

Organizations that may look at and/or copy your research records for research, quality assurance, and data analysis include: UCSF's Committee on Human Research.

What are the costs of taking part in this study?

You will not be charged for any of the study procedures.

Will I be paid for taking part in this study?

In return for your time, effort and travel expenses, you will be compensated $15/hr for participating in the EEG, behavioral testing (both in the lab and for the home training), and saliva samples, and $20/hr for the fMRI testing. A check will be mailed to you about 6-8 weeks after you complete your participation in the study (thus requiring us to obtain your social security number).

Only select sections of this study are eligible to earn a 'completion bonus'. If your section of the study is eligible for a 'completion bonus', your experimenter will ask you to initial below.

Initials ☐ Eligible to earn a "completion bonus" of $50, if and only if ALL assigned tasks are completed during the study. If this bonus is earned, $50 will be added to your check at the end of the study.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Adam Gazzaley, M.D., Ph.D., if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at 415-476-2162.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, treatment will be available. The costs of the treatment may be covered by the University of California or the study sponsor, Robert Wood Johnson Foundation, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415-476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you in any way. You will not lose any of your regular benefits, and you can still get your care from our institution the way you usually do.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to the researcher(s) about any questions or concerns you have about this study. Contact Dr. Gazzaley or a member of his lab at 415-476-2164.

If you have any questions, comments, or concerns about taking part in this study, first talk to the researcher above. If for any reason you do not wish to do this, or you still have concerns after doing so, you may contact the office of the **Committee on Human Research**, UCSF's Institutional Review Board (a group of people who review the research to protect your rights).

You can reach the CHR office at **415-476-1814**, 8 am to 5 pm, Monday through Friday. Or you may write to: Committee on Human Research, Box 0962, University of California, San Francisco (UCSF), San Francisco, CA 94143.

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CONSENT

You have been offered a copy of this consent form to keep, in addition to the University of California, San Francisco Experimental Subjects Bill of Rights outlining the rights of every person who is asked to be in a research study.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to be in this study, or to withdraw from it at any point without penalty or loss of benefits to which you are otherwise entitled. If you wish to participate in this study, please sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent