

Effect of T6 Dermatome
Electrical Stimulation on Gastric
Motor Functions, Appetite,
Satiating, Satiety and Weight
Loss in Individuals with
Overweight and Class I Obesity

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Title of the Study: **Effect of T6 Dermatome Electrical Stimulation on Gastric Motor Functions, Appetite, Satiety, Satiety and Weight Loss in Individuals with Overweight and Class I Obesity**

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Abstract

Background

Previous studies demonstrated that upper abdominal dermatome electrical stimulation inhibited postprandial antral motility, possibly through activation of somatovisceral stimulation or central mechanisms. Electrical stimulation of the dorsal columns of the spinal cord to prevent the perception of intractable neuropathic pain signals was associated with appetite reduction and weight loss; percutaneous electrical neurostimulation of dermatome T6 was associated with appetite reduction and, along with a proper diet, achieved a significantly greater weight reduction than diet alone in morbidly obese subjects. The effects of T6 dermatomal electrical stimulation on gastric motor functions and body weight in otherwise healthy overweight or class I obese volunteers are unclear.

Hypothesis

T6 dermatomal electrical stimulation results in delay of gastric emptying of solids, reduction in gastric volume, inhibition of appetite, and weight loss in healthy volunteers who are overweight or have class I obesity.

Aim

In participants with BMI 25-34.99kg/m², treated before and after two meals of the day with T6 dermatomal electrical stimulation (delivered by a TENS unit), we aim to compare baseline measurements of gastric emptying of solids, fasting and postprandial gastric volume, satiety, satiety, appetite, and body weight with measurements after three months of treatment.

Methods

We shall perform scintigraphic testing of gastric emptying of solids, as well as tests of satiation, satiety, gastric volume, appetite assessment, plasma ghrelin (total), GLP1 and PYY in 16 healthy overweight or class I obese volunteers receiving T6 dermatomal electrical stimulation.

Significance

This study will form the foundation for the potential subsequent application of dermatome electrical stimulation for treatment of overweight and/or class I obesity.

Research Plan

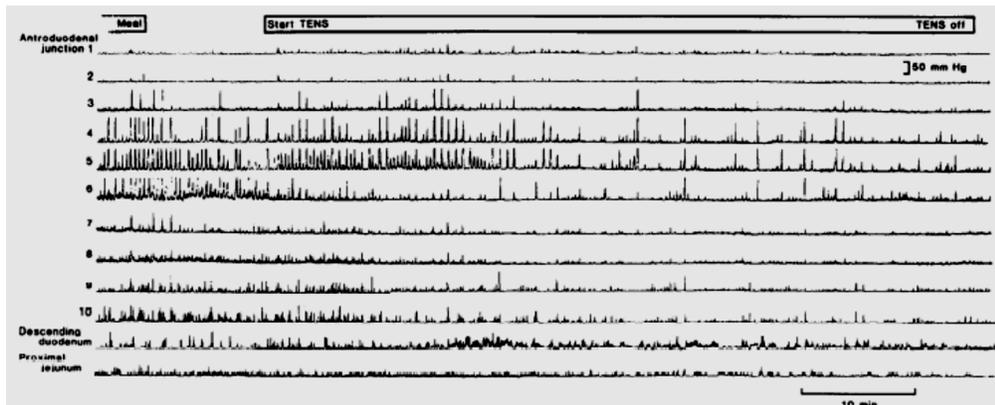
BACKGROUND

An implantable gastric stimulator (gastric pacemaker) has been used to treat obesity; this achieves excess weight loss up to 40% in approximately 1 year. The stimulator can be placed laparoscopically or endoscopically, but is invasive (1-3). The modulation of neuronal activities and release of certain hormones with an implantable gastric stimulator may explain the reduction of appetite and the increase of satiety, such as a decrease in ghrelin levels (4).

Viscerovisceral spinal sympathetic reflexes appear to play an important role in the autonomic control of thoracoabdominal viscera, such as the heart and great vessels (5). However, somatic stimulation may also affect visceral function through autonomic reflexes. The best known somatovisceral response is the effect of cold pain on vasomotor reactions (6). Evidence suggests that the gastrointestinal tract may also be influenced by such somatovisceral reflexes; thus, in anesthetized rats, cutaneous stimuli applied to the abdomen and hind paw decrease and increase stomach motility, respectively. Whereas the latter reflex response appears to relay centrally and the efferent limb of the reflex is located in vagal fibers, the response to abdominal stimulation involves a somatosympathetic reflex that relays at the level of the spinal cord, being retained in cervical cord-transected rats (7).

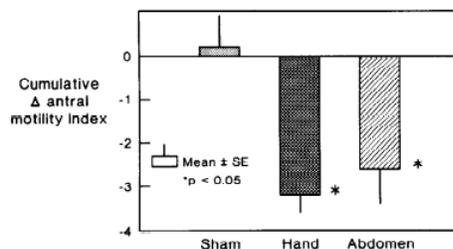
In studies performed by the Principal Investigator 30 years ago (8), sustained somatic stimulation by transcutaneous electrical nerve stimulation (TENS) was applied to the skin of human volunteers while simultaneously monitoring their upper gastrointestinal phasic pressure activity, extraintestinal vasomotor indices, and plasma levels of putative humoral mediators of autonomic reflexes (Figure 1).

Figure 1.



Stimuli were applied either to the hand (C8-T1) or to the upper abdomen (T5-T10) to determine whether impulses at these two dermatomes produced different effects on fed antral phasic pressure activity. TENS resulted in significant reduction ($p=0.007$) in antral motility index when applied to the hand and abdomen, as compared with sham stimulation (Figure 2). This was associated with increases in skin conductance and plasma beta-endorphin levels, but there were no changes in pulse, blood pressure, or circulating catecholamine levels. No qualitative changes in proximal intestinal pressure activity were detected. These studies suggested that sustained somatic stimuli resulted in reduced postprandial antral phasic pressure activity and the similarity in the responses to TENS applied to the hand and abdominal dermatomes suggests that the somatovisceral responses may relay at the central level.

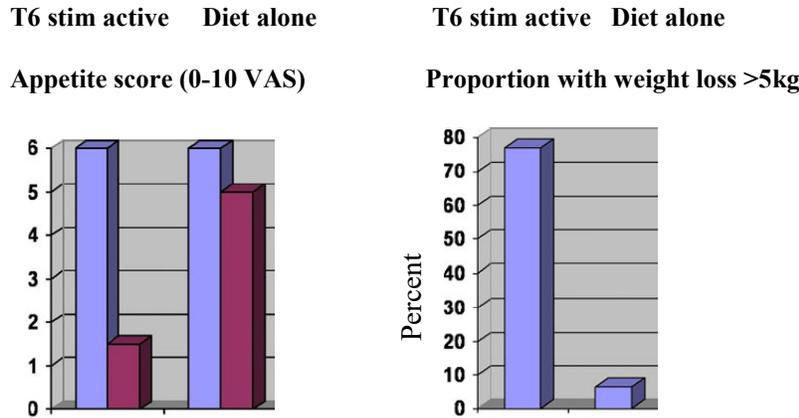
Figure 2.



While effects of TENS dermatomal stimulation on gastric emptying was not evaluated in the earlier studies, more recent data suggested that cutaneous gastric electrical stimulation slowed gastric emptying (9). Furthermore, Electrical stimulation of the dorsal columns of the spinal cord to prevent the perception of intractable neuropathic pain signals in two patients was associated with appetite reduction and weight loss (10). In a large study, Ruiz-Tovar et al. showed that percutaneous electrical neurostimulation of dermatome T6 was associated with appetite reduction and, along with a proper diet, achieved a significantly greater weight reduction than diet alone in morbidly obese patients (11).

Figure 3 shows effects on pre-treatment and post-treatment appetite scores and proportion with weight loss >5kg (11).

Figure 3.



The effects of T6 dermatomal electrical stimulation on gastric motor functions in otherwise healthy overweight or class I obese volunteers are unclear.

HYPOTHESIS AND SPECIFIC AIM

Hypothesis

T6 dermatomal electrical stimulation results in delay of gastric emptying of solids, reduction in gastric volume, inhibition of appetite, and weight loss in healthy volunteers who are overweight or have class I obesity.

Aim

In 16 participants with BMI 25-34.99 kg/m², treated before and after two meals of the day with T6 dermatomal electrical stimulation (delivered by a TENS unit), we aim to compare baseline measurements of gastric emptying of solids with measurements on day 1 of treatment and after 4 weeks and 3 months of treatment. We also aim to compare baseline measurements of fasting and postprandial gastric volume, satiation, satiety, appetite, and weight with measurements after three months of treatment.

EXPERIMENTAL DESIGN

Overweight or class I obesity participants who are not on metformin and have not been diagnosed with type 2 diabetes mellitus (other than dietary advice for borderline hyperglycemia) will be recruited for the study.

Participants will undergo baseline measurements of height, weight, BMI, pulse, blood pressure, gastric function, satiation, satiety, and incretin hormones, over a period of 3 to 7 days. In an open-label study, all 16 participants will receive 15-minute T6 dermatome cutaneous stimulations with a TENS unit applied immediately before ingestion of two of the main meals of the day (breakfast and evening meal), and 60-minute stimulations applied immediately after ingestion of these meals.

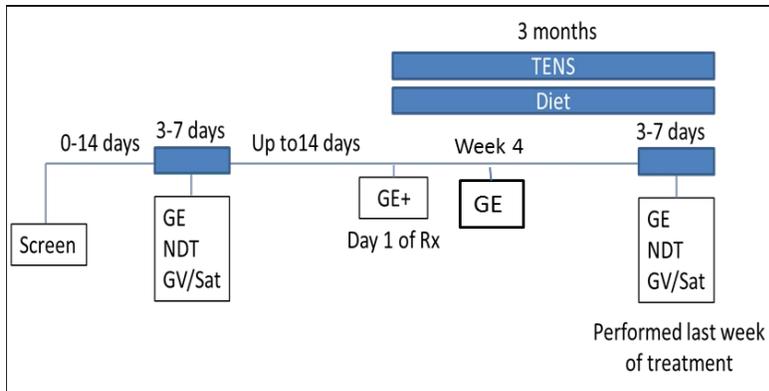
Participants will attend the Mayo Clinic Clinical Research Trials Unit during the first day of treatment, within 2 weeks from completion of baseline testing. During this visit (day 1 of treatment), devices will be provided and participants will receive training on self-administering electrical stimulation. Hence, the first set of electrical stimulations will take place at Mayo Clinic. On this day, participants will also undergo a gastric emptying test as a measure of the acute effect of T6 dermatome cutaneous stimulation on gastric emptying.

Participants will apply the stimulus four times daily for a treatment period of at least 3 months, at the time of breakfast and evening meals (starting 15 minutes preprandially and immediately postprandially for 60 minutes). After 4 weeks of treatment, the participants will be asked to return to the Clinical Research and Trials Unit for a repeat of the gastric emptying study identical to the procedure performed at baseline. During the three-month treatment period, participants will keep a diary of weight, measured on the same weighing scales in their homes once weekly, and a weekly appetite record (0-10cm VAS, paper diary). The stimulation parameters will be: 200 μ sec pulse width at 20 Hz with a goal amplitude range of 18-20 mA. Each stimulation will begin at 0 mA and increase quickly to achieve the 18-20 mA dose. Clinical trial stimulation will be limited to an accumulated maximum of 150 Joules each day; For example, two 15-minute and two 60-minute stimulation sessions at 200 μ sec pulse width, 20 Hz and 25 mA deliver an accumulated 40.5 Joules per day. . Participants that do not tolerate the discomfort or develop nausea likely caused by the TENS unit, will report to the investigational team the post-prandial duration of stimulation may be reduced from the targeted duration of 60 minutes postprandially).

During the final week of the three-month treatment period or at the time of early withdrawal, participants will undergo the same measurements as performed during the previous gastric emptying test days. **During these studies, participants will receive 15-minute T6 dermatome cutaneous stimulations with the TENS unit immediately before meal ingestion and 60-minute stimulations immediately after meal ingestion, in the different tests.**

Figure 4 is a schematic that summarizes the main events that will take place in this study.

Figure 4.



METHODS

Participants

Overweight or class I obese participants who are not on metformin and have not been diagnosed with type 2 diabetes mellitus (other than dietary advice for borderline hyperglycemia) will be recruited for the study. The objective is to have 16 participants complete all investigative testing over approximately 14 weeks. Therefore, we may screen and enroll up to 36 participants in order to ensure 16 fulfill eligibility criteria and complete the study.

Inclusion Criteria

- Overweight and obese adults ($BMI \geq 25 \text{ kg/m}^2$ and $\leq 34.99 \text{ kg/m}^2$) residing within 125 miles of Mayo Clinic in Rochester, MN; these will be otherwise healthy individuals with no unstable psychiatric disease and not currently on treatment for cardiac, pulmonary, gastrointestinal, hepatic, renal, hematological, neurological, or endocrine (other than hyperglycemia on diet) disorders.
- Age: 18-65 years
- Gender: Men or women. Women of childbearing potential will be using an effective form of contraception, and have negative pregnancy tests within 48 hours of enrollment and before each radiation exposure.
- Subjects must have the ability to provide informed consent before any trial-related activities.

Eligible individuals will be asked to avoid taking additional medications and supplements for the duration of the study, unless reviewed and approved by the study team.

Exclusion Criteria

- Abdominal surgery other than appendectomy, Caesarian section or tubal ligation

- b. Positive history of chronic gastrointestinal diseases, systemic disease that could affect gastrointestinal motility, or use of medications that may alter gastrointestinal motility, appetite or absorption, e.g., Orlistat
- c. Positive history of diabetes mellitus or use of hypoglycemic medications
- d. Positive history of spinal cord injury and/or chronic back pain
- e. Significant untreated psychiatric dysfunction based upon screening with the Hospital Anxiety and Depression Inventory (HAD) (12), a self-administered alcoholism screening test (AUDIT-C) (13), and the Questionnaire on Eating and Weight Patterns (binge eating disorders and bulimia) (14). If such a dysfunction is identified by a HAD score >11 or difficulties with substance or eating disorders, the participant will be excluded and given a referral letter to his/her primary care doctor for further appraisal and follow-up.
- f. Intake of medication, whether prescribed or over the counter (except multivitamins), within 7 days of the study. Exceptions are birth control pill, estrogen replacement therapy, thyroxine replacement therapy, low dose analgesia or anti-inflammatory medications (Acetaminophen and Ibuprofen) and any medication administered for co-morbidities as long as they do not alter gastrointestinal motility including gastric emptying and gastric accommodation.
- g. Subjects may also be excluded from participation for other factors at the discretion of the principal investigator.

Recommended Diet (modified from ref. 11)

The Participants will be encouraged to consume a diet of 1200 kcal for women and 1400 kcal for men (estimated mean macronutrient proportions: carbohydrates 51%; proteins 23%; fats 26%). Upon enrollment in the study, they will meet with a registered dietitian for a pertinent diet education. Throughout the duration of the study, the participants will record their food intake on a daily food diary that will be reviewed by the study dietitian.

1200 Kcal:

Breakfast: Skimmed milk (240ml) or two natural yogurts - bread (100g) or two cookies – granola or whole grain cereal (1/2 cup) – nuts (15 mixed)

Mid morning: Fruit (100g of apple, pear, orange, peach, or kiwi)

Lunch and dinner:

First course to choose from:

- Vegetables (200g) spinach, chard, eggplant, watercress, endive, lettuce, cauliflower, mushrooms, leeks, asparagus, cabbage, cucumber, peppers, tomatoes, alternating cooked or salad
- Vegetables (150g) green beans, beets, carrots, artichokes or brussel sprouts
- Vegetable soup (1 cup)
- Pasta, semolina or rice (1/3 cup cooked)

Second course to choose from:

- Fish (120g)
- Chicken, turkey, rabbit, veal (100g)
- Two eggs

Bread (30 g)

Dessert, choice of:

- Fruit (100g of apple, pear, orange, peach, or kiwi OR 200g melon, watermelon, or strawberries)
 - **Snack:** 200ml of skimmed milk alone or with coffee or tea
- Olive oil** for the entire day: 30ml (2 tablespoons)

1400 Kcal:

Breakfast: Skimmed milk (240ml) or two natural yogurts - bread (100g) or two cookies - cottage cheese (60 g) - granola or whole grain cereal (1/2 cup) – nuts (15 mixed)

Mid morning: Fruit (100g of apple, pear, orange, peach, or kiwi)

Lunch and dinner:

First course to choose from:

- Vegetables (250g) spinach, chard, eggplant, watercress, endive, lettuce, cauliflower, mushrooms, leeks, asparagus, cabbage, cucumber, peppers, tomatoes, alternating cooked or salad
- Vegetables (200g) green beans, beets, carrots, artichokes or brussel sprouts
- Vegetable soup (1 cup)
- Pasta, semolina or rice (1/2 cup cooked)

Second course to choose from:

- Fish (160g)
- Chicken, turkey, rabbit, veal (130g)
- Two eggs with cheese

Bread (30 g)

Dessert, choice of:

- Fruit (100g of apple, pear, orange, peach, or kiwi OR 200g melon, watermelon, or strawberries)

Snack: 200ml of skimmed milk alone or with coffee or tea – Corn flakes (1/2 cup)

Olive oil for the entire day: 30ml (2 tablespoons)

T6 Dermatomal Stimulation

T6 dermatomal stimulation will be achieved by utilizing an Elira TENS device (Elira Therapeutics, Inc., St. Louis, MO), following the company's protocol. The Elira device provides a broad range of options for stimulation parameters. In particular, pulse width is programmable from 25 μ sec to 400 μ sec, pulse amplitude from 1 mA to 45 mA, pulse frequency from 1 Hz to 200 Hz, session duration from 5 min to 60 min, and number of sessions per day from 0 to 8 sessions.

- Participants will undergo four stimulation sessions per day (daily for at least 3 months) distributed around 2 meals (breakfast and dinner) as follows: A 15-minute pre-prandial session (starting 15 minutes before the meal) and a 60-minute post-prandial session (starting immediately after the meal), during which the participant can walk around and continue to perform regular activities as desired, with the exception of driving and operating machinery
- The stimulation parameters will be: 200 μ sec pulse width at 20 Hz with a goal amplitude range of 18-20 mA (depending on the subject's pain threshold). Participants will be instructed to begin each stimulation at 0 mA and increase as tolerated (within 5 minutes) to achieve the 18-20 mA goal.

Clinical trial stimulation will be limited to an accumulated maximum of 150 Joules per day, with a maximum of 0.001 Joules (1 mJ) per pulse. For example, two 15-minute and two 60-minute stimulation sessions at 200 μ sec pulse width, 20 Hz and 25 mA deliver an accumulated 40.5 Joules per day, with only 0.23 mJ per pulse, allowing for upward titration as needed. The principal investigator may increase or decrease any of the stimulation parameters at his discretion up to the maximum 150 Joules daily limit.

Blood Samples

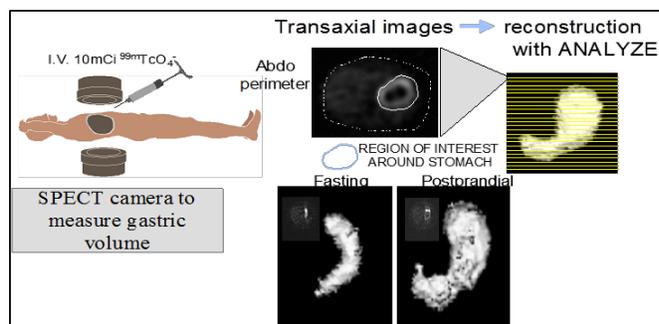
Fasting, 15, 45, and 90 minute post-prandial blood samples will be collected at the baseline and treatment conclusion visits, and will be stored at -70°C for assay analysis of plasma gastrointestinal hormone levels as well as storing a blood-based DNA sample for possible future genetic testing. Fasting blood glucose will be measured at one of the baseline visits using a glucometer (CRTU nurses).

Quantitative Traits

On different days, participants will attend Mayo Clinic Clinical Research Trials Unit at a prescheduled time after an 8-hour fasting period, and the following validated quantitative traits will be measured.

1. **Gastric emptying (GE) of solids** by scintigraphy: Scans will be obtained immediately after consumption of test meal and then every 15 minutes for the first hour, every 30 minutes for the second hour and then at the 3 and 4 hour timepoints. The primary endpoint is gastric half-emptying time ($\text{GE } T_{1/2}$), and the secondary endpoints are proportions emptied at 2 and 4 hours (15). The normal range for $\text{GE } T_{1/2}$ is based on 10th and 90th percentiles in healthy volunteers, based on gender (16). In general, GE of liquids is noncontributory in the context of upper gastrointestinal symptoms (17). In order to reduce radiation burden (needing two isotopes to assess both liquid and solid emptying), we will study exclusively GE of solids.

Figure 5



2. **Fasting and postprandial gastric volume (GV)** by single photon emission computed tomography (SPECT), developed and validated (including performance characteristics) in our lab [Figure 5 (18-20)].

3. **Satiation** by Ensure® nutrient drink test (1kcal/mL, 11% fat, 73% carbohydrate, 16% protein) with ingestion at a rate of 120

mL every 4 minutes equivalent to a constant rate of 30ml/minute to measure volume to fullness (VTF) and maximum tolerated volume (MTV) (21). Briefly, participants record their sensations of fullness using a numerical scale from 0 to 5, with level 0 being no symptoms, level 3

corresponding to fullness sensation after a typical meal (“volume to fullness”), and level 5 corresponding to the MTV (maximum or unbearable fullness/satiation). Nutrient intake is stopped when subjects reach the score of 5. Postprandial symptoms of fullness, nausea, bloating, and pain are measured 30 minutes after the meal using 100mm horizontal visual analog scales (VAS), with the words “none” and “worst ever” anchored at each end.

4. **Satiety- Buffet Meal (for assessment of kcal intake as a measure of appetite)** by ad-libitum buffet meal to measure total caloric intake and macronutrient distribution in the chosen food (15). Five hours after ingesting 300mL liquid nutrient (Ensure®) as part of the SPECT gastric volume study, participants will be invited to eat, during a 30-minute period, a standard ad libitum meal that includes five cheese lasagna (Stouffers®, Nestle USA, Inc., Solon, OH [nutritional analysis of each 304g box: 340kcal (19g protein ((23% of energy)), 41g carbohydrate ((48% of energy)), and 11g fat ((29% of energy))]; vanilla pudding (Jell-O®, Kraft Foods North America, Tarrytown, NY [nutritional analysis of each 110-g carton: 110 kcal (1g protein ((4% of energy)), 23g carbohydrate ((84% of energy)), and 1.5g fat ((12% of energy))]; and skim milk (Kemps Select, Kemps LLC®, St. Paul, MN [nutritional analysis of each 236mL carton: 90kcal (9g protein ((40% of energy)), 13g carbohydrate ((60% of energy)), and 0g fat])). The total amount (grams and kilocalories) of food consumed and the kilocalories of each macronutrient at the ad libitum meal are analyzed by the study dietitian using validated methods.

Participants will be subdivided into “excessive eaters” [the top tertile (1176 kcal) as defined in a prior study of 264 overweight or obese participants] and the bottom 2 tertiles, defining non-excessive intake among overweight or obese participants.

5. **Ratings of appetite** will be measured every 30 minutes between the time of ingestion of standard liquid breakfast and the start of the ad libitum meal. Ratings for appetite (satiety, fullness, hunger and prospective food consumption), thirst, wellbeing and nausea will be recorded using VAS, as described by Flint et al. (22). VAS, 100mm in length with words anchored at each end expressing the most positive and the most negative ratings, will be used to assess hunger, satiety, fullness, prospective food consumption, desire to eat something fatty, salty, sweet or savory, and the palatability (5 questions) of the test meal (Figure 6).

I am not hungry at all	How hungry do you feel?	I have never been more hung
I am completely empty	How satisfied do you feel?	I cannot eat another bite
Not at all full	How full do you feel?	Totally full
Nothing at all	How much do you think you can eat?	A lot
Yes, very much	Would you like to eat something sweet?	No, not at all
Yes, very much	Would you like to eat something salty?	No, not at all
Yes, very much	Would you like to eat something savoury?	No, not at all
Yes, very much	Would you like to eat something fatty?	No, not at all

Good	Visual appeal	Bad
Good	Smell	Bad
Good	Taste	Bad
Much	Aftertaste	None
Good	Palatability	Bad

Overall appetite score will be calculated as the average of the four individual scores (satiety + fullness + 100-prospective food consumption + 100-hunger / 4).

6. **Plasma gastrointestinal hormones (ghrelin, GLP-1 and PYY)** by radioimmunoassay measured at fasting, and 15, 45, and 90 minutes

postprandially during the NDT. The primary endpoint is the peak postprandial level. CCK levels will not be measured in the current study, since they were non-informative in our prior studies. Total ghrelin will be measured by a radioimmunoassay technique (Linco Research, Inc., St. Charles, MO). The assay uses ^{125}I -labeled ghrelin and a ghrelin antiserum to determine the level of total ghrelin in plasma. GLP-1 will be measured as the biologically active GLP-1 (active and total) using a 2-site non-competitive immunoassay based on enzyme-labeled quantification of GLP-1 detected by a fluorogenic substrate. PYY will be measured by radioimmunoassay (Linco Research, Inc., St. Charles, MO). PYY exists in at least 2 molecular forms, 1-36 and 3-36, both of which are physiologically active and are detected by the assay.

7. **Self-administered questionnaires** assessing affect, exercise performance, attitudes, satisfaction with body image, and eating behavior (12-14,23-26).

Statistical Analysis

Sample size assessment - Sample size assessment is based on the results of primary endpoints in the Mayo Clinic lab. Assuming the intra-individual coefficient of variation (or standard deviation) is similar to the inter-individual variation, we have used the SD_{inter} for estimating the power of the study (n=16, baseline versus post-treatment).

Response	Mean	SD	Predicted detectable effect size (%(absolute #)), n=16 on treatment compared to baseline, paired analysis
Gastric emptying, $T_{1/2}$ min*	121.7	29.8	18.4% (22.4 min)
Fasting gastric volume, ml**	225	65	21.8% (49mL)
Gastric accommodation, ml**	507	100	14.7% (75mL)

Data obtained from *ref. 16 and **ref. 20; predicted detectable effect size is shown with 80% power, $\alpha=0.05$.

The sample size of 16 on-treatment relative to baseline will have sufficient power to detect a difference in gastric emptying of 22.4 min, of fasting gastric volume of 49mL, and in gastric accommodation of 75mL.

Statistical Methods

It is anticipated that all primary and secondary endpoints will be normally distributed. We shall use a paired student's t-test to compare study parameters (differences between baseline and on-treatment). An analysis of covariance may be examined using gender and BMI as covariates, since these may significantly affect gastric functions such as satiation, maximum tolerated volume, and gastric emptying.

Interim Analysis

An administrative interim analysis will be completed after 6 subjects have completed at least 4 weeks of treatment. The data will be submitted in a blinded fashion to the study sponsor's statistician while the investigative team remains blinded to the treatments. This interim analysis will be conducted for administrative purposes to provide information about future planning of other research activities. The

conduct of this study will not be altered and all planned research activities will proceed until the completion of the targeted 16 subjects.

Primary endpoints

1. Body weight change from baseline
2. Gastric emptying $T_{1/2}$ after day 1 treatment
3. Gastric emptying $T_{1/2}$ after 3 months treatment

Secondary endpoints

1. Fasting gastric volume
2. Postprandial gastric volume or accommodation volume
3. Gastric emptying % at 1 hour in day 1 and end of three months of treatment
4. Satiation: volume to fullness (grade 3) and maximum tolerated volume (grade 5)
5. Satiety: kcal intake at buffet meal
6. Appetite score during satiety meal test and at weekly intervals (at home)
7. Plasma ghrelin, GLP-1 and PYY fasting
8. Peak postprandial plasma ghrelin, GLP-1 and PYY fasting

Anticipated Results and Significance

We anticipate greater weight loss with active treatment with dermatomal stimulation compared to baseline. The sample size is not sufficient to appraise twice versus once daily treatment. However, the data will be tabulated for descriptive analysis. The physiological measurements will provide information about the potential mechanisms involved in any beneficial effects on weight and appetite.

Potential Pitfalls, Precautions Taken, and Alternative Strategies

- a. Feasibility - Given our 500-person database with baseline quantitative traits and genotype, we are confident we will recruit sufficient numbers of participants for these studies that involve mainly noninvasive tests.
- b. The pilot study is intended to document feasibility to recruit and retain subjects in such a 12 to 14-week, *hypothesis-generating* treatment trial, and to appraise the weight loss achieved in order to characterize the coefficient of variation for planning the sample size of a future *hypothesis testing* trial.
- c. Exploratory analyses will be performed using the other quantitative traits which are all measured in these studies to assess physiological parameters that may be relevant to any beneficial effects of the treatment in these overweight or class I obese subjects.
- d. In order to develop pre-specified monitoring and analysis plans, we shall establish a DATA SAFETY MONITORING PLAN which will involve review by experts independent of the study, using a team comprised of researchers with track records in biostatistics and clinical trials and expertise in the quantitative biomarker

Device Safety: Designation of Non-Significant Risk

Based on the FDA guidance on Significant Risk and Nonsignificant Risk Medical Device Studies (27), the proposed study does not meet the definition for a significant risk (SR) device study and hence is a non-significant risk (NSR) clinical study.

Moreover, the Elira TENS device is regarded as an NSR device on the following basis:

- It is not implantable
- It does not support or sustain human life
- It is not for use of substantial importance in diagnosing, curing, mitigating or treating a disease (no claims related to obesity have been made by the manufacturer)
- It does not present a potential for serious risk to the health, safety or welfare of the participant

It is important to note that the Elira TENS device is essentially similar to commercially-available, over-the-counter TENS units that can be purchased at local pharmacies and are commonly utilized for self-administered therapy.

Lastly, participants will keep a diary that will serve as a tool for evaluating risk/discomfort potentially associated with the use of the Elira TENS unit. Nausea, dyspepsia and local discomfort on anterior abdominal wall (treatment site) may occur with over-stimulation.

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