Evidence for Long-Term Pancreatic Damage Caused by Laxative Abuse in Subjects Recovered from Anorexia Nervosa

Nigel W. Brown,[1*] Janet L. Treasure,[1] and Iain C. Campbell[2]

[1] Eating Disorders Research Unit, Institute of Psychiatry, King's College London, United Kingdom
[2] Department of Neuroscience, Institute of Psychiatry, King's College London, United Kingdom

Accepted 2 February 2000

Abstract: **Objective:** *This study examined whether a prior history of laxative abuse results in long-term changes in gastrointestinal function.* **Method:** *The functioning of the enteroinsular axis was examined by measuring the insulin response to a standard meal. The study involved 18 subjects who had fully recovered from anorexia nervosa (AN) and an age and weight-matched control group. In the recovered group, 10 of 18 subjects had a history of laxative abuse.* **Results:** *Subjects with a prior history of laxative abuse show a more gradual increase and decrease in insulin secretion, but no differences in glucose response or hunger ratings.* **Discussion:** *Because there are no differences in the glucose response to the meal, it is hypothesized that the difference in insulin response is due to changes in the enteroinsular axis. These data indicate that chronic laxative abuse induces long-term changes in gastrointestinal function. © 2001 by John Wiley & Sons, Inc.* Int J Eat Disord 29: 236–238, 2001.

Key words: *anorexia nervosa; laxative; enteroinsular axis; pancreas*

INTRODUCTION

Anorexia nervosa (AN) is associated with a wide range of physical and mental abnormalities and it is unclear whether these abnormalities completely disappear in long-term recovered subjects. Subjects with AN at a low weight exhibit abnormalities in the insulin response to a meal (Casper, 1996). We have recently reported that this is present in subjects who have fully recovered from the disorder (Brown et al., 1999). In addition to food restriction, subjects with AN may engage in a number of purging behaviors. Laxative

Dr. Brown's current address is Institute of Liver Studies, IDM Section, King's College Hospital, Denmark Hill, London, SE5 9RS, UK.
Correspondence to: Nigel W. Brown, Ph.D., Institute of Liver Studies, IDM Section, King's College Hospital, Denmark Hill, London, SE5 9RS, UK. E-mail: nigel.brown@kingshc.nhs.uk

abuse has been reported to cause gastrointestinal dysfunction, in particular, pancreatic damage (Kobayashi et al., 1988). To assess this possibility, the present study examined the enteroinsular axis by measuring the insulin response to a meal in a group of 18 recovered subjects and in age and weight-matched controls. Of the 18 recovered subjects, 10 had a history of laxative abuse (LAX). In the recovered subject group, there were no significant differences in age, body mass index (BMI), length of eating disorder, or length of time recovered between subjects who had abused laxatives and those who had not. Also, there were no significant differences in the number of subjects who had binged or vomited within the two subgroups. Recovery was defined as (1) resumption of menses for at least 3 months, (2) a BMI greater than 18.5 kg/m^2, and (3) normal eating habits, that is, no evidence of dietary restriction or purging. The study was approved by the Bethlem and Maudsley Hospital's Ethical Committee and all subjects gave informed consent.

METHODS

The insulin response to a standard meal (consisting of cottage cheese sandwiches; for details of method, refer to Brown et al., 1999) was measured. Briefly, the subjects fasted from 12 midnight and arrived in the test center at 10:45 a.m. An indwelling cannula was inserted for blood sample collection. Blood specimens were collected at 11:00 a.m. and thereafter at 15-min intervals until 12:15 p.m., then at 12:45, 1:45, and 2:45 p.m. At these times, the subjects were issued with a series of visual analogue scales for assessing mood and hunger. The meal was presented at 11:15 a.m. and had to be eaten by 12:15 p.m. The meal consisted of cottage cheese sandwiches, which contained the following macronutrients: 24.6 g of protein, 46.8 g of carbohydrate, 10.7 g of fat, and 9.36 g of fiber. Subjects were allowed either diet cola or unsweetened black coffee during the meal and free access to mineral water throughout the test period. Insulin was measured by coated tube radioimmunoassay (DPC, Ltd., Glyn Rhonwy, Llanberis, UK).]

RESULTS AND DISCUSSION

The LAX group showed an apparent difference in the pattern of insulin secretion compared with the other recovered subjects and controls. To quantify this, the rate of change of insulin secretion (δ) was calculated using the formula: $\delta\ [\text{insulin}] = [\text{insulin}]_{t(x)} - [\text{insulin}]_{t(x-1)}$, where t(x) = the sample at time (x) and t(x-1) = the sample before sample t(x). The results are shown in Figure 1. The LAX group show a more gradual increase and decrease in insulin secretion with significantly lower rates of change in insulin secretion (δ) at Points 2 and 4. The reason for this difference in the LAX group is unclear but can be hypothesized to be due to one of two mechanisms. First, the rate of gastric emptying may be decreased in the LAX group. However, there were no significant differences in the plasma glucose response, indicating that nutrients were arriving in the small intestine at similar times after the start of the meal. In addition, there were no differences in hunger ratings between the two recovered subgroups. Both these factors indicate that there is no gross difference in the gastric emptying rate in LAX subjects. Second, the observed difference in the rate of change in insulin secretion (δ) may lie in the enteroinsular axis (Lavin et al., 1998), in particular a decrease in the release or actions of either the glucose-dependent insulinotropic polypeptide (GIP) or glucagonlike peptide-1 (GLP-1). Both of these hormones are produced by cells located in the intestinal mucosa. It can be hypothesized that the laxative abuse resulted in permanent damage to this tissue. Interestingly,

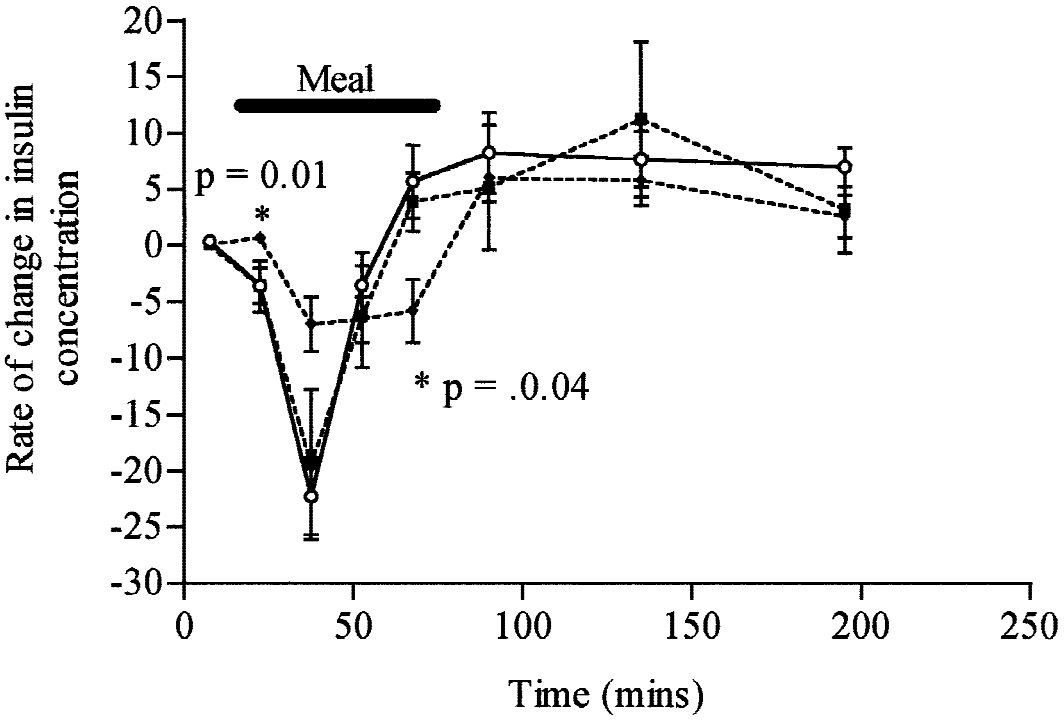

Figure 1. Rate of change of insulin secretion. Open circles = control; closed sqaures = no laxatives; closed diamonds = laxatives.

GIP release is dramatically reduced in patients with AN (Alderdice, Dinsmore, Buchanan, & Adams, 1985). However, it is not known whether release of this hormone is reduced in the recovered state or is further reduced by laxative abuse. It is proposed that prolonged laxative abuse caused long-term damage to this system. Thus, there is a slower release of insulin after a meal, as the hormone is responding to the increases in plasma glucose levels. In conclusion, data are presented that indicate that laxative abuse during a period of AN causes a degree of impairment in the enteroinsular axis and that this persists after recovery.

This study was funded by the Wellcome Trust, which also provided the salary for N.W. Brown.

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