

**AWARD NUMBER: W81XWH-17-1-0490**

**TITLE:** Using Multimodal Imaging to Examine the Neural Mechanisms of an Integrative Exercise Program for Individuals with Dementia

**PRINCIPAL INVESTIGATOR: Linda Chao**

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**PREPARED FOR: U.S. Army Medical Research and Materiel Command**  
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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> The goal of this project is to investigate whether participation in the Preventing Loss of Independence through Exercise (PLIÉ) program for 4 months will result in neurobiological changes that improve cognitive function, leading to improvements in physical function and quality of life (QOL). We will estimate the impact of PLIÉ on brain atrophy rates, Default Mode Network (DMN) functional connectivity, and cerebral perfusion and determine if improvements in cognition, function, and QOL are associated with changes in brain volume, DMN functional connectivity, and cerebral perfusion in individuals who participated in PLIÉ.					
<b>15. SUBJECT TERMS</b> Exercise, Alzheimer's disease, other dementias, mild cognitive impairment, quality of life, neuroimaging					
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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

The goal of this project is to investigate whether participation in the Preventing Loss of Independence through Exercise (PLIÉ) program for 4 months will result in neurobiological changes that improve cognitive function, leading to improvements in physical function and quality of life (QOL). We will estimate the impact of PLIÉ on brain atrophy rates, Default Mode Network (DMN) functional connectivity, and cerebral perfusion and determine if improvements in cognition, function, and QOL are associated with changes in brain volume, DMN functional connectivity, and cerebral perfusion in individuals who participated in PLIÉ.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Exercise, Alzheimer's disease, other dementias, mild cognitive impairment, quality of life, neuroimaging.

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

**What were the major goals of the project?**

*List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.*

1. Obtain local and HRPO IRB approval (months 1-7)
2. Obtain neuroimaging data from MRI-eligible MCI participants of VA-funded trial of PLIÉ (months 1-10).
3. Recruit first DOD PLIÉ cohort of MCI participants where neuroimaging will be obligatory part of study (months 11-15).
4. Obtain behavioral and clinical data before and after PLIÉ intervention in first DOD MCI cohort (months 15-24).
5. Obtain neuroimaging data from MCI participants in first DOD PLIÉ cohort (months 15-24).
6. Recruit second DOD PLIÉ cohort of MCI participants where neuroimaging will be obligatory part of study (months 17-23).
7. Obtain behavioral and clinical data before and after PLIÉ intervention in second DOD MCI cohort (months 23-32).
8. Obtain neuroimaging data from MCI participants in second DOD PLIÉ cohort (months 24-32).
9. Process imaging data (months 15-32).
10. Analyze imaging data together with PLIÉ behavioral outcome measures (months 32-35).
11. Disseminate study findings (months 12, 24, 26).
12. Write final report for DOD (month 36).

**What was accomplished under these goals?**

*For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.*

Major activities and achievements:

- Obtained local IRB and HRPO approval to obtain neuroimaging data from MR-eligible MCI participants in VA-funded trial of PLIÉ.
- Obtained local IRB and HRPO approval to establish a second (DOD-funded) PLIÉ study that will enroll only participants with MCI who consent to neuroimaging before and after the PLIÉ intervention.
- Acquired neuroimaging data from MCI participant enrolled in VA-funded trial of PLIÉ.
- Established new PLIÉ site at the San Francisco VA.

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

*If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. “Training” activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. “Professional development” activities result in increased knowledge or skill in one’s area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.*

Nothing to report.

**How were the results disseminated to communities of interest?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.*

Nothing to report.

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

*If this is the final report, state “Nothing to Report.”*

*Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.*

- Recruit MR-eligible MCI participants for PLIÉ intervention at the SF VAMC.
- Obtain baseline behavioral/cognitive data from these MCI participants
- Obtain baseline neuroimaging data from the MCI participants.

- 4. IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

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

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).*

Nothing to report.

**What was the impact on other disciplines?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.*

Nothing to report.

**What was the impact on technology transfer?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:*

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report.

**What was the impact on society beyond science and technology?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:*

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report.

5. **CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, “Nothing to Report,” if applicable:

**Changes in approach and reasons for change**

*Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.*

Nothing to report.

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

*Describe problems or delays encountered during the reporting period and actions or plans to resolve them.*

There were four participants with MCI who were enrolled in the last cohort of Dr. Barnes’ VA-funded trial of PLIÉ. Although all four MCI participants expressed interested in participating in the neuroimaging sub-study, only one was MR-eligible. We will avoid this complication in the subsequent DOD-funded PLIÉ cohorts because we will only target individuals with MCI who are eligible for MRI for recruitment in those cohorts.

**Changes that had a significant impact on expenditures**

*Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.*

Nothing to report.

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

*Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.*

**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:

Study #17-23518 (imaging VA-PLIÉ participants): approved: 11/15/2017; expires 11/14/2018

Study # 17-23034 (DOD- PLIÉ): approved: 12/15/2017; expires: 12/14/2018

**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:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state “Nothing to Report.”

• **Publications, conference papers, and presentations**

Report only the major publication(s) resulting from the work under this award.

**Journal publications.** *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report.

**Books or other non-periodical, one-time publications.** Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).

Nothing to report.

**Other publications, conference papers, and presentations.** Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (\*) if presentation produced a manuscript.

Nothing to report.

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

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report.

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to report.

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

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report.

- **Other Products**

*Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:*

- *data or databases;*
- *biospecimen collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

N/A

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### **What individuals have worked on the project?**

*Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change.”*

Name: Linda Chao  
Project Role: PI  
Researcher Identifier: 0000-0002-8593-2434 (eRA Commons: lindachao)  
Nearest person month worked: 0.51 calendar months  
Contribution to Project: Dr. Chao has 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 has held monthly meetings with the research team to discuss progress, technical. and scientific issues, and subject flow issues.

Name: Deborah Barnes  
Project Role: Co-Investigator  
Researcher Identifier: 0000-0002-2953-4079 (eRA Commons: BANESD)  
Nearest person month worked: 0.6 calendar months  
Contribution to Project: Dr. Barnes has worked closely with Dr. Chao to identify and recruit participants with MCI from the community, from the San Francisco VA Memory Disorders Clinic, and from UCSF Memory and Aging Center for the PLIÉ cohorts. In addition, Dr. Barnes has assisted in data quality control.

Name: Margaret Chesney  
Project Role: Co-Investigator  
Researcher Identifier: 0000-0002-1066-5490 (eRA Commons: chesneymar)  
Nearest person month worked: 0.6 calendar months  
Contribution to Project: Dr. Chesney has worked closely with Dr. Chao to oversee the conduct of the proposed research. In particular, she has worked with Dr. Chao to develop and implement optimal approaches to interest MCI participants in the imaging aspects of the project, and specific methods to help participants with cognitive impairment to get through the MRI experience with minimal stress and movement. She has applied her expertise as a clinical psychologist in her work with Dr. Chao and the team on all aspects of the assessments of cognitive function and quality of life, including maintaining the highest quality of data collection, and analyses of these measures in conjunction with the neuroimaging. She has meet regularly with Dr. Chao, including attending monthly team meetings.

Name: Wolf Mehling  
Project Role: Co-Investigator  
Researcher Identifier: 0000-0002-0932-9844 (eRA Commons: mehling)  
Nearest person month worked: 0.6 calendar months  
Contribution to Project: Dr. Mehling has worked closely with Dr. Chao to oversee the conduct of the proposed research. He has meet regularly with Dr. Chao to discuss the study's progress, technical, and scientific issues. In addition, Dr. Mehling has assisted with data quality control.

Name:	Derek Flenniken
Project Role:	neuroimaging database manager
Researcher Identifier:	N/A
Nearest person month worked:	0.6 calendar months
Contribution to Project:	Mr. Flenniken has built a customized database for the specific needs of this project and has ensured that neuroimaging data generated by this project is stored in a timely manner and accessible at all times.

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

*If there is nothing significant to report during this reporting period, state "Nothing to Report."*

*If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed*

Name: Linda Chao

- Changes:
1. Effort on this grant was reduced from 0.6 calendar months to 0.48 calendar months.
  2. Effort on DOD/CDMRP grant W81XWH-16-1-0558 was reduced from 0.6 calendar months to 0.51 calendar months.
  3. Effort on VA grant I01CX000798-04 has been reduced from 6 calendar months to 5.16 calendar months
  4. Dr. Chao is co-investigator on DOD/CDMRP grant W81XWH-17-1-0685 at 0.3 calendar months.
  5. DOD/CDMRP grant AZ170018 has been recommended for funding. Dr. Chao will be a co-investigator at 0.24 calendar months.

Name: Deborah Barnes

- Changes:
1. Effort on VA grant IORX001507 has been increased from 5.46 to 6.3 calendar months.
  2. Effort on VA grant I0CX001246-01 has been decreased from 2.04 to 1.2 calendar months.
  3. Effort on the Program for the Aging Century, funded by the S.D. Bechtel, Jr. Foundation has been reduced from 3 to 0.6 calendar months.
  4. NIA grant "Improving Advance Care Planning by Preparing Diverse Seniors for Decision Making" ended on 6/30/2018
  5. Patient Centered Outcomes Research Institute grant "Preparing Spanish-Speaking Older Adults for Advance Care Planning and Medical Decision Making" ended on 3/31/2017.
  6. Effort on Alzheimer's Association grant "Paired Integrative Exercise Program for People with Dementia and Caregivers" has been reduced from 1.2 to 0.6 calendar months
  7. Dr. Barnes is a co-investigator on the UCSF Tideswell Innovation Center for Action-Oriented Aging Research, 0.5 calendar months.
  8. Dr. Barnes is a co-investigator on DOD grant W81XWH-16-1-0507 at 0.6 calendar months.
  9. Dr. Barnes is PI of a pilot project "UCSF Older Americans Independence Center" supported by a NIA (P30AG044281) grant at 0.3 calendar months.
  10. Dr. Barnes is PI of an NIA R56 AG056417 grant at 3 calendar months.
  11. Dr. Barnes is co-investigator on a NIA R01 AG0 51508 grant at 1.8 calendar months.

Name: Margaret Chesney

- Changes:
1. NIA grant R01 AT005820 ended 8/31/2017
  2. Effort on VA grant IORX001507 has been reduced to 0 calendar months.
  2. Effort on DOD/CDMRP grant W81XWH-16-1-0558 was reduced from 0.6 calendar months to 0.51 calendar months.
  4. “Integrative Exercise for Veterans with PTSD Symptoms” funded by the Osher Center Philanthropic Gift Fund ended 9/20/2017
  5. Dr. Chesney is co-investigator on VA grant I01 RX001939-01A1 at 0.5 calendar months.
1. NIA grant R01 AT005820 ended 8/31/2017
  2. Effort on VA grant IORX001507 has been reduced to 0 calendar months.
  2. Effort on DOD/CDMRP grant W81XWH-16-1-0558 was reduced from 0.6 calendar months to 0.51 calendar months.

Name: Wolf Mehling

- Changes:
1. “Paired Integrative Home Exercise for Seniors with Dementia and their Caregivers: A Pilot Study,” funded by the UCSF Pepper Center and Tideswell ended 01/31/2017.
  2. Effort on VA grant IORX001507 has been reduced to 0 calendar months.
  3. Effort on Alzheimer’s Association grant “Paired Integrative Exercise Program for People with Dementia and Caregivers” has been increased from 0.6 to 1.2 calendar months.
  4. “Integrative Exercise for Veterans with PTSD Symptoms” funded by the Osher Center Philanthropic Gift Fund ended 9/20/2017
  5. Dr. Mehling is a co-investigator on VA grant I01 RX001939-01A1 at 1.55 calendar months.

**What other organizations were involved as partners?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.*

*Provide the following information for each partnership:*

Organization Name:

Location of Organization: (if foreign location list country)

Partner’s contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*
- *Collaboration (e.g., partner’s staff work with project staff on the project);*

**8. SPECIAL REPORTING REQUIREMENTS: N/A**

9. **APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

N/A