

CIRCULATING GHRELIN LEVELS ARE NOT ASSOCIATED WITH CRAVING AND WITHDRAWAL SYMPTOMS IN ACUTE NICOTINE WITHDRAWAL

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Dear Editors,

Recently ghrelin has been shown to be involved in reward-associated craving during alcohol withdrawal (Koopmann et al. 2011). Additionally, an impaired neuroendocrine regulation of appetite regulating hormones (orexin and leptin) have been repeatedly associated with tobacco craving (al'Absi et al. 2011, von der Goltz et al. 2010). However, ghrelin, an orexigenic hormone, suggested to be also involved in mesolimbic dopaminergic pathways (Abizaid et al. 2006), which play a central role in the development and maintenance of addictive disorders, such as nicotine addiction, has not been investigated so far.

In this experimental study we included 11 male heavy smokers (age 51.4 ± 13.5 ; FTND: 7.3 ± 1.7 ; cigarettes smoked on baseline day: 20.45 ± 9.1 ; duration of smoking (years): 33.9 ± 10.3 ; previous quit attempts: 1.1 ± 1.22 ; cigarettes per day (usually): 25.45 ± 9.34), and 10 male nonsmokers. A positive approval from the local ethics committee was present; all procedures were carried out with the written consent of the participants. During baseline session, participants completed self-report measures to assess history and level of their nicotine dependence, including the Fagerström Test of Nicotine Dependence (FTND), the Minnesota Nicotine Withdrawal Scale (MNWS) and the Questionnaire of Smoking Urges (QSU). Participants were not suffering from any other current psychiatric diagnoses, as defined by the DSM-IV. To verify the abstinence from smoking, participants provided expired carbon monoxide (CO) levels on "withdrawal day", and at baseline (in each case in the evening hours). Blood samples were assessed at baseline and after a 24-hour period of nicotine abstinence. To minimize confounding effects of food intake/hunger on ghrelin levels, participants were instructed to have a light meal at least 2 hours before each session. Ghrelin analyses were performed in Institute of Clinical Chemistry (University Hospital Zurich) using a commercial radioimmunoassay kit (Phoenix Pharmaceuticals, Inc). Intra-assay variation (CV%) for ghrelin was 5-7%, inter-assay variation (CV%) was 12-15%.

Exhaled air CO levels decreased significantly between baseline and 24-hours later (baseline 20.36 ± 9.92 ; 24-hours later 3.45 ± 2.07 ; $p < 0.001$), parallel urge to smoke (QSU: baseline 99.27 ± 28.38 , 24-hours later 154.27 ± 30.17 ; $p < 0.001$) and nicotine withdrawal symptoms (MNWS: baseline 0.45 ± 0.69 , 24-hours later 10.18 ± 4.56 ; $p < 0.001$) increased significantly in the smoker group. However, we found no statistic differences between the ghrelin levels in smokers versus non-smokers (baseline: $p = 243$; 24-hours later: $p = 0.530$). Ghrelin levels in smokers decreased during acute withdrawal (1292.3 ± 401.8 pg/L vs. 1207.8 ± 550.9 pg/L), however, this reduction was not significant ($p = 0.483$). Furthermore we found no correlation between ghrelin levels (ghrelin baseline – ghrelin withdrawal) and the FTND (Spearman's $\rho = -0.231$ ($p = 0.494$)), Minnesota Nicotine Withdrawal Scale ($\rho = -0.159$ ($p = 0.640$)) and urge to smoke (QSU ($\rho = -0.173$ ($p = 0.612$))).

The preliminary finding of this study is, that ghrelin seem to be not associated with nicotine withdrawal symptoms and tobacco craving in smokers suffering from acute nicotine withdrawal. Furthermore, we found no differences concerning ghrelin levels between smokers and non-smokers. However, these findings should be interpreted with caution because of the small sample size and thus limited statistical power. Furthermore, the descriptive phenomenon "craving" is difficult to measure precisely (Vukovic et al. 2008). Further studies are warranted to investigate the role of ghrelin in nicotine withdrawal, and for a better understanding of the mechanisms and pathways underlying appetite regulating hormones in induction of craving and withdrawal symptoms in general.

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Conflict of interest: None to declare.

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