



Grasser, Lana Ruvolo¹; Wanna, Cassandra¹; Minton, Sean²; Phillips, Karlye A³; Durmornay, Nathalie³; Seligowski, Antonia³; McClean, Sam⁴; & Jovanovic, Tanja¹

1. Wayne State University; 2. Emory University; 3. McLean Hospital/Harvard University; 4. University of North Carolina
CONTACT: Lana Ruvolo Grasser, lgrasser@med.wayne.edu @scientificruvvy on Twitter

ABSTRACT

Background: Exposure to trauma increases risk for mental health disorders, including substance use. As a putative biomarker for PTSD, fear-potentiated startle (FPS) may also have clinical utility as a predictive biomarker for substance use disorders in the context of trauma exposure. This study recruited participants in the Emergency Department (ED) as part of the AURORA study; we hypothesized that FPS immediately following trauma would predict more severe substance use later.

Methods: Trauma-exposed individuals completed a differential fear conditioning FPS paradigm within 2 weeks of trauma exposure. Participants were followed longitudinally at 2, 8 weeks and 3 months, and responded to questionnaires regarding PTS symptoms and substance use. A linear regression model was used to test whether FPS to danger (CS+) or safety (CS-) cues predicted substance use, after controlling for PTS symptoms

Results: FPS to the CS+ within 2 weeks of trauma exposure significantly predicts frequency of concurrent alcohol use and alcohol use two months following exposure when controlling for age, sex, race, and posttraumatic stress symptoms, $R=.26$, $R^2=.07$, $R^2\text{change}=.03$, change in $F(1,145)=4.97$, $p=.03$, $b=.01$, $t=2.23$, $p=.03$ for W2; $R=.22$, $R^2=.05$, $R^2\text{change}=.03$, change in $F(1,137)=4.15$, $p=.04$, $b=.01$, $t=2.037$, $p=.04$. There was not enough variance in use patterns for marijuana, cocaine, heroin, hallucinogens, sedatives, barbiturates, nor stimulants to explore FPS as a predictor of use. Mindfulness was not associated with substance use nor FPS, and did not mediate the relation between FPS and use. Use prior to trauma significantly moderated the relation between FPS and future alcohol use, change in $R^2=.03$, change in $F(1,142)=7.116$, $p=.01$.

Conclusions: FPS may be a clinically viable indicator of future alcohol use patterns in individuals exposed to trauma, especially in previous frequent users, and this method could potentially identify individuals in need of early intervention to prevent substance use disorders.

INTRODUCTION

Exposure to trauma and subsequent psychopathology—PTSD, anxiety, depression, etc.—puts individuals at increased risk for physical health conditions such as cardiovascular disease and metabolic syndrome, as well as substance use disorders. Fear-potentiated startle quantifies fear responses, overgeneralization of fear, and impairments in safety learning. Previous studies have indicated that enhanced startle is observed as a negative reinforcer of alcohol dependence and that FPS is elevated in adults with PTSD. However, other studies have also shown diminished startle response in chronic substance users with co-morbid PTSD. As a candidate biomarker for PTSD, FPS may also have utility as a predictive biomarker for substance use disorders, with differential characteristics for chronic versus acute users. Use of FPS in clinical settings could aid in determining those who may be at increased risk and require early intervention; exploring the mediating role of mindfulness characteristics within this relationship could point towards a viable intervention option.

Specific Hypothesis:

Startle response will predict substance use habits, with greater startle response (EMG) predicting greater usage of substances for acute users; diminished startle response will predict greater usage of substances for chronic users. The relationship between the two aforementioned variables will be mediated by mindfulness characteristics, where individuals who report more mindful tendencies will be less likely to use substances, even if they do present with heightened FPS.

METHODS

AURORA Study of Adverse Posttraumatic Neuropsychiatric Sequelae (APNS)

Individuals exposed to trauma are enrolled at emergency departments across the United States within 72 hours of exposure

Psychological Assessments

Participants complete self-report questionnaires and interviews at multiple timepoints following trauma exposure which assess posttraumatic stress symptoms, mindfulness characteristics, and substance use patterns

Fear-Potentiated Startle

Fear-potentiated startle is defined as the increase in the acoustic startle response elicited by the pairing of a conditioned stimulus (CS+) with an unconditioned stimulus (US; air blast to the larynx). Electromyogram (EMG) is used to measure startle magnitude (eyeblink component). CSs are two different colored shapes. During acquisition, the startle probe—a white noise burst—is delivered through headphones followed by presentation of a CS on a computer screen. The US follows the CS+ and is not paired with the non-reinforced cue (CS-). During the extinction phase, neither CS is presented with the US.

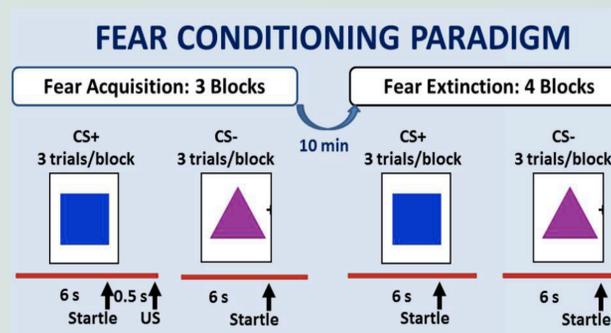


Figure 1. Fear-potentiated startle (FPS) paradigm. Participants complete this task two weeks following exposure to trauma

Statistical Design

A two-step hierarchical regression was used to test whether FPS explained a significant portion of variance in substance use when controlling for age, sex, race, and posttraumatic stress symptoms.

The PROCESS macro, model 4, was used to test the mediating role of mindfulness on the relation between FPS and substance use.

A two-step hierarchical regression was used to test the moderating effects of alcohol use prior to trauma exposure, with FPS to threat cue and prior use entered in block one, and FPS, prior use, and the interaction term in block two.

RESULTS

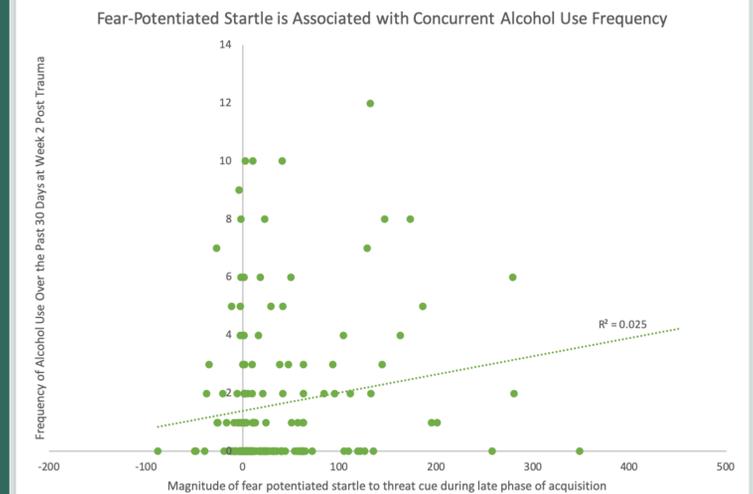


Figure 2. FPS to threat cue during the late phase of acquisition is significantly associated with concurrent alcohol use frequency (in days) two weeks following trauma exposure, $n=151$, $R=.26$, $p=.03$

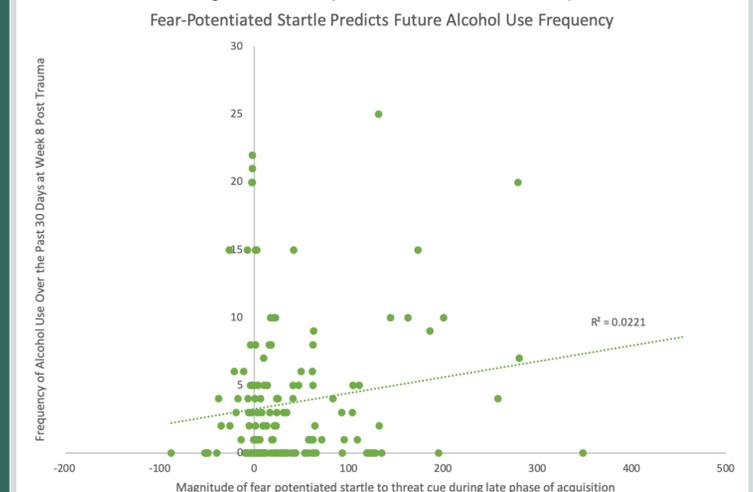


Figure 3. FPS to threat cue during the late phase of acquisition is significantly associated with future alcohol use frequency (in days) eight weeks following trauma exposure, $n=143$, $R=.22$, $p=.04$

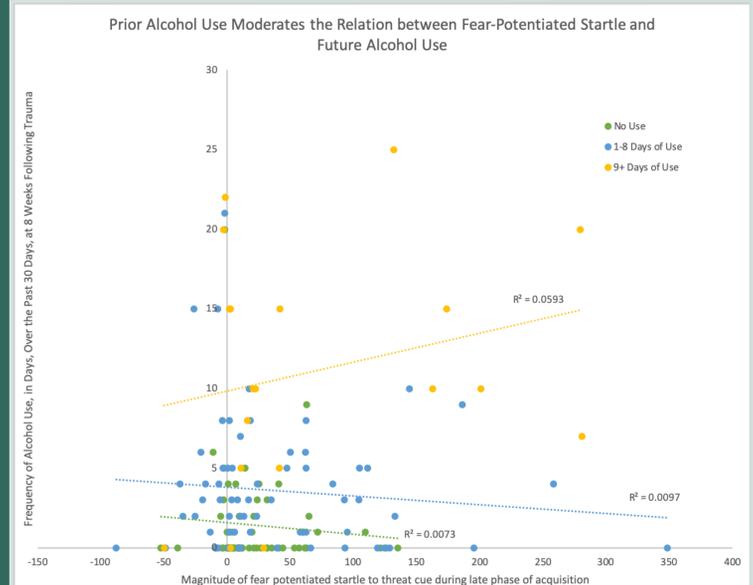


Figure 4. The relation between FPS and future use is significantly moderated by greater prior use (9+ days of drinking in a 30 day period prior to trauma), $n=146$, $R=.56$, $R^2=.32$, $b=.01$, $t=2.67$, $p=.01$.