

The NPU Task: Evaluating a Surrogate Endpoint for Stress Mechanisms in Research on Smoking Cessation Interventions



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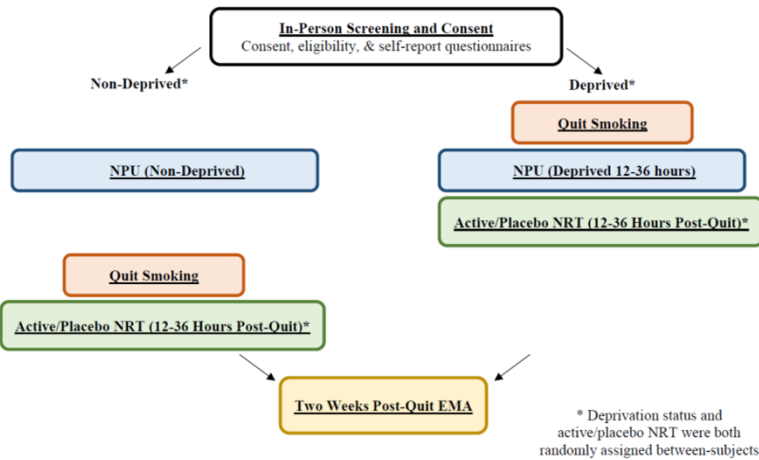
BACKGROUND & SIGNIFICANCE

- Surrogate endpoints are robust, early predictors of clinically relevant outcomes. Surrogate endpoints are advantageous for three reasons:
 - Available much earlier than ultimate clinical outcomes^{1,2}
 - Establish an intervention's mechanism of action^{3,4}
 - More power to test impact of intervention on this mechanism^{5,6}
- Stressor reactivity is a target for many interventions in addiction but we do not have well-validated surrogate endpoints for stress-induced relapse mechanisms.
- Basic science combines with preliminary clinical research to suggest that overall stressor reactivity and relative unpredictable stressor reactivity as measured by startle potentiation in the NPU task may be attractive surrogate endpoints for this purpose.^{7,8}

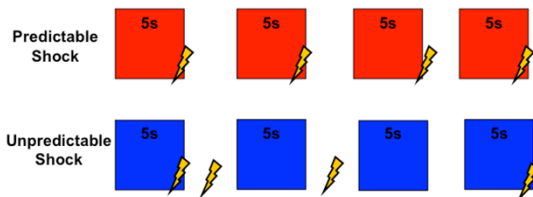
OBJECTIVES

- The goal of this study was to evaluate a key requirement for two potential surrogate endpoints – their ability to predict clinical outcomes.
- We tested if overall stressor reactivity and relative unpredictable stressor reactivity for recently abstinent daily cigarette smokers ($N = 128$) predicts probability of lapsing during two-week cessation attempt.

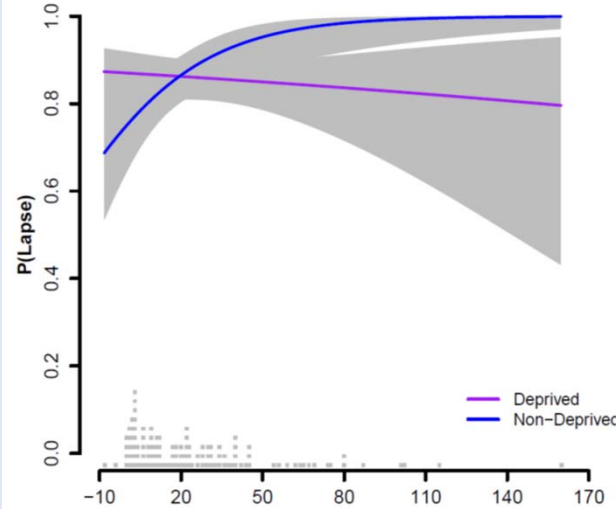
METHODS



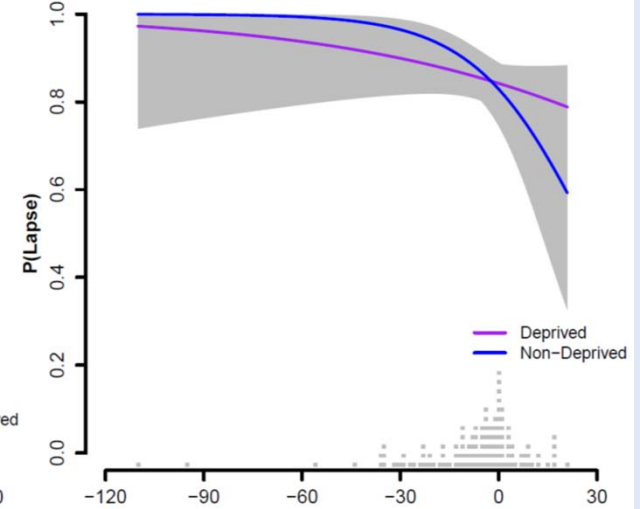
NPU STRESSOR TASK



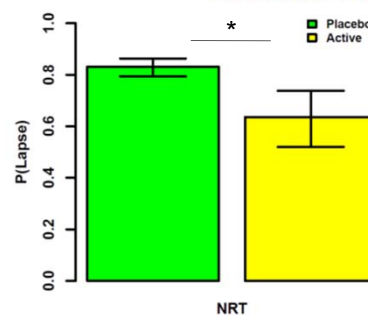
Overall Stressor Reactivity Fails to Significantly Predict Probability of Lapsing



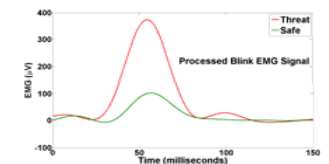
Relative Unpredictable Stressor Reactivity Fails to Significantly Predict Probability of Lapsing



Overall Stressor Reactivity



Relative Unpredictable Stressor Reactivity



SUMMARY & FUTURE DIRECTIONS

- Our pre-registered hypotheses were not supported. Specifically, overall stressor reactivity and selective unpredictable stressor reactivity did not significantly predict probability of lapsing during two-week cessation attempt.
- These results raise some concern about overall and selective unpredictable stressor reactivity as surrogate endpoints in research on smoking cessation interventions. However, these null results must be tempered by important study limitations of low power:
 - Relapse broadly vs. stress-induced relapse
 - Rates of continuous abstinence

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