Prolonged Exposure Therapy for Combat-Related PTSD: 20 Years of Progress

Alan Peterson, PhD, UT Health San Antonio, South Texas Veterans Health Care System, and UTSA

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Conflict of Interest, Disclosures, and Disclaimers

- Dr. Peterson does not have any conflicts of interest related to this presentation.
- Some of the content of this presentation may be distressing. Viewer discretion is advised.
- The views expressed herein are solely those of the author and do not reflect an endorsement by or the official policy or position of the Department of Defense, the Department of Veterans Affairs, or the US Government.

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Brief Bio, Alan Peterson, PhD, ABPP

- **Retired USAF Clinical Health Psychologist (1980-2005)**
  - Wilford Hall Air Force Medical Center, San Antonio, TX
  - Department Chair and Postdoctoral Fellowship Director
  - Completed 3 post-9/11 deployments
- **UT Health San Antonio (2005-present)**
  - Professor and Chief, Division of Behavioral Medicine
  - Director, STRONG STAR Consortium
  - Director, Consortium to Alleviate PTSD
- **UTSA Dept of Psychology (2012-present)**
  - Professor, Military Health Psychology PhD Program
- **South Texas Veterans Health Care System (2014-present)**
  - Supervisory Research Health Scientist

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Where were you?

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Operation Enduring Freedom

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Operation Iraqi Freedom
21. 10. 2004
AF THEATER HOSPITAL
BALAD IRAQ
ENTRANCE

8


The Air Force Theater Hospital

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Contingency Aeromedical Staging Facility

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The First Patient

- Some of the content of this presentation may be distressing. Viewer discretion is advised.
- 22-year old active duty US Air Force Airman performing convoy protection duty in Iraq
- Lead vehicle hit with 500-pound vehicle borne improvised explosive device (VBIED)
- Airman performed Combat Life Saving, secured area, provided security for medic
- Seen for intake 10 days after attack
- Initial PCL-M = 67 (range = 17-85)
- Frequent flashbacks of the event
- Frequent nightmares
- Significant avoidance

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The First Patient

- What did he think happened to the child?
- Who's fault was it?
- What did he think about:
  - Himself?
  - Military leaders and the decisions they make?
  - Insurgents?
  - The world

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The First Patient

- Completed 4 sessions of PE modified for combat theater
- Final PCL-M = 20 (range = 17-85)
- Returned to convoy protection duty
- Completed deployment
- Voluntarily extended deployment to train replacements
- 8-year follow-up
  - Had been promoted 4 times
  - Had successfully completed a second deployment
  - Does not have PTSD

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Pragmatic Case Studies in Psychotherapy, http://pcsp.libraries.rutgers.edu
Volume 1, Module 2, Article 1, pp. 1-25, 07-27-2005 [copyright by authors]

Three American Troops in Iraq: Evaluation of a Brief Exposure Therapy Treatment for the Secondary Prevention of Combat-Related PTSD*

JEFFREY A. CIGRANG[a,d], ALAN L. PETERSON[b], & RICHARD P. SCHOBITZ[c]

[a] Wright-Patterson Medical Center, Dayton, Ohio
[b] Wilford Hall Medical Center, San Antonio, Texas
[c] Tripler Army Medical Center, Honolulu, Hawaii
[d] Correspondence concerning this article should be addressed to Jeff A. Cigrang, 88th Medical Operations Squadron/SGOH, 4881 Sugar Maple Drive, Wright-Patterson Air Force Base Ohio 45433-5529.
Email: jeff.cigrang@wpafb.af.mil
*Note: The views expressed in this article are those of the authors and are not the official policy of the Department of Defense or the United States Air Force.

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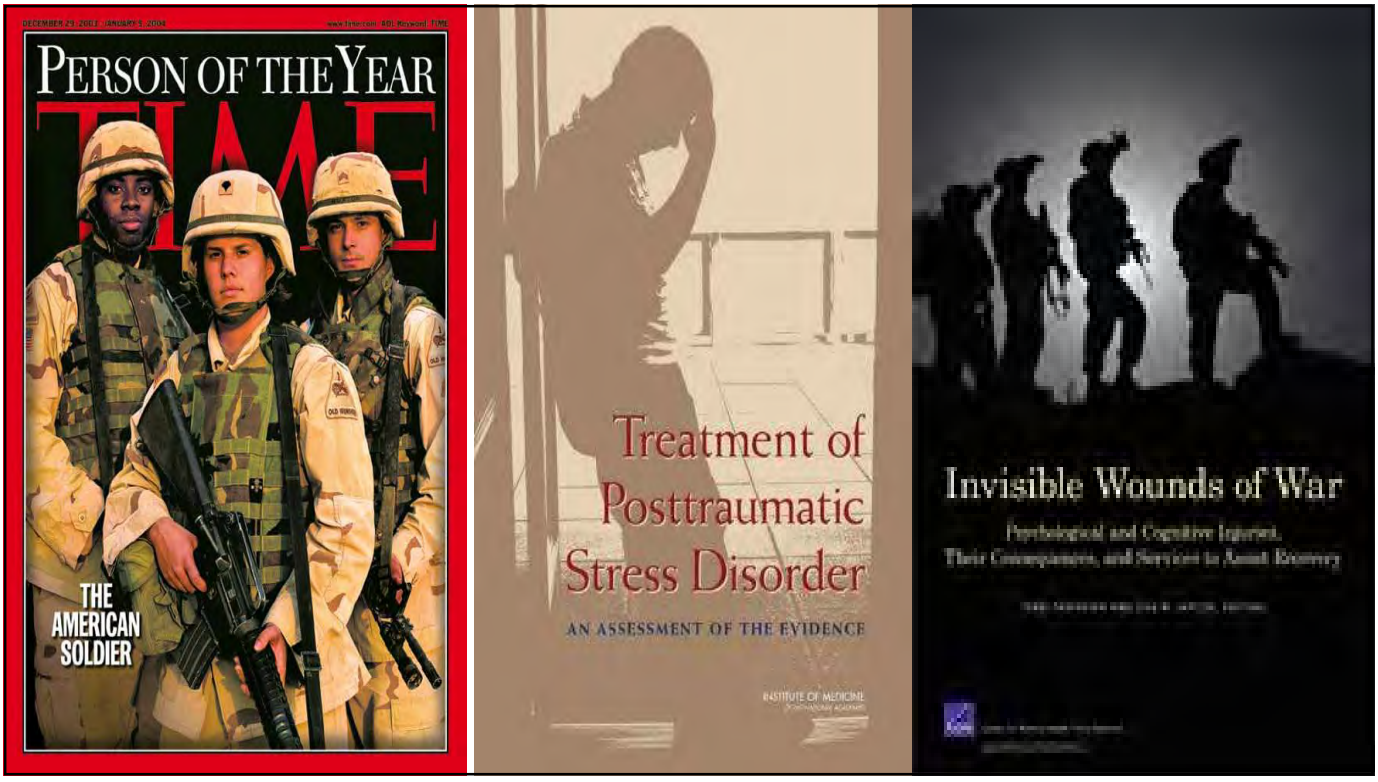

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Some Considerations in Conducting Clinical Trials with Active Duty Military Personnel

- What is the current state of the science?
  - Research with civilians, veterans, and military personnel
- Start small, identify a possible signal, take the next logical step in the design of clinical trials
  - Clinical case study
  - Open-label, nonrandomized clinical trial, clinical replication series
  - Small randomized clinical trial
  - Randomized clinical trial (RCT) of active versus comparison
  - Multi-site RCTs
  - RTCs including the combination of psychotherapies, medications, and medical devices
- Importance of not using placebo treatment arms with active duty

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STRONG STAR Prolonged Exposure Studies: 20 Years of Progress

1. **Cigrang et al. 2005; Peterson et al., 2005**: Case study of PE delivered in combat zone
2. **Cigrang et al. (2011, 2015, 2017)**: Abbreviated PE (four 30-minute sessions) in primary care
3. **Foa et al., (2018)**: Spaced (weekly) PE versus Massed (daily) PE for PTSD
4. **Peterson et al., (2020)**: Modified PE delivered in active combat theater
5. **Foa et al. (2020):** Evaluation of PE workshop with and without clinical case consultation
6. **Foa et al., (2022):** 60-minute versus 90-minute PE for PTSD in Active Duty Military
7. **Peterson et al., (2022):** Pilot study of single stellate ganglion block combined with massed PE
8. **Peterson et al., (2023):** Massed vs. Intensive Outpatient Program (IOP) PE
9. **Straud et al., (2024):** Pilot RCT of Cannabidiol (CBD) for PTSD
10. **Fox et al., (2025):** Image-Guided, Robot-Controlled TMS plus PE for PTSD
11. **Peterson et al., (in progress):** Combining SGB with Massed PE for PTSD
12. **Peterson et al., (in progress):** Shared Decision Making for PTSD
13. **Straud et al., (in progress):** Open label pilot of esketamine for PTSD
14. **Peterson et al., (in preparation):** MDMA-Enhanced Massed PE for PTSD in Active Duty Military

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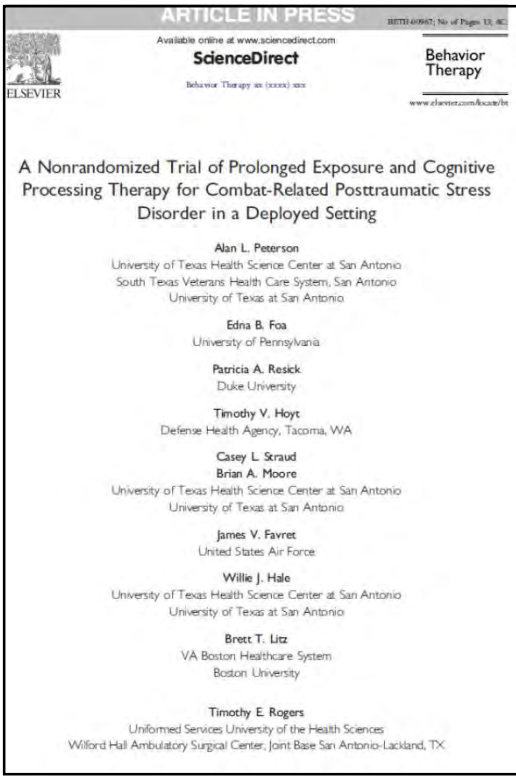

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A Nonrandomized Trial of Prolonged Exposure and Cognitive Processing Therapy for Combat-Related Posttraumatic Stress Disorder in a Deployed Setting

Alan L. Peterson
University of Texas Health Science Center at San Antonio
South Texas Veterans Health Care System, San Antonio
University of Texas at San Antonio

Edna B. Foa
University of Pennsylvania

Patricia A. Resick
Duke University

Timothy V. Hoyt
Defense Health Agency, Tacoma, WA

Casey L. Straud
Brian A. Moore
University of Texas Health Science Center at San Antonio
University of Texas at San Antonio

James V. Favret
United States Air Force

Willie J. Hale
University of Texas Health Science Center at San Antonio
University of Texas at San Antonio

Brett T. Litz
VA Boston Healthcare System
Boston University

Timothy E. Rogers
Uniformed Services University of the Health Sciences
Wilford Hall Ambulatory Surgical Center, Joint Base San Antonio-Lackland, TX

Peterson et al., (2020): Modified PE delivered in active combat theater

- (*N* = 12) received either PE (*n* = 6) or CPT (*n* = 6) by deployed military behavioral health providers who had been trained in PE or CPT prior to deployment.
- Participants not randomized to conditions, but received treatment based on the clinical judgment of the provider.
- Treatment sessions were scheduled and conducted flexibly to allow for adaptations needed to meet the work demands in the deployed location.

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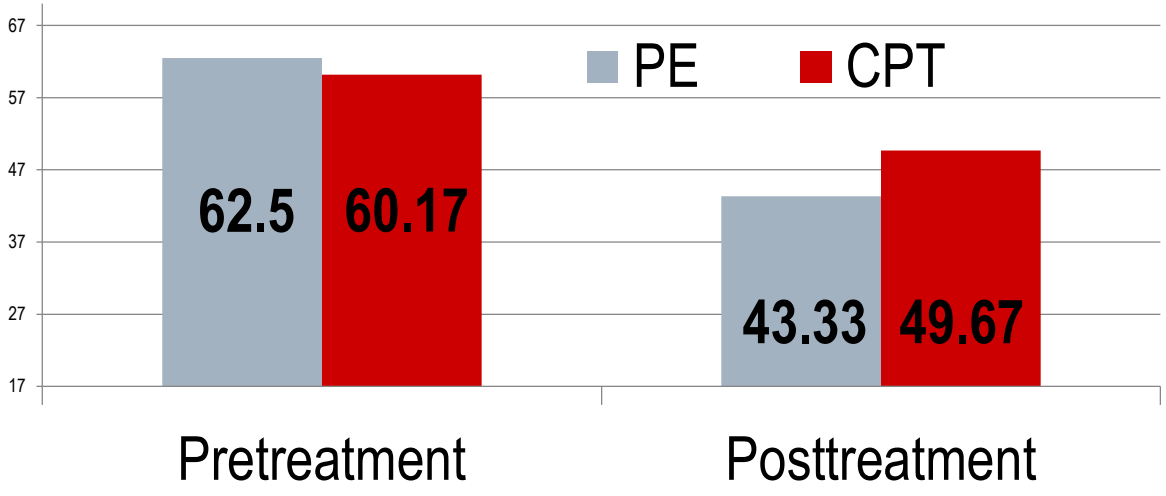
Peterson et al., (2020): Modified PE delivered in active combat theater



Results of PCL-M

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Moving Effective Treatment for Posttraumatic Stress Disorder to Primary Care: A Randomized Controlled Trial With Active Duty Military

Jeffrey A. Cigrang, PhD
Wright State University

Sheila A. Rauch, PhD
Emory University School of Medicine and Atlanta VA Medical Center, Atlanta, Georgia

Jim Mintz, PhD
and Antoinette R. Brundige, MA
University of Texas Health Science Center at San Antonio

Jennifer A. Mitchell, PsyD
Randolph Family Health Clinic, Joint Base San Antonio–Randolph, San Antonio, Texas

Elizabeth Najera, PhD
Wilford Hall Ambulatory Surgical Center, Joint Base San Antonio–Lackland, San Antonio, Texas

Brett T. Litz, PhD
VA Boston Healthcare System, Boston, Massachusetts, and Boston University School of Medicine

Stacey Young-McCaughan, RN, PhD
and John D. Roache, PhD
University of Texas Health Science Center at San Antonio

Elizabeth A. Hembree, PhD
University of Pennsylvania

Jeffrey L. Goodie, PhD
Uniformed Services University of the Health Sciences

Scott M. Sonnek, PhD
Wilford Hall Ambulatory Surgical Center, Joint Base San Antonio–Lackland, San Antonio, Texas

Alan L. Peterson, PhD
University of Texas Health Science Center at San Antonio and South Texas Veterans Health Care System, San Antonio, Texas

For the STRONG STAR Consortium

- **Research Question:**
- Will a brief PE for Primary Care protocol (four 30-minute appointments) delivered by behavioral health consultants reduce PTSD symptoms in OIF/OEF/OND service members?

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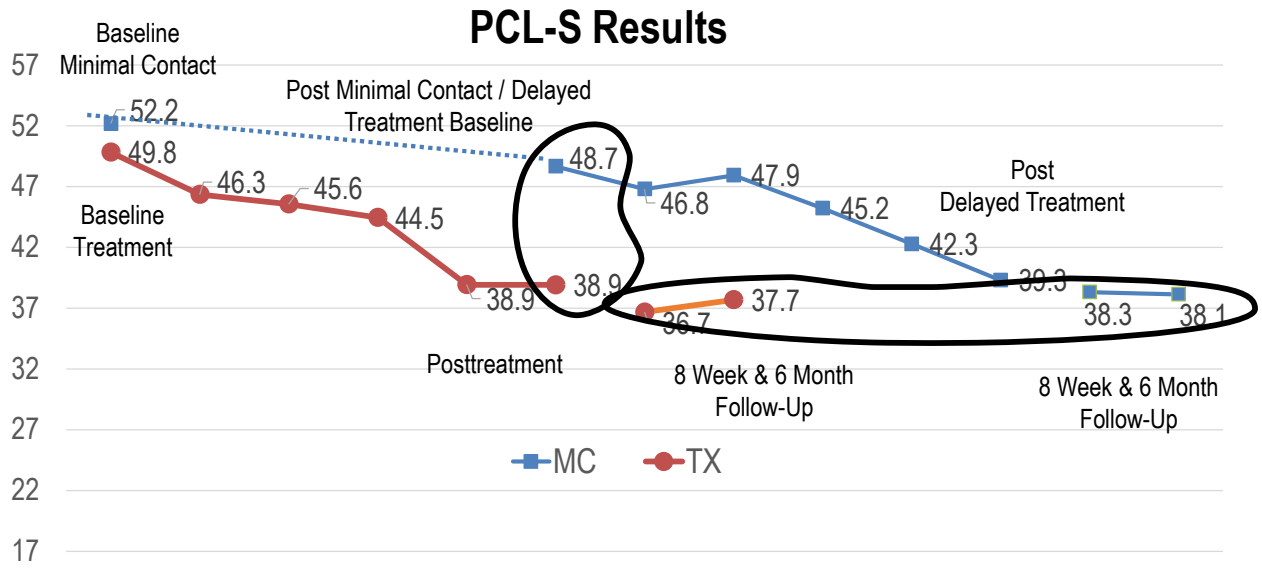
Cigrang et al. (2017): Abbreviated PE in Primary Care



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Research

JAMA | Original Investigation

Effect of Prolonged Exposure Therapy Delivered Over 2 Weeks vs 8 Weeks vs Present-Centered Therapy on PTSD Symptom Severity in Military Personnel

A Randomized Clinical Trial

Edna B. Foa, PhD; Carmen P. McLean, PhD; Yinyin Zang, PhD; David Rosenfield, PhD; Elna Yadin, PhD; Jeffrey S. Yarvis, PhD; Jim Mintz, PhD; Stacey Young-McCaughan, RN, PhD; Elisa V. Borah, PhD; Katherine A. Dondanville, PsyD; Brooke A. Fina, MSW; Brittany N. Hall-Clark, PhD; Tracey Lichner, PhD; Brett T. Litz, PhD; John Roache, PhD; Edward C. Wright, PhD; Alan L. Peterson, PhD; for the STRONG STAR Consortium

- PI: Edna Foa, University of Pennsylvania
- 366 participants at Ft Hood, Texas were randomized to:
  - **M-PE**: 10 PE sessions delivered in 2 weeks ("massed"); **(n = 110)**
  - **S-PE**: 10 PE sessions delivered in 8 weeks ("spaced"); **(n = 109)**
  - **PCT**: 10 present centered therapy sessions delivered in 8 weeks; **(n = 107)**
  - **MCC**: 2 weeks of twice weekly minimal contact via phone calls;**(n = 40)**

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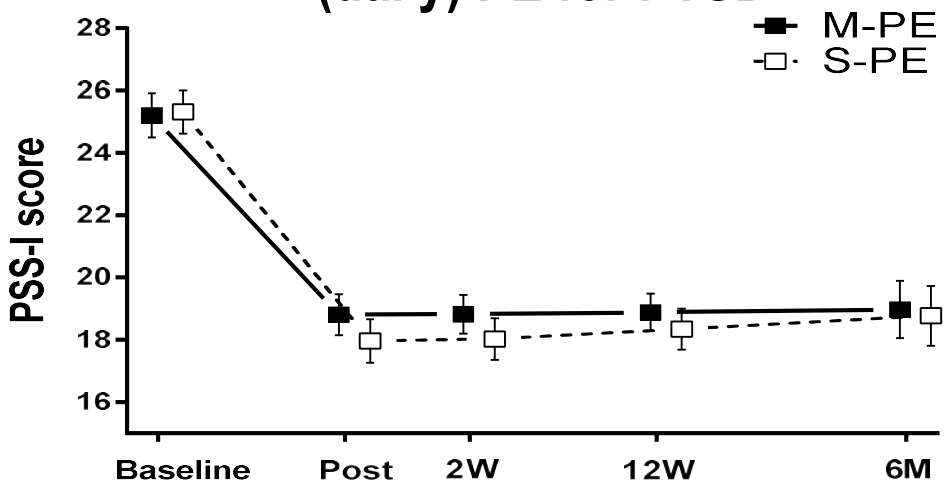
Foa et al., (2018): Spaced (weekly) PE versus Massed (daily) PE for PTSD



Foa et. al (2018) Effect of PE therapy delivered over 2 weeks vs 8 weeks vs present-centered Therapy on PTSD symptom severity in military personnel: A RCT. *JAMA*

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Limitations of Foa et al. (2018)

- Mean reduction on PCL-5 with massed PE = 14 points
- Only about 50% of patients were has clinically significant reductions in symptoms or lost PTSD diagnosis
- Compared to about 80% in previous studies with civilian female assualt victims
- Massed-PE patients returned to duty after each 90-minute PE session and did not have adequate time to complete daily out-of-session homework activities (i., listed to audio recording of session, complete in-vivo exercises)
- Many patients had multiple traumas in addition to the Criterion A event
- Although standard 10-session PE protocol is not limited to addressing just one trauma, it is difficult to treat more than 1 trauma in 10 sessions
- The standard PE protocol may benefit from some enhancements

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Peterson et al., (2023): Massed vs. Intensive Outpatient Program (IOP) PE

- **Massed-PE (M-PE)**: 15 daily, individual, 90-minute PE treatment sessions over 3 weeks
  - 15 sessions allowed additional time to focus on a second trauma, if necessary
  - Released from duty for 3 weeks to complete daily PE out-of-office homework exercises
- **Intensive Outpatient-PE (IOP-PE)**: 15 daily, individual, 90-minute PE treatment sessions over 3 weeks
  - Released from duty for 3 weeks to complete daily PE out-of-office homework exercises
  - 8 additional treatment augmentations

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IOP-PE Augmentations

1. Team-Based Treatment
2. Clinic-Based Completion of Homework
3. Brief Therapist Feedback Sessions
4. Enhanced Social Support
5. Top Three Traumas
6. Graduated Imaginal Exposure
7. Brief Timeline Review of all Traumas
8. Posttreatment Booster Sessions

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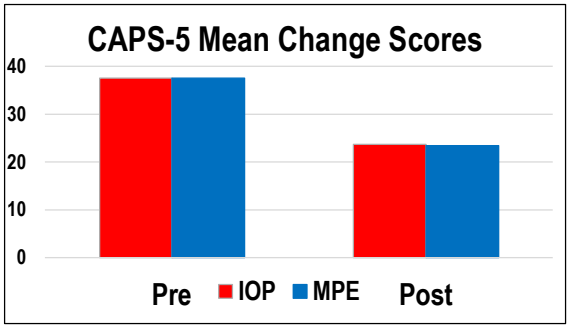
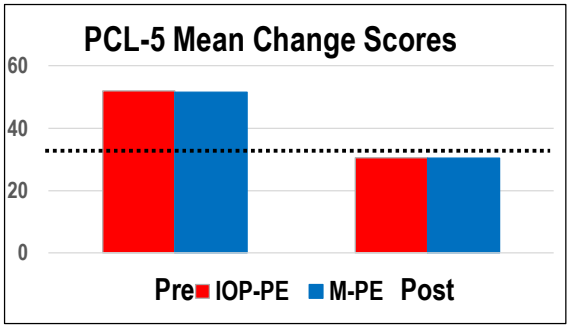
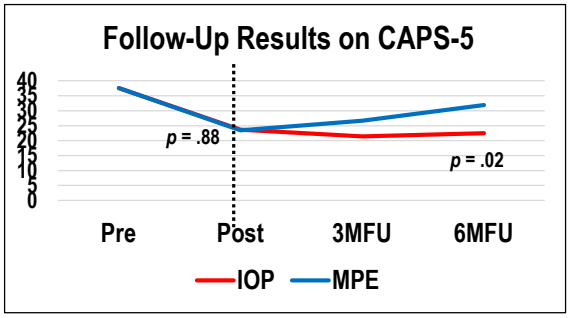
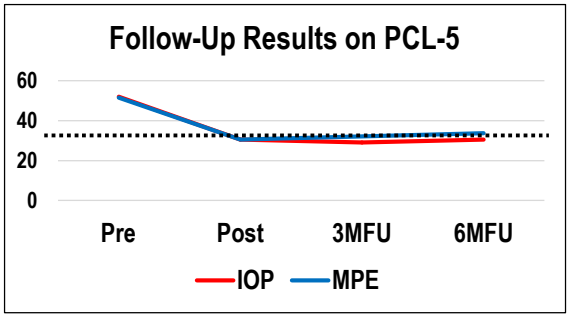
Findings: CAPS-5 and PCL-5









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Foa et al. (2020): Evaluation of PE workshop with and without clinical case consultation

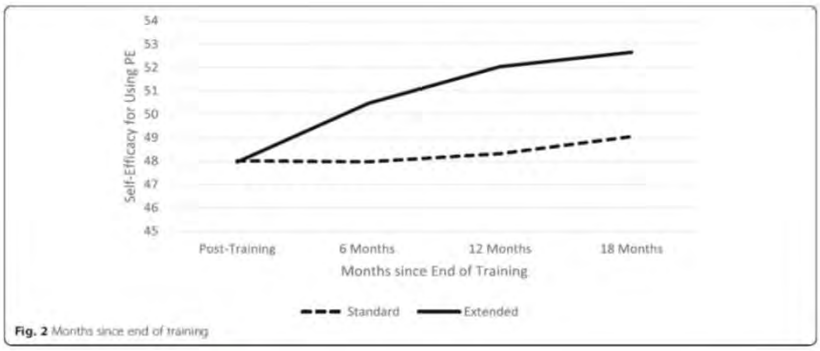

Fig. 2 Months since end of training

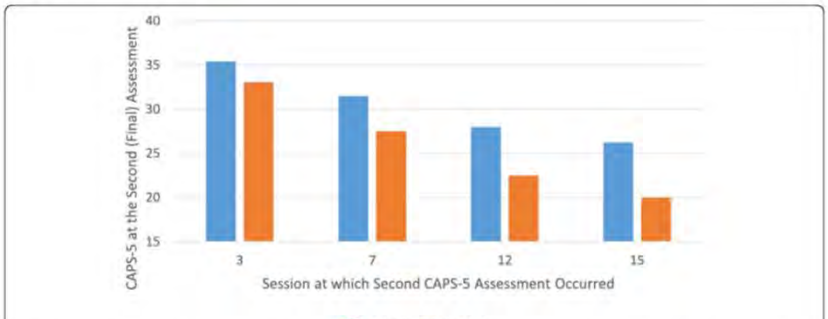

Fig. 3 CAPS-5 for Patients at Their Second (Final) Assessment. Note: CAPS-5, Clinician Administered PTSD Scale for DSM-5. The session at which the second assessment occurred varied from session 3-15. This graph illustrates the treatment condition differences at 4 of those assessment points

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Foa et al., (2022): 60-minute versus 90-minute PE Sessions for PTSD in Active Duty Military

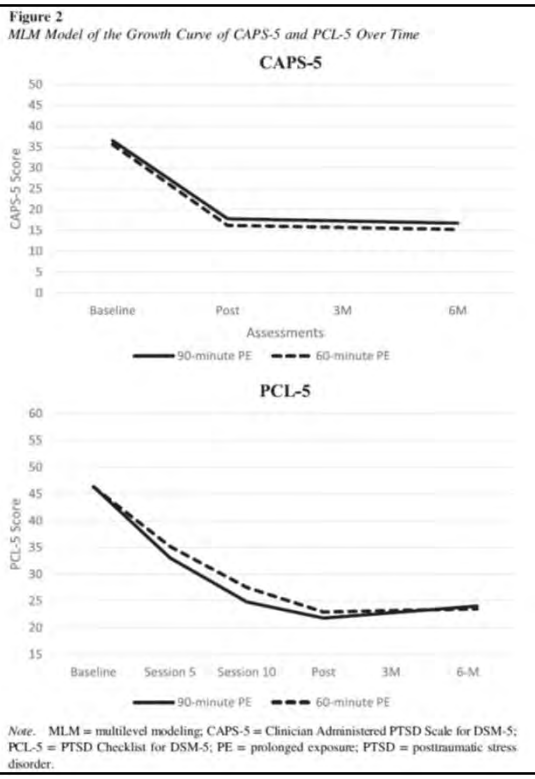

Figure 2
MLM Model of the Growth Curve of CAPS-5 and PCL-5 Over Time

Note. MLM = multilevel modeling; CAPS-5 = Clinician Administered PTSD Scale for DSM-5; PCL-5 = PTSD Checklist for DSM-5; PE = prolonged exposure; PTSD = posttraumatic stress disorder.

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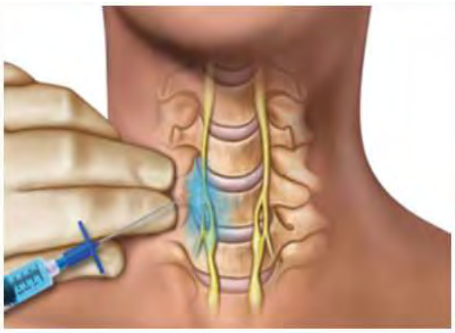
Peterson et al., (2022): Pilot study of a single stellate ganglion block combined with massed PE



- Injection of a local anesthetic in the sympathetic nerve tissue of the neck located on either side of the voice box
- Blocks the nerves that go to the arms and the sympathetic nerves that go to the face
- Indicated for: facial pain, neck pain, or arm pain
- For PTSD, blocks physiological stress response symptoms
- Rae Olmstead et al., 2019 RCT PCL-5 changes: **-13 points** with SGB; **-5 points** with saline sham SGB in musculature near stellate ganglion

- Pilot project: 12 active duty military treated with 10 Daily 90-Minute PE Sessions over 2 weeks
- SGB (6.5 mL of 0.5% ropivacaine) given between PE sessions 1 and 2
- **92%** completion rate
- **32-**point average reduction on the PCL-5
- **89%** no longer met CAPS-5 diagnostic criteria/clinically significant reductions on PCL-5 at the 3-month follow-up point

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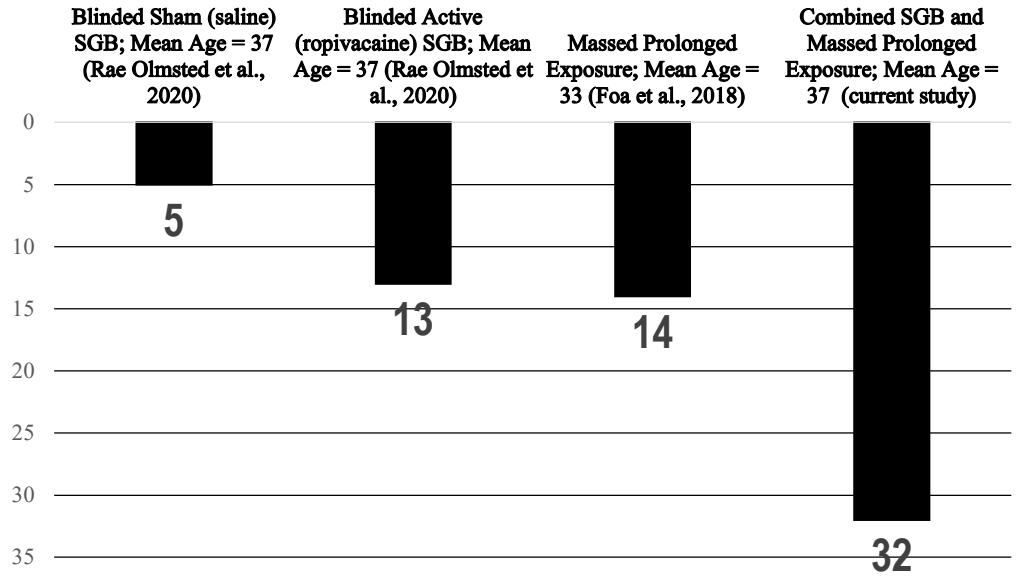
Reductions in PCL-5 PTSD Symptom Scores with SGB



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Combining Stellate Ganglion Block With Prolonged Exposure For PTSD: A Randomized Clinical Trial (PI: Peterson)

- **Participants:** 140 active duty military and veterans with PTSD
- **Recruitment Sites:** San Antonio and Fort Cavazos, Texas
- **Aim 1:**To conduct a 2-arm randomized clinical trial to evaluate the efficacy of a SGB injection combined with M-PE (*n* = 70) as compared to a saline sham SGB injected directly into stellate ganglion combined with M-PE (*n* = 70) for the PTSD.
- **Aim 2:** To evaluate differences in psychophysiological arousal during the imaginal exposure portion of PE as a potential mechanism of change in trauma-focused treatments for PTSD.
- **Primary End Point:** 1-month follow-up after completion of 2-week M-PE
- **Active SGB:** Offered to participants in sham SGB arm at 1-month follow-up

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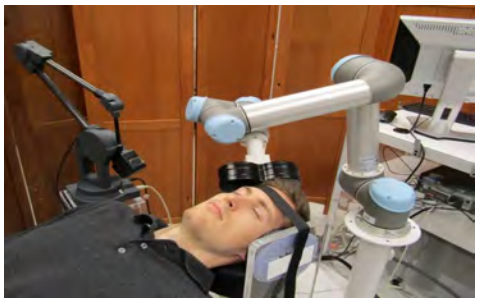
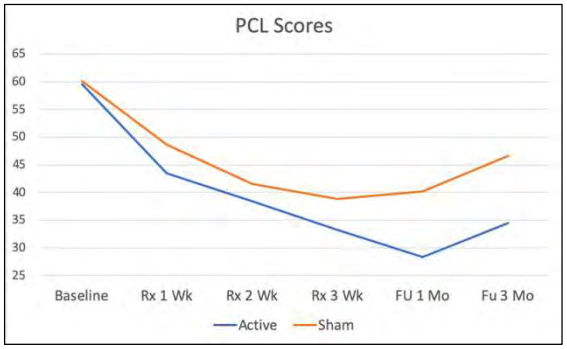
Image-Guided, Robotically Delivered Transcranial Magnetic Stimulation (irTMS) for Combat-Related PTSD: A Double-Blind, Randomized, Placebo-Controlled Clinical Trial (PI: Peter Fox)

- Results: Active irTMS was more effective than sham irTMS (N = 119)



C^3*Stim* irTMS System



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Straud et al., (2024): Pilot RCT of Cannabidiol for PTSD

- **Participants:** 21 veterans and civilians with PTSD
- **Recruitment Site:** San Antonio, Texas
- **Aim 1:** To evaluate the combination of (1) cannabidiol (CBD) plus massed PE vs. (2) Placebo plus massed PE for PTSD.
- **Aim 2:** To evaluate biological and physiological markers associated with CBD.
- **Results at 1-Month Follow-Up:**
  - CBD + M-PE reduced CAPS-5 (Baseline = 43; posttreatment = 15)
  - Placebo + M-PE reduced CAPS-5 (Baseline = 43; posttreatment = 10)
  - No difference between treatment arms

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Peterson et al. (in progress): Shared Decision-Making for the Treatment of PTSD

- **Research Design:** Partially Randomized Preference Trial
- **Objectives:** To evaluate the impact of Shared Decision Making to match patients to evidence-based cognitive behavioral treatments for PTSD:
  - **Prolonged Exposure (PE)**
  - Cognitive Processing Therapy (CPT)
  - Written Exposure Therapy (WET)
- **Participants:** Active duty military provided description of the risks/benefits and advantages/disadvantages of PE, CPT, and WET
- **Treatments:** Offered in different frequencies and modalities:
  - Massed (daily) or Spaced (weekly) treatment protocols
  - In-office or telehealth delivery modalities

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Straud et al., (in progress): Open label pilot of esketamine for PTSD

- **Participants:** 8 veterans and civilians with PTSD
- **Recruitment Site:** San Antonio, Texas
- **Aim 1:** To evaluate the feasibility of a novel combination treatment of esketamine and massed PE for PTSD as indicated by success in recruitment, enrollment, initiation, and adherence.
- **Aim 2:** To examine the acceptability of combining esketamine and massed PE for PTSD.
- **Aim 3:** To evaluate the benefits of the combined intervention that suggests a larger, RCT is warranted.
- **Primary End Point:** Scores on the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) and the PTSD Checklist for DSM-5 (PCL-5) and the 1-month follow-up after completion of 2-week massed PE

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Peterson et al. (recommended for funding): MDMA-Enhanced Massed Prolonged Exposure for PTSD in Active Duty Military Personnel

Principal Investigator: Alan Peterson, PhD, ABPP
Co-PIs: Jessica Maples-Keller, PhD, & Barbara Rothbaum, PhD
Performance Site: UT Health San Antonio with recruitment from San Antonio and Fort Cavazos, Texas
Funding Source: FY24 Defense Medical Research & Development Program Psychedelic Treatment Research Clinical Trial

Study Aims

- Aim 1: To compare the efficacy of 100 mg of MDMA (ecstasy; delivered as the active treatment) to 20 mg of MDMA (delivered as the control comparison group) when dosed in combination with Massed PE given to both groups as the standard of care therapy for the treatment of posttraumatic stress disorder (PTSD) in active duty military, guard, and reserve personnel.
- Aim 2: To evaluate secondary outcomes including return to duty readiness, psychosocial functioning, intimate relationship functioning, suicidal ideation, and depression at the 1-month posttreatment follow-up point.
- Aim 3: To evaluate differences in subjective and psychophysiological arousal during the imaginal exposure portion of prolonged exposure as a potential mechanism of change in trauma-focused treatments for PTSD.

Approach

Two-armed, double-blind, randomized clinical trial.

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The Future of PTSD Research with Service Members and Veterans

- Combination treatments including evidence-based cognitive behavioral therapies, medications, and medical devices
- Treatment of PTSD and common comorbid conditions (TBI, sleep disorders, SUD, chronic pain, tinnitus, suicide risk)
- Precision Medicine
- Prevention of PTSD

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9TH ANNUAL SAN ANTONIO COMBAT PTSD CONFERENCE

UT Health San Antonio

Save the Date!

Mark your calendars and plan to join us for the San Antonio Combat PTSD Conference

- **October 20 – 21, 2025**
- **October 29 – 30, 2026**

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