

## **Circulating Orexin Changes During Withdrawal are Associated with Nicotine Craving and Risk for Smoking Relapse**

### **Supplemental Text**

In addition to the main analyses presented in the main paper, we were interested in examining the association between orexin and craving measures. To do this exploratory analysis, orexin was correlated with craving measures (craving, appetitive, and aversive urges), withdrawal symptoms, and affect measures (positive affect and distress). As these were exploratory analysis only, no correction for multiple correlations was made. A series of correlation analyses was done separately per session for each group (nonsmokers, relapsers and successful abstainers) and sex.

Neither depressive affect (PHQ-9 Prime MD) nor anxiety (STAI) measured at baseline was associated with orexin at either time point. During ad libitum smoking, however, the measure of appetitive urges was correlated with orexin only for female relapsers ( $r(44) = .35, p < .05$ ). During this time point there was no association between orexin and any of the withdrawal symptoms for any of the abstainers (male or female) or relapsing men (see Supplementary Table 1).

At the 24-hour abstinence period, there were several statistically significant correlations between orexin and self-reported mood and withdrawal measures. During this time period, abstaining women had consistent negative correlations between orexin and physical complaints ( $r(38) = -.32, p < .05$ ), MNWS ( $r(38) = -.32, p < .05$ ) and aversive smoking urges ( $r(37) = -.39, p < .05$ ) while abstaining men had positive correlations with MNWS ( $r(38) = .42, p < .01$ ) and cigarette craving ( $r(38) = .32, p < .05$ ). Relapsing men also showed a negative correlation between orexin and positive affect ( $r(57) = -.28, p < .05$ ) as well as positive correlations with distress ( $r(57) = .28, p < .05$ ) and MNWS ( $r(57) = .26, p < .05$ ). Relapsing women did not show any significant correlations between orexin and withdrawal measures (Supplementary Figure 1 & Supplementary Table 1). Nonsmoking females showed no significant association between

orexin concentration and positive affect or negative mood. At the 24 hour abstinence session, the only significant association was for male nonsmokers, between orexin and positive affect ( $r(34) = .38, p < .05$ ). Per standard interpretation in the social sciences, these associations all represent medium effect sizes (Cohen, 1992).

---

Insert Supplementary Table 1 here

---

---

Insert Supplementary Figure 1 here

---

## References

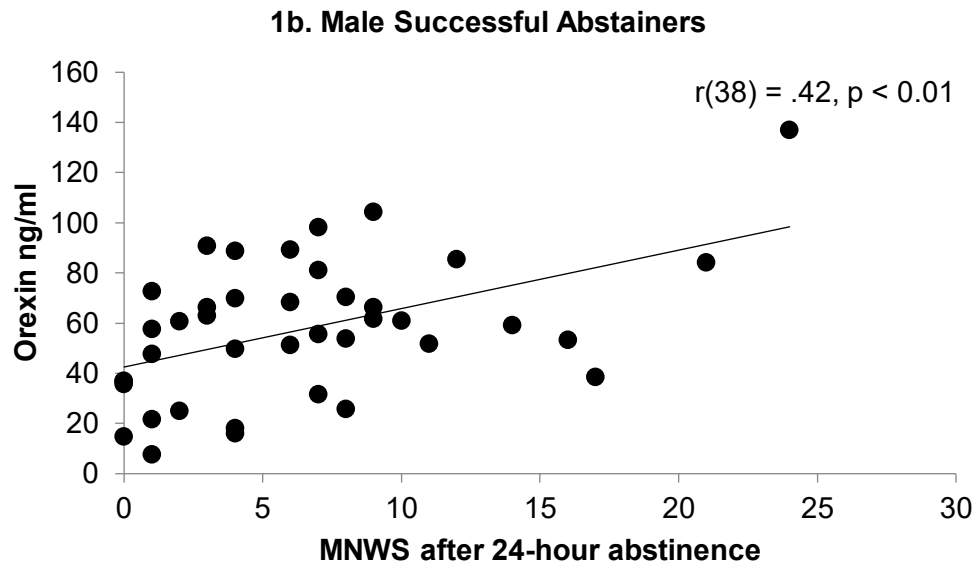
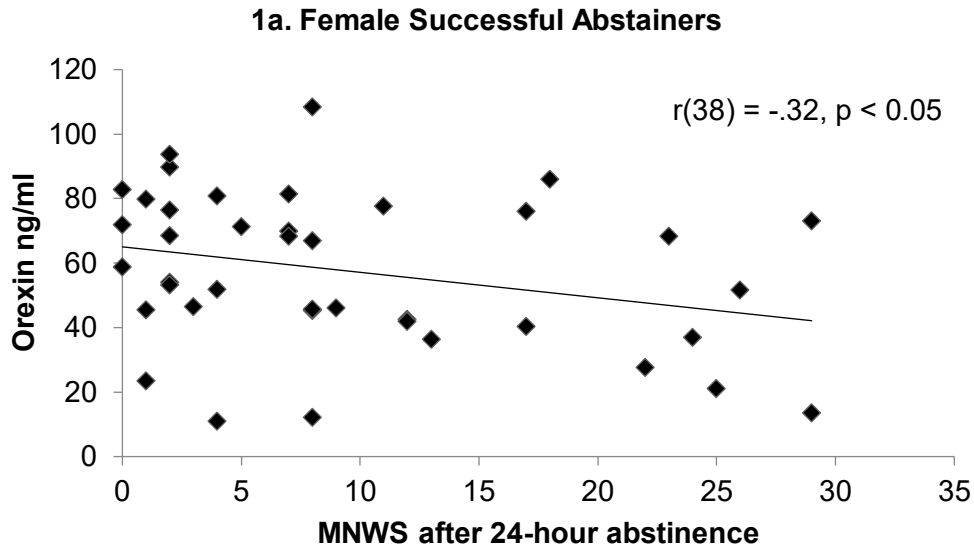
Cohen J (1992) A power primer. *Psychol Bull* 112:155-159.

Supplementary Table 1. Correlations between orexin and craving and withdrawal symptoms, by gender and group.

	Nonsmokers		Successful Abstainers		Relapsers	
	Female	Male	Female	Male	Female	Male
Ad libitum Session						
Positive Affect	-0.05	0.06	-0.15	-0.17	0.05	-0.24
Distress	0.03	0.14	0.05	0.03	-0.09	-0.01
Physical Symptoms	0.19	0.28	0.13	0.15	0.05	-0.07
MNWS	-0.01	0.14	0.20	0.10	-0.08	0.07
Craving			0.00	0.08	0.22	-0.22
QSU-B F1			0.16	0.11	<b>0.35*</b>	-0.21
QSU-B F2			0.13	0.04	0.19	-0.07
24 Hr Abstinence Session						
Positive Affect	0.06	<b>0.38*</b>	-0.01	-0.29	0.04	<b>-0.28*</b>
Distress	-0.10	-0.23	-0.17	0.28	0.03	<b>0.28*</b>
Physical Symptoms	-0.06	-0.09	<b>-0.32*</b>	0.31	0.03	-0.04
MNWS	0.05	-0.13	<b>-0.32*</b>	<b>0.42**</b>	-0.05	<b>0.26*</b>
Craving			-0.29	<b>0.32*</b>	-0.04	0.13
QSU-B F1			-0.27	0.22	-0.02	-0.00
QSU-B F2			<b>-0.39*</b>	0.28	0.03	0.00

\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001

Supplementary Figure 1



Supplement figure legend

Supplement Figure 1. A scatter plot depicts the association between orexin and withdrawal symptoms (MNWS) in smoking females (1a.) and smoking males (1b.).