AWARD NUMBER: W81XWH-15-2-0005

TITLE: Can a Canine Companion Modify Cardiac Autonomic Reactivity and Tone in PTSD?

PRINCIPAL INVESTIGATOR: Steven H. Woodward

RECIPIENT: Palo Alto Veterans Institute for Research

Palo Alto, CA 94304-0038

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14. ABSTRACT									
We are active	ly acquiring an	d processing	data that tests the	impact of par	ticipation in	the Service Animal Training			
Intervention pi	rogram at the	APAHCS-II	auma Recovery Pr	ogram autono	omic regula	tion, social experience, and social			
cognition in P	TSD. Overall, I	ecruitment h	as been on target, k	out enrollmen	it in the inte	nsive arm of the study has slowed due			
to canine med	lical and behav	vioral issues.	New canines are ex	xpected to joi	n the progra	am soon and recruitment for this study			
arm is expecte	ed to return to	previous leve	ls. Preliminary resu	ilts suggest a	n effect of c	anine companionship on attentional			
bias. Prelimina	ary analyses o	f the impact of	of canine companio	nship on slee	p and socia	l behaviors are underway.			
15. SUBJECT TI	ERMS								
Posttraumatic	stress disorde	r. animal-ass	isted therapy, auto	nomic regulat	tion. autono	mic reactivity, mood, sociality, social			
cognition slee	en ambulatory	monitoring	defense response f	acial affect	,				
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1. INTRODUCTION:

The subject of this research is the impact of canine companionship on cardiac autonomic regulation, mood, social experience, and social cognition in U.S. Military Veterans undergoing inpatient treatment for deployment-related posttraumatic stress disorder. Its purpose is to confirm or disconfirm in such Veterans the positive impacts of canine companionship that have been reported in civilian samples. Its scope is the inpatient treatment context; however, its results may have implications for less severely affected populations and similar but less intensive interventions.

2. KEYWORDS:

Posttraumatic stress disorder, animal-assisted therapy, autonomic regulation, autonomic reactivity, mood, sociality, social cognition, sleep, ambulatory monitoring, defense response, facial affect

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.

The major goals for this project were to perform strong tests of a set of hypotheses relating canine companionship to autonomic regulation, social experience, and social cognition.

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.



In the fourth 12-months of this project, we have received a 12-month extension and revised the recruitment goals to reflect the changes in clinical programs. The major goals were to recruit 200 and complete 174 participants. Recruitment rates have stabilized, and our study completion rates stand at 96% of the current projected for the intensive limb of the design and 95% of the non-intensive limb.

Tabular form: Enrollment since recruitment began in April 2015:						
	Actual	SOW target	SOW target			
	(n)	to date	final			
Total Enrolled	194	200 (97%)	251 (77%)			
Dog (intensive)	60	58 (103%)	77 (78%)			
Non-dog	134	142 (94%)	174 (77%)			
Total Completed	166	174 (95%)	200 (83%)			
Dog (intensive)	46	48 (96%)	60 (77%)			
	[+1 current]					
Non-dog	120	126 (95%)	140 (86%)			

Withdrawals (April 2015 – January 2019):

	Actual	SOW expected	Withdrawal reasons		
		to date			
	n (% of enrolled)	n (% of enrolled)			
Total Withdrawals	27 (14%)	40 (20%)			
Dog (intensive)	13 (22%)	17 (30%)	6 discharged early from clinical program;		
			5 changed mind about dog program; 2 found study too burdensome		
Non-dog	14 (10%)	14 (10%)	7 changed mind;		
			4 discharged early from clinical program;		
			2 clinically contraindicated;		
			1 ineligible		

There have been no AE, SAEs, or UPs.

We have continued to perform interim analyses of data as they are acquired, and to publish them when appropriate. Our second journal article, Miller et al, *two independent predictors of nightmares in posttraumatic stress disorder*, has been published in the *Journal of Clinical Sleep Medicine*, (vol. 14, pp. 1921-1927). As reported in the last MOMRP review, we did not find any effect of service dog presence in the sleep environment on nightmare reports.

While interim analyses continue to find no main effect of canine presence on sleep heart rate, support for a canine presence x time of night interaction has strengthened. We have upgraded our modeling of sleep heart rate to include effects of time-of-night and time-since-sleep-onset, day of week, and early vs late in treatment. With these improvements have come indications that this metric is exquisitely sensitive to what can be inferred as "stress". For example, there is a small but statistically significant increase in sleep heart rate over days of the week as participants engage in treatment. This effect interacts with the canine presence x time of night interaction. It is tempting to conjecture that the canine presence x time of night interaction derives from moderation, by dog presence, of the pre-awaking activation that includes elevation of circulating levels of cortisol and epinephrine. This is also the circadian phase associated with elevated risk for myocardial infarct. As such, this finding may represent an important modulation of sleep heart rate even in the absence of a main effect. We believe publication of this finding should await acquisition of the full sample.

Preliminarily analyses of the Reading the Mind in the Eyes Test, our primary laboratory measure of social cognition, have also failed to find an effect of canine presence. This contrasts with our findings on attention bias and startle. It is broadly aligned, however, with our preliminary findings that canine accompaniment over the course of the day is not associated with elevated self-reports of sociality. We believe these negative findings should await publication with the highest statistical power our design can achieve.

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.

Dr. Jamison has acquired a strong basis in qualitative research design while executing an add-on to this study. Ms. Gala and Ms. Villasenor both acquired significant training in structured clinical interviewing while members of the study staff. Dr. Woodward, the PI, has acquired new training in the R statistical package and in linear mixed effects modeling while leading this study.

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.

We have used journal articles and conference presentations to disseminate data from this study. These are listed below.

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.

During the next reporting period, data acquisition and processing will continue as proposed. When and if obtained, additional positive results deemed reliable and replicable will be submitted for publication. Analyses of effects on all outcomes are underway.

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).

It is still premature to attribute any changes in the practice of providing service animals to Veterans or in the conduct in animal-assisted therapy to this project.

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.*

Our findings regarding attention bias represent the first demonstration of an impact of canine presence on a non-subjective outcome relevant to the broad proposition that the company of a service dog makes veterans with PTSD "feel better".

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.

There are no changes in objectives or scope.

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.

As we described at the recent MOMRP review, and in communications with our past and current science officers, we have experienced significant challenges recruiting participants into the intensive limb of our study since mid-summer, 2016. The shortage of service dogs contributing to this problem has been alleviated; however, a remaining constraint on recruitment derives from the permanently reduced census of the Trauma Recovery Program. At the suggestion of Inna Williams, we requested and were granted a no-cost extension. We have continued with reduced staffing and increased reliance with student volunteers. Recruitment has continued at a slow but steady pace, as our numbers indicate. We expect to achieve our originally-proposed sample sizes by November 2019.

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.

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

None.

Significant changes in use or care of vertebrate animals.

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS: List any products resulting from the project during the reporting period. If there are no products to report for the current quarter, state "Nothing to report."

6. 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).

Woodward, S. H., Jamison, A.L., Gala, S., & Holmes, T.H. 2017. Canine companionship is associated with modification of attentional bias in posttraumatic stress disorder. *PloS One*, *12*, e0179912. doi: 10.1371/journal.pone.0179912

Miller, K. E., Jamison, A. L., Gala, S., & Woodward, S. H. (2018). Two Independent Predictors of Nightmares in Posttraumatic Stress Disorder. Journal of Clinical Sleep Medicine, 14(11), 1921-1927.

Woodward, S. H., Jamison, A.L., Gala, S. Psychophysiologic Responses to Loud Tones in Posttraumatic Stress Disorder with and without a Familiar Service Dog Present. (*under review*)

Federal support is acknowledged in all of the above.

• 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.

Woodward, S.H., Lawlor, C., Jamison, A.L., Gala, S. Does Canine Companionship Improve sleep in severe deployment-related PTSD? Presented at the International Society for Traumatic Stress Studies, November 2018, Washington, D.C.

Miller, K. E., Jamison, A.L., Gala, S., Woodward, S.H. Night-to-night subjective and objective predictors of trauma-related disturbed dreaming reports. Presented at the International Society for Traumatic Stress Studies, November 2018, Washington, D.C.

• 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.

Nothing to report.

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."

Example:

Name:

Mary Smith

Project Role:Graduate StudentResearcher Identifier (e.g. ORCID ID):1234567Nearest person month worked:5

Contribution to Project:

Funding Support:

Ms. Smith has performed work in the area of combined error-control and constrained coding. The Ford Foundation (Complete only if the funding support is provided from other than this award).

Name: Project Role: Nearest person month worked: No change	Steven Woodward Principal Investigator 2
Name: Project Role: Nearest person month worked: No change.	Andrea Jamison Coordinator 12
Name: Project Role: Nearest person month worked:	Diana Villasenor Research Assistant 8

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 and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report.

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: <u>Organization Name:</u> <u>Location of Organization: (if foreign location list country)</u> 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);
- Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and
- Other.

Paws for Purple Hearts

Menlo Park, California

Non-profit organization that provides and manages the service dogs, and the service animal training intervention. We have included them in this second annual report because monies were requested to defray their costs incurred in transferring two service dogs from San Diego and Virginia whose behavioral profiles are compatible with the SATI program and the original design of this project. (Two of the three PPH dogs that came into service earlier this project year proved unable to perform as needed.)

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES:

Can a Canine Companion Modify Cardiac Autonomic Reactivity and Tone in PTSD ERMS# 13046055 Award # W81XWH-15-2-0005

PI: Steven H. Woodward, PhD Org: Palo Alto Veterans Institute for Research Award Amount: \$1,283,573

Study/Product Aim(s)

• We propose to provide a strong test of the ability of canine-assisted therapy to mitigate recognized symptoms of PTSD that are relevant to medical and rehabilitative status. Based on studies in non-veteran, non-military samples, canine companionship may mitigate both elevated basal heart rate and poor social/interpersonal function. We will also assess the impact of canine companionship on laboratory tasks of social cognition and stress reactivity.

Approach

•We will record waking and sleeping heart rate for up to 42 days/nights in a completer sample of 60 Veterans engaged in inpatient PTSD treatment and participating in a service animal training intervention (SATI). The latter program includes extended periods both with and without the 24/7 companionship of the service animal, allowing us to use participants as their own controls. Selected between-subjects comparisons will contrast the diagnostic status' and treatment progress of SATI program participants and non-participants.

Timeline and Cost

Activities FY	15	16	17	18	19
hiring, approvals, contracting, stim development and piloting, statistical consultation					
recruitment, structured interviewing, laboratory assessments, ambulatory psychophysiology, sleep actigraphy, preliminary data analyses, data archiving					
summary data analyses, manuscript prep & submission					
Estimated Budget (\$K) (direct)	\$317k	\$317k	\$325k	\$189k	\$136k

Updated: 1/2019



Accomplishment: Plot illustrating lack of association between canine presence and performance on the Reading the Mind in the Eyes task, a common test of social cognition. These results argue against a canine-companionship induced-upregulation of emotion perception underlying reported effects on sociality.

Goals/Milestones

CY15 Goal - Complete startup tasks and commence recruiting ☑ all startup tasks completed ☑ 52 participants enrolled (vs 55 planned in SOW) CY16 Goals - Continue accrual/ process data ☑ 110 participants enrolled, 97 completed (vs 104 planned in SOW) ☑ ongoing data processing/archiving/methods development CY17 Goals - Continue accrual/ process data ☑ 153 participants enrolled, 131 completed (vs 164 planned in SOW) ☑ ongoing data processing/archiving/methods development CY18 Goals - Continue accrual/ process data ☑ 194 participants enrolled, 166 completed (vs 174 planned in SOW) ✓ ongoing data processing/archiving/methods development CY19 Goals - Continue accrual/ process data Complete enrollment/testing \Box complete data analysis Budget Expenditure to Date (through November, 2018) Projected Expenditure:: \$1,283,573 Actual Expenditure:: \$ 1,066,765