

# Physiological Responses Induced by a Surgical Procedure Increase Leptin Sensitivity and Signaling

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## Introduction

Obesity is a critical health care issue due to its positive correlation to cardiovascular disease, liver disease, and diabetes. Leptin is a polypeptide that targets neurons in the brain involved in the control of energy balance. Since leptin administration reduces feeding and body weight (BW,) it is a candidate for treating obesity.

## Hypothesis

Hyperleptinemic obese individuals are resistant to the effects of exogenously administered leptin. However, cranial surgery (Sx) induces a larger body weight loss in hyperleptinemic, diet-induced obese (DIO) mice than in lean, chow fed mice. Obese mice, which lack leptin, do not show an exaggerated BW loss. We assessed whether the BW loss induced by surgery in leptin resistant DIO mice is due to the restoration of leptin action.

## Methods

We used C57Bl6 male mouse, maintained on either a low fat chow diet (lean) or a high fat diet (DIO.) A stainless steel canula was fixed in the lateral cerebral ventricle and connected to an osmotic minipump. We tested whether icv administration of a leptin receptor antagonist prevented the BW loss induced by Sx on both lean and DIO mice. To test if the effects were exclusive to ICV Sx, we monitored the effect on BW and feeding after laparotomy in DIO mice.

## Results

Cranial surgery as well as laparotomy is associated with significant BW loss in DIO mice (n=8.) Administration of a leptin antagonist in the brain prevents the effects of ICV Sx on BW loss and anorexia but only after 72 hours. The reduction of circulating leptin action with the pretreatment with a leptin antagonist (10 mg/kg, ip daily) significantly increased BW, feeding, and impaired glucose tolerance in both lean and DIO mice. Pretreatment with the leptin antagonist was unable to block the acute BW loss and anorexia induced by ICV Sx.

## Conclusion

Our data demonstrate that signals mediating Sx-induced BW loss and anorexia in DIO mice are common to any major surgical insult. The acute BW loss induced by Sx in DIO mice is independent of sensitization to hyperleptinemia. However, leptin action is required for the maintenance of the BW loss induced by SX.

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