Original Article

Subcutaneous Oxyntomodulin Reduces Body Weight in Overweight and Obese Subjects

A Double-Blind, Randomized, Controlled Trial

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This study investigated the effect of subcutaneously administered oxyntomodulin on body weight in healthy overweight and obese volunteers. Participants self-administered saline or oxyntomodulin subcutaneously in a randomized, double-blind, parallel-group protocol. Injections were self-administered for 4 weeks, three times daily, 30 min before each meal. The volunteers were asked to maintain their regular diet and level of physical exercise during the study period. Subjects’ body weight, energy intake, and levels of adipose hormones were assessed at the start and end of the study. Body weight was reduced by 2.3 ± 0.4 kg in the treatment group over the study period compared with 0.5 ± 0.5 kg in the control group (P = 0.0106). On average, the treatment group had an additional 0.45-kg weight loss per week. The treatment group demonstrated a reduction in leptin and an increase in adiponectin. Energy intake by the treatment group was significantly reduced by 170 ± 37 kcal (25 ± 5%) at the initial study meal (P = 0.0007) and by 250 ± 63 kcal (35 ± 9%) at the final study meal (P = 0.0023), with no change in subjective food palatability. Oxyntomodulin treatment resulted in weight loss and a change in the levels of adipose hormones consistent with a loss of adipose tissue. The anorectic effect was maintained over the 4-week period. Oxyntomodulin represents a potential therapy for obesity. 

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The prevalence of obesity is rapidly increasing worldwide; currently >65% of adults in the U.S. are overweight (1). Although even a modest weight loss can improve the health of obese individuals, efforts to treat the obesity pandemic have been unsuccessful. Novel therapeutic targets are urgently required.

Several gut hormones have been found to modulate appetite (2–4). Oxyntomodulin is a peptide product of the proglucagon gene released from the L-cells of the small intestine in response to food ingestion (5). Oxyntomodulin has been reported to reduce food intake by 19.3% during an intravenous infusion administered to normal-weight humans, an effect that continues for >12 h after infusion (6). Furthermore, in rodents, repeated intraperitoneal administration over 7 days has been associated with reduced white adipose tissue and a highly significant reduction in weight compared with controls (7). Thus, oxyntomodulin may offer a novel treatment for human obesity.

We hypothesized that self-administered subcutaneous oxyntomodulin would induce weight loss, reduce appetite, and alter the levels of adipose hormones in overweight and obese volunteers investigated in a 4-week community-based study.

RESEARCH DESIGN AND METHODS

Healthy male and female volunteers, ages 18–55 years, with a stable BMI of 25–40 kg/m² were recruited by advertisement and followed between January and August 2004. All potential subjects were nonsmokers with normal physical examination, routine blood tests, and electrocardiograms. Subjects were screened using the standard Dutch Eating Behavior Questionnaire (8) and SCOFF Questionnaire (9) and were excluded if they demonstrated abnormal eating behavior. Food preferences were assessed using a nine-point hedonistic scale to ensure that the study meal was acceptable. Subjects were given a subcutaneous injection of saline to assess whether they would find regular injections acceptable. A power calculation was used to estimate the number of subjects required to detect a significant effect of oxyntomodulin on a participant’s body weight. Assuming a difference of 1 ± 0.2 kg to be clinically significant and using a significance level of P < 0.05 and 90% power, it was calculated that 12 subjects were required in each group; the final treatment group consisted of 14 subjects, and the final control group consisted of 12 subjects. Women of child-bearing age were advised to avoid pregnancy by OLI, oxyntomodulin-like activity.

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between the two groups.

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check injection technique, and monitor subjects for side effects and compliance. Identical protocol for injection preparation was used as in the previous week, the control and treatment groups were not significantly different. Groups were therefore matched for BMI and age and had similar mean height

subjects were removed from the study. Of the 33 eligible subjects, 31 agreed to enter the study.

Participants were withdrawn at 3 weeks. Both subjects cited a dislike of exercise and usual diet in a regimen of three meals per day. For 1 week infusion study that demonstrated a reduction in calorie intake (6).

participants administrated oxyntomodulin. Visual analog scales, 100 mm in length, were completed throughout the study meal day to evaluate subjective feelings of hunger, nausea, and meal palatability.

Blood samples were taken at t = −30, 0, 15, 30, 60, 90, 150, 210, and 240 min to screen for any effect of oxyntomodulin on other analytes (Table 3). All blood samples were collected from an antecubital fossa cannula into lithium/heparin tubes (LIP, Cambridge, U.K.) containing 2,000 kallikrein inhibitor units of aprotinin (Trasylol; Bayer) and stored on ice. After centrifugation, plasma was immediately separated and stored at −20°C until being analyzed. Blood pressure and pulse were measured before each blood sample on each of the study meal days.

**Hormone measurements.** Commercially available assays were used to measure plasma leptin and adiponectin (Linco Research, St. Charles, MO). Plasma oxyntomodulin-like activity (OLI) was measured using an established in-house radioimmunoassay (5). Plasma taken 30 and 90 min after injection was analyzed by gel permeation chromatography to assess oxyntomodulin degradation (6). Insulin, peptide YY, and ghrelin-like immunoreactivity were measured using in-house radioimmunoassays (11–13). All samples were assayed in duplicate and within one assay to eliminate interassay variation. Glucose and total and HDL cholesterol were measured by an Olympus Analyzer.

**Statistical analyses.** Combined data are expressed as means ± SE. Data were compared using paired t tests for within-group analyses and unpaired t tests for between-group analyses. The changes in body weight, food intake, and adipose hormones. Oxyntomodulin was synthesized by Bachem U.K., sterile for culture and negative for pyrogen, as previously described (10). A subcutaneous dose of 400 nmol was chosen, which allowed us to achieve the same blood concentration as a previous human intravenous infusion study that demonstrated a reduction in calorie intake (6).

From recruitment, subjects were instructed to continue their current level of exercise and usual diet in a regimen of three meals per day. For 1 week before the study, all subjects self-administered saline injections three times daily, 30 min preprandially, into their abdominal subcutaneous tissue. All subjects prepared their injections by adding 0.25 ml sterile water to vials containing freeze-dried sodium chloride and self-administered injections using a 27-gauge needle. Subjects who failed to comply with the protocol during this week were removed from the study.

Subjects were randomly allocated to the control or treatment group by an independent investigator. Randomization was performed by stratification using the parameters BMI and age; subsequent randomization into the control or treatment group was performed by coin toss. The control and treatment groups were therefore matched for BMI and age and had similar mean height and weight (Table 1). The estimated energy requirements for the control and treatment groups were not significantly different.

During the 4-week study period, subjects self-administered normal saline or oxyntomodulin (400 nmol), three times daily, 30 min preprandially. An identical protocol for injection preparation was used as in the previous week, and the saline and oxyntomodulin vials were indistinguishable. The subjects were reviewed weekly by blinded investigators to measure body weight, check injection technique, and monitor subjects for side effects and compliance. Adverse events during the injection period were recorded by diary. Protocol compliance was 94.4 ± 1.1% in the control group and 95.3 ± 1.2% in the treatment group, estimated by counting the number of returned empty vials. Compliance was also confirmed by checking for cutaneous sites of injection and inspecting the number of subjects’ accumulated used needles. Subjects were weighed on each visit, and three fasting weights were recorded on three separate days at both the start and end of the study using a calibrated electronic scale (Marsden, London, U.K.) accurate to the nearest 100 g. Subjects wore the same light clothing and voided urine before each measurement. Premixture blood samples were taken at the start and end of the study to measure leptin and adiponectin levels.

Energy intake was measured during three lunchtime study meals on days 1, 2, and 29. The day before each study meal, subjects refrained from alcohol and strenuous exercise and fasted overnight. Subjects first ingested a fixed 200-kcal breakfast and 210 min later self-administered their injection (designated as t = 0). A meal of known energy content was provided in excess of exercise and usual diet in a regimen of three meals per day. From recruitment, subjects were instructed to continue their current level of exercise and usual diet in a regimen of three meals per day.

**RESULTS**

**Participant flow.** Eligibility for the study was assessed in 89 subjects; 33 healthy subjects were eligible according to study criteria, and 56 were excluded because of either abnormal eating behavior or coexisting health problems. Of the 33 eligible subjects, 31 agreed to enter the study. After 2 subjects were excluded in the week before randomization because of noncompliance with saline injections, 29 were randomized into the study phase: 16 into the treatment group and 13 into the control group. One female subject, randomized to the treatment group, withdrew at 2 weeks. Another female subject, randomized to the control group, withdrew at 3 weeks. Both subjects cited a dislike of self-administering injections as their reason for withdrawal. A male volunteer, subject X, was removed from the treatment group after day 2 due to nausea. Intention-to-treat analysis was not possible as these subjects were lost to follow-up. Thus 26 subjects completed the entire 4-week injection period, 14 within the treatment group and 12 within the control group.

**Effect of oxyntomodulin on body weight.** Repeated preprandial subcutaneous injection of oxyntomodulin resulted in a 2.4 ± 0.4% reduction in body weight, compared with a 0.5 ± 0.6% reduction in the control group (P = 0.0129) over the 4-week study period. This represented a significant weight loss of 2.3 ± 0.4 kg in the treatment group and 0.5 ± 0.5 kg weight loss in the control group (P = 0.0106) (Fig. 1). After 2 weeks, interim data demonstrated a significant weight loss of 1.1 ± 0.3 kg in the treatment group (P = 0.0343), which increased to 1.4 ± 0.4 kg after 3 weeks (P = 0.0331). Thus, on average, there was an additional 0.45-kg weight loss per week in the oxyntomodulin group.

Over the study period, there was a change in adipose hormones in the treatment group consistent with a reduction in adipose tissue. At the start of the study, the plasma
leptin and adiponectin levels in the control and treatment groups were not significantly different. In the treatment group, the plasma leptin levels were reduced from baseline (325 ± 50 ng/ml) by 79 ± 35 ng/ml (19.5 ± 6.2%); this change was significant when compared with the control group (P = 0.0185) (Table 2). The plasma adiponectin levels were increased from baseline (83.6 ± 9.5 μg/ml) by 8.3 ± 4.3 μg/ml (9.4 ± 4.9%) in the treatment group; this change was also significant when compared with the control group (P = 0.0068) (Table 2).

**Effect of oxyntomodulin on food intake and appetite.** A subcutaneous injection of oxyntomodulin reduced energy intake during the study meal. The energy intake of the control group was not significantly different on day 1 (716 ± 108 kcal), 2 (660 ± 99 kcal), or 29 (711 ± 87 kcal). On day 1, when the treatment group self-administered a saline injection, energy intake (678 ± 45 kcal) was not statistically different from that of the control group. However, subjects who self-administered oxyntomodulin had significantly lower energy intake on days 2 (508 ± 46 kcal; P = 0.0007) and 29 (428 ± 61 kcal; P = 0.0023) when compared with their energy intake on day 1 (Fig. 2).

There were no significant differences in the preprandial visual analog scales for hunger and nausea in the control and treatment groups 30 min after injection (data not shown). There also was no difference in the postprandial assessment of subjective palatability of the food between the control (day 2, 44 ± 6 mm; day 29, 48 ± 8 mm) and treatment (day 2, 43 ± 5 mm; day 29, 44 ± 7 mm) groups.

Only two subjects in each group failed to complete the study meal protocol. These subjects did not consume the same food type at each study meal. In the interest of accuracy, these subjects were excluded from food intake and appetite analysis before unblinding. Thus, study meal data were analyzed with n = 10 for the control group and n = 12 for the treatment group.

**Plasma levels of oxyntomodulin.** After an injection of oxyntomodulin, plasma OLI increased to a peak of 972 ± 165 pmol/l at 30 min (Fig. 3). In comparison, on the days that subjects administered saline, the mean baseline level of OLI was 97.4 ± 5.5 pmol/l and the peak postprandial level of OLI was 116.5 ± 10.4 pmol/l at 150 min.

Gel permeation analysis (14) of plasma samples from the treatment group demonstrated a single immunoreactive peak eluting at the same position as synthetic oxyntomodulin, with no indication of any degradative fragments. There was also no antibody formation at the end of the study, as assessed by plasma binding of the oxyntomodulin label.

**Hormone, lipid, and glucose levels.** There was a statis-

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**TABLE 2**

Changes in screened analytes over the 4-week study period

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Treatment group</th>
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<tbody>
<tr>
<td></td>
<td>Initial value</td>
<td>Change in value at 4 weeks</td>
</tr>
<tr>
<td>n</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>283 ± 24</td>
<td>31 ± 25</td>
</tr>
<tr>
<td>Adiponectin (μg/ml)</td>
<td>111.4 ± 11.3</td>
<td>-7.6 ± 3.0</td>
</tr>
<tr>
<td>Insulin (pmol/l)</td>
<td>26.7 ± 8.5</td>
<td>-1.1 ± 5.4</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>4.61 ± 0.09</td>
<td>0.21 ± 0.09</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>4.71 ± 0.26</td>
<td>-0.26 ± 0.15</td>
</tr>
<tr>
<td>HDL (mmol/l)</td>
<td>1.07 ± 0.06</td>
<td>-0.01 ± 0.03</td>
</tr>
<tr>
<td>Ghrelin (pmol/l)</td>
<td>493 ± 87</td>
<td>47 ± 58</td>
</tr>
<tr>
<td>Peptide YY (pmol/l)</td>
<td>11.8 ± 1.6</td>
<td>-2.6 ± 1.5</td>
</tr>
</tbody>
</table>

Data are means ± SE. An unpaired t test was used to compare changes in the control vs. the treatment group. *Significant difference.
A significant increase in preprandial insulin levels 30 min after subcutaneous administration of oxyntomodulin, but the increase was small compared with the effect of meal ingestion and not sufficient to affect plasma glucose levels (Table 3). This effect on insulin was present on both day 2 and day 29 (Fig. 4). The area under the curve for the incremental insulin level was nonsignificantly lower on day 2 (18.0 ± 0.9 nmol·min⁻¹·l⁻¹; P = 0.1378) and significantly lower on day 29 (14.9 ± 0.7 nmol·min⁻¹·l⁻¹; P = 0.0398) over the 4-h postinjection period compared with the day saline was administered (day 1: 21.6 ± 1.1 nmol·min⁻¹·l⁻¹). The injection of oxyntomodulin did not acutely affect plasma levels of peptide YY or ghrelin 30 min after injection (Table 3). There were no other significant chronic preinjection changes observed over the 4-week study period in the analytes screened (e.g., in lipid parameters or insulin levels) (Table 2).

**Adverse events.** Short-lived minor discomfort at the injection site was reported by 8 of 14 of the subjects in the treatment group and 5 of 12 of the control group. In total, 6.9% of all oxyntomodulin injections and 6.6% of all saline injections were reported to cause minor discomfort; thus discomfort did not appear related to the substance injected.

Transient mild nausea was reported with 3% of oxyntomodulin injections compared with 0.2% of all saline injections (P = 0.0389). These data included subject Y, who experienced nausea associated with 13 of the first 47 injections. The dose subject Y administered was halved, and the incidence of nausea decreased to 2 out of the remaining 37 injections. On day 29, subject Y had a peak OLI level of 868 pmol/L, compared with the mean peak for the group of 972 ± 619 pmol/L, despite taking only half the dose of oxyntomodulin. A second participant, subject X, was removed from the treatment group after day 2 because of adverse effects and was not included in the analysis; after each of the initial three oxyntomodulin injections, subject X had significant nausea that interfered with daily activities. This subject’s plasma OLI levels peaked at 2,140 pmol/L 15 min postinjection and were significantly higher than the rest of the treatment group over the entire 4-h study period (P < 0.0001 by two-way ANOVA). Another subject regularly experienced nausea for 2 days during her midmenstrual cycle and was included in the treatment group data in the interest of stringency. The incidence of all other reported adverse events was <2% and not significantly different between the treatment and control groups. There were no effects of oxyntomodulin self-administration on pulse rate or systolic or diastolic blood pressure as measured during the study meal days.

**Follow-up data.** The treatment group regained 1.1 ± 0.4 kg 2 weeks after terminating the oxyntomodulin injections. The control group gained 0.5 ± 0.2 kg and were 0.0 ± 0.6 kg different from their initial weight. The difference in weight loss between the control and treatment group was no longer significant 2 weeks after the end of the study period (P = 0.134). One subject in the control group and one in the treatment group were lost to follow-up after the end of the study; therefore, the follow-up data were analyzed with n = 11 in the control group and n = 13 in the treatment group.

**TABLE 3**

<table>
<thead>
<tr>
<th></th>
<th>Day 1 (saline)</th>
<th></th>
<th>Day 2 (oxyntomodulin)</th>
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<th>Day 29 (oxyntomodulin)</th>
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<tbody>
<tr>
<td></td>
<td>Initial value</td>
<td>Change at 30 min</td>
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<td>Change at 30 min</td>
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<td></td>
<td></td>
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<td></td>
<td>Initial value</td>
</tr>
<tr>
<td>Insulin (pmol/L)</td>
<td>34.5 ± 4.7</td>
<td>−6.1 ± 3.2</td>
<td>27.4 ± 3.6</td>
<td>32.6 ± 7.7</td>
<td>0.0004*</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>4.79 ± 0.09</td>
<td>−0.04 ± 0.06</td>
<td>4.75 ± 0.10</td>
<td>0.07 ± 0.08</td>
<td>0.300</td>
</tr>
<tr>
<td>Ghrelin (pmol/L)</td>
<td>370 ± 65</td>
<td>−5 ± 23</td>
<td>375 ± 74</td>
<td>−42 ± 35</td>
<td>0.3429</td>
</tr>
<tr>
<td>Peptide YY (pmol/L)</td>
<td>12.2 ± 2.1</td>
<td>1.1 ± 2.2</td>
<td>15.2 ± 4.4</td>
<td>−3.5 ± 4.1</td>
<td>0.3377</td>
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<td>26.7 ± 4.3</td>
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<td>40.5 ± 10.1</td>
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<td>0.0008*</td>
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<td>0.1637</td>
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</tbody>
</table>

Data are means ± SE. A paired t test was used to compare the change from baseline 30 min after an injection of oxyntomodulin with the change on day 1 when the treatment group injected saline. *Significant difference.
DISCUSSION
Self-administering oxyntomodulin subcutaneously effect-
vively reduced body weight by 2.4% over a 4-week period in
healthy overweight and obese volunteers. This effect was
substantial considering that all subjects were asked to
continue their usual diet and level of exercise. The accom-
panying reduction in leptin and increase in adiponectin
suggest that the weight loss demonstrated was at least
partly due to a reduction in adipose tissue. A significant
reduction in energy intake with preservation of subjective
food palatability was also observed. The magnitude of this
anorectic effect was sufficient to account for the weight
loss in the treatment group (15).

The plasma OLI levels achieved by subcutaneous injec-
tion were similar to those achieved by an intravenous
infusion of 3.0 pmol · kg⁻¹ · min⁻¹ in a study that reduced
food intake by 19.3% in normal weight subjects (6). This
anorectic effect was comparable with the effect observed
in overweight subjects in the current study. This suggests
that oxyntomodulin has an equipotent anorectic effect in
normal weight and overweight subjects and that obesity
does not confer resistance to the anorectic effect of
oxyntomodulin.

A recent human intravenous infusion study demon-
strated no effect of oxyntomodulin on insulin or glucose
levels in normal-weight humans (6). In the current study,
there was no evidence of a postprandial incretin effect.
There was a small increase in preprandial plasma insulin
after oxyntomodulin injection. However, this increase was
not sufficient to alter plasma glucose levels. Other gut
hormones, such as glucagon-like peptide, are known to
have a powerful incretin effect (12). Indeed, glucagon-like
peptide 1, while improving glucose tolerance when given
to type 2 diabetic subjects (16), can cause hypoglycemia in
nondiabetic subjects (17). There was no evidence of a
change in baseline insulin, glucose, or lipid levels over the
4-week study period in this group of healthy obese sub-
jects. Further studies are needed to assess to what degree
long-term oxyntomodulin administration leads to an im-
povement in metabolic parameters in obese subjects with
abnormal glucose and lipid metabolism.

The current study did not demonstrate an effect of
oxyntomodulin on the circulating level of the orexigenic
hormone ghrelin. It has been suggested that a proportion
of the anorectic effect of intravenously administered oxyn-
tomodulin is secondary to its suppressant effect on ghrelin
(6). However, this does not seem a likely mechanism for
the dose administered subcutaneously in the current
study. The decrease in body weight was secondary to a
significant reduction in energy intake. This reduction in
energy intake was likely due to a reduction in appetite, as
there was preservation of food satisfaction and therefore
no evidence of taste aversion. Indeed, a previous study
demonstrated that administration of intravenous oxynto-
modulin reduces preprandial hunger scores in normal-
weight humans (6). However, the current study did not
demonstrate a change in subjective appetite scores before
the meal after a subcutaneous injection of oxyntomodulin.
This may have reflected a perception of early satiety rather
than a reduced preprandial appetite or a failure of the
visual analog scores as a tool of appetite measurement.

The self-administration of subcutaneous oxyntomodulin
was well-tolerated by the subjects, and good compliance
rates were achieved. This was a fixed initial dose study; a
dose of 400 nmol oxyntomodulin may not be appropriate
for all subjects. Indeed, subject Y experienced a much
lower incidence of nausea after the dose was reduced.
Subject X demonstrated extremely high plasma OLI levels
after oxyntomodulin injection and experienced significant
nausea. These subjects may have absorbed oxyntomodulin
more rapidly or metabolized the peptide more slowly.
Larger groups studies are needed to assess if this was an
idiosyncratic response.

These preliminary data suggest that the administration
of oxyntomodulin could be an effective treatment for
obesity. The reduction in food intake seen at the end of the
study was statistically no different to the reduction on day
2, indicating that the efficacy of oxyntomodulin was main-
tained. In addition, the rate of weight loss was consistent
over the 4-week study period. Oxyntomodulin levels are
increased in patients who have had jejunooileal bypass
surgery (18,19). This sustained elevation of plasma oxy-
tomodulin may be one of the factors leading to successful
weight reduction in these patients. There was no evidence
of oxyntomodulin antibody formation from the assay data.
Together, this suggests that administration of oxyn-
tomodulin beyond the 4-week study period may be expected
to result in continued weight loss. However, these data are
limited by our small sample size and the 4-week duration of
the study. Longer-term clinical trials involving larger
numbers of participants are required to demonstrate the
long-term efficacy of oxyntomodulin as an antiobesity
therapy.

In summary, subcutaneous self-administration of oxyn-
tomodulin three times daily in the community reduced
body weight, decreased food intake, and altered the levels
of adipose hormones in overweight and obese nondiabetic
human subjects. The anorectic effect was well maintained
over the 4-week study period, and the weight loss com-
pared favorably with that achieved through other drug
therapies. Currently available pharmacological agents li-
censed for weight reduction therapy have limited efficacy
(20). Several drugs now in development affect widely
distributed central neurotransmitter systems and may
therefore have a broad spectrum of side effects. Mimicking
postprandial satiety by administering a natural postpran-
dial hormone such as oxyntomodulin may provide a more
specific treatment for obesity.

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the Wellcome Trust and Medical Research Council. The
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the study; collection, management, analysis, and interpre-
tation of the data; or preparation, review, and approval of
the manuscript.

The study was conceived by K.W., A.J.P., and S.R.B. The
study protocol and ethical application was formulated by
and performed the study interventions, hormone assays,
and data analysis. Dietetic support and data analysis were
performed by S.M.E. in collaboration with G.S.F. K.W. and

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A.J.P. drafted the manuscript, and all authors were involved in its critical appraisal and final approval.

The use of oxyntomodulin for the treatment of obesity is the subject of two pending patent applications (WO 2003/022904 and WO 2004/06285) in the name of Imperial College Innovations, which have been exclusively licensed to Thiakis Limited.

We thank the volunteers for their invaluable help with the study. We also thank Dr. David Stephens for statistical advice and the Department of Biochemistry, Charing Cross Hospital, for its assistance with the measurement of glucose and lipids.

REFERENCES

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