Psychophysiological Alterations in Posttraumatic Stress Disorder

Development Over Time and Response to Treatment

Michael G. Griffin, Ph.D.

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"Now I want you to relax completely!"
Eventually, Billy came to dread his father’s lectures over all other forms of punishment.
Why Study Biological Changes in PTSD?

- Normative Stress Response vs Abnormal Stress Response
- Objective Indicator of PTSD: Biological Markers
  - Diagnosis
  - Differential Diagnosis
  - Treatment Outcome & Predictors of Tx Outcome
- Risk Factors for Development of Disorder
- Identification of PTSD Subtypes (e.g., Dissociative?)
Biological Approaches to the Study of PTSD

- Psychophysiological Approach
  - Responses to Trauma-Specific Stimuli (e.g., scripted imagery, lab monologue)
  - Responses to Intense Neutral Stimuli (e.g., startle / loud tone)

- Psychoendocrine Approach
  - Response to Endocrine Challenge (e.g., DST)
Trauma Samples

- Acute Trauma Survivors studied longitudinally (1Mo Post and 6Mo Post)
  - Trauma Cue Reactivity and Startle/Loud Tone Reactivity

- Treatment Outcome Studies
  - CBT with Cognitive Processing Therapy
  - Trauma Cue Reactivity and Startle/Loud Tone Reactivity
Enhanced Startle in PTSD

- Previous studies have generally shown that participants with PTSD have a greater magnitude startle response than those without PTSD.

  - **Combat veterans** (Butler, et. al., 1990; Grillon et.al., 1996; Morgan et. al., 1995a, 1995b; Orr et.al., 1995, 1997)

  - **Mixed trauma** victims including motor vehicle accidents, sexual assault, and childhood sexual abuse (Shalev et. al., 1992, 1997, 2000; Morgan et. al., 1997; Orr et. al., 1999)
Startle in Combat Vets

Heart Rate

Eye Blink EMG

Skin Conductance

Data from Orr, et.al., 1995 J. Abnorm. Psych.
Startle Reactivity in PTSD

- There is little information about the development of startle following trauma.
- There is even less information about how or if startle responding is modified by treatment.
- We have examined these questions by assessing psychophysiological startle reactivity in the laboratory.
A Prospective Assessment of Auditory Startle Alterations in Rape and Physical Assault Survivors

Michael G. Griffin
Department of Psychology & Center for Trauma Recovery, University of Missouri-St. Louis, St. Louis, MO

This study used a prospective design to investigate startle reactivity following trauma exposure. Startle response was evaluated using loud tones during which measures of eyeblink electromyogram (EMG) and heart rate (HR) were collected. Participants were 40 female sexual or physical assault survivors assessed at 1 month and 6 months postassault. There were no significant differences in startle reactivity between posttraumatic stress disorder (PTSD) and non-PTSD groups at the initial assessment. However, at 6 months postassault there was a significantly greater EMG and HR response in the PTSD group as well as a significant increase in startle reactivity from 1 month to 6 months postassault. The findings lend support to a sensitization model of trauma reactivity in which startle response develops over time along with PTSD symptoms.
Methods

**Auditory Startle Stimuli**

- Stimuli were ten 95 dB, 1000Hz pure tones presented for 500ms with nearly instantaneous rise and fall times
- Intertrial intervals were randomly varied from 32 - 52 seconds
- Startle stimuli were presented binaurally over headphones
Results

Heart Rate: Startle Reactivity

One-Month Post

<table>
<thead>
<tr>
<th>Startle Stimuli</th>
<th>PTSD</th>
<th>Non PTSD</th>
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<tbody>
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Six-Months Post

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<th>Startle Stimuli</th>
<th>PTSD</th>
<th>Non PTSD</th>
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<td>Sig</td>
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Heart Rate: Startle Reactivity

n.s.

.05
Results

EyeBlink EMG: Startle Reactivity

One-Month Post

Six-Months Post
PTSD Group Response x Time Post Assault

< 10 Days Post
N = 6

> 20 Days Post
N = 10

* p < .05
Treatment Outcome Research

Does Physiologic Response to Loud Tones Change Following Cognitive–Behavioral Treatment for Posttraumatic Stress Disorder?

Michael G. Griffin, Patricia A. Resick, and Tara E. Galovski

1Department of Psychology and Center for Trauma Recovery, University of Missouri-St. Louis, St. Louis, Missouri, USA
2National Center for PTSD, VA Boston Healthcare System and Boston University, Boston, Massachusetts, USA

- Comparisons Pre – Posttreatment
- Treatment Responders vs Treatment Nonresponders
Utility of Biological Measures in Treatment Studies

- Objective indicators of treatment outcome.
- Biological markers may be helpful in determining treatment strategy. For example, biological measures that can be assessed within therapy may allow an evaluation of exactly where treatment begins to produce efficacy or relief from PTSD symptoms.
- Discussion of biological alterations can be therapeutic for the client. This includes helping the client understand why they are having symptoms and normalizing their reactions.
- Added benefit of objectively demonstrating alterations in biological variables following treatment.
Methods

Cognitive-Behavioral Treatment for PTSD

- Data were collected as part of an ongoing treatment outcome study for rape and physical assault survivors with PTSD
- Treatment Summary:
  - Assist the client to cognitively process accurate, emotion-laden memories and resolve conflicts between memories of the event which cannot be avoided
  - Specific modules to help the client modify problematic beliefs in areas frequently affected by victimization: safety, trust, power/control, esteem, and intimacy
  - Exposure component in which clients are encouraged to activate their memory of the event and to experience their emotions
- Treatment duration was 6 - 12 weeks
Methods

Data Analyses

Main Effect Variables:

- **Group**: Based upon
  - Treatment responders (N=53) (defined as not meeting CAPS criteria for PTSD diagnosis at posttreatment)
  - VS
  - Treatment Non-responders (N=21) (defined as continuing to meet CAPS criteria for PTSD at posttreatment)

- **Time**: Based upon
  - Pre- vs Posttreatment assessment

Interaction Effect:

- Group x Time
Results

Clinical Findings

<table>
<thead>
<tr>
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<th>Pretreatment</th>
<th>Posttreatment</th>
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<tr>
<td>CAPS Total</td>
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<tr>
<td>BDI</td>
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<tr>
<td>PDEQ</td>
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</table>

- Pretreatment: p<.001
- Posttreatment: p<.001

Legend:
- Treatment Responders (N=53)
- Treatment NonResponders (N=21)
Results

Clinical Findings

![Bar chart showing clinical findings for Responders and Non Responders before and after treatment.](chart)

- Pretreatment scores for Reexp, Avoid, Arous, CAPS Startle are compared between Responders and Non Responders.
- Posttreatment scores show significant reductions for Responders compared to Non Responders.

** p<.001, * p=.05
Results

Heart Rate: Startle Reactivity

Pretreatment

Posttreatment

Group x Time Interaction ($F_{1,57} = 9.0$, $p<.01$)

Simple Main Effects:

Group Effects: Pretreatment = n.s.

Posttreatment ($F_{1,57} = 15.2$, $p<.001$) NR > R

Time Effects: Nonresponders Pre-Post = n.s.

Responders Pre-Post ($F_{1,41} = 23.4$, $p<.001$) Pre > Post

$n.s.$
Results

EyeBlink EMG: Startle Reactivity

Group x Time Interaction ($F_{1,59} = 4.5, p<.05$)
Simple Main Effects:
- Group Effects: Pretreatment = n.s.
- Posttreatment ($F_{1,59} = 9.8, p<.01$) NR > R
Time Effects: Nonresponders Pre-Post = n.s.
- Responders Pre-Post ($F_{1,43} = 12.2, p<.001$) Pre > Post
Discussion

- Findings indicate that treatment responders showed a significantly smaller startle response to auditory tones after treatment compared to treatment non responders.

- Treatment non responders showed no significant change in startle responding from pre- to posttreatment.
Discussion

- Previous studies of trauma survivors suggest that heightened startle reactivity may become a chronic response.
- Results suggest that startle response can be modified with successful treatment.
Psychophysiological Alterations Following Cognitive Processing Therapy with Hypnosis

Michael G. Griffin, Ph.D.
University of Missouri - St. Louis
Department of Psychological Sciences & Center for Trauma Recovery

Tara E. Galovski, Ph.D.
National Center for PTSD & Boston VA Medical Center

&

Kimberly B. Werner, Ph.D.
Washington University in St. Louis Brown School of Social Work

This work was supported by NCCAM grant MH55688 (PI- Galovski)
Current Study

- Randomized controlled trial of Cognitive Processing Therapy (CPT) preceded for 3 weeks by either a hypnosis (hyp) component or a sleep and symptom monitoring (ssm) component.

- A primary goal was to evaluate if hypnosis would be effective to improve sleep difficulties in trauma survivors.

- Additional goals included incorporating objective physiological assessments of treatment outcome.
Treatment Conditions

- **Sleep & Symptom Monitoring (3 weeks) then Cognitive Processing Therapy (ssmCPT)**
  - Three weeks of daily monitoring of symptoms of Sleep, PTSD, & Depression with weekly phone checks by their therapist

- **Hypnosis Training (3 weeks) along with ssm then Cognitive Processing Therapy (hypCPT)**
  - Hypnosis protocol included 3 weekly 60min sessions targeting sleep issues including sleep onset and mid-sleep awakening (relaxation, hypnotic trance induction, guided imagery)
Cognitive Processing Therapy (CPT)

- CPT was administered individually and consisted of 12 weekly, 60-minute sessions (Resick et al., 2010).
- CPT is predominantly a cognitive therapy in which patients are taught to identify, question, challenge and replace faulty assumptions and thoughts about the traumatic event.
- Patients engage with the traumatic memory and allow natural affect to run its course.
- CPT first targets specific, inaccurate interpretations of the trauma itself and then targets current and future maladaptive and inaccurate beliefs about world, self, and others.
Methods

Inclusion Criteria

- Female
- Sexual or Physical Assault
- PTSD diagnosis (CAPS DSM-IV)
- Clinically significant sleep impairment (severity score 3 or greater on CAPS D1)
- At least 3Mo post trauma
- Stable on any psychotropic meds

All study procedures were approved by the Institutional Review Board at the University of Missouri- St. Louis
Measures

- Clinician Administered PTSD Scale (CAPS DSM-IV; Blake et al., 1990)
- Beck Depression Inventory (BDI-II; Beck et al., 1996)
- Pittsburgh Sleep Quality Index (PSQI; Buysse et al, 1989)
- Insomnia Severity Index (ISI; Morin 1993)
- Script-Driven Imagery Psychophysiology (Lang et al., 1983)
Participant Demographics

- Age: 18 -70 (M=36.9, SD=11.8)
- Race: 50% African American; 50% White
- Marital Status: 54% single; 16% married/cohabiting; 30% divorced/sep/widowed
- Education: M=14.2 years, SD=2.9 years
- Income: 74% < 20K
Trauma Characteristics

- Lifetime endorsement of child sexual abuse 71%; child physical abuse 58%; adult sexual assault 63%; other adult victimization 32%; domestic violence 56%

- Index event for treatment and assessment:
  - 39% Child Sexual Abuse
  - 11% Child Physical Abuse
  - 26% Adult Sexual Assault
  - 24% Adult Physical Assault
Assessments

- Conducted at the following time points:
  - Pre-treatment (prior to any intervention)
  - Status Check (following hyp or ssm)
  - Post-treatment (after CPT)
  - Follow-up (3 months post)
### Script-Driven Imagery Procedure

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Script</th>
<th>Imagine</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>Playback over headphones</td>
<td>Imagine scene as vividly as possible</td>
<td>Rest</td>
</tr>
</tbody>
</table>

30 sec

Response scores were calculated:

- Script Mean – Baseline Mean
- Imagery Mean – Baseline Mean

* Adapted from Pitman & Orr
Scripts

- 2 Personalized Trauma Scripts
- 2 Neutral Scenes (Living Room & Sitting in a Lawn Chair)
- 1 Positive Scene (Beach)
- 1 Generic Stressor (Public Speaking)
BDI Score

- ssmCPT
- hypCPT

Pre Trt | Status Check | Post Trt | 3Mo Post
CAPS Sleep Item

- Pre Trt
- Status Check
- Post Trt
- 3Mo Post

- ssmCPT
- hypCPT
CAPS Nightmares Item

Graph showing the comparison of ssmCPT and hypCPT over time:
- Pre Trt
- Status Check
- Post Trt
- 3Mo Post

The graph indicates a decrease in nightmares for both groups with ssmCPT showing a slightly more rapid decrease compared to hypCPT.
PSQI Sleep Latency

- ssmCPT
- hypCPT

Pre Trt | Status Check | Post Trt | 3Mo Post
Clinically Significant Change in Sleep Scores

**PSQI Total**
(Decrease > 1SD)

**ISI Total**
(Decrease > 8points)

<table>
<thead>
<tr>
<th>Group</th>
<th>Percent of Participants</th>
</tr>
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<tbody>
<tr>
<td>hypCPT</td>
<td>50%</td>
</tr>
<tr>
<td>ssmCPT</td>
<td>20%</td>
</tr>
<tr>
<td>hypCPT</td>
<td>40%</td>
</tr>
<tr>
<td>ssmCPT</td>
<td>10%</td>
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Trauma Scripts: HR Change from Baseline

HR Change from Baseline

<table>
<thead>
<tr>
<th></th>
<th>Script</th>
<th>Imagery</th>
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<tbody>
<tr>
<td>Pre-Trt</td>
<td>ssmCPT</td>
<td>ssmCPT</td>
</tr>
<tr>
<td>Post-Trt</td>
<td>hypCPT</td>
<td>hypCPT</td>
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</tbody>
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HR (bpm)
Trauma Scripts: SC Change from Baseline

![Graph showing SC change from baseline for scripts and imagery](image)
Public Speaking Script: HR Change from Baseline

![Bar chart showing HR change from baseline for Script and Imagery conditions. The chart compares pre-trial (Pre-Trt) and post-trial (Post-Trt) conditions for ssmCPT and hypCPT.](chart.png)
Lawn Chair Script: HR Change from Baseline

HR (bpm)

Script

Imagery

Pre-Trt  Post-Trt

Pre-Trt  Post-Trt

ssmCPT  hypCPT
Beach Script: HR Change from Baseline

Script

Imagery

HR (bpm)

Pre-Trt  Post-Trt  Pre-Trt  Post-Trt

ssmCPT  hypCPT
Trauma Scripts
Trt Responder vs Non Responder (& Dropouts): HR Change from Baseline

Script

Imagery

HR (bpm)

Pre-Trt  Post-Trt  Pre-Trt  Post-Trt

Trt Responders

Trt NonResponders & Dropouts
Conclusions

- **Treatment clinical outcome:**
  - Both conditions successfully treated PTSD and depressive symptoms (depression better in hypCPT)
  - Sleep impairments improved more quickly in the hypCPT condition
  - The ssmCPT condition did catch up and show similar sleep improvements by the follow-up assessment
Conclusions

- Treatment Psychophysiology Outcome
  - No significant differences between the treatment conditions on psychophysiology
  - Treatment was accompanied by a significant reduction in psychophysiological arousal.
  - This was specific to trauma cues
  - This was also specific to successful treatment (losing a PTSD Dx)
  - Biology can be altered by successful treatment
Acknowledgements

Collaborators:
- Dr. Patricia Resick, Ph.D.
- Dr. Tara Galovski, Ph.D.
- Dr. Mindy Mechanic, Ph.D.
- Dr. Kimberly Werner, Ph.D.

Current Graduate Students in my Lab:
- Brittany Preston, M.A.
- Rebecca Delgado, M.A.
- Sydney Harris, B.A.
“It’s time we face reality, my friends. ... We’re not exactly rocket scientists.”
Participant Flow Chart

181 Assessed for Eligibility

108 Randomized

56 Symptom Monitoring + Cognitive Processing (ssmCPT)
25 Completers (21 Physio)
23 Drop-outs
8 Removed

25 Completed post-treatment
23 Lost to post-treatment
2 Completers
11 Drop-outs

52 Hypnosis + Cognitive Processing (hypCPT)
26 Completers (21 Physio)
18 Drop-outs
8 Removed

29 Completed post-treatment
15 Lost to post-treatment (all drop-outs)

62 Ineligible
11 Did not complete assessment
Affect-Startle Effect

Data from Vrana, Spence & Lang 1988
Neural Systems Involved in Acoustic Startle Response

- Ventral Cochlear Nucleus (VCN)
- Ventral Nucleus of the Lateral Lemniscus (VLL)
- Nucleus Reticularis Pontis Caudalis (RPC)
- Medial Longitudinal Fasciculus (MLF)
- Spinal Cord
- Muscle Response