COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY
YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: GLP-1 analogue effects on food cues, stress, motivation for highly palatable foods, and weight

Principal Investigator: Ania Jastreboff, MD, PhD

Phone Number: 1-888-Y-STRESS

Research Study Summary:

- We are asking you to join a research study.

- The purpose of this research study is to evaluate if food craving and intake and weight is changed in response to taking a medication called semaglutide compared to taking placebo medication.

- Study procedures will include:

  1) Initial evaluation including health status assessment; questionnaires about eating, stress, mood, fatigue, quality of sleep and physical activity; and laboratory sessions to assess how the medication affects your response to food triggers, including stress and food triggers which are provoked using guided imagery of stress, food and neutral situations
  2) An oral glucose tolerance test with lab drawn to see if you have pre-diabetes before you start the medication/placebo
  3) One eating /lab draw session [video recorded(optional)] before you start the medication/placebo
  4) Weekly medication administration and side effect assessment visits
  5) An oral glucose tolerance test with lab draw to see if you have pre-diabetes during the last two weeks of taking the medication/placebo
  6) Three eating /lab drawn sessions [video recorded(optional)] during the last two weeks of taking you start the medication/placebo
  7) An eating /lab draw session [video recorded(optional)] 3-6 weeks after you finish taking the medication/placebo
  8) Phone calls throughout the study to assess your eating patterns as well as checking in to see how you are doing on the medication or placebo medication.

- 19-22 visits are required over 3.5 to 4 months.
- The screen visit is estimated to take 3h, the OGTT visit is estimated to take 3h, the food snack task visits are estimated to take 4.5h-5h, the med administration and side effect visits are estimated to take less than an hour
- We will ask that you do not start any additional medications that can impact weight or any structured weight loss programs during the course of the study (until after the one month post-treatment follow-up visit).

- There are some risks from participating in this study, including side effect to the medication such as gastrointestinal side effects, most commonly nausea, abdominal discomfort, feeling of fullness.
- The study may have no benefits to you. Some individuals may lose weight during participant in this study while others may not lose weight.
- There are other choices available to you outside of this research. You can choose not to participant in this study. You can talk with your doctor about how to lose weight or change your eating behavior.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?

We are asking you to take part in a research study because your Body Mass Index (BMI) is greater than or equal to 30kg/m^2 (defined as having obesity). We are looking for 96 participants to be part of this research study.

Who is paying for the study?

The National Institutes of Health (NIH) is providing funding for this study.

What is the study about?

The purpose of this study is to examine whether a glucagon-like peptide medication called semaglutide (FDA approved for the treatment of diabetes and obesity) changes food craving and intake behavior and affects our response to food triggers, including stress and food triggers. The study will also look out how different hormones in our body respond to this medication and whether these changes are related to weight loss. Semaglutide is FDA approved for the treatment of type 2 diabetes and for the treatment of obesity in individuals without diabetes in the United States. It is also being investigated for the potential of decreasing cardio vascular events, such as heart attacks.

What are you asking me to do and how long will it take?

If you agree to take part in this study, this is what will happen:

Assessments before starting semaglutide or placebo medication:

When you enter the study, we will ask you about your food preferences and other psychological and physical problems that you may have now or in the past. We will also ask you to complete several paper and pencil tests regarding eating habits. These tests will take 2-3 sessions and a total of 5-6 hours of your time.

You will also complete a physical health screening to make sure you are in good physical health and determine menstrual cycle status in women. You will be cleared for further participation by the study physician. If you decide to take part in this study, you must be free of major medical illnesses as determined by the physical health screening and urine analysis. Women will also be given a

urine pregnancy test and hormone levels will be assessed for menstrual cycle functioning.

You will also participate in an **Oral Glucose Tolerance Test (OGTT)** which assesses insulin resistance. After an overnight fast (beginning at 9PM), you will come to the office at 8AM. An IV will be put into the vein in one of your arms so that we can draw blood at regular intervals. Approximately 15 minutes later, you will be given 8 ounces of a sugar drink. Blood will then be drawn at several time points over the next two hours. Total amount of blood draw during this time is approximately 2 ½ ounces, a little more than a quarter cup of blood. This session will take approximately 2-3 hours of your time. The oral glucose tolerance test will be repeated again at week 11-14 of the study.

We may ask to videotape your interview sessions and will only do so after asking for your signed permission to do so. You will know when you are being videotaped. The videotape recording will be used for research only. The recording will not be shown to the general public and will not be identified with your name. Declining to be videotaped will not affect your study participation in any way.

We will ask that you do not start any additional medications that can impact weight or any structured weight loss programs during the course of the study (until after the one month post-treatment follow-up visit).

Food Lab Assessments

One food laboratory session will be conducted, prior to starting the medication. Three food laboratory sessions will be repeated at the end of treatment and described below. The final food laboratory session will be conducted 3-6 weeks after you complete the treatment with the medication/placebo. The laboratory session will last for four and a half hours scheduled from 12:00 PM to ~5:00 PM in the afternoon. No smoking is permitted on the Yale Stress Center and during the laboratory sessions.

The **food laboratory sessions** will begin at 2:00 PM at the Yale Stress Center. When you come into the testing room we will first set you up to draw blood samples. An IV will be put into the vein in one of your arms so that we can draw blood at regular intervals. About 90ml (less than 1/2 cup of blood) of blood will be taken during each session which your body can easily tolerate. Over the final weeks you are on the medication and for the follow-up post treatment visit, this will amount to approximately 376 ml a little more than 1 1/2 cups of blood a cup of blood which is less than the amount of blood drawn during a blood donation. While your body can tolerate this level of blood draw, you should not donate blood for a period of 8 weeks after the laboratory sessions.

The blood samples will be analyzed for naturally occurring chemicals that your body produces regularly.

On the afternoon of each lab session, 3 electrodes will be attached to your chest to allow recording of your heart rate. You will also wear a special strap across your chest or upper stomach area that has a small strain gauge on it which will also assist us in recording your heart rate. These are non-invasive measure of your heart rate.

Next, we will attach a sensor (like a clothespin) to your finger to monitor your heart rate, and place a blood pressure cuff on your arm to measure blood pressure. These are painless procedures. You

will remain seated and be allowed to relax. Then you will participate in a food taste test. You will be given snack foods and will be instructed to taste each snack and rate how much you like the taste. You can eat as much of the snacks as you like to fully make your taste ratings.

After the taste test, we will ask you to stay quietly in the testing room for an additional one-hour. At various times during this period we will collect blood samples and ask you to make ratings of your feelings and urges for specific foods.

The same procedure will be done at the end of treatment (weeks 11-14). Two additional food laboratory sessions will take place during the last week of treatment which is the same as described above but you will be asked to periodically submerge your hand in either cold water (4 degrees) or room temperature water (37 degrees) at different time points.

One additional food laboratory session will take place 3-6 weeks after you complete the treatment.

Randomization and Medication versus Placebo description

After you complete the above sessions you will then be assigned randomly (by a computer program) to either the medication (semaglutide group) or the placebo group. Neither you nor the individuals you are interacting with during the course of the study will know if you are receiving the study medication or the placebo medication. The placebo group will receive and inactive (inert) substance, in this case salt water (saline). The semaglutide group will receive Semaglutide.

Semaglutide is a glucagon-like peptide medication, FDA approved for the treatment of type 2 diabetes and for the treatment of obesity in adults. In a study of individuals with diabetes and obesity this glucagon like peptide medication resulted in 7-10 more pounds that the group which did not receive semaglutide.

The medication semaglutide and placebo will be administered once per week subcutaneously (a small shot) by a nurse at the Yale Stress Center. The study drug will be given to you subcutaneously (under your skin) in the region of the thigh, upper arm, or belly. (Once during the course of the study, in order to give the prescribed dose, you may receive two shots instead of one shot.) After each dose administration you will meet with the study nurse practitioner or physician at the Yale Stress Center (YSC) to review how you are doing over all on the medication or placebo. At these weekly visits side effects will be reviewed and assessed including the most common adverse reactions (reported in ≥5%) such as nausea, vomiting, diarrhea, abdominal pain, constipation.

Your dose of semaglutide will be titrated up (increase slowly) based on FDA medication recommendations as well as your side effect assessment. You will receive placebo or semaglutide 0.25mg subcutaneous injection once weekly for 4 weeks; then 0.5mg once weekly for 4 wks; and finally, 1mg once weekly until the end of the study (4 weeks). We will work with you if you are not able to tolerate doses (due to gastrointestinal side effects).

For your safety and for continuity of your care, we will communicate with your primary care provider that you are participating in the study.

<u>What are the risks and discomforts of participating?</u>

Before you decide to take part in this research study, there are some risks and inconveniences that you should know about. These include: 1) risks associated with placement of an intravenous (IV) catheter, 2) risks associated with having blood drawn, 3) some risks associated with the cold water immersion procedure, and 4) taking the medication vs. placebo injections once per week. These risks are described below.

1) Intravenous (IV) Placement: When an intravenous catheter is started, there is some risk that you may develop a bruise where the IV enters the vein. Usually these go away in several days without any treatment. On extremely rare occasions, a blood clot or infection may occur.

2) Drawing of Blood: During each laboratory session, about 90ml blood (less than ½ cup of blood) will be drawn to measure levels of naturally occurring chemicals hormone that may change during the session. The total amount of blood drawn during the baseline tests is less than the amount of blood obtained during a regular blood donation. We are drawing 156 ml (slightly more than ½ a cup). During the treatment phase and follow up lab session we will collect a total of 446 ml of blood which is similar to 1 blood donation (a blood donation is 500 ml). People who are in good health are not usually affected by this kind of blood loss. However, to be safe, you should not donate blood for at least 8 weeks after completing the laboratory sessions and not enroll in this study until 8 weeks has passed since you last gave blood. The table below describes in detail the amount og blood that will be drawn in total for the whole study.

Blood draw during first 6 weeks	**Amount (ml)**
Baseline: Oral glucose stress test (OGTT)	70
Baseline (pre-treatment): Food Snack Test (FST) with no stressor	86
TOTAL throughout study baseline	**156**

Blood draw during following 10-14 weeks	**Amount (ml)**
During-treatment: OGTT	70
During-treatment: FST with no stressor (2)	86
During-treatment: FST with cold water test	102
During-treatment: FST with warm water	102
Post treatment follow-up FST with no stressor	86
TOTAL throughout study 12-14 weeks (during and post treatment)	**446**

3) The Cold Water Immersion Procedure: The cold water immersion procedure can be associated with some mild discomfort but you are allowed to remove your hand if the procedure becomes intolerable and it has not been shown to have any lasting effects.

4) Medication (semaglutide) vs. placebo: As described above you will be randomly assigned (by a computer) to receive the medication (semaglutide) or placebo (inactive saline, salt water) via subcutaneous injection (small shot) on a weekly basis for 12-14 weeks. The side effect of getting an injection is possible irritation or rash at the injection site. This usually self-resolves. If this does not resolve, the study physician and nurse practitioner working with the investigators will assess whether you should continue or stop the medication (semaglutide an placebo). Taking semaglutide there are some common side effects

(described below) and rare side effects. Some of the rare side effects include development of gall stones, pancreatitis (inflammation of the pancreas), and an ileus [lack of movement in the intestine which can lead to a blockage of food material (obstruction) in the intestine] and we will monitor you closely for these rare side effect and will conduct blood draw for safety. If any are suspected, we will have you stop taking the medication and refer you to appropriate medical care. The more common side effects, which occur include nausea, vomiting, diarrhea, abdominal pain constipation, and fatigue, particularly when weight loss occurs. We will also monitor you for injection site discomfort, rash or redness as well as increases in heart rate, and tiredness. You will receive a call during the first week of dose increase of the medication to assess for side effects and address any questions/concerns you may have.

5) To minimize any of the above risks as well as medication interaction, we ask that you please let us know immediately if you need so start any other new medications during the course of the study. We will check for possible interactions for safely.

How will I know about new risks or important information about the study?

We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?

You may or may not lose weight in this study and this this study is not designed to provide you with any direct health benefit. We expect that the results of the study, however, may benefit science and others through increasing our knowledge about the mental and physical effects of stress and its relation to behavior.

How can the study possibly benefit other people?

The benefits to science and other people may include a better understanding of how semaglutide works to change food craving and intake and response to stress and food triggered eating.

Are there any costs to participation?

You will not have to pay for taking part in this study or the medication or placebo you will be provided for three months. The only costs include transportation and your time coming to the study visits. We can provide help with transportation to get to the Center, if needed.

Will I be paid for participation?

You will be paid for taking part in this study. You will be compensated as follows: $100 for the intake appointment and OGTT appointment, $100 for each of the 5 food laboratory sessions, $10 for each week of dietary recall telephone calls (5 weeks), $25 bonus for completing all of the dietary recalls, $20 for each of the visits for medication shot and med check (12-14 visits, maximum of $280 for med check visits), $50 for second oral glucose tolerance test (OGTT), and a $100 bonus for completing all the visits - for a total compensation of $1105 for participation in the study. If an injection visit happens on the same day as a lab visit (to minimize trips to our

office for you) then you will receive the higher visit compensation (lab visit). If you needed an additional visit for any reason, you will receive a bonus compensation. Additionally, we will reimburse your parking costs. You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments.

What are my choices if I decide not to take part in this study?

Instead of participating in this study, you have some other choices.
You could:

- Get treatment without being in a study. Semaglutide is now available for the treatment of obesity, and there are other medications your doctor can prescribe.
- Take part in another study.
- Receive care only, without any treatment for your disease.

How will you keep my data safe and private?

We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if we learn that you are hurting a child or an older person.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission.

We will also share information about you with other researchers for future research but we will not use your name or other identifiers. We will not ask you for any additional permission.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called “Protected Health Information.” It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this Study.
- The entire research record and any medical records held by Yale University School of Medicine created from: July 1, 2020 to June 30, 2025.
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research regarding
    - HIV / AIDS test results (if you have preexisting condition)
    - Hepatitis infection
    - Sexually transmitted diseases
    - Other reportable infectious diseases
    - Physical exams

- Laboratory, x-ray, and other test results
- Diaries and questionnaires
- The diagnosis and treatment of a mental health condition
- Use of illegal drugs or the study of illegal behavior
- Records about any study drug you received

Of note, if any concering mood issues come up on questionnaires, we will refer you to your primary care provider or if emergent situation to the Emergency Department.

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The U.S. Food and Drug Administration (FDA) This is done so that the FDA can review information about Semaglutide (the medication) involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- The study sponsor or manufacturer of study drug/device
- Drug regulatory agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- The primary investigator, Dr. Ania Jastreboff
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. Researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of such as child abuse and neglect, or harm to self or others.

Investigator Interest

The principal investigator, Dr. Jastreboff, has received compensation from Novo Nordisk, the manufacturer of study drug semaglutide, for consulting services. You may ask to speak with Dr. Jastreboff about this interest.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record. However, this is a double-blinded study and if you sign this permission form, you will not be allowed to look at or copy your study related information until after the research is completed.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to Dr. Ania Jastreboff and Dr. Rajita Sinha at 2 Church Street South, Suite 209, The Yale Stress Center, at the Yale University, New Haven, CT 06519.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to insure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?

You and/or your insurance carrier would be responsible for the cost of any injury or illness relating to the study. Financial compensation for injury is not available.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

We would still treat you with standard therapy or, at your request, refer you to a clinic or doctor who can offer you treatment. Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary, for example is you develop serious side effect we will withdraw you from the study for your safety.

What will happen with my data if I stop participating?

If you stop participating in the study for any reason, we will stop collecting data at that point. Data collected to that point is de-identified and therefor will be included in the analysis until the point at which you stop participating.

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigators at 1-888-Y-STRESS.

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date