

# Negative Affect During Nicotine Withdrawal

## Insights from Explicit-cue and Contextual Fear Conditioning Models

John J. Curtin, Ph.D., Joanne M. Hogle, M.A. & Jesse Kaye, University of Wisconsin, Madison

### ABSTRACT

Numerous theorists have suggested one primary motive for nicotine and other drug use is to alleviate negative affect experienced during drug withdrawal (e.g., Baker et al., 2004, Koob & LeMoal, 2001). A core assertion of these models is that repeated drug use produces neuroplastic changes in affect systems, resulting in dysregulated affect during drug withdrawal. Substantial self-report data exist to confirm this thesis for drug dependent users. However, human psychophysiological research to corroborate these data and explicate neurobiological mechanisms is limited. In this study, nicotine withdrawn and non-withdrawn dependent smokers completed explicit-cue and contextual conditioning procedures. Explicit-cue conditioning involved the contingent administration of electric shock on CUE+ only trials. Contextual conditioning involved the non-contingent administration of shock on both CUE+ and CUE- trials. These procedures were modeled on previously validated animal conditioning procedures and yield indices of fear vs. anxiety with established neurocircuitry (Davis, 1998). Fear potentiated startle was measured to examine the expression of fear and anxiety. Results suggest increases in anxiety but not fear during nicotine withdrawal. Specifically, withdrawn smokers selectively displayed exaggerated contextual conditioning (i.e., increased fear potentiated startle for CUE- vs. BASELINE trials) when shocks were administered non-contingently. In contrast, withdrawn smokers exhibited normal explicit-cue conditioning (comparable fear potentiated startle for CUE+ vs. CUE- trials) when shocks were administered contingently. Results are interpreted with respect to differential involvement of bed nucleus of the stria terminalis vs. amygdala in these conditioning procedures.

### STUDY GOALS

- To evaluate the effect of nicotine withdrawal in laboratory procedures designed to elicit fear vs. anxiety.
- Anxiety, but not fear, is predicted to increase among withdrawn (relative to non-withdrawn) smokers. This should be observed primarily in the non-contingent shock condition, which most powerfully manipulates anxiety.

### METHOD

#### Participants

132 dependent smokers across 2 smoking groups: Non-withdrawn vs. Withdrawn (24hrs)

#### Conditioning Procedures

All participants completed a baseline assessment followed by one of three conditioning procedures involving the presentation of a series of colored squares:

- Contingent Shock:** Shocks administered during only one specific square color (only CUE+)
- Non-Contingent Shock:** Shocks administered randomly during both square colors (CUE+ and CUE-)
- Non-Contingent Tone:** Non-aversive tones administered randomly during both square colors (CUE+ and CUE-)

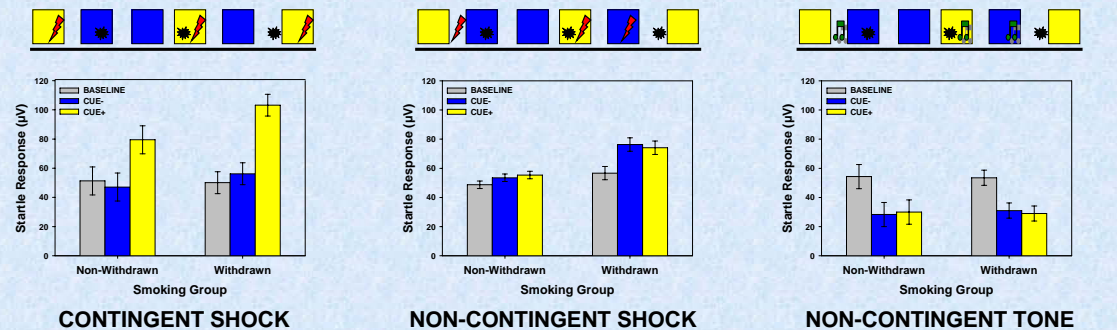
#### Measures

Startle response to white noise probes was measured during both square colors (CUE+ and CUE-) and during baseline assessment via eye-blink EMG.

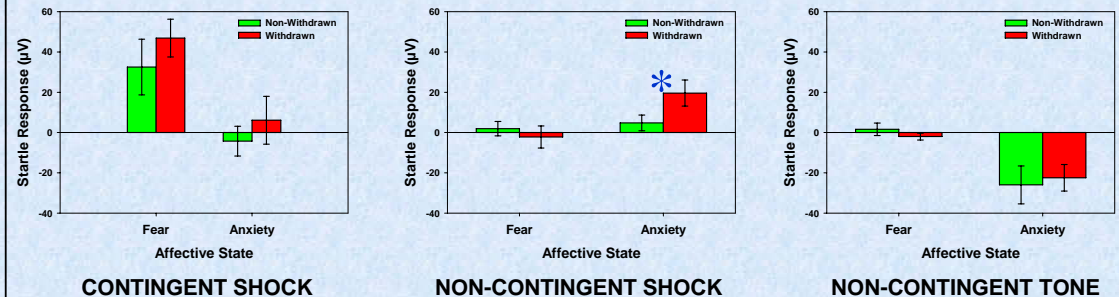
Fear potentiated startle was calculated via two methods to assess **FEAR** vs. **ANXIETY**:

- FEAR** = CUE+ vs. CUE- trials
- ANXIETY** = CUE- vs. BASELINE trials

### STARTLE RESPONSE



### FEAR POTENTIATED STARTLE: FEAR VS. ANXIETY



The Smoking Group effect was tested separately for **FEAR** and **ANXIETY** scores in each conditioning procedure:

- As predicted, Withdrawn Smokers displayed elevated **ANXIETY** relative to Non-Withdrawn Smokers in the Non-Contingent Shock condition ( $p = .029$ , one tailed).
- Consistent with previous research (Hogle & Curtin, 2006), no significant Smoking Group effect was observed for **FEAR** in the Contingent Shock condition ( $p = .196$ , one tailed).
- No significant Smoking Group effects were observed in the Non-Contingent Tone condition, indicating comparable startle responding (and habituation) in the absence of aversive conditioning.

### CONCLUSIONS

- Initial analyses confirmed the successful manipulation of Fear vs. Anxiety with Contingent vs. Non-Contingent administration of electric shock, respectively.
- Consistent with previous research (Hogle & Curtin, 2006; Piper & Curtin, 2006), no effect of nicotine withdrawal was observed on **FEAR** response when shocks were administered contingently.
- In contrast, our novel manipulation of **ANXIETY** revealed significant group differences when shocks were administered non-contingently. Withdrawn Smokers displayed increased **ANXIETY**, consistent with the frequent self-report of problems with negative affect in smokers on cessation of tobacco use.
- Extrapolation from animal model analogs of these conditioning procedures suggests that the bed nucleus of the stria terminalis, rather than the amygdala, may mediate the affective disruption during nicotine withdrawal.