PARTICIPANT INFORMATION SHEET

STUDY TITLE: A question of taste: Do sweet substances alter pain perception in adults?

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Ethical approval number: 60062

Please contact Dr. Elizabeth Mooney elizabeth.mooney@bristol.ac.uk or 07729 401657 if you have any questions about this study

You are being invited to take part in a research study at the University of Bristol looking at how sweet tastes affect the sensations of warmth and painful heat.

This leaflet explains why the project is being done and details of what happens during the study. It is important that you read this if you are interested in participating in the study so that you understand what is involved. Feel free to discuss it with friends, family and your GP. Also, please do contact us if you have any questions.

1. Why is this study being done?

Pain is an unpleasant sensation familiar to us all. It is important to protect our body from damage. However, sometimes pain is not helpful in protecting us and becomes inconvenient to our everyday lives, which is why we try to reduce it by taking painkillers. The way in which pain works at a biological level is still not very well understood, and the medications that we have available to treat pain are not perfect. Therefore researchers are constantly trying to find out more about how pain works and how doctors may be able to provide better treatments for pain. This project will look at how the feeling of pain and the sensation of sweet taste interact.

2. What will taking part involve?

The investigation involves one testing session at the Clinical Research and Imaging Centre at the University of Bristol. The session will last about 1.5 hours. During the session we will use a small heated device held against your arm and ask you to tell us when the device feels hot or painful. The sensation may be likened to touching a warm radiator. We will adjust the temperature to a level that you tell us causes a moderately intense pain (ranked as 6/10 by you where 10 is extremely painful). The device will be turned off as soon as you report it as painful, and it will never be allowed to become hot enough to damage your skin. Each heat stimulus will last only for a short time (15 seconds) and you will be able to terminate the stimulus at any point. We have previously done this sort of test on many study subjects and they have found it tolerable and to not cause any lasting harm.

While this testing is being carried out, we will ask you to taste a number of different sweet-flavoured solutions by holding them in your mouth before spitting them out or swallowing them as you prefer. At the end of the session, we will ask you to fill in a short questionnaire about food preferences. The general procedure of participating is as follows:

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2.1. Before consent

- Once you have read this form and if you are interested in taking part please contact one of the research team listed on the top of this information sheet.
- We will discuss any questions that you might have, and we will ask you a few questions to ensure that you meet the inclusion/exclusion criteria for the study. We can then arrange a suitable date for your visit.

2.2. Study session

This session will be at the Clinical Research and Imaging Centre, University of Bristol. In preparation for the study you will be asked to follow these restrictions prior to reporting visit:

- No over the counter medications on the day of the study, such as pain killers. You may take your normal prescription medications, but please inform the research of any medication taken.
- No alcohol on the evening before the study and the day of the study.

**Please wear comfortable clothing and ensure that we will be able to apply the warming stimulus to your forearm** (e.g. wear short sleeves or sleeves that can be easily rolled up).

At the beginning of the session we will check your understanding of the study and give you further opportunity to ask questions. We will then ask a few some questions about your health and lifestyle to ensure that it is safe for you to participate. If you are happy to give us your informed consent to participate, we will ask you to sign a consent form and the study session will begin.

**NB: It should be noted that these tests are for research purposes only, and do not provide any information on medical diagnosis.**

Below is a list of procedures that will happen during the study session and a diagram of the sequence of events. The total time we expect to complete the main study is ~**1.5 hours**.

At the beginning of the study session we will determine your warm detection threshold and heat pain threshold using standard testing procedures. This is to ensure that you are able to detect temperature changes and therefore make sure that participation in our project is safe for you. In the very unlikely event that your results are outside of our reference range we will suggest that you contact your GP for further advice. Please do note that “outside of the reference range” does not necessarily mean that you are unwell.

2.4. Procedures

**Thermal stimulation**

Thermal stimulation is a validated and safe method used to produce a sensation of pain. During the study we will apply a series of warm stimuli to your arm over an area a few centimetres across. It is important for you to know that none of the temperatures used will cause skin damage, but there may be a slight reddening of the skin under the probe, which may last for up to 4 hours.

**Tasting solutions**

We will ask you to take sips of the test solutions into your mouth and to hold them there for up to 10 seconds before spitting them out or swallowing them as you prefer. We will ask you to rinse your mouth with water in between each solution. The solutions will be sucrose (sugar) or sucralose (sweetener such as Splenda) dissolved in drinking water. These are all normal things that you might have in an ordinary kitchen, and will cause no harm if swallowed. The solutions will all be prepared hygienically with clean drinking water and provided in single-use disposable cups.
6. Must I take part?
No. It is entirely your decision if you would like to take part. If you are interested, please let us know by email and one of the research team will be in touch. We will arrange to meet you to answer any questions. Signing a consent form only happens when you are completely happy that all of your questions have been answered, and even once you have signed the consent form you are free to withdraw from the experiment at any time.

7. What are the possible side-effects of taking part?
Thermal stimulation:
Slight reddening of the skin around the site of heating/cooling.

Pain:
We will minimise this unwanted side-effect of thermal stimulation at all times, however, it is important to note that you will experience short periods of discomfort. Remember: you are in control of the experiment at all times, and can tell us to stop if it is too painful.
8. Who is excluded from taking part in this study?
For safety and scientific reasons the following exclusion criteria are used, unfortunately, you cannot take part if you:
Are diagnosed with acute or chronic pain conditions.
Are diagnosed with a confounding medical (particularly neurological) or psychiatric condition
Are taking pain killers regularly.
Have a pacemaker for your heart, or similar device.
Use recreational drugs
Unable to understand verbal and/or written instructions given in English

Please inform the investigator straight away if you have any of the conditions above. Please fill out the screening form so we are sure you do not meet exclusion criteria.

9. What are the possible benefits of taking part?
The current research project is investigating how sweet tastes affect how we feel warmth and heat pain. There are no direct medical benefits for you. Taking part in this study will help us understand how the effect of sweet tastes on pain sensation.

10. What about the time that I have to take to do this study?
Your participation in the study is estimated to take no more than 2 hours. We will reimburse you for your time (see below).

11. What will happen if I don’t want to carry on with the study?
You are free to withdraw at any time, without giving a reason. A decision to withdraw at any time, or a decision not to take part, is completely voluntary.

12. What if something goes wrong?
In the unlikely event that you are harmed as a result of this study, there are no specific compensation arrangements. Please note it is advisable for people with private healthcare insurance to inform their insurers about participation in research studies. If you have any general complaints regarding the study please contact Dr. Mooney or Dr. Pickering.

13. Will my identity be protected?
All information identifying you will be kept in a locked room at the University of Bristol and held in the strictest confidence. All computer and paper records relating to the study will be stored in accordance with the provisions of the Data Protection Act. No other researchers, companies or individuals either in the UK or abroad will have access to information which identifies you. Your data will simply carry a code number, which only the Research team can trace back to you.

14. Will my taking part in this study be kept confidential?
All information collected about you during the course of the research will be kept strictly confidential.

15. What will happen to the results of the study?
The full results of the studies being conducted will not be known until the last participant has been tested, which may take up to 2 years. The results will be reported in professional publications and at meetings, but

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you will not be identified by name. If you are interested in receiving a summary of the results, please contact Dr Mooney.

18. Who is funding and organising the study.
Academic Foundation Program at the University of Bristol

19. Who has reviewed the study?
The study has been reviewed by the University of Bristol Faculty Research Ethics Committee for Health Sciences and adheres to approved safety and ethical procedures at the Clinical Research and Imaging Centre.

20. Will I receive any remuneration for taking part in this study?
For participating in this study you will be reimbursed at a rate of £10 per hour.

21. What do I do now?
If you are interested in taking part or if you want more information, please contact Dr Elizabeth Mooney (details at the head of this brochure). Arrangements will then be made to provide you with further information.

Thank you for reading this and for considering whether you would like to take part in the study.
Volunteer Questionnaire Form

Study title: Investigation of the interaction between temperature sensation and sweet tastes.

Sex: M / F
Age:

<table>
<thead>
<tr>
<th>Please answer all questions</th>
<th>Circle answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you have or have you had any form of acute or chronic pain? (e.g. slipped disc, hernia, fibromyalgia)</td>
<td>YES/NO</td>
</tr>
<tr>
<td>2. Do you have or have you had any form of neurological disorder, disease or diagnosis? (e.g. multiple sclerosis)</td>
<td>YES/NO</td>
</tr>
<tr>
<td>3. Do you have any ongoing medical or psychiatric conditions? (e.g. clinical diagnosis of anxiety and/or depression)</td>
<td>YES/NO</td>
</tr>
<tr>
<td>4. Have you taken any pain killing medicines in the last week?</td>
<td>YES/NO</td>
</tr>
<tr>
<td>5. Do you have any implanted stimulating devices such as cardiac pacemakers or defibrillator?</td>
<td>YES/NO</td>
</tr>
<tr>
<td>6. Do you take recreational drugs? (e.g. cannabis, amphetamines)</td>
<td>YES/NO</td>
</tr>
<tr>
<td>7. Are you or could you be pregnant?</td>
<td>YES/NO</td>
</tr>
<tr>
<td>8. Have you ever been diagnosed with diabetes or impaired glucose tolerance?</td>
<td>YES/NO</td>
</tr>
<tr>
<td>Is there any other information you wish to disclose which may influence the study or your safety during the study?</td>
<td>YES/NO</td>
</tr>
</tbody>
</table>

SIGNED
(Researcher).............................................................................................DATE..........................

(Name) ..........................................................................................................................

Subject ID    029    Researcher initials:   ERM    Date:    2 0 1 8
CONSENT FORM: Investigation of the interaction between temperature sensation and sweet tastes.

Please answer the following questions to the best of your knowledge

DO YOU CONFIRM THAT:

- You understand that the screening is not for medical screening or diagnostics ☐ ☐
- Your participation in the study is voluntary ☐ ☐
- You are between 18-65 years of age ☐ ☐
- You do not suffer from any of the listed conditions (see information sheet) ☐ ☐
- You are not a current user of drugs, other than prescription ☐ ☐
- You understand that the information collected about you will be used to support other research in the future, and may be shared anonymously with other researchers. ☐ ☐

HAVE YOU:

- Read and understood the information sheet explaining the study? ☐ ☐
- Had an opportunity to ask questions and discuss this study? ☐ ☐
- Received satisfactory answers to all questions you asked? ☐ ☐
- Received enough information about the study for you to make a decision about your participation? ☐ ☐

DO YOU UNDERSTAND:
That you are free to withdraw from the study and free to withdraw your data prior to anonymization

- at any time? ☐ ☐
- without having to give a reason for withdrawing? ☐ ☐

I hereby fully and freely consent to my participation in this study.
I understand the nature and purpose of the procedures involved in this study. These have been communicated to me in the information sheet accompanying this form.
I understand and acknowledge that the investigation is designed to promote scientific knowledge and that the University of Bristol will use the data I provide for no purpose other than research.
I understand that the data I provide will be kept confidential, and that on completion of the study my data will be anonymised by removing all links between my name or other identifying information and my study data. This will be done immediately after the study, and before any presentation or publication of my data.
I understand that the University of Bristol may use the data collected for this project in a future research project but that the conditions on this form under which I have provided the data will still apply.

Participant’s signature: ___________________________ Date: ________________

Name of participant: __________________________________________________________

Signature of person taking consent: ___________________________ Date: ________________

Name of person taking consent: __________________________________________________
Dear students and staff,

**What does pain taste like?**

We are currently recruiting healthy volunteers to take part in a study looking at how the sensation of pain interacts with the taste of sweet flavours.

The study involves applying heat to a small area of skin on the arm and asking when it feels warm or painful. The effect of concurrently taking a sweet drink will be tested.

The study will take about 1.5 hours and participants will experience some transient discomfort or pain during the study. The heat applied will not be hot enough to burn the skin. Participants will be reimbursed for their time (£10/hour).

If you are interested in taking part or receiving more information regarding the study, please contact Dr Elizabeth Mooney (elizabeth.mooney@bristol.ac.uk). There is no obligation to participate in the study.

Thank you for your interest,

Best regards,

Elizabeth Mooney
What does pain taste like?

We are RECRUITING VOLUNTEERS for a RESEARCH STUDY.

We are investigating how the sensation of pain interacts with the taste of sweet flavours.

The study involves applying heat to the skin on the arm and reporting how warm or painful it feels before and after tasting some sweet liquids.

You will feel some transient pain on occasion but you will be in control at all times. None of the stimuli are hot enough to burn or damage your skin.

You will be REIMBURSED for your time (£10/hour).

Please contact Dr Elizabeth Mooney on elizabeth.mooney@bristol.ac.uk for more information.
Investigation of the interaction between temperature sensation and sweet tastes – investigator script

Thirst assessment

To avoid the possibility of thirst interfering with our results, we first need to do a quick assessment of your current level of thirst.

Please rate your current level of thirst on the scale, from no thirst at all to the most intense thirst imaginable.

**OPTIONAL**

Please drink as much water as you wish from the jug provided.

Please rate your current level of thirst on the scale, from no thirst at all to the most intense thirst imaginable.

(repeat as required)

Warm and heat pain detection threshold.

Next we are going to use this device to assess your ability to feel warm temperatures. The device will be attached to your arm. It will start to warm up gradually. Please press the button immediately when you perceive a change in temperature to warm for the first time.

Now we will test when you perceive the warming of the device as painful. Your skin will be slowly warmed. At some point in time you will feel a second sensation on top of the “warm” sensation. The impression of “warmth” or “heat” will change its quality towards an additional impression of a “burning”, “stinging”, “drilling” or “aching” sensation. Please press the stop button immediately once you perceive such a change. Please do not wait to press the stop button until the sensation has become unbearably painful.

We will now repeat those two tests twice. For ramp 1, please press the button immediately when you perceive a change in temperature to warm for the first time. For ramp 2, please press the button immediately once you perceive the change in quality of the sensation to painful.

Sweet pain modulation parameter assessment

Next we are going to heat the device to different temperatures and ask you to rate the pain that you feel each time. The different temperatures will be delivered at random. You will feel the device warm up and then stay at the same temperature for 5 seconds. At the end of the stimulus, please rate the overall pain sensation that you felt on the scale, which ranges from no pain at all to the most intense pain imaginable. If you want to stop the test immediately at any time, raise your free hand.
Taste sensation assessment

Now we will assess how the test solutions taste. I will give you a small sample of solution and ask you to hold it in your mouth for 10 seconds. After this you may spit out the solution and rinse your mouth with water. Then you will rate the sweetness and pleasantness of the solution on separate scales. The first scale ranges from “not sweet at all” to “extremely sweet” and the second from “neutral” to “extremely pleasant”. If you find the solution actively unpleasant, please do not rate it on the second scale but place a mark in the box provided.

Test warm and heat pain detection threshold.

Now we will repeat the first test that we performed to assess your ability to feel warm temperatures, but this time while you have a test solution in your mouth. I will give you a small sample of solution to hold in your mouth, after which the device will start to warm up gradually – ramp 1. Please press the button immediately when you perceive a change in temperature to warm for the first time. The device will then heat up again – ramp 2. At some point in time you will feel a second sensation on top of the “warm” sensation. The impression of “warmth” or “heat” will change its quality towards an additional impression of a “burning”, “stinging”, “drilling” or “aching” sensation. Please press the stop button immediately once you perceive such a change. Please do not wait to press the stop button until the sensation has become unbearably painful.

Once the test is complete you may spit out the solution and rinse your mouth with water.

Sweet pain modulation test

Next we will use the same protocol as earlier in which I asked you to rate the painfulness of 5 second periods of warming on the scale. I will give you a small sample of solution to hold in your mouth, and the device will warm up and then stay at a temperature for 5 seconds. At the end of the stimulus, please rate the overall pain sensation that you felt on the scale, which ranges from no pain at all to the most intense pain imaginable. If you want to stop the test immediately at any time, raise your free hand.

Anticipation test

We will now return to the warming ramps testing your ability to feel warm and hot temperatures. First we will do this with no solution in your mouth. Then we will repeat it 3 times with a sample of sweet solution in your mouth. For ramp 1, please press the button immediately when you perceive a change in temperature to warm for the first time. For ramp 2, please press the button immediately once you perceive the change in quality of the sensation to painful. Please do not wait to press the stop button until the sensation has become unbearably painful.
Repeat taste sensation assessment

Finally, we will re-assess how the test solutions taste. I will give you a small sample of solution and ask you to hold it in your mouth for 10 seconds. After this you may spit out the solution and rinse your mouth with water. Then you will rate the sweetness and pleasantness of the solution on separate scales. The first scale ranges from “not sweet at all” to “extremely sweet” and the second from “neutral” to “extremely pleasant”. If you find the solution actively unpleasant, please do not rate it on the second scale but place a mark in the box provided.

Questionnaires

That was the last of the tests. Next I would like you to complete some questionnaires. Please take a much time as you like to fill these in.

Debrief

Thank you for taking part in this study. Do you have any comments or questions about the tests that we have performed today?