UNIVERSITY OF CALIFORNIA LOS ANGELES
CONSENT TO PARTICIPATE IN RESEARCH

STUDY TITLE:

Brain connectivity and response to Tai Chi in geriatric depression

INTRODUCTION:

Helen Lavretsky, M.D., and associates from the Department of Psychiatry at the University of California, Los Angeles are conducting a research study. You have been asked to participate in this study because you are at least 60 years old and have reported that you are have experienced symptoms of depression and you are on a stable form of treatment for at least 4 (four) months. Approximately 220 subjects will participate in this study. This study will require that you make up to 17 (seventeen) visits in 12 (twelve) months to the study site during your participation and 12 weekly training sessions for 60 minutes.

The researchers will explain this study to you. **Research studies are voluntary and include only people who choose to take part.** Please take your time about deciding whether to participate in this study. Before deciding:

- You can discuss this study with friends and family.
- You can also discuss it with your health care doctor or request a second opinion.
- If you have any questions, you can ask the researchers for more information before deciding to participate.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to compare Tai Chi to health and wellness education with older adults experiencing symptoms of depression. We will conduct a randomized, controlled design for this 12-week pilot trial of the behavioral intervention of Tai Chi to health and wellness education training programs to cognitive performance in older subjects. We will investigate and compare cognitive functioning, performance, and mood in older subjects in the Tai Chi group and the health and wellness education group.

The purpose of the functional magnetic resonance imaging (fMRI) scan is to better understand depression. We will be performing 3 (three) fMRI scans. This study has 4 (four) parts:

1) The first part of the study is to measure your physical and mental condition.

2) In the second segment of the study, you will complete an fMRI scan which will take a picture of the brain structure. The pictures from the fMRI scan will help the investigators better understand the relationship between the structure and function of the brain and how it works. This will be done three times: once at baseline, once after 12 weeks of treatment, and once at the 12-month follow up visit.

3) You will complete follow-up visits and you will have 12 weekly 60 minute Tai Chi or health and wellness education classes.

4) You will complete a blood draw for genetic analysis. The purpose of this is to determine the role of genes that are involved in the mechanisms of stress and depression and its possible relationship to mood (depression) and treatment response. We will also explore changes in gene expression, immune system, and telomerase levels with treatment using special tests. This will be done three times: once at baseline, once after 12 weeks of treatment, and once at the 12-month visit.

The following definitions may help you understand how this research study is designed:

- Electrocardiogram (ECG) – electrical activity of your heart.
- Randomized/ randomization – assigned to a group by chance, like flipping a coin.
- Functional Magnetic Resonance Imaging (fMRI) Scan – a medical imaging technique used in radiology to visualize internal images of the body in detail.

This study is being funded by the National Institutes of Health.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Two hundred and twenty (220) people will take part in this study at UCLA.

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

Before you begin the study:

Screening Procedures and Initial Visits (Screening / Visit 1-3):

Before you begin the study, you will need to read and sign this consent form. You will have a general medical and psychiatric history taken, your vital signs (blood pressure, pulse) (5 minutes duration), and an ECG (electrocardiogram - a measure of the electrical activity of your heart) will be performed (25 minutes). Various questionnaires about your condition will be administered asking about your mood, daily functioning, and patterns of thinking and memory (2 hours). The questionnaires and screening procedures are performed to determine eligibility and are for research purposes. You must be on a form of stable treatment and we will determine that there are no changes in your depression for the first 12 weeks of the study.

Blood Samples. At this initial visit, blood will be drawn by needlestick from your arm for routine laboratory testing and genetic analysis (15 minutes). The blood samples will be processed at the UCLA Clinical and Translational Research Center (CTRC). Approximately 8 tablespoons of blood will be drawn. Venipuncture is a routine procedure used for obtaining blood samples by inserting a needle into a vein in the arm and withdrawing a small blood sample. Although one attempt at venipuncture is usually sufficient, additional attempts may be necessary if the first attempt proves unsuccessful.

These tests will also be done to ensure that you meet the medical requirements for participating in the study. A phlebotomist will perform blood drawing and measure your vital signs. A sample of 10ml of blood will be collected and it will be processed by the Core Laboratories of UCLA Department of Human Genetics. You are eligible for the genetic portion of the study if you are participating in the active intervention study.

The initial visit will last approximately 2 ½ to 3 hours.

<u>During the study</u>:

Diagnostic / Neuropsychological Evaluation Visit (Visit 2):

If you are eligible and take part in this study, during the second visit you will randomly assigned to weekly 60 minute sessions of Tai Chi training or health and wellness education training. Dr. Lavretsky or a member from the study staff will conduct a neuropsychiatric evaluation using questionnaires and cognitive assessments during the baseline visit.

Magnetic Resonance Imaging (MRI) Scan (Visit 3). You will be asked to have one MRI scan of your brain in the beginning of your treatment course. The procedure involves making brain images with magnetic fields and does not involve radiation, blood samples or injections. MRI scans use a large magnet to form a structural image of your brain. The scan will occur at the UCLA Brain Mapping Center. You will be asked to remove all metal from your body before the scan and lie still for about 60 minutes while the scan is taking place.

Follow-Up Visits (Visits 4-9 and 12-13):

Follow-up visits will occur weekly, bi-weekly (every 2 weeks), and then monthly in order to ensure your safety and to understand your response to the study procedures. Each visit will last approximately 30 minutes. You will be interviewed by the study doctor or the research study staff during all visits. Interviews and questionnaires will be used to determine if the treatment is working and useful. At each follow-up visit, your vital signs will be measured (5 minutes), your practice and homework log will be reviewed with you, and questionnaires will be administered (25 minutes). The follow-up visits will be scheduled around the time that you attend your training classes.

Weekly Tai Chi or Health and Wellness Education (12 classes):

Weekly Tai Chi or health and wellness education training will occur every week for 60 minutes for 12 weeks. The weekly sessions will last approximately 60 minutes per class.

Final follow-up visits (Visits 10-11 and 14-17):

During the final visit, a physical, psychiatric examination, and a follow-up blood draw for genetic analysis will be repeated. The follow-up visits 10-11 (at 3 months) and visits 14-17 (12 months) will be approximately 3 hours for all procedures. The follow-up visit 13 (at 6 months) will be approximately 2 hours long. The study doctors will be responsible for doing the physical and psychiatric examinations. (Please see the Summary Table in the end of the consent). All screening and follow-up procedures are done for research purposes.

In the event that you tell the research staff that you are thinking about killing yourself or you answer "yes" to a question about the thoughts of suicide, the investigator will ask you more questions about those thoughts. Depending on how intense your thoughts are or how much you feel like hurting yourself, the research staff may provide you with referrals for treatment, work with you to contact your personal physician, trusted family member, or therapist to discuss your thoughts of harming yourself; or work with you on a plan that may include getting you to a hospital for safety.

Management of Insomnia:
If you experience insomnia or anxiety in the course of the study, the investigator may recommend behavioral relaxation techniques such as walks in the evening, or warm bath.

We may discover undiagnosed mental and medical conditions in the process of the study, and we will ask for your permission to report the results of your examination to your primary physician or psychiatrist.

Monitoring of Alcohol Use:
At each visit you will be asked questions about your alcohol use. It is recommended that you do not drink alcohol while participating in the study because it may lead to impaired attention and judgment, which may be detrimental if you are operating machinery or driving.

HOW LONG WILL I BE IN THIS STUDY?

This study will last up to 12 months. The screening visits (1-2) may take up to 4 hours altogether, and the baseline visit (3) will be approximately 30 minutes. All follow-up visits during the classes will last 30 minutes. The 12 week follow-up visits will last approximately 3 hours, the 6 month follow-up will last 2 hours, and the 12-month follow-up visit will last approximately 3 hours. The weekly wellness training classes (60 minutes) will occur once a week for 12 weeks.

WHAT KINDS OF RISKS OR DISCOMFORTS COULD I EXPECT?

Known risks and discomforts:
The possible risks and/or discomforts associated with the procedures described in this consent form include: This research study may involve risks that are currently unforeseeable. Other side effects of significant concern include increased irritability, agitation, or restlessness. Please, contact the study team immediately if you notice any of these symptoms or have any concerns.
Blood drawing may produce pain, infection, bruising, swelling at the site and rarely fainting.

Risks Associated with Loss of Privacy in Genomic Research:
While the controlled-access databases developed for this project will contain information that is traditionally used to identify you, such as your name, address, telephone number, or social security number, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For

example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you.

As part of the study, your samples will be subjected to whole genome or exome sequencing, techniques that allow to read and decode each letter of your DNA that makes you who you are. This means that people who have access to your personal sequence will be able to know the color of your eyes, hair as well as whether you are susceptible to certain type of medical conditions. The information generated through the study may also be relevant to close family members such as your parents or siblings that could share some of those unique sequences. Because the data can be stored and used indefinitely, there is the possibility that your privacy or that of close family members may be affected.

Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her blood relatives. Therefore, your genetic information could potentially be used in ways that could cause you or your family distress, such as by revealing that you (or a blood relative) carry a genetic disease. There also may be other privacy risks that we have not foreseen.

Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record.

In the event of an unexpected breach of confidentiality, a federal law called the Genetic Information Non-Discrimination Act (GINA) will help protect you from health data breach. In general, this law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Potential Risks and Discomforts with MRI:

There are no known risks to you from psychological testing or interviewing; however, you may get tired or feel nervous if questions are asked that you cannot or wish not to answer. If this occurs, you will be allowed to take a break or ask questions. Under no circumstances will you be pressured to respond.

The MRI scanning procedure requires that you be lying in a small, partially-enclosed space. Some people find this to be uncomfortable and may feel symptoms of claustrophobia including nervousness, sweating or other minor discomfort. You will be provided with a special ball (or button) to squeeze should you become anxious or agitated during the MRI session. Squeezing the ball will set off an alarm bell and the MRI scan will be immediately discontinued. The sound of the MRI scanner can be quite

loud; you will be given special earplugs and/or headphones to minimize the noise. The magnetism of the machine attracts certain metals; therefore, people with these metals in their bodies (such as pacemakers, infusion pumps, aneurysm clips, metal prostheses, joints, rods, or plates) will be excluded from the study. The metal in most dental fillings is less responsive to magnetism and is therefore allowed. You will be asked to fill out a metal screening form before you can undergo an MRI scan in order to notify the investigator conducting the study of any metal in your body, other than dental fillings. There are no other known side effects resulting from exposure to the MRI scan. In the studies performed so far, there have been no significant risks reported in animals or humans for similar exposures. However, the potential risks to a fetus are unknown. Thus, if you are pregnant, or you think you may be pregnant, you should not participate in this study.

Unknown risks and discomforts:
The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

If you notice a negative change in your condition, notify your study doctor at (310) 825-0511 for 24 hours a day, 7 days a week. It is also important that you discuss with your study doctor or the research study staff all unpleasant or unusual symptoms that you may experience. Any positive effects that are experienced should be discussed as well.

ARE THERE ANY BENEFITS IF I PARTICIPATE?

Possible benefits to me:
You may not experience any benefit from participating in this study. The possible benefits you may experience from being in this study may include an evaluation of symptoms, general health discussions with the study doctor and help in referrals for additional treatment if needed.

Possible benefits to others or society:
There will be no direct benefit to you from participating in this study. This study will help the researchers learn more about the study procedures such as Tai Chi Chih and health and wellness education that may help improve knowledge of a more effective treatment for depression in the elderly. Hopefully this information will help in the treatment of future patients with depressive symptoms like yours. There are potential benefits for both the subjects and broader segments of society. Volunteers often express great satisfaction from knowing they have been able to make a personal contribution to the advancement of human understanding and to the search for solutions to health problems -- either their own or others'. For society, the increased understanding gained through this study may provide further information about biomarkers for depression, and may eventually benefit many older adults.

WHAT OTHER CHOICES DO I HAVE IF I DON'T WANT TO PARTICIPATE?

If you decide not to take part in this study, or if you withdraw from this study before it is completed, there may be alternative procedures or courses of treatment are available.

One alternative is not to participate. Other alternative therapies are available to treat your condition. The alternative options include psychotherapy, cognitive behavioral therapy, and other methods like exercise. You may choose to be treated with one or more of these rather than participate in the study. You may choose to receive these therapies at any point during the study, and if you do, your participation in the study will be discontinued. If you have questions about alternative therapy, ask your study doctor for additional information.

CAN THE RESEARCHERS REMOVE ME FROM THIS STUDY?

The researchers may end your participation in this study for a number of reasons, such as if your safety and welfare are at risk, if you do not follow instructions or if you miss scheduled visits. The researchers or the study sponsor might also decide to stop the study at any time.

If you decide to stop being in the study, are removed from the study, or the study is stopped, the researcher will ask you to withdraw from participating in this research if circumstances arise which warrant doing so. If you experience any of the following side effects like chest pain, aggravated hypertension with blood pressure above 160/90 mm Hg on two consecutive appointments, exhibit changes or have an abnormal reading on your ECG; develop any severe side-effects, or if you become ill during the research, you may have to drop out, even if you would like to continue. The investigator, Helen Lavretsky, M.D., M.S., will make the decision and let you know if it is not possible for you to continue. The decision may be made either to protect your health and safety, or because it is part of the research plan that people who develop certain conditions may not continue to participate. The PI will ask you to discontinue the study treatment if you demonstrate worsening symptoms in your depression and you will be referred for clinical care at UCLA or the community. The PI will continue be in contact for safety until the appointment is scheduled with your primary psychiatrist.

If you must drop out because the investigator asks you to (rather than because you have decided on your own to withdraw), you will be paid $10.00 per visit.

The data collected about you up to the point of withdrawal will remain part of the study and may not be removed from the study database.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT CONFIDENTIAL?

The only people who will know that you are a research subject are members of the research team. No information about you, or provided by you during the research, will be disclosed to others without your written permission except:

- if necessary to protect your rights or welfare (example, if you are injured and need emergency care); or
- if required by law

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

The researchers will do their best to make sure that your private information is kept confidential. Information about you will be handled as confidentially as possible, but participating in research may involve a loss of privacy and the potential for a breach in confidentiality. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security.

Use of personal information that can identify you:
After you provide identifying information, the research coordinator will assign a number code to track the questionnaires and interview materials. We will be removing identifying information from all data during the data analysis phase of the project and removing identifying information from all data presented publicly in lectures, seminars, or publications.

How information about you will be stored:
All files will be kept in locked cabinets, as will copies of the signed informed consent forms, to maintain the anonymity of participants and to bar any unauthorized access. The computerized database will be protected through the use of entry codes available only to authorized personnel.

People and agencies that will have access to your information:
Under California law, the privilege of confidentiality does not extend to information about sexual or physical abuse of a child/elderly/dependent adult. Although all private information will be kept confidential and will not be discussed outside of the research group, investigators are obligated by law to report a suspected or known sexual and physical abuse of a child or an elderly person, or a subject's threatened violence to self or others. If any member of the program staff has or is given such information, they will be obligated by law to report it to the appropriate authorities.

The research team and authorized UCLA personnel, the study sponsor, National Institutes of Health (NIH), and regulatory agencies such as the Food and Drug Administration (FDA), may have access to study data and records to monitor the study. Research records provided to authorized, non-UCLA personnel will not contain identifiable information about you. Publications and/or presentations that result from this study will not identify you by name.

Genetic information in your sample and possible limits to individual confidentiality:
Every tissue or fluid sample contains genetic information. Recent studies have found normal and disease producing genetic variations among individuals. Such variations may permit identification of individual participants. Despite this possible limitation, every precaution will be taken to maintain your confidentiality now and in the future.

We have learned from past research that we will not always be able to predict future research findings and new technologies. You should be aware that unforeseeable

problems might arise from new developments. Possible problems include insurance or employment discrimination based on genetic information. Sometimes genetic information suggesting different parentage is obtained during research. We do not plan to report such findings to participants. Within the limits imposed by technology and the law, every effort will be made to maintain the privacy of your genetic information.

Your specimen and information about you are protected by a federal Certificate of Confidentiality. This means that we can't be forced to release your specimen or information about you for any legal proceeding, even if a court of law asks.

The Certificate allows us to use your specimen and information about you for purposes of this research, or to disclose it for other research when allowed by law. The Certificate requires other researchers to also protect specimens and information we share with them.

There are limits to this protection. The Certificate does not protect your information when:

- You or your family voluntarily release information about yourselves.
- You consent to release of information (for example, the uses described in this form, or if you sign release forms for employment, insurance or medical care).
- A federal agency audits or evaluates research that it funds.
- [Researchers [intend/are required] to report possible intent to harm yourself or others, child abuse, elder abuse, or infectious disease cases.
- The Food & Drug Administration requires information as part of overseeing drugs, devices or other products.

How information about you may be used for future research

We would like to use de-identified data from this study for other future research projects studying mental health. If you agree, this would mean that your data will be used for studies going on right now as well as studies that are conducted 10 or 20 years from now.

We would also like your permission to share your de-identified sample and results with investigators at the other research centers, doing research in mental health. It is possible that other investigators conducting other research might request that de-identified data collected for this study be shared for further research. For example, investigators associated with the government agency supporting this study might make this request. Even if you agree that your de-identified data may be shared with other investigators, your name or other personal identifying information would not be revealed. Your information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative.

ARE THERE ANY COSTS FOR TAKING PART IN THIS STUDY?

The study sponsor will supply and pay for the cost of supplying and administering the extra related laboratory tests. Neither you nor your insurance company will be billed

for your participation in this research. Research procedures that will be covered include all procedures required by the protocol to be performed during the study visits (i.e., ECGs, laboratory examination, physical and psychiatric examination, training costs). All the study materials and associated charges will be covered free of charge for the duration of the study. You will be responsible for costs associated with seeing your primary care physician (co-pay, etc.).

WILL I BE PAID FOR MY PARTICIPATION?

You will receive a payment of $100.00 honorarium for your participation in the 12-week trial, which will also help to cover travel costs. Those participating in baseline and 12-week fMRI scans will be reimbursed at $50.00 per scan up to a total of one hundred dollars ($100). Those participating in the 6-month follow up will receive $100.00, and those who complete the 12-month follow-up including a final fMRI scan will receive $150. Thus, if you participate in all portions of the study you will receive $450. If you participate in all portions of the study except the brain scans, you will be followed for 6 months only and receive $200. You will incur no financial obligations.

You will be reimbursed for out of pocket expenses for parking. We will offer reimbursement of $12.00 per visit for up to $204.00.

You will be asked for your Social Security number for the purposes of payment. UCLA employees other than the study team may know that you are participating in a research study, but this information will only be for specific reasons such as making payments and they will not know specific details of the study. Information such as the study title, the nature of the research or the names of procedures undergone will not be indicated in the check request. This information will be protected and stored in a locked cabinet and shredded as soon as payment has been received. If you received more than $600 from UCLA in the course of a year, UCLA must report such income to the Internal Revenue Service.

WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

The Research Team:

Principal Investigator: Helen Lavretsky, M. D.
760 Westwood Plaza, UCLA NPI
Los Angeles, CA 90095
(310) 794-4619

You may contact Helen Lavretsky, M.D. at (310) 794-4619 with any questions or concerns about the research or your participation in this study. You can also call the UCLA Page Operator at (310) 825-6301 to reach Helen Lavretsky, M.D. 24 hours a day, 7 days week.

UCLA Office of the Human Research Protection Program (OHRPP):

If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, you may contact the UCLA OHRPP by phone: (310) 825-5344; by email: Box 951694, Los Angeles, CA 90095-1694.

Public Information about this Study:
ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. 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.

WHAT HAPPENS IF I BELIEVE I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number(s) listed above.

If you are injured as a result of being in this study, UCLA will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or the study sponsor Alzheimer's research and Prevention Foundation, or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call the UCLA Office of the Human Research Protection Program at 310-825-5344 or send an email to mirb@research.ucla.edu.

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You can choose whether or not you want to participate. Whatever decision you make, there will be no penalty to you and you will not lose any of your regular benefits.

- You have a right to have all of your questions answered before deciding whether to take part.
- Your decision will not affect the medical care you receive from UCLA.
- If you decide to take part, you can leave the study at any time.
- If you decide to stop being in this study you should notify the research team right away.
- The researchers may ask you to complete some procedures in order to protect your safety.
- If you decide not to take part, you can still get medical care from UCLA.

HOW DO I INDIC ATE MY AGR EEMENT TO PARTICIPATE?

If you agree to participate in this study you should sign and date below. You have been given a copy of this consent form and the Research Participant's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

SIGNATURE OF THE PARTICIPANT

_____
Name of Participant

_____ _____
Signature of Participant Date

Please check the appropriate boxes below and initial:

☐ _____ I agree to have MRI scans.

☐ _____ I do not agree to have MRI scans.

☐ _____ I agree to provide blood samples for genetic analysis.

☐ _____ I do not agree to provide blood samples for genetic analysis.

SIGN ATURE OF PERSON OBTAINING CONSENT

_____ _____
Name of Person Obtaining Consent Contact Number

_____ _____
Signature of Person Obtaining Consent Date

Table 1. The assessment schedule:

Week	**Screen**	**Baseline**	**2**	**4**	**6**	**8**	**10**	**12**	**16**	**20**	**24**	**1-Year**
Visits	1-2	3	4	5	6	7	8	9-10	11	12	13	14-15
Time	4 hrs	30 min	30 min	30 min	30 min	30 min	30 min	3 hrs	30 min	30 min	2 hrs	3 hrs
Assessment	X	X	X	X	X	X	X	X	X	X	X	X
Informed Consent	X											
History	X											
Physical Exam	X							X			X	X
Blood Draw	X							X				X
fMRI	X							X				X
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X
SCID – I/P	X											
Rating Scales	X	X						X			X	X

Table 2. The Tai Chi Chih and Health Education and Wellness schedule:

Week	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
60 min training	X	X	X	X	X	X	X	X	X	X	X	X