Dr. Harry Kissileff

The goal of this project is to identify predictors of success in the treatment of obesity after roux-en-y bariatric surgery. "To understand predictors of success and risk and examine mechanisms of behavior change, research is needed that allows detailed measurement of psychosocial and behavioral variables in the targeted population before and after bariatric surgery" (NIH REF-DK-13-026). The specific aims of this proposal are to: 1) employ behavioral tests of mechanisms that control food intake in normal weight individuals, to determine which intake control mechanisms lead to changes after Roux-en-y gastric bypass; and 2) measure behavioral and psycho-social predictors of weight loss and food intake reduction, so as to determine which are most predictive of successful weight loss and food intake reduction. The mechanism we propose to account for success is reduction in food intake brought about by the pattern of hormone release, particularly GLP-1, and gastric distention, both known to underlie satiation, coupled with postingestive changes in reinforcing value of food and motivation to consume. Tests of the hypothesis will be done by measuring responses to tasting, working for, and consuming, foods on sensory, motivational, cognitive, and physiological variables, including amount consumed and rate of eating under standardized conditions, before surgery and at a two year follow up visit. In addition the inhibitor exendin-9-39 (EX9) will be infused before a meal to determine whether blockade of GLP-1R after surgery partially reverses intake reduction. We predict that successful patients will show changes that favor reduction in food intake, rate of eating, motivation to consume, reward value of foods, and a hormone profile that has been shown to generate satiation and maintain reduction in intake (e.g. increased CCK, GLP-1, reduced ghrelin). To the extent that psycho-social and cognitive factors may override physiological brakes to eating behavior, the subjects may fail to achieve success, and consequently the failure may be predicted from overimpulsiveness or inability to suppress working for rewarding food stimuli. To test these hypotheses, a total of 100 patients will be enrolled prior to RYGBP and restudied 2 years after the surgery. Based on known high attrition in this population and our past 10 year experience with bariatric research, it is estimated that 100 patients will need to be enrolled over 2 years to obtain 50 who complete testing at 2 years. Ex9 studies will be done in a subset of 30 completers, only after RYGBP, 15 failure (<15% weight loss) 15 success (>30% weight loss). The strength of predictors for weight loss will be assessed by steepness of regression and level of significance of outcomes from predictors