TRIAL PROCEDURES

1. RECRUITMENT

Advertisements will be done on social media, outbound calls will be made to prior research subjects at Boston Clinical Trials and posters will be displayed in the waiting areas. At Jacobi, patients will also be recruited when they come for a regular dental visit and are waiting in the waiting room.

2. SCREENING: TELEPHONE ELIGIBILITY INTERVIEW

A call will be made to recruit subjects and confirm, followed by scheduling the one-time research testing. The caller will use the **Eligibility Telephone Questionnaire**.

3. VISIT

A. OVERVIEW

Enrollment and eligibility determination will be done prior to or during the visit.

B. ENROLLMENT & CONSENT

Advertisements will be sent by email to recruit subjects and posters will be displayed in the waiting areas.

The researcher will review with the prospective subject eligibility and demographic information and the **Eligibility Questionnaire** and **Demographic Data** forms completed.

After confirming eligibility, the Investigative site will consent/assent the subject prior to any procedures, using the **Consent forms** and answer any patient questions.

C. TEST "ADHD-RS"

The subject does the baseline ADHD-RS test cataloging ADHD symptoms and their impact.

D. ASSESS "CGI-S"

The MD gathers the baseline Clinical Global Impression Severity (CGI-S).

E. RESEARCH QUESTIONNAIRES

Each subject/family will complete a **Research Survey, including a custom PMS questionnaire and questions about sensory overstimulation**.

They will also complete a **Food and Activity Diary** for the day of testing to assess factors affecting lidocaine effectiveness.

F. LIDOCAINE TESTING

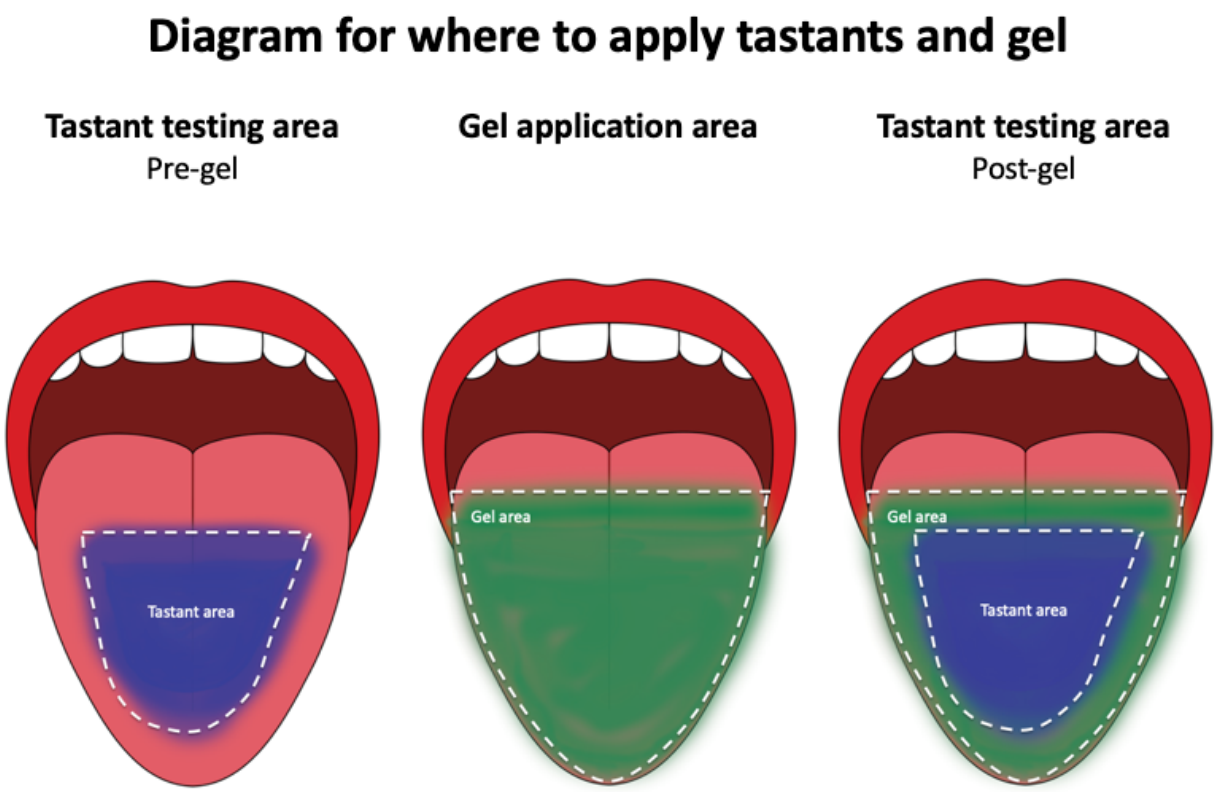
The **Lidocaine tester** will apply lidocaine to the tongue and test for numbness, using the pain-free taste tests.

Lidocaine: we will use Septodont 5% oral lidocaine gel (NDC 0362-0221-10).

The taste solutions will be identical in appearance and odorless, and prepared in 7 one-use vials, 2 with 25% sodium chloride by weight (25 grams NaCl: 75 ml water), 2 with 60% sucrose by weight (60 grams sucrose: 40 ml water), and 2 with just water and one surprise container containing one of the three, to prevent guessing post-lidocaine. Only purified water will be used.

The order of testing the three tastes will be randomized, each will be labeled with a one-time code, prepared by a certified research compounding pharmacy or manufacturer; the labeling will be blinded such that neither the administrator of the test nor the subject will know in advance of the application which taste is in which bottle.

The following diagram shows where the tastants and gel should be applied.



The testing will be performed in a calm setting.

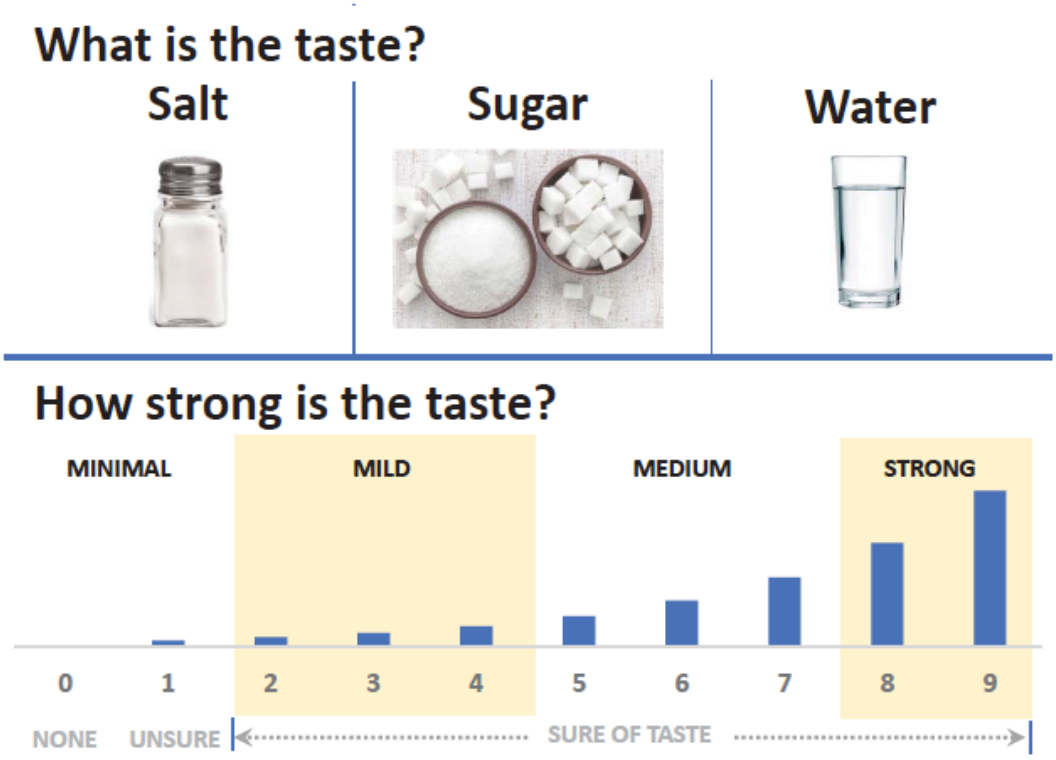
Step 1: Tastants pre-gel

- Before application of the gel, one taste solution will be rubbed across the tongue using a swab, being careful to cover the middle section of the tongue and rub the swab back and forth and to avoid the edges, per the diagram above.
- The subject asked to describe the taste, if any, and its intensity on a scale from 0 (none) to 10 (very intense). We will use a card with sugar, salt, and water and a 10-point scale for intensity to prompt the subject

- For assessing the taste intensity, subjects will be told if they are "guessing" to mark the intensity as no more than zero or one. Only if they are sure what the tastant is, should the intensity be > 1.
- Pre-testing: do 1 each, water, salt, sugar
- Rinse between flavors in pre-test and spit out water

The procedure will be repeated with a second swab with a different tastant, and again with a third swab and the final tastant.

To assist the subject, after the application of each taste the researcher will show them this **Oral Lidocaine Tastant Card**.



Step 2: The lidocaine gel will be rubbed onto the surface and sides of the front half of the tongue using a swab. We will use blister packs of the lidocaine to increase the consistency of dosing.

- Dry tongue before applying lidocaine
- "**Use all the gel in the blister pack**" to standardize dose. (We will adjust quantity in blister to 0.75g of Septodont)
- Provide each subject a paper cup and a towel during the 2-minute wait post lidocaine to catch drool.

- ***There will be no rinsing during the two minutes***.

Step 3: Two minutes after application of lidocaine, the taste assessment is repeated.

- Apply tastant to the center of the tongue, rubbing back and forth, being careful to avoid the margins of the tongue and gel.
- Tell subjects, "**there will be a random assortment of the 4 tastants, not be one of each**".
- Rinse between tastants

The Lidocaine tester will complete the **Oral Lidocaine Testing Data Collection Form.** The subject and those doing the testing will be instructed not to discuss the results of the lidocaine effectiveness testing.

G. LABELS

ALL SITES: Bag around kit, with label of instructions and site identification

COLOR OF LABEL: PINK	**COLOR OF LABEL: White**
PRE-GEL: Tastants & Swabs Inner Bag *Use at room temperature **Contains one of each tastant* Use by: mm/dd/yyyy Contains material from lot number xxxxxxxx@x lot number xxxxxxxx@x lot number xxxxxxxx@x	**POST-GEL: Tastants & Swabs Inner Bag** *Use at room temperature **Contains random assortment of 4 tastants, minimum of 1 each* Use by: mm/dd/yyyy Contains material from lot number xxxxxxxx@x lot number xxxxxxxx@x lot number xxxxxxxx@x lot number xxxxxxxx@x

ALL SITES:

Lidocaine blister & Applicator Inner Bag
Use by dd/mm/yyyy
Contains material from
lot number xxxxxxxx@x

Tastant bottle labels: white

(tastant NOT revealed on label)

Tastant	**All**
Label	**Shake before using** # xxxxx

H. SUBMIT RESULTS USING ELECTRONIC DATA COLLECTION FOR ANALYSIS

The results of the endpoints of the lidocaine effectiveness testing will be submitted electronically using the **Oral Lidocaine Testing Results** form.

I. THANK SUBJECTS FOR PARTICIPATION AND PROVIDE TRAVEL REIMBURSEMENT

Subjects will receive a $75 travel reimbursement at Boston Clinical Trials. Subjects at Jacobi Medical Center will receive $50 Amazon Gift Certificates.

J. CLINICIAN PROVIDES GUIDANCE ON FUTURE USE OF ANESTHETICS

After results have been analyzed, the site will inform the subjects of their lidocaine effectiveness status. These results of the lidocaine test will be shared with the local principal investigator, so that the clinician can provide guidance about future use of anesthetics. We believe bias will be avoided by not unblinding until this point, together with aspects of the study design, including with the inclusion of pure water as a taste, resulting in no one tasting every taste, the separation of roles, and the presence of tingling in the tongue, even among those who do not get numb.

DATA ANALYSIS / STATISTICAL METHODS

1. Sample Size Determination

The sample size of n=50 with ADHD and 50 without ADHD to assess the prevalence of lidocaine ineffectiveness in ADHD vs. those without ADHD. The initial results will guide calculations of future sample sizes to extend the analysis.

We aimed to recruit half the subjects at BCT and the rest at Jacobi Medical Center.

2. Effect Size Analysis

Based on prior studies, we anticipate 30-60% lidocaine ineffectiveness in ADHD and 3-11% in those without ADHD. We further hypothesize that women with PMS may be more significantly affected.