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 In this study, nicotine withdrawn and non-withdrawn dependent smokers completed explicit-cue and contextual conditioning procedures.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 Specifically, withdrawn smokers selectively displayed exaggerated contextual conditioning (i.e., increased fear potentiated startle for CUE- vs. BASELINE trials) when shocks were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 In contrast, withdrawn smokers exhibited normal explicit-cue conditioning (comparable fear potentiated startle for CUE+ vs. CUE- trials) when shocks were administered contingently.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 terminals vs. amygdala in these conditioning procedures.

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Anxiety, but not fear, is predicted to increase among withdrawn (relative to non-withdrawn) smokers.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.

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As predicted, Withdrawn Smokers displayed elevated ANXIETY relative to Non-Withdrawn Smokers in the Non-Contingent Shock condition (p = .029, one tailed).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.

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.