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TITLE: Threat Monitoring and Behavioral Health Throughout the Deployment and Career Cycles: A Translational Study

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CONTRACTING ORGANIZATION: Tel Aviv University

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Threat Monitoring and Behavioral Health Throughout the Deployment and Career Cycles: A Translational Study

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6. AUTHOR(S)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Background: Biased processing of threat-related information confers vulnerability to stress-related psychopathology. Studies indicate that threat-related attention bias and attention bias variability (ABV; fluctuation of attention toward and away from threat) are modulated by traumatic exposure and correlate with stress-related symptoms.

Objectives: **a)** To provide longitudinal information on the plasticity of threat monitoring throughout the transitions of military deployment and career cycles, and on its relations to combat exposure and stress-related symptoms. **b)** To elucidate the neuro-cognitive mechanisms underlying this plasticity. And **c)** to test the efficacy of a feedback-based application in reducing ABV and PTSD symptoms among veterans.

Specific Aims and Design: ***Study 1*** - Longitudinal follow-up of 579 IDF infantry soldiers in 5 time-points: 1) shortly after recruitment in basic training; 2) one year into the service; 3) two years into the service; 4) four-months post-discharge; and 5) one year of post-discharge, civilian life. At each assessment the following data will be collected: cognitive threat-monitoring, combat experiences, and self-reports on symptoms. In the last two assessments information on adjustment to civilian life will be added. Specific aims are: a) delineate the natural course of threat monitoring and mental health throughout the deployment and career cycles; and b) describe the interplay between changes in threat monitoring and changes mental health and adjustment over time. ***Study 2*** – This laboratory study of 60 participants will measure baseline threat-related attention bias and ABV, followed by instructed fear conditioning to safe (CS-) and danger (CS+) contexts. The effects of this induced stress on attention bias and ABV, and the effects of perceived control over the stressor will be measured. Specific aims are: a) to detailing the effects of induced stress on attention bias and ABV; and b) to detail how a sense of perceived control over threats acts to moderate the effects of stress on threat monitoring. ***Study 3*** – Randomized controlled trial designed to test the efficacy of a novel feedback-based application in reducing both ABV and PTSD symptoms in combat veterans with PTSD. Sixty IDF veterans with PTSD will be randomized to receive either 8 feedback-based ABV reduction training sessions or 8 training sessions of a placebo control condition. Threat-related attention bias, ABV, and clinical outcome measures will be collected before and after treatment/placebo as well as at a 3-month and 12-month follow-ups.

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON** USAMRMC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified		

TABLE OF CONTENTS

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Biased processing of threat-related information has been shown to confer vulnerability to anxiety and stress-related psychopathology. Studies further indicate that threat-related attention is modulated by traumatic exposure, and that aberrations in threat monitoring correlate with elevated symptoms such as PTSD, anxiety, and depression. These attention modulations present potential targets for preventative and treatment programs for soldiers and veterans applying cognitive bias modification (CBM) programs. Three studies are performed in the grant period: a) A longitudinal follow-up on behavioral health and threat-related processing biases in soldiers throughout the deployment and career cycles. This study will provide a basis for developing evidence-based cognitive bias modification prevention/intervention programs that match the changing needs of soldiers and veterans; b) a controlled laboratory study of the effects of induced stress on attention bias and attention bias variability; and c) a randomized controlled trial testing the efficacy of a feedback-based attention bias variability and symptom reduction protocol for veterans with PTSD.

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

Combat Stress, Deployment, Attention Bias, PTSD, Cognitive Bias Modification

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official 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.

Study 1:
a) To delineate the natural course of threat monitoring and mental health throughout the deployment and career cycles
b) To reveal the associations and interplay between these two factors
c) To reveal the structural and functional neural changes associated with these transitions

Study 2:
a) To shed light on the effects of induced stress on threat-related attention bias and attention bias variability
b) To explore how a sense of perceived control over threats acts to moderate the effects of stress on threat monitoring

Study 3:
a) To test the efficacy of a novel feedback-based attention bias modification protocol in reducing both bias variability and symptoms in combat veterans with PTSD

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

Study 1:

a) IRB approvals, preparation of equipment, recruitment and training of study personnel
b) Session 1 of data collection (right after recruitment into the IDF has been completed – data from 579 soldiers has been collected, coded, and stored
c) 50 soldiers of the 579 were MRI scanned (structural and functional)
d) Preparations for Session 2 of data collection has started – expected May-June 2020

Study 2:

a) Development of study protocol and tasks - completed
b) Recruitment and training of study personnel - completed
c) Data collection from 28 participants - completed

Study 3:

a) IRB approvals, preparation of equipment, recruitment and training of study personnel – completed
b) Piloting of the ABV-feedback technique – completed successfully.
c) Social media advertising campaign for patient recruitment – up and running
d) 49 potential patients have been screened, 9 were clinically interviewed, 4 met study inclusion criteria, 1 of those declined participation, 3 were enrolled.
e) Two patients completed the full protocol, one still running

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

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

Study 1:
a) Preparation, analysis, and review of data from Session 1 - ongoing
b) Preparations for data collection from 579 IDF soldiers, one year into service – Session 2 – expected May-June 2020.
c) MRI re-scanning of the 50 soldiers from Session 1

Study 2:
a) Data collection from 32 participants to complete the study

Study 3:
a) Data collection from 13 veterans with PTSD

4. **IMPACT:** D*escribe 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).

Given the longitudinal nature of study 1 and the blind in study 3 meaning information and impact awaits further data collection. Study 2 will be completed soon.
Thus "Nothing to Report" at this time.

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 PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official 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:*

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.

Nothing to Report

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

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

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. Describe the technologies or techniques were shared.

Piloting of the ABV-feedback protocol we developed for the PTSD trial of study 3 indicate both feasibility and effective cognitive target engagement. This technology and technique is a novel breakthrough in cognitive bias modification research even as a proof of concept.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. 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;*
  - *physical 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.*

a) A unique data base of 579 soldiers' behavioral health, attention patterns, and brain data (n=50) was formed – data point 1 out of 5. b) Proof of concept ABV-feedback therapy has been established this software and clinical protocol, if proved efficacious in clinical trials, could offer a novel treatment for PTSD.

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 Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name: Prof. Yair Bar-Haim
Project Role: PI
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0002-4630-9180
Nearest person month worked: 12
Contribution to Project: Overarching scientific supervision and coordination.

Name: Prof. Paul Bliese
Project Role: Co PI
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 12
Contribution to Project: Research design and data analyses planning and execution.

Name: Noa Hertz
Project Role: Post-doctoral student
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 12
Contribution to Project: Protocols development, IRB coordination, training and supervision of research assistants.

Name: Dana Shamai
Project Role: PhD level student
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0003-1397-9214
Nearest person month worked: 9
Contribution to Project: Protocols development, IRB coordination, training and supervision of research assistants.

Name: Yaron Alon
Project Role: PhD level student
Researcher Identifier (e.g. ORCID ID): https://orcid.org/0000-0002-9400-0911
Nearest person month worked: 8
Contribution to Project: Protocols development, IRB coordination, training and supervision of research assistants.

Name: Nimrod Hertz
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 10
Contribution to Project: practicing research protocols

Name: Mai Gelman
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 11
Contribution to Project: practicing research protocols

Name: Ruba Maklada
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 10
Contribution to Project: practicing research protocols

Name: Nitsan Saban
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 10
Contribution to Project: practicing research protocols

Name: Chen Klein
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 8
Contribution to Project: practicing research protocols

Name: Ofek Gradshtein
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 7
Contribution to Project: practicing research protocols and preparing research equipment

Name: Naama Avni
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 3
Contribution to Project: practicing research protocols

Name: Ofer Meiri
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 6
Contribution to Project: practicing research protocols

Name: Tuval Krispal-Orad
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2
Contribution to Project: practicing research protocols

Name: Hagar Manor
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: practicing research protocols

Name: Shachar Lando
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: practicing research protocols

Name: Emily Klinger
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: practicing research protocols

Name: Nili Neuthal
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1
Contribution to Project: practicing research protocols

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:
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);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*

- *Other.*

Organization Name: Israel Defense Force
Location of Organization: Israel
Partner's contribution to the project: Facilitating IRB process; Facilitating coordination with the studied units; Collaboration on study implementation and IDF data gathering.

Organization Name: University of South Carolina
Location of Organization: South Carolina, USA
Partner's contribution to the project: Research design and data analyses planning and execution

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ers.amedd.army.mil*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.*

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.