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Grady
Trauma
Project

Dysregulated Fear Responses in Adults and Children from a Traumatized Inner City Population

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Grady Trauma Project: Risk and Resiliency



www.gradytraumaproject.com

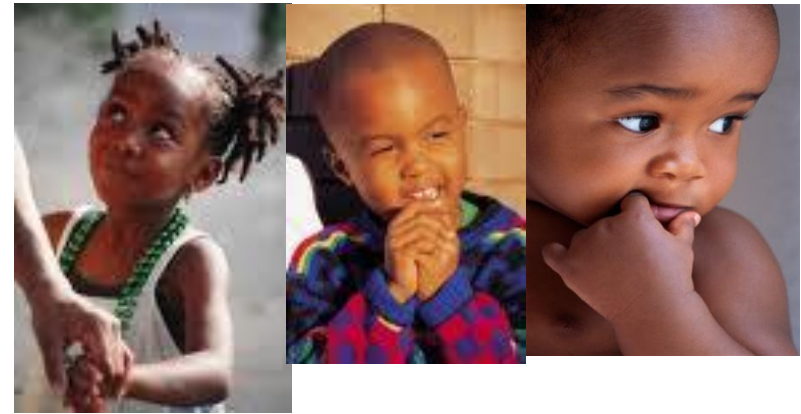
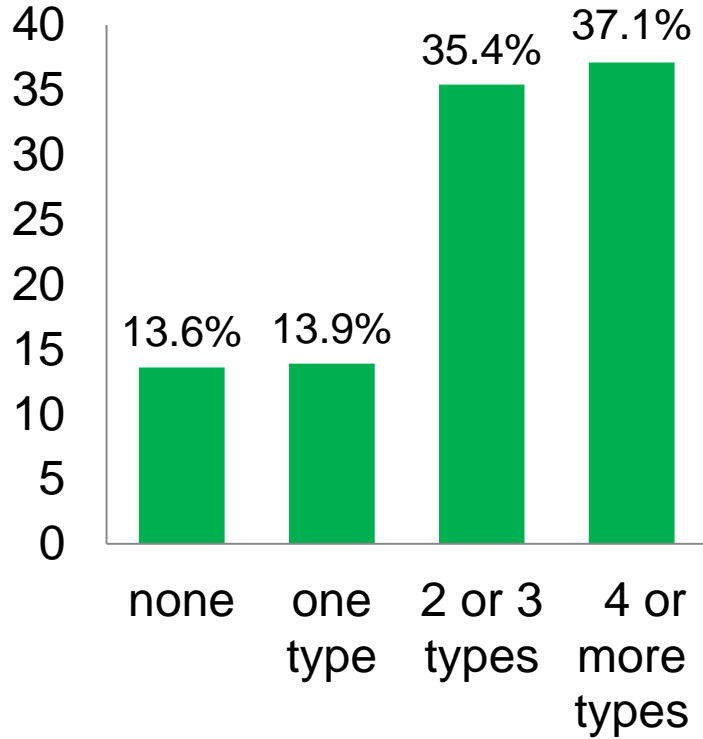
PIs: Kerry Ressler, MD, PhD and Bekh Bradley, PhD

Severe Inner-city Trauma

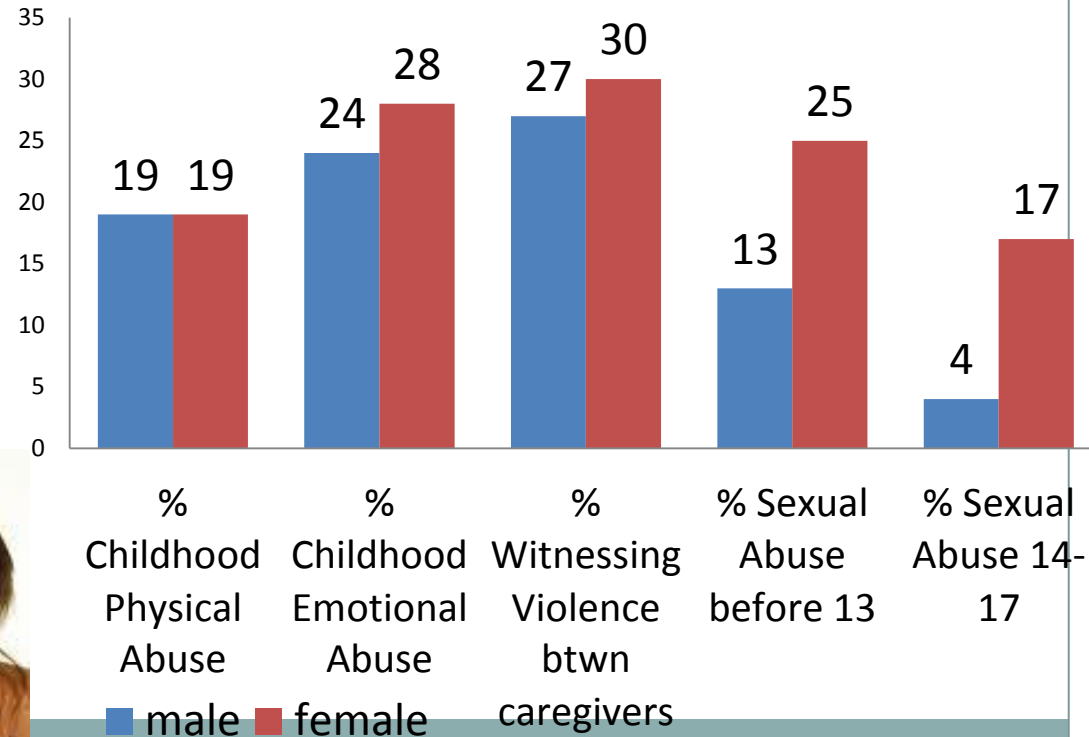


TRAUMATIC EVENTS INVENTORY	Percent of Sample
Natural Disaster	20.69
Serious Accident or Injury	55.77
Sudden Life-Threatening Illness	38.60
Military Combat	9.26
Close Friend or Family Member Murdered	3.57
Close Friend or Family Member Committed Suicide	8.77
Attacked with Weapon	35.09
Attacked Without Weapon	34.55
Violence Between Parents or Caregivers	35.19
Beaten as a Child	35.71
Sexual Contact Before Age 13	21.43
Forced Sexual Contact Between 14 and 17	9.09
Forced Sexual Contact After Age 17	9.80

- Exposure to multiple types of trauma is the rule rather than the exception



Trauma Exposures Often Include Childhood Abuse and Other Types of Family Violence



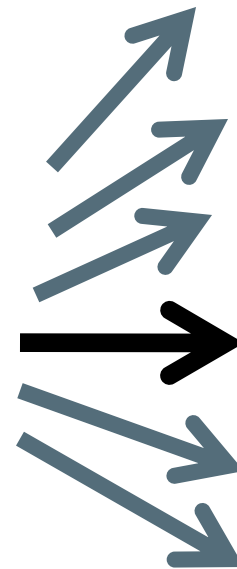
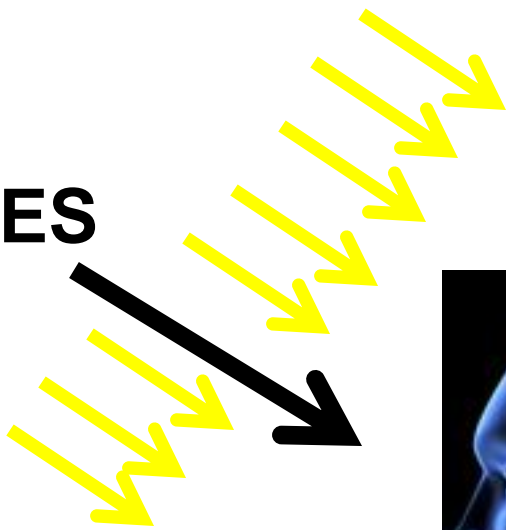
PTSD—The Disorder



- Onset determined by traumatic event, but low rates of illness relative to trauma exposure: gene X environment risk factors
- Heterogeneous: three major symptom clusters
 - Re-experiencing (intrusive) symptoms
 - Avoidance symptoms
 - Hyper-arousal symptoms
- High rates of comorbidity with depression, other anxiety disorders, substance abuse



GENES



PTSD



**ENVIRONMENT
TRAUMA**



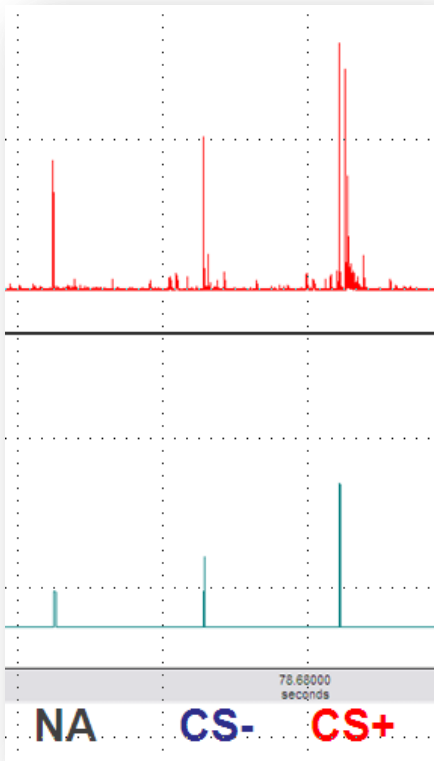
**NEUROBIOLOGICAL
BIOMARKERS**



"Did I startle you?"



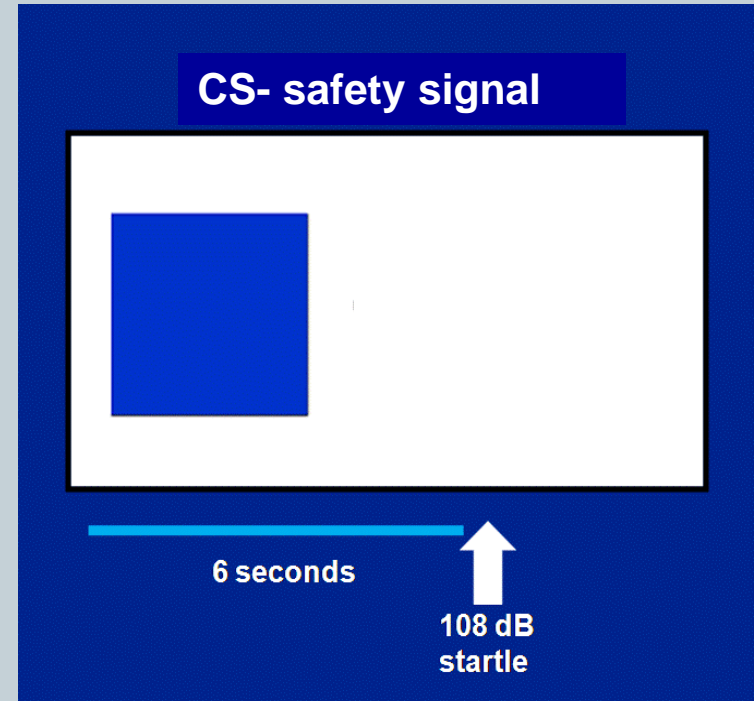
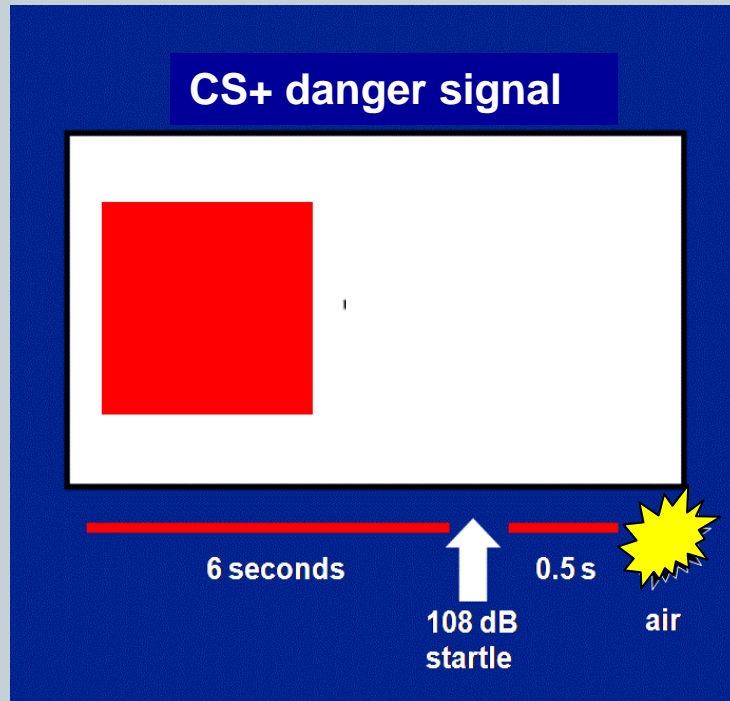
Biomarker: ACOUSTIC STARTLE RESPONSE



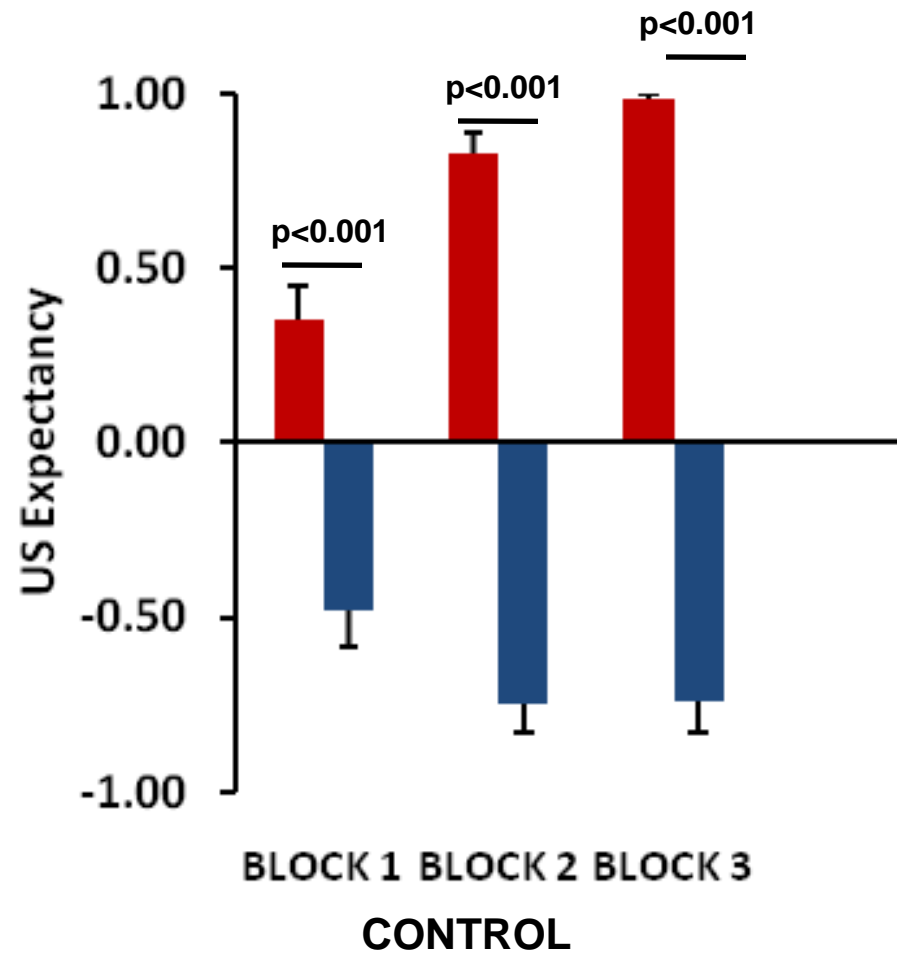
Simple Discrimination: A+/B-



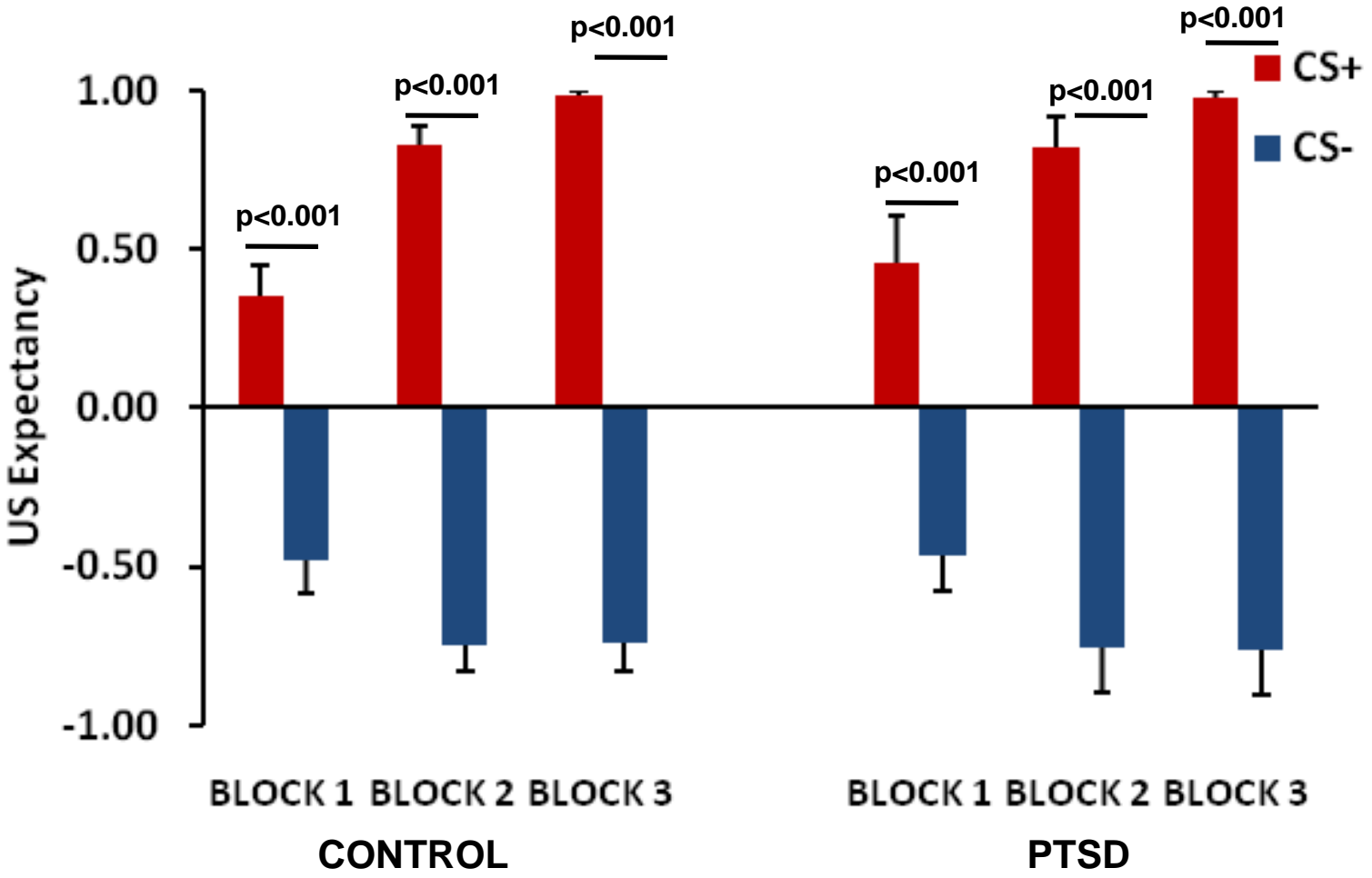
Acquisition: 3 blocks of 4 trials



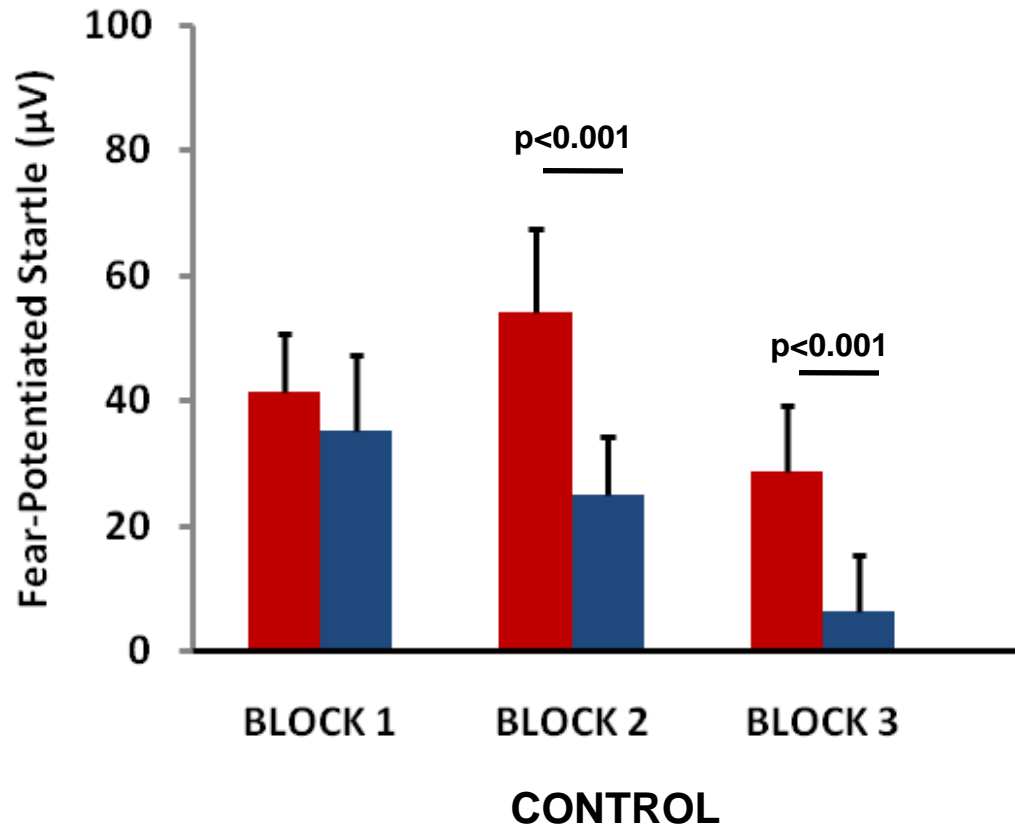
Cognitive discrimination between CS+ and CS-



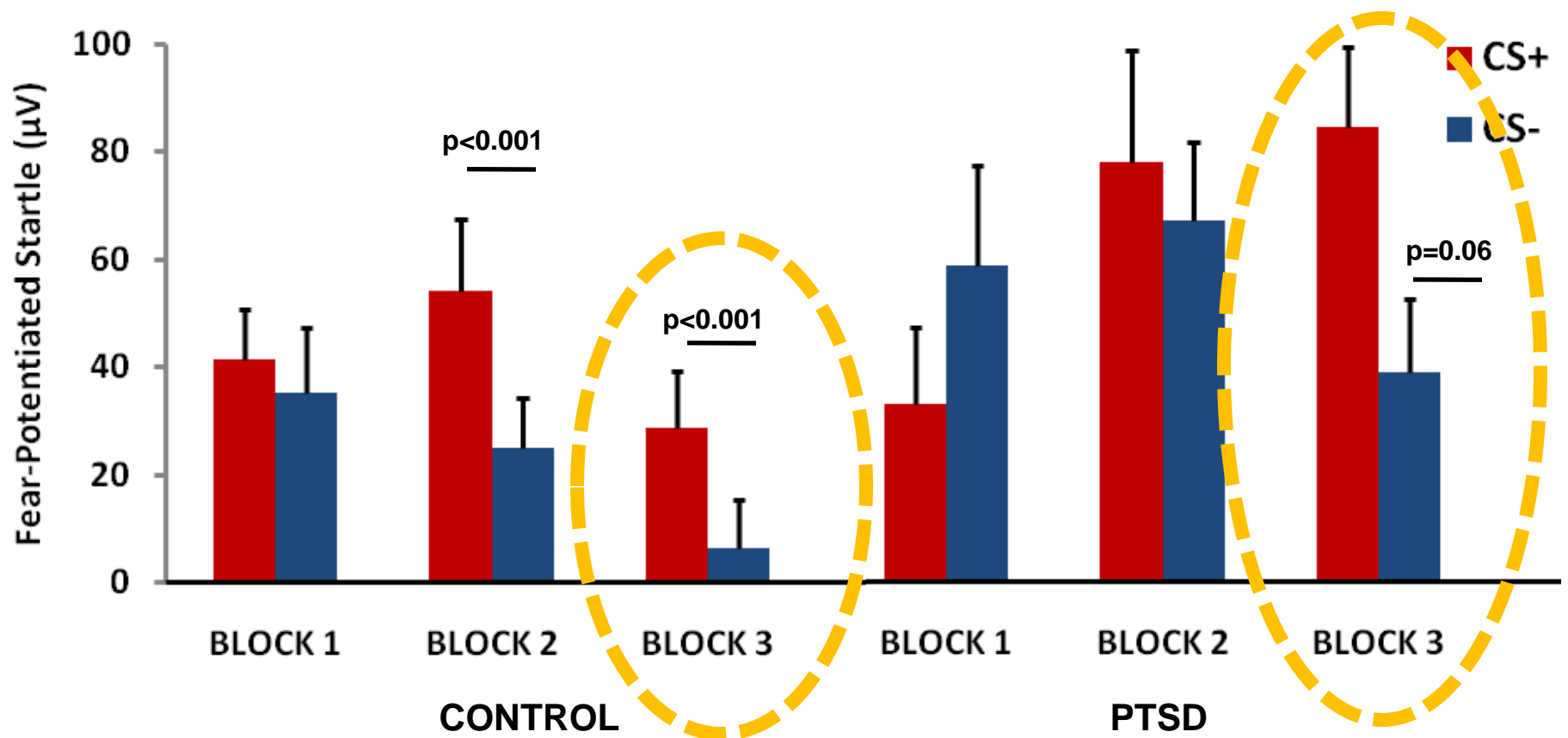
Cognitive discrimination between CS+ and CS-



Startle discrimination between CS+ and CS-



Startle discrimination between CS+ and CS-



Correlation between startle to CS+ and CS- and PTSD symptoms

		TEI	CTQ	BDI	PSS Intrusive	PSS Avoidance	PSS Hyperarousal
CS+ DANGER	Pearson r	.07	.04	.18	.27*	.03	.19
	p	.57	.74	.15	.03	.84	.13
CS- SAFETY	Pearson r	.14	.08	.19	.18	.09	.31*
	p	.26	.58	.13	.15	.45	.01

B) Outcome: Hyper-Arousal PTSD Symptoms

Predictors:	R ²	R ² Change	F Change	p
1. Age, Sex, and Race	0.003	0.003	0.11	ns
2. Childhood and Adult Trauma	0.134	0.131	7.56	0.001***
3. Startle to Safety Cue	0.191	0.057	7.00	0.009**
4. SCR to Safety Cue	0.194	0.003	0.32	ns

Fear inhibition is impaired in PTSD

frontiers in
BEHAVIORAL NEUROSCIENCE

Tanja Jovanovic^{1*} and Seth Davin Norrholm^{1,2}



Contents lists available at ScienceDirect

Neuropharmacology

journal homepage: www.elsevier.com/locate/neuropharm

Tanja Jovanovic^{a,*}, Andrew Kazama^b, Jocelyne Bachevalier^b, Michael Davis^{a,b}

Table 1

Summary of human clinical findings with the AX+/BX- paradigm.

	Fear learning (AX+ > NA)	Safety signal learning (BX- < AX+)	Safety signal transfer (AB < AX+)
Healthy volunteers	Yes	Yes	Yes
Combat PTSD	Yes	Yes/No	No
Civilian PTSD	Yes	No	No
Depression w PTSD	Yes	No	No
Depression w/o PTSD	Yes	Yes	Yes

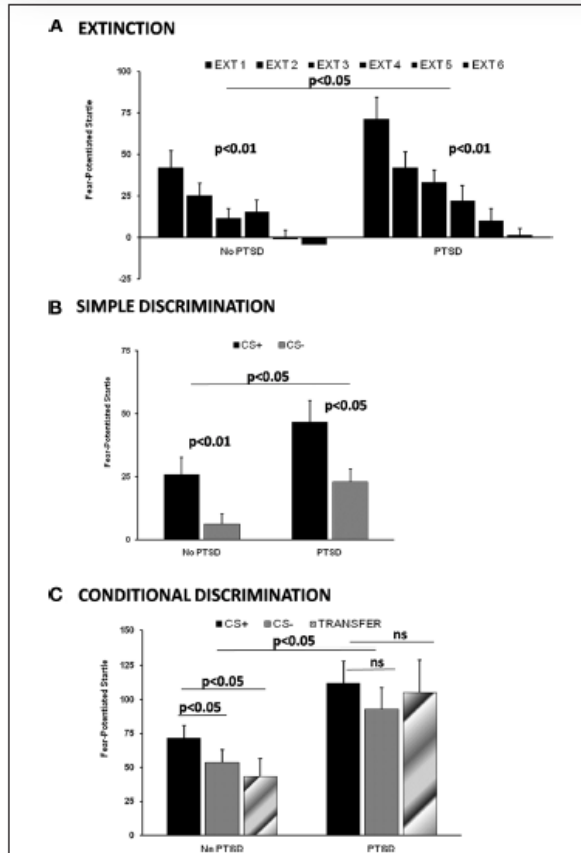


FIGURE 2 | Fear-inhibition data from our studies on a traumatized civilian population. (A) Extinction, adapted from (Norrholm et al., 2011); (B) Simple

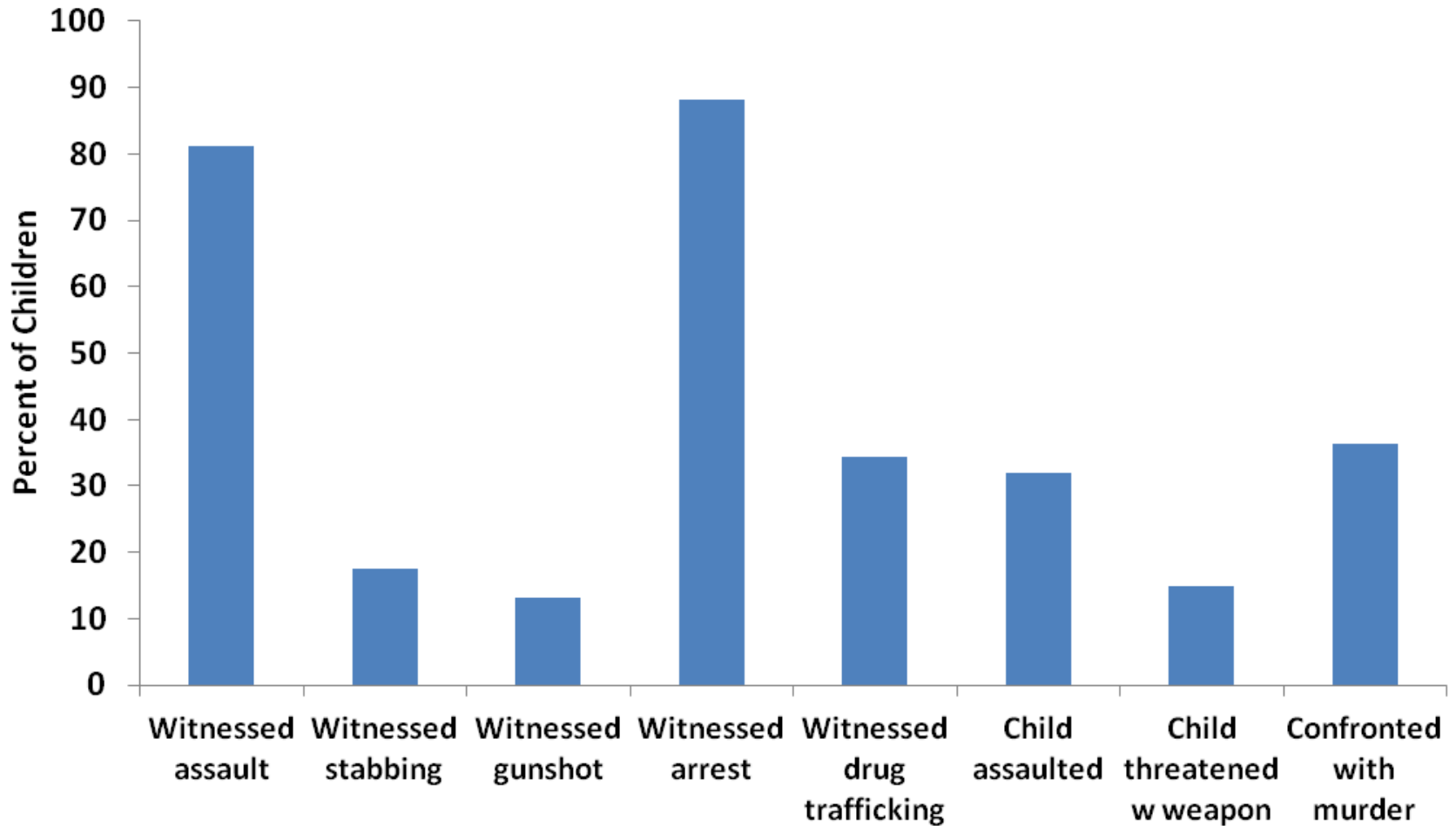
- PTSD is associated with impaired fear inhibition using 3 fear-potentiated startle paradigms
- Impaired fear inhibition is a biomarker of PTSD in different trauma populations



Longer-term effects:

**NEUROBIOLOGY OF
FEAR AND ANXIETY IN
THE NEXT
GENERATION**

Child trauma exposure at Grady :

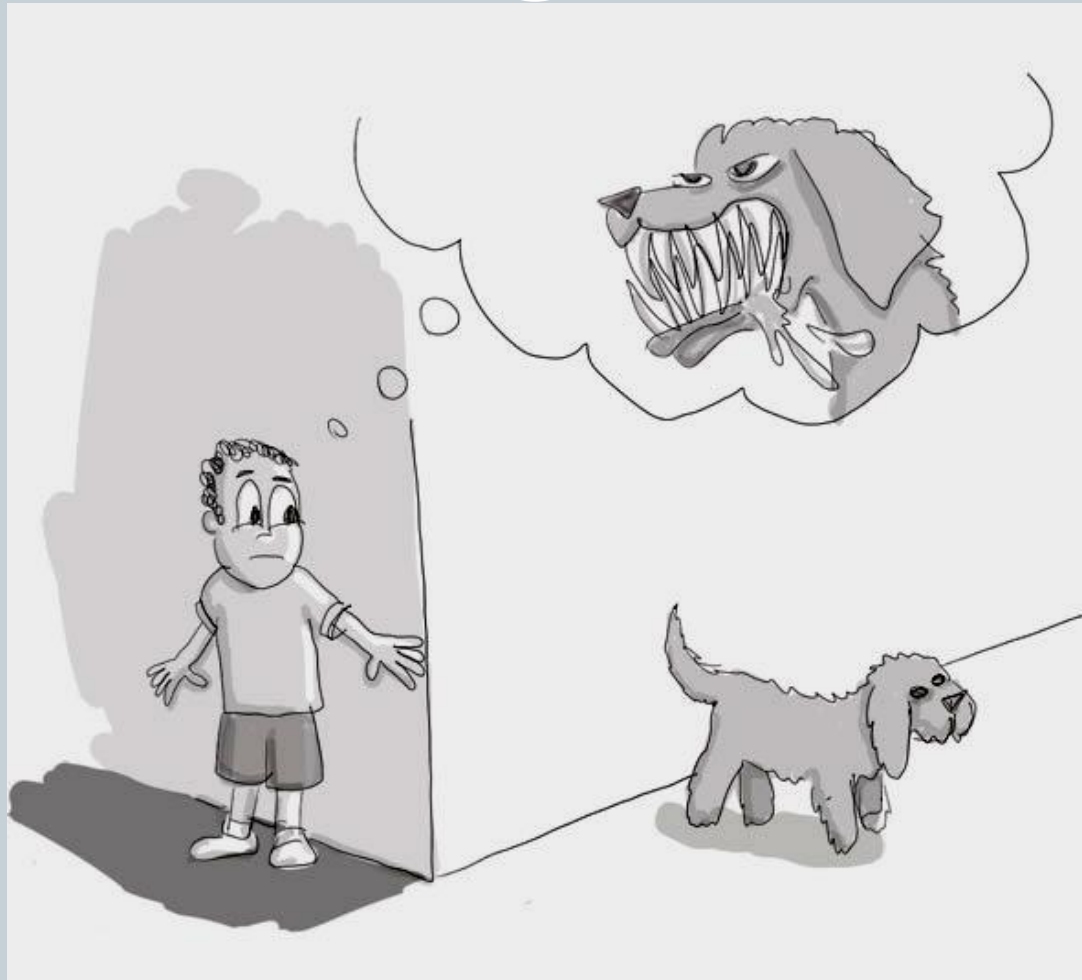


PTSD Symptoms in Children



- Bad Dreams and Fears
- Externalizing or “acting out” behaviors including impulsivity, irritability/anger and inattentiveness.
- Re-enact traumas (e.g., aggression, sexualized behaviors, need to control others). Such behaviors may emerge in an automatic manner in response to reminders of their traumatic experiences.

Generalization of Danger



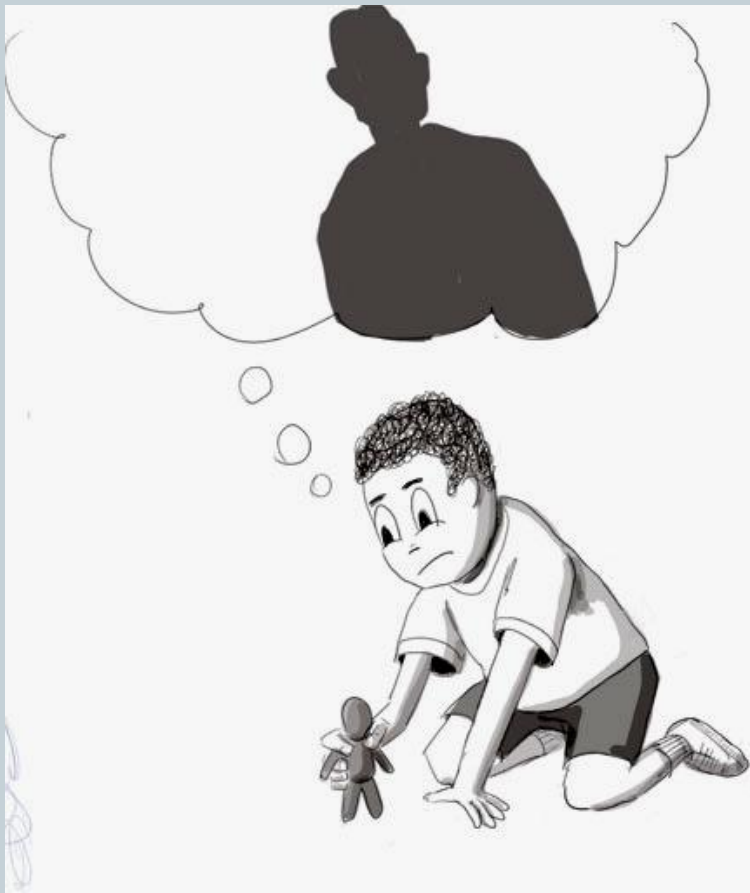
Nightmares



Re-enacting



Play or drawing of trauma



Kid Startle Team:

GTP Researchers:

Ami Smith, PhD

Dorthie Cross, MA

Will Holland

Jannifer Winkler

Sarah Spann

Jennifer Davis

Alicia Nelson

Bekh Bradley, PhD

Collaborators:

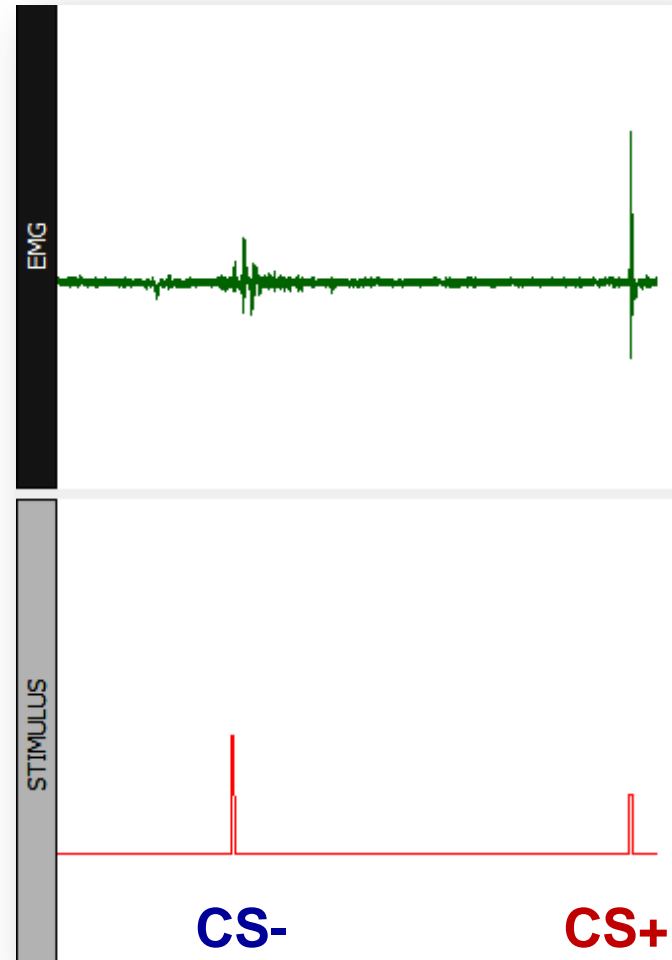
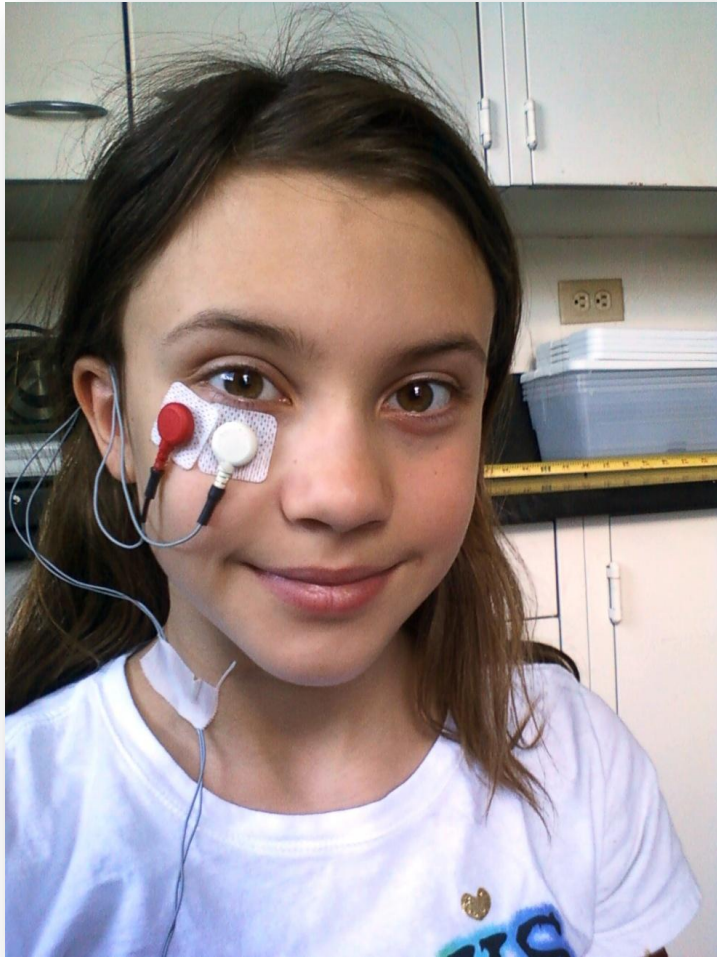
Erin Tone, PhD

Chaundrissa Smith, PhD

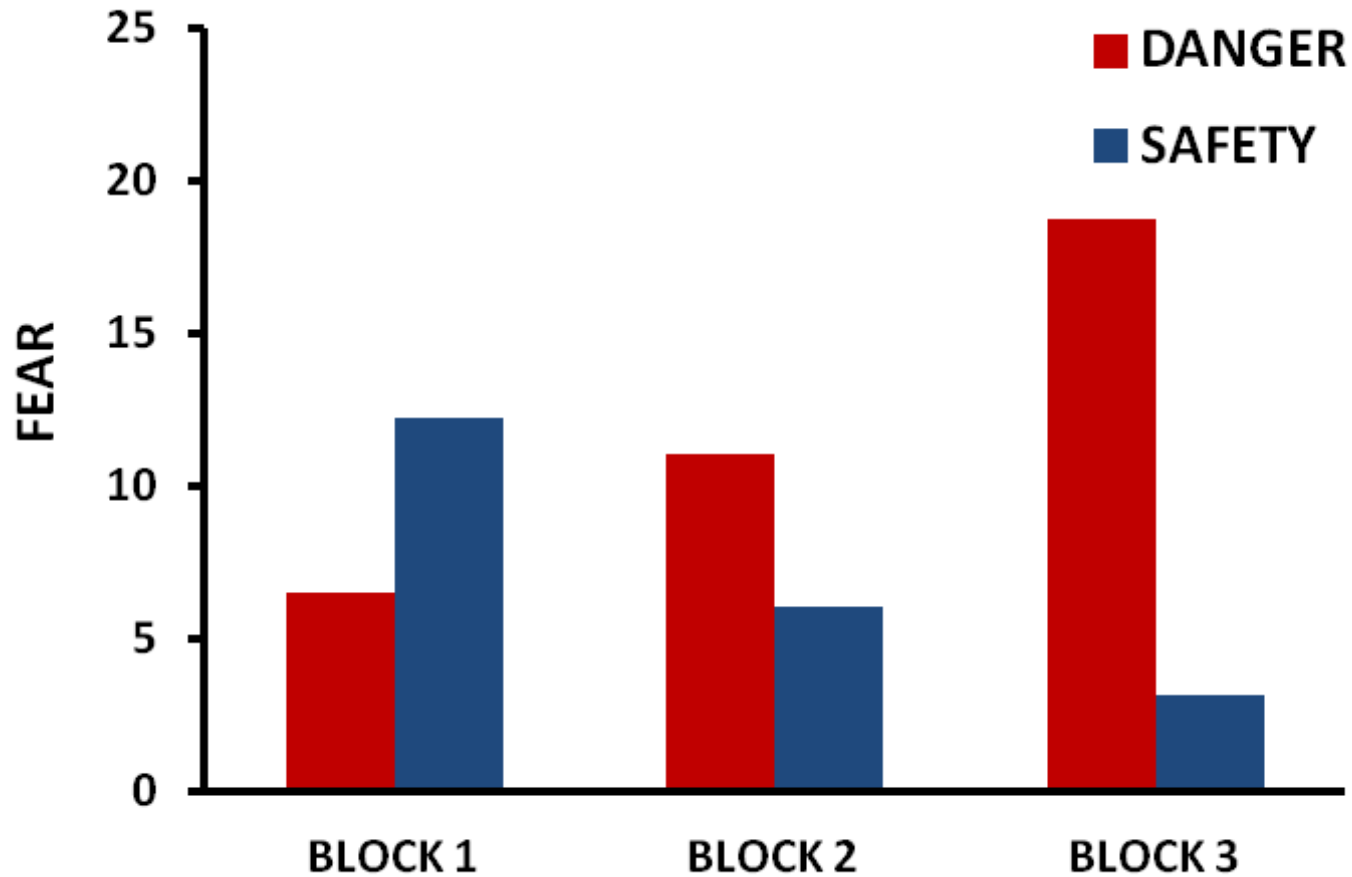
MaryAnn Jacobs, MD



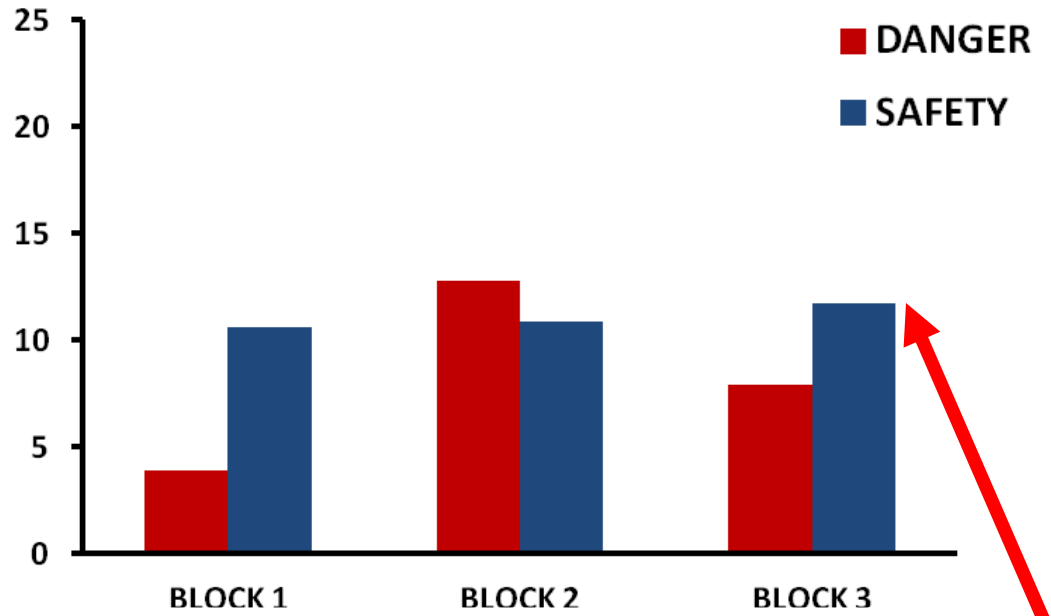
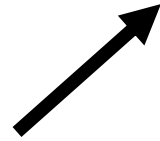
Fear conditioning in children



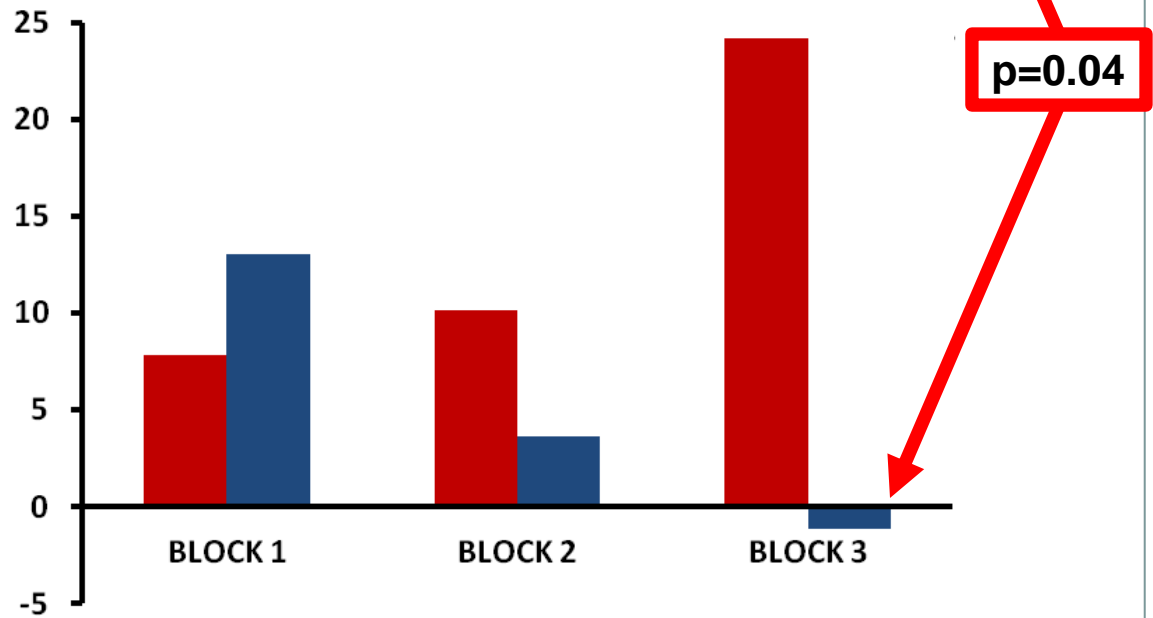
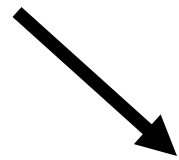
Preliminary data: fear-potentiated startle in children



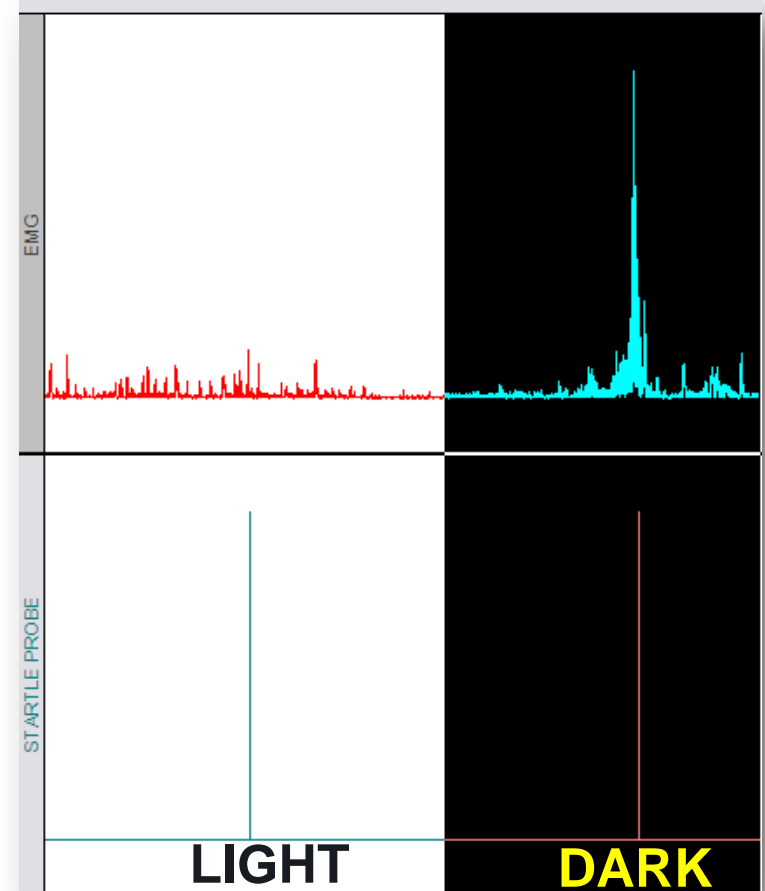
AGE<10



AGE=10-12



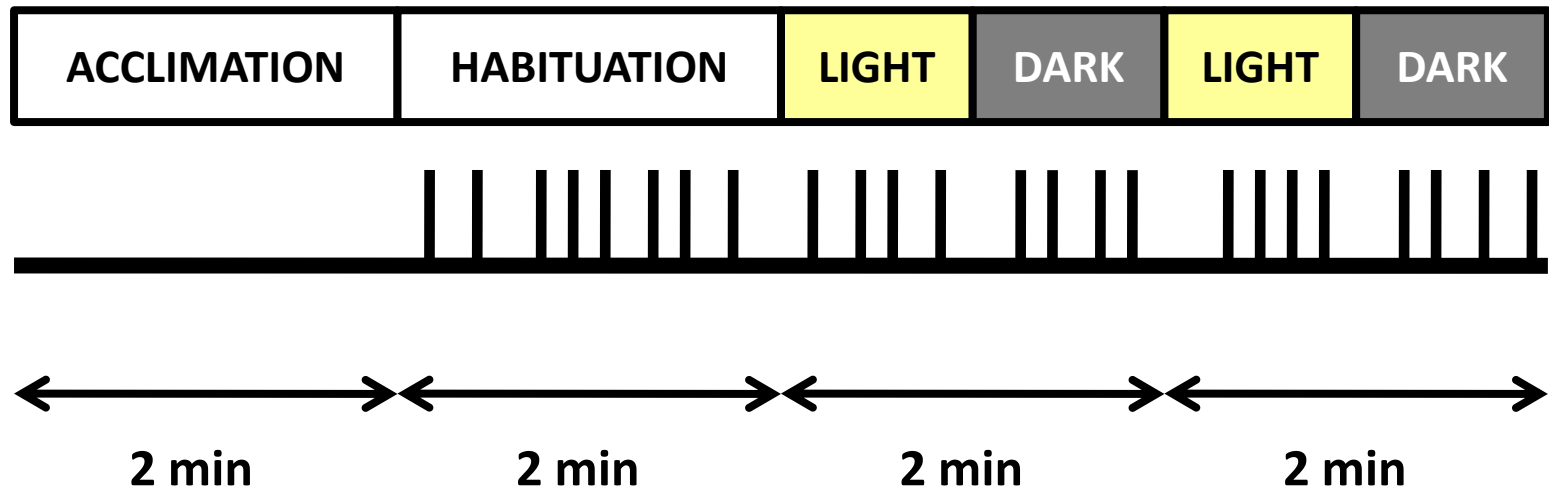
Startle in Children of Abused Mothers



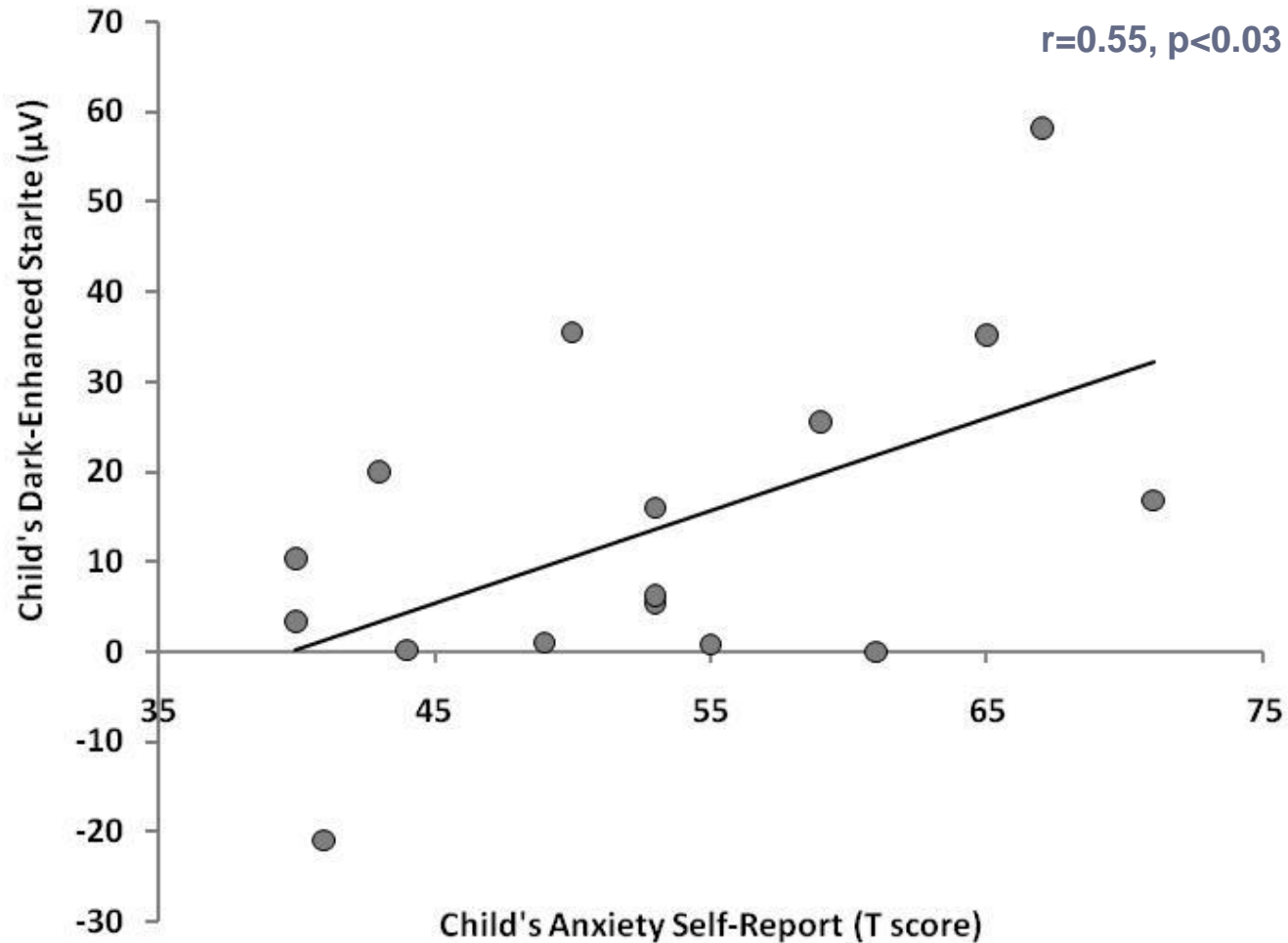
Dark-Enhanced Startle



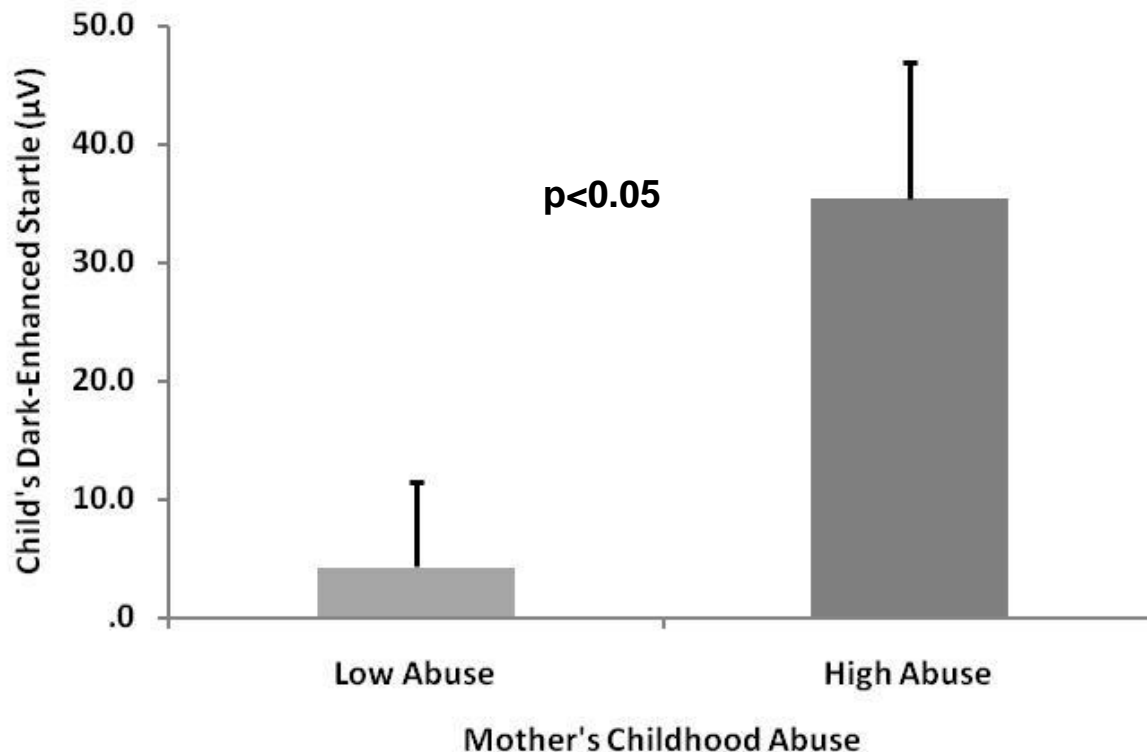
- Startle magnitude greater in dark than light
- Nonspecific anxiety marker
- Greater in “high-risk” adolescents (risk defined by parental anxiety or depression)



Dark-enhanced startle is associated with anxiety in children



Children of abused mothers startle more in the dark



- Children of mothers with high levels of abuse have higher dark-enhanced startle than children of mothers with low levels of childhood physical abuse

Increased dark-enhanced startle is not due to maternal mental illness or child's own trauma

Dark-Enhanced Startle				
MODEL	R²	R² Change	F Change	p
1. Child's Age and Sex	0.06	0.06	0.71	0.50
2. Child's Trauma	0.09	0.03	0.75	0.40
3. Maternal PTSD	0.13	0.04	0.90	0.35
4. Maternal Depression	0.13	0.00	0.10	0.76
5. Maternal Childhood Physical Abuse	0.42	0.28	9.24	0.007

Conclusions



- Physiological markers such as the startle response provide potential biomarkers of PTSD risk in adults and children
- Trauma has long-term neurobiological consequences for the victim as well as the victim's children: multigenerational effects

Acknowledgements:

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- ❖ Neurological Disorders
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