

# Sucrose-Induced Modification of Peri-Neuronal Nets May Potentiate Stress- Related Chronic Obesity

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**Introduction:** 60-70% of people report they eat high-sugar foods that provide a palatable taste during times of stress. People with a history of eating comfort foods have reduced hypothalamic- pituitary-adrenocortical (HPA) axis responses to stress, but consumption of these foods is detrimental to metabolic health, with stress-related eaters being 2-3 times more likely to become obese. Similar stress responses are observed in normal-weight rats, but rats with Western diet (WD)-induced obesity do not exhibit stress relief unless larger volumes of sucrose are consumed. Previous studies found parvalbumin (PV) interneurons with perineuronal nets (PNNs) in the basolateral amygdala (BLA) are disinhibited and mediate reduction of the HPA stress response. We hypothesize obesity's stress relief-blunting effects are mediated by a decrease in the proportion of BLA PV interneurons with PNNs.

**Methods:** Rats fed chow, WD, or a pair-fed diet were given twice-daily access to 4 or 6 mL of pleasurable sucrose solution (30%) for 14 days, followed by an acute stress challenge at the end of two weeks. The rats were then sacrificed and transcardially perfused using a 3.7% paraformaldehyde solution. The brains were fixed overnight, then switched to a 30% sucrose solution. The brains were then serially cut on a freezing microtome. A triple-label immunohistochemical procedure was performed to label PV interneurons and PNNs in the BLA and prelimbic (PL) area. Image J was used for analysis of confocal images to quantify number of PV interneurons and PNNs and determine intensity of PNNs. A 2-way ANOVA statistical analysis was used to compare the groups using diet type and type of drink as the factors.

**Results:** The number of BLA PV interneurons with full PNNs was significantly higher in WD vs. pair-fed rats ( $p=0.032$ ) with no difference significant observed between WD vs. chow. There was no significant difference in the ratio of PV cells with PNNs vs. PV cells without PNNs between the groups ( $p=0.098$ ). Similarly, in the PL area, there was a significantly higher number of PV interneurons with full PNNs in WD vs. chow rats ( $p=0.027$ ). Again, there was no significant difference in the ratio of PV cells with PNNs vs. PV cells without PNNs between the groups ( $p=0.99$ ).

**Conclusion:** Since the number of PV interneurons with PNNs was increased in rats with WD- induced obesity, obesity's stress relief-blunting effects may not be mediated through inhibition of BLA PV interneurons as expected and PV interneuron disinhibition may be heightened in obesity. We believe obesity impacts a different part of the HPA axis to produce the stress relief- blunting previously observed. Future research is needed to determine the mechanism underlying decreased efficacy of comfort feeding on stress reduction in obese rats to elucidate a biological pathway and possible pharmacological targets for obesity treatment.

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