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TITLE: MOTION: MOTION: Moving Online Together Investigation of Neurocognition

PRINCIPAL INVESTIGATOR: Linda Chao

**RECIPIENT: Northern California Institute for Research and Education (NCIRE)
San Francisco, CA**

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14. ABSTRACT The goal of this study is to examine a novel, integrative mind-body movement program, Preventing Loss of Independence through Exercise (PLIÉ), with Tai Chi for the ability to improve cognition and enhance brain connectivity in people with mild cognitive impairment (MCI) and subjective memory decline (SMD). The two mind-body interventions will also be compared with an active control, Health and Wellness Education (HWE) in a randomized controlled trial (RCT). Aim 1 will evaluate the effects of PLIÉ and Tai Chi versus HWE, all delivered remotely via tele-health techniques, on the Alzheimer's Disease Assessment Scale - cognitive subscale (ADAS-cog). Aim 2 will evaluate the effects of the three interventions on default mode network (DMN) functional connectivity. Aim 3 will explore the association between changes in functional connectivity with changes in cognition.					
15. SUBJECT TERMS Exercise, mind-body, Alzheimer's disease, mild cognitive impairment, neuroimaging.					
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1. INTRODUCTION:

The goal of this study is to examine a novel, integrative mind-body movement program, Preventing Loss of Independence through Exercise (PLIÉ), with Tai Chi for the ability to improve cognition and enhance brain connectivity in people with mild cognitive impairment (MCI) and subjective memory decline (SMD). The two mind-body interventions will also be compared with an active control, Health and Wellness Education (HWE) in a randomized controlled trial (RCT). Aim 1 will evaluate the effects of PLIÉ and Tai Chi versus HWE, all delivered remotely via tele-health techniques, on the Alzheimer’s Disease Assessment Scale - cognitive subscale (ADAS-cog). Aim 2 will evaluate the effects of the three interventions on default mode network (DMN) functional connectivity. Aim 3 will explore the association between changes in functional connectivity with changes in cognition.

2. KEYWORDS:

Exercise, mind-body Alzheimer’s disease, other dementias, mild cognitive impairment, subjective memory decline, quality of life, neuroimaging.

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Major Task/Milestone	Timeline	Date Completed
Major Task 1: Prepare regulatory documents and research protocol		
<i>Milestone: Local IRB approval at UCSF/SFVAHCS and UCLA</i>	Mos. 1-3	08/09/2021
<i>Milestone: HRPO approval for all protocols</i>	Mos. 1-6	11/12/2021
Major Task 2: Train and coordinate staff across sites		
<i>Milestone: Research staff trained and calibrated</i>	Mos. 3-6	11/30/2021
Subtask: Develop study database and data collection forms	Mos. 4-6	9/30/2021
Major Task 3: Train and coordinate staff across sites		
<i>Milestone: Harmonized neuroimaging measures</i>	Mos. 6-7	4/20/2022
<i>Milestone: Harmonized mind-body interventions and developed HWE control</i>	Mo. 6	2/28/2022
Subtask: Train Tai-Chi instructor on TSH platform	Mo. 7	Feb. 2022
Major Task 4: Participant Recruitment		
Subtask: Initiate and maintain recruitment through clinicaltrials.gov, Alzheimer’s Association TrialMatch; UCSF and UCLA sites/resources	Mos. 6-20	began 1/31/2022
Subtask: Perform VINCI data pulls of veterans in CA with MCI and send recruitment letters	Mos. 6-20	12/06/2021
<i>Milestone: 1st participant consented, screened and enrolled</i>	Mo. 7	2/23/2022
Major Task 5: Assessment & Intervention of Study Cohorts		
Subtask: Obtain baseline behavioral and imaging data	Mos. 7-8 (cohort 1)	5/3/2022 - 6/28/2022
Subtask: Deliver study intervention to study participants	Mos. 9-12 (cohort 1)	Started on 6/28/2022

What was accomplished under these goals?

Major activities:

1. Obtained local IRB and HRPO approval for protocols (November 2021)
2. Hired, trained, and coordinated study staff across UCLA and SFVA/NCIRE sites (November, 2021)
3. Developed study database and data collection forms (August, 2021)
 - a. Screening:
 - a. Brief SCID for DSM5
 - b. Montreal Cognitive Assessment (MoCA)
 - b. Baseline, 3-, and 6-month behavioral assessments:
 - a. ADAS-cog
 - b. Dual Walking-task
 - c. Timed Up and Go
 - d. Trail Making Test
 - e. RBANS stories and symbols tests
 - f. D-KEFS Color-Word Interference Test
 - g. FAS word fluency
 - c. Baseline, 3-, and 6-month self-report assessments:
 - a. Neuro QOL Well being
 - b. Neuro QOL lower extremity function
 - c. Neuro QOL Emotional and Behavioral Dyscontrol
 - d. Neuro QOL Cognitive Function
 - e. Freiburg Mindfulness Index
 - f. PROMIS29
 - g. PROMIS Social Isolation
 - h. Body Experience Questionnaire - subset
 - i. Multidimensional Assessment of Interoceptive Awareness - subset
4. Harmonized Neuroimaging Measures for the SFVA Siemens Skyra and the UCLA Brain Mapping Center Prisma scanners (April, 2022)
 - a. T1-structural, ABCD MPR (voxel size: 1x1x1)
 - b. T2-structural, ABC SPC (voxel size: 1x1x1)
 - c. Resting state fMRI (voxel size: 2x2x2)
 - d. Diffusion tensor imaging (voxel size: 1.7x1.7x1.7)
 - e. Pseudocontinuous arterial spin labeling perfusion (PCASL, voxel size: 2.5x2.5x2.3)
5. Harmonized study interventions (February, 2022)
 - a. 2 hour-long classes per week for 12 weeks
 - b. Moving Together and Tai Chi classes live-streamed, initially over Together Senior Health (TSH)'s platform, later switched to Zoom
 - c. Health and Wellness Education (HWE) active control consists of videos of lectures from UC professors about various health topics, delivered over EdPuzzle platform
6. Initiated recruitment (December, 2021, first participant enrolled in February, 2022)
 - a. **121** screen completions out of 372 sign-ups/contacts
 - i. 42 Male/79 Female
 - ii. Mean age: 73.1 ± 8.0
 - iii. Mean education: 17.1 ± 8.0
 - iv. 42 with formal MCI diagnosis, 75 with subjective memory decline
 - b. **60** follow-up screens with MoCA and brief SCID
 - i. 24 Male/36 Female
 - ii. Mean age: 73.3 ± 7.4
 - iii. Mean education: 16.9 ± 2.2
 - iv. 20 with formal MCI diagnosis, 37 with subjective memory decline
 - v. Mean MoCA scores: 25.1 ± 2.9
 - vi. **40/60** had eligible MoCA scores (≤ 26 , >17)

Major activities (cont):

- c. Randomized **19** subjects in Cohort 1 to intervention
 - i. 7 to Moving Together (PLIE); 6 to Tai Chi; 6 to Health and Wellness Education (HWE)
 - ii. 6 Male/13 Female
 - iii. Mean age: 72.7 ± 8.8
 - iv. Mean education: 17.4 ± 2.1
 - v. 10 with formal MCI diagnosis, 9 with subjective memory decline
 - vi. Mean Baseline ADAS-cog score: 12.2 ± 7.3
 - vii. Mean MoCA: 23.2 ± 2.6

What opportunities for training and professional development has the project provided?

Nothing to report.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

- Continue to enroll and recruit participants with MCI and SMD for trial at SF and UCLA sites
- Continue to obtain behavioral/cognitive/imaging data from participants and deliver PLIE, Tai Chi, and Health and Wellness intervention on-line
- Obtain 6-month follow-up data from first cohort participants.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them

We moved delivery of the Tai Chi intervention from Together Senior Health (TSH) platform to UCSF Zoom because the Tai Chi instructor and most of the study participants were more familiar and comfortable with Zoom and because of some intermittent sound issues with the TSH platform. Later, the sound issues on the TSH platform prompted us to move the Moving Together intervention to Zoom as well

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

There are no significant deviations or changes in approved protocols for the use of human subjects. The current IRB approval dates are:
MOTION: Moving Online Together Investigation of Neurocognition (PI: Linda Chao); University of California San Francisco IRB. The protocol was approved on 07/29/2021; the current expiration date is: 06/15/2023.

Protocol [HRPO Assigned Number]: E02185, approved 11/12/2021

Significant changes in use or care of vertebrate animals.

N/A

Significant changes in use of biohazards and/or select agents

N/A

6. PRODUCTS:

- **Publications, conference papers, and presentations**
- **Journal publications.**

Nothing to report.

Books or other non-periodical, one-time publications.

Nothing to report.

Other publications, conference papers, and presentations.

Nothing to report.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

A 12-week, 24 session Health and Wellness Education curriculum was developed under this project.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Linda Chao
Project Role: PI
Researcher Identifier: 0000-0002-8593-2434 (eRA Commons: lindachao)
Nearest person month worked: 0.96 calendar months
Contribution to Project: Dr. Chao has supervised general aspects of the project and worked closely with the study co-investigators to ensure the successful coordination of all aspects of project, from study procedures, data collection, to data quality control. She holds bi-monthly meetings with the co-investigators and weekly meetings with the intervention team to discuss the study's progress, technical and scientific issues, and subject flow issues.

Name: Gary Tarasovsky
Project Role: Database Manager
Researcher Identifier: N/A
Nearest person month worked: 1.2 calendar months
Contribution to Project: Mr. Tarasovsky has constructed a web-based data collection and management system for the MOTION study, and a centralized database that accommodates both direct data entry and electronic upload of summary files from the San Francisco and UCLA study sites. Mr. Tarasovsky has been managing the study database system, performing daily maintenance, including log analysis, performance tuning, and backup. Mr. Tarasovsky has also submitted data requests to the VHA's Corporate Data Warehouse and VA Informatics and Computing Infrastructure to identify veterans at the San Francisco and Greater Los Angeles VA who have a diagnosis of MCI in support of subject recruitment efforts.

Name: Sarah Slain
Project Role: San Francisco Study Coordinator
Researcher Identifier: N/A
Nearest person month worked: 8.8 calendar months
Contribution to Project: Ms. Slain has been responsible for recruitment, screening, and data base entry for Northern California subjects for the MOTION study. She has collected demographic information, schedule the different procedures and tests, and has been responsible for reimbursement of study participants.

Name: Courtney Sheen
Project Role: San Francisco Study Coordinator
Researcher Identifier: N/A
Nearest person month worked: 9 calendar months
Contribution to Project: Ms. Sheen has been responsible for recruitment, screening, and data base entry for Southern California subjects for the MOTION study. She has collected demographic information, schedule the different procedures and tests, and has been responsible for reimbursement of study participants.

Name:	Riya Jacob
Project Role:	Research Assistant
Researcher Identifier:	N/A
Nearest person month worked:	1.5 calendar months
Contribution to Project:	Ms. Jacob was responsible for assisting Ms. Slain and Ms. Sheen with recruitment, screening, and data base entry for MOTION subjects for the MOTION study for both sites. She collected demographic information, scheduled procedures and tests, and helped reimburse MOTION study participants.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Name: Linda Chao

- Changes:
1. Dr. Chao was awarded a VA Research Career Scientist award (K6CX002552-05) on 04/01/2022. This award supports 100% of Dr. Chao's VA FTE.
 2. Dr. Chao's SF VA appointment has increased from 7/8th to 8/8th
 3. Dr. Chao's UCSF and the San Francisco VA has increased from 26.5% FTE to 50% FTE. Her combined UCSF and SFVA effort is now 150%.
 3. Dr. Chao's effort on VA Merit award "An Investigation of the Relationship between Toxicant Exposures during Gulf War Deployment and Prodromal Parkinson's Disease" (2I01CX00079805) has been decreased to "as needed."
 4. Dr. Chao is now PI of VA Merit award "Preventing Loss of Independence through Exercise in Community Living Centers (PLIE-CLC)" (1I01HX002764). Her effort on this project as "as needed."
 5. DOD/CDMRP/PRARP grant "Using Multimodal Imaging to Examine the Neural Mechanism of an Integrative Exercise Program in Individuals with Mild Cognitive Impairment" has ended.
 6. DOD/CDMRP/GWIRP grant "Examination of plasma PON1 paroxonase activity and genotype in Gulf War Veterans" has ended.
 7. DOD/CDMRP/GWIRP grant "Incidence of Mild Cognitive Impairment in Gulf War Veterans" has been awarded. Dr. Chao is PI at 1.2 calendar months.
 8. DOD/CDMRP/GWIRP grant "Pilot Test of Apnea and Insomnia Relief for Veterans with Gulf War Illness" has been awarded. Dr. Chao is PI at 1.2 calendar months.
 9. DOD/CDMRP/GWIRP grant "Generational and Family Health in Veterans with Gulf War Illness; Address Longstanding Questions about Effects of Gulf War Service on Birth Outcomes, Reproductive Health, and Health Conditions Affecting Veterans' Spouses and Children" has been awarded. Dr. Chao is co-investigator at 0.3 calendar months.
 10. DOD/CDMRP/GWIRP grant "Enrichment of Data Collection for the Boston Biorepository and Integrative Network for GWI: The Non-Exclusionary Wave (NEW BBRAIN) Cohort" has been awarded. Dr. Chao is co-investigator at 0.3 calendar months.

Name: Helen Lavretsky

- Changes:
1. NIH/NICIH grant "Mentoring and Research in Translational Neuroscience of Integrative Medicine" has ended.
 2. NIH/NICIH grant "Brain Connectivity and Response to Tai Chi in Geriatric Depression" has ended.

Name: Helen Lavretsky
Changes: 3. NIH/NIA and NIH/NIMH Administrative supplements to address prevention of cognitive decline have ended.
4. NIH/PCORI grant “Optimizing Outcomes in Treatment Resistant Late Life Depression Investigates treatment strategies in geriatric depression” has ended.
5. Alzheimer’s Research and Prevention Foundation grant “Reducing Risk for Alzheimer’s Disease in High-Risk Women through Yogic Meditation Training” has ended.
6. NIH/NIAMS grant “Genetic factors of bone loss in older adults taking antidepressants” has ended.
7. NIH/NCCIH grant “Mind-Body Intervention to reduce symptoms among people aging with HIV” has ended.

Name: Cynthia Benjamin
Changes: 1. NIH/NIA grant “Brain Health Together: A Livestreaming Group-Based Digital Program” has been awarded. Ms. Benjamin is co-PI contributing 3.6 calendar months.
2. NIH/NIA grant “Extending Independence and Quality of Life for People with Alzheimer’s disease or dementia through Telehealth Program Delivery” has been awarded. Ms. Benjamin is co-PI contributing 2.0 calendar months.

Name: Deborah Barnes
Changes: 1. Dr. Barnes previously had a joint appointment with the University of California, San Francisco (UCSF) and the San Francisco VA (SFVA) Health Care System. Effective 4/1/2022, Dr. Barnes separated from SFVA and is currently 100% UCSF.
2. Effort on VA grant 1I01HX002764 has been reduced to 0 calendar months. This grant has been transferred to Dr. Linda Chao.
3. Effort on VA grant 5I01RX002946 has been reduced to 0 calendar months.
4. Effort on VA grant 5I01CX001761 has been reduced to 0 calendar months.
5. Effort on VA grant 1I01CX002096 is pending transition from VA salary to VA contract. Effort will be reduced from 1.2 calendar months to 0.8 calendar months.
6. NIH/NIA grant “Multi-domain Alzheimer’s Risk Reduction Study” has ended.
7. DOD/CDMRP/PRARP grant “Using Multimodal Imaging to Examine the Neural Mechanisms of an Integrative Exercise Program for Individuals with Mild Cognitive Impairment” has ended.
8. Effort on NIH/NIA grant “Prognostic calculators for patients with Alzheimer’s disease and related dementias” has been reduced from 1.2 calendar months to 0.4 calendar months.
9. Effort on NIH/NIA “AD/ADRD Health Care Systems Research Collaboratory” has increased from 1.2 calendar months to 1.4 calendar months.
10. California Department of Public Health grant “Identifying Key Modifiable Risk Factors for Alzheimer’s Disease in California” has ended.
11. NIH/NIA grant “Brain Health Together: A Livestreaming Group-Based Digital Program” has been awarded. Dr. Barnes is co-PI contributing 2.4 calendar months.
12. NIH/NIA grant “Identifying and supporting patients with undiagnosed dementia using the HER Risk of Alzheimer’s and Dementia Assessment Rule (eRADAR): a pilot clinical trial” has been awarded. Dr. Barnes is co-PI contributing 3.0 calendar months.

Name: Deborah Barnes

Changes: 13. NIH/NIA grant “Multidomain Alzheimer’s Risk Reduction Study (MARRS) Pilot” has been funded. Dr. Barnes is a co-investigator contributing 1.2 calendar months.
14. Dr. Barnes is contributing 0.4 calendar months as a co-investigator on NIH/NIA grant “Prognostic calculators for patients with Alzheimer’s disease and related dementias.”
15. NIH/NIA grant “Extending Independence and Quality of Life for People with Alzheimer’s disease or dementia through Telehealth Program Delivery” has been awarded. Dr. Barnes is co-PI contributing 1.2 calendar months.

Name: Margaret Chesney

Changes: 1. VA grant “Improving Mind/Body Health with Integrative Exercise” has ended.
2. DOD/CDMRP/PRARP grant “Using Multimodal Imaging to Examine the Neural Mechanisms of an Integrative Exercise Program for Individuals with Mild Cognitive Impairment” has ended.
3. NIH/NIA grant “Extending Independence and Quality of Life for People with Alzheimer’s disease or dementia through Telehealth Program Delivery” has been awarded. Dr. Chesney is co-investigator contributing 0.36 calendar months.

Name: Wolf Mehling

Changes: 1. Effort on NIH/NIAMS grant “UCSF Core Center for Patient-centric Mechanistic Phenotyping in Chronic Low Back Pain (UCSF REACH)” has increased from 1.8 calendar months to 3.0 calendar months.
2. DOD/CDMRP/PRARP grant “Using Multimodal Imaging to Examine the Neural Mechanisms of an Integrative Exercise Program for Individuals with Mild Cognitive Impairment” has ended.
3. NIH/NIA grant “Extending Independence and Quality of Life for People with Alzheimer’s Disease or Dementia Through Telehealth Program Delivery” has been awarded. Dr. Mehling is co-investigator at 0.6 calendar months.
4. NIH/NCCIH grant “Feasibility Clinical Trial of Integrated Mind-Body Therapy for Chronic Low Back Pain” has been awarded. Dr. Mehling is co-PI at 2.4 calendar months.

Name: An Vu

Changes: 1. VA grant (CX002322) “Neural and cognitive consequences of COVID-19 survival” has been awarded. Dr. Vu is co-investigator at 0.24 calendar months. His salary support and effort is contained within is VA physicist duties.
2. VA grant (CX001973) “Neurofunctional differences in cognitive and behavioral impulsivity in veterans with PTSD” has been awarded. Dr. Vu is co-investigator devoting effort “as needed” to the project. His salary support and effort is contained within is VA physicist duties.
3. Effort on NIH R01 EB028670 grant “Breaking the Barriers to Microscale fMRI” was reduced from 2.30 calendar months to 2.04 calendar months.
4. UCSF Resource Evaluation and Allocation Committee grant “Evaluation of spin-echo based gSLIDER for sub-millimeter, mesoscale fMRI at 3T” has been granted a no-cost extension. The new end date is 12/31/2022.
5. Effort on NIH-NIAMS grant (U19AR075737) “UCSF Core Center for Patient-centric Mechanistic Phenotyping in Chronic Low Back Pain (UCSF REACH)” has been increased from 0.54 calendar months to 1.78 calendar months.

Name:

An Vu

6. NIH-NIMH grant “Highly Accelerated Simultaneous Multi-Slice Phase Contrast MRI.” ended on 7/31/2020.

7. DOD grant “TBI Endpoints Development (TED)” ended on 9/29/2020.

8. Marcus Program in Precision Medicine Innovation grant “The Neural Basis of Approach Bias Modification in Opioid Users with Chronic Pain” has been awarded. Dr. Vu is co-investigator at 0.9 calendar months without compensation.

9. NIH/NIMH grant (R21MH12749) “Can neural network instability in schizophrenia be improved with a very low carbohydrate ketogenic diet?” has been awarded. Dr. Vu is co-investigator at 0.24 calendar months.

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS: N/A

9. APPENDICES:

N/A