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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

NONE LISTED

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1. INTRODUCTION:

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:

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

3. ACCOMPLISHMENTS:

What were the major goals of the project?

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

Study 1:

a) Assessment wave 3 data collection is in full gear, data from 421 IDF soldiers were collected, and some more is due until the end of November when the participants will be honorably discharged.
b) Wave 3 MRI data were collected from 41 participants.
c) Six new research assistants were recruited and trained for the job and have started participating in data collection.
d) Coding and processing of Wave 2 data have been completed.
e) Coding and processing of Wave 3 data is ongoing.

Study 2:

a) 60 participants completed the full protocol.
b) Data processing and analyses have been started.

Study 3:

a) 662 potential patients have been screened, 78 were clinically interviewed, 32 met study inclusion criteria and enrolled.
b) 23 patients completed the full protocol, 18 of them also completed a follow-up clinical evaluation, and 8 are still running.
c) New research assistants and a clinician were recruited and trained.

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?

Study 1:

a) Preparation, analysis, and review of data from wave 3 – ongoing – preliminary results to be reported in the next quarterly report.
b) Preparations for data collection in Wave 4 (post discharge) is expected on spring of 2022.
c) Wave 4 MRI re-scanning of the 50 soldiers from waves 1-3.
d) Data analyses and publication of interim results from waves 1-3 is expected.

Study 2:

a) Complete data analysis.
b) Write-up and publication of the study.

Study 3:

a) Data collection from additional 28 veterans with PTSD.

4. IMPACT:

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

Given the longitudinal nature of study 1 and the blind in study 3 meaningful information and impact awaits further data collection. Interim reports and publication is expected from waves 1-3. As to Study 2, preliminary results are presented below and full analyses and publication will ensue.

Study 2: Effects of induced stress on attention bias and attention bias variability

Preliminary results

Manipulation check of fear conditioning. Results support a successful fear conditioning. Specifically, higher distress levels were reported during the CS+ blocks compared to the CS- blocks, $t(59) = 18.85$, $p < .001$ (Figure 1a), and higher amplitude of skin conductance response (SCR) was noted for the CS+ blocks relative to the CS- blocks, $t(59) = 2.97$, $p = .004$ (Figure 1b).

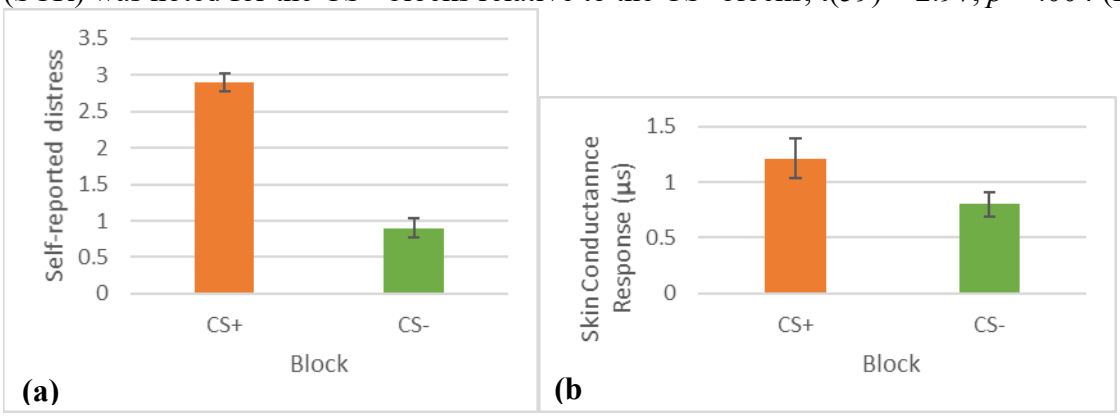

Figure 1. Self-reported distress (a) and skin conductance response (b) in the different dot-probe blocks.

Attention bias. The current study did not replicate previous results according to which attentional avoidance emerges during CS+ blocks. Specifically, attention bias during CS+ blocks and CS- blocks did not differ, $t(59) = 0.457$, $p = .649$ (Figure 2). This result remained consistent even when controlling for baseline attention bias or the difference in self-reported distress or SCR between CS+ and CS- blocks. This non-replication may be partly explained by the low psychometrics of the attention bias score with split-half reliability of $r(60) = 0.135$, $p = .305$.

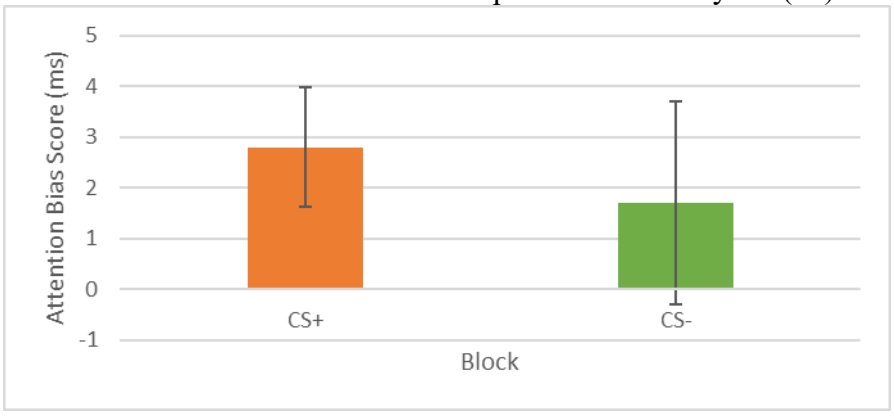

Figure 2. The effect of fear conditioning on threat-related attention bias.

Attention Bias Variability. This is the first study to explore the effect of stress induction on attention bias variability (ABV) among healthy participants. ABV deceased in CS+ blocks compared to CS- blocks when controlling for baseline ABV, $F(1,58) = 12.37$, $p < .001$ (Figure 3). This result suggests a different pattern of threat monitoring in health participants relative to patients with PTSD.

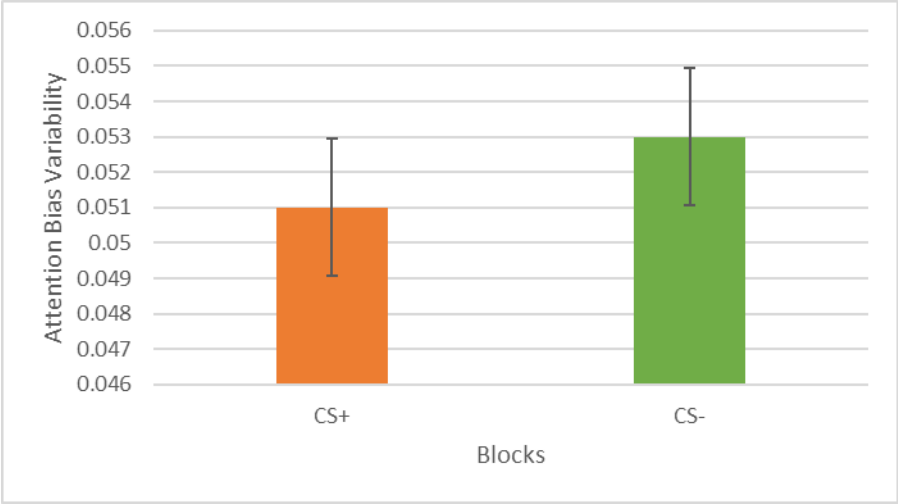

Figure 3. The effect of fear conditioning on attention bias variability.

The effect of sense of control on ABV. Data processing and analyses of session 2 data, designed to address the effect of sense of control over threat on ABV, has started. We expect to completed analyses in the coming months.

What was the impact on other disciplines?

The preliminary findings appear to support a main theme in recent literature emphasizing the role of variability indices in attentional deployment research. The ABV results are of great interest here and the measurement techniques we developed for these analyses could serve the research community at large.

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

Nothing to Report

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

Nothing to Report

Significant changes in use or care of vertebrate animals

Significant changes in use of biohazards and/or select agents

Nothing to Report

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**

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

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

Nothing to Report

- **Other Products**

a) A unique data base of 421 soldiers' behavioral health, attention patterns, and brain data (n=43) was formed – data point 3 out of 5.
b) Proof of concept ABV-feedback therapy has been established. This software and clinical protocol, if proved efficacious in the current trial (Study 3) and additional clinical trials, could offer a novel treatment for PTSD.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Prof. Yair Bar-Haim
Project Role: PI
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Contribution to Project: Overarching scientific supervision and coordination.

Name: Prof. Paul Bliese
Project Role: Co PI
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Contribution to Project: Research design and data analyses planning and execution.

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Name: Yaron Alon
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Contribution to Project: practicing research protocols and data collection

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Name: Bar Gabso
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Contribution to Project: practicing research protocols and data collection

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Name: Roni Rom-Laor
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Contribution to Project: assessing PTSD symptoms of patients in study 3.

Name: Gal Weiner
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Name: Mai Gelman
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Nearest person month worked: 2
Contribution to Project: protocols development, IRB coordination, training and supervision of research assistants.

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Name: Dvir Caspi
Project Role: research assistant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 3
Contribution to Project: practicing research protocols and data collection

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
Nothing to Report

What other organizations were involved as partners?
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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:

QUAD CHARTS:

9. APPENDICES: