DONDERS INSTITUTE

Donders Centre for Cognition

INFORMATION FOR PARTICIPATION IN THE RESEARCH: THE ROLE OF SEROTONIN IN LEARNING AND DECISION MAKING: A BEHAVIOURAL STUDY

With this information, we would like to invite you to take part in the scientific study 'the role of serotonin in learning and decision making: a behavioural study' at the Donders Centre for Cognition. Participation is voluntary. In this very comprehensive information sheet, you can read about the study, what it means for you and what the pros and cons are.

In the attachments you fill find

- Contact details of the independent expert Dr. Robbert-Jan Verkes
- Information about the insurance for participants
- An example of the consent form that must be signed before participation
- Prescription of the medication that is used within this study
- A medical checklist that is used by the researchers to assess whether you can be invited to the intake interview.

Can you please read the information and decide if you want to take part?

Ask your questions

This information could help you to decide whether you would like to participate. We also suggest the following:

- Ask questions to the researcher who gave you this information.
- Talk to your partner, family or friends about this study.
- Ask questions to the independent expert Dr Robbert-Jan Verkes (see contact details Appendix A).

General information

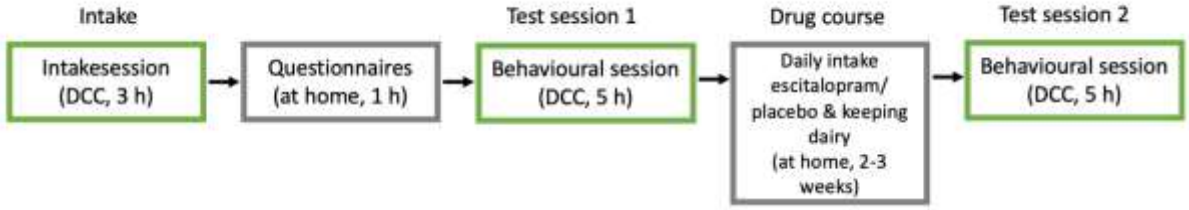
The Donders Centre for Cognition (DCC) has set up this study, and in this document it is referred to as the 'sponsor' or DCC. Researchers or research assistants conduct the study. Our research has been reviewed independently by the Medical Ethical Reviewing Committee Oost Nederland (METC; https://www.ccmo.nl/metcs/erkende-metcs/metc-oost-nederland). There is no formal objection against this study.

What is the purpose of the study?

In this study, we focus on the link between serotonin in the brain and brain functions. This brain substance is known to affect several brain functions, such as decision-making and motivation. However, because of the complexity of the serotonergic system, it is still unclear what role serotonin plays precisely in making decisions. The aim of this study is therefore to understand how changes in serotonin in the brain affect learning and decision-making. To achieve this goal, we will give you a drug that enhances serotonin by keeping it active for longer (escitalopram, also known as Lexapro or Cipralex) and a placebo (a dummy pill with no active ingredient) for a period of 2-3 weeks. During the study sessions, we will study your behaviour in several computerized tasks.

Escitalopram is prescribed, among other things, for treatment of depression and anxiety disorders. Previous studies have used the same or higher dose of escitalopram safely in healthy participants. Because of the low dose we will use in the current study, we expect that you will not experience severe side effects of the drug, and that there will be no long-term effects. It is, however, of utmost importance that you follow the study's rules (see 'what agreements do we make with you')

What happens during the study?



This study involves three in-person sessions with the researchers at the DCC in Nijmegen. The sessions will take place in the **Maria Montessori** building. You can take a seat in room **01.302** (see also Appendix A for further information). The researcher will pick you up there and take you to the room where the experiment will be conducted.

As part of the study, you will also need to take escitalopram or placebo tablets for 2-3 weeks, with the exact duration depending on your availability for the final testing session. Before you participate, we will send a letter to your GP informing them of your participation in this study.

It is important for the success of our study that you attend all scheduled appointments with us and carefully follow the instructions you are given. For safety reasons, for the duration of the study you will be asked not to smoke (e.g., tobacco or cannabis), not to consume alcohol or severely limit its use, **and not to use stimulants** (**e.g., LSD, MDMA, XTC**), as this can lead to dangerous interactions with the drug.

It is also important that you do not drink alcohol 24 hours before each appointment, have breakfast in the morning and do not smoke (in addition to not smoking and avoiding alcohol during the drug course). Drinking one caffeinated beverage (coffee, tea) in the morning is allowed. Furthermore, we would also like to ask you to try to be well rested for the three appointments where you come into the lab.

Step 0: Pre-screening (by phone)
Before we schedule an appointment for you to come to the lab, we will schedule a phone appointment with you at least one week after you receive this brochure. To participate in the study, you must meet several medical criteria. For this purpose, we have prepared a short medical questionnaire (see Appendix E). We ask you to complete this questionnaire before the appointment is made with you for the phone screening. The researchers will go over these questions with you over the phone. If you have to answer yes to any of the questions, you cannot participate in the study. You do not have to indicate to which question the affirmation applies. If you do not have to answer affirmatively to any one of the questions, an appointment will be made for the intake. Only after this appointment we can determine whether you can be admitted to the study safely.

Step 1: Intake session (DCC)

Before the actual examination begins, an appointment will be made with you for an intake interview. During this visit, a member of the research team will explain the purpose of the study to you, tell you what is expected of you, and how everything will work. You will be instructed on what to do during the study. Again, you can ask questions at any time. Once you have been fully informed, the researcher will ask you to sign the consent form. Furthermore, we will ask you to fill out a number of questionnaires and one of the researchers will go through a list of questions with you that are important for the results of the study, but also for your own safety. The following people cannot participate in the experiment due to safety reasons:
- Pregnant people
- People who are breastfeeding
- People who have had a past diagnosis of a mental illness (such as depression)
- People who have been treated with antidepressants or antipsychotics
- People who are currently or have had suicidal thoughts in the past.

During the intake interview, your blood pressure, heart rate, and electrocardiogram (ECG) will be measured. The ECG measurement requires you to undress from the waist down, and then the researcher or medical staff will place electrodes on your chest and limbs. These measurements are necessary to determine whether you can take escitalopram without risk. Here, the researchers are taking a precaution: if it is decided based on these readings that you should not participate, it does not mean that you are not healthy. The intake session will conclude with some baseline measurements of cognition and practice of cognitive tasks.

If, based on this initial visit, you are able and willing to participate, two follow-up appointments will be made with you to come to the DCC to be tested.

Step 2: Questionnaires (at home)
After the intake interview, when the follow-up appointments are scheduled, you will receive a set of questionnaires to fill out online before your second appointment. These questionnaires will take about an hour of your time. They include a series of questions about your personality and general lifestyle (e.g., impulsivity, stress, perfectionism).

Step 3: Behavioural session (DCC)
For the behavioural session, you will come again to the DCC in Nijmegen. First, you will be asked to fill out some questionnaires. Women will undergo a pregnancy test to rule out pregnancy. Then, after measuring blood pressure, heart rate, and body temperature, you will perform various tasks on the computer, which will take about 4 hours, including breaks. You will have a longer break halfway through the measurements to have a snack from us.

After completing the behavioural tasks, you will receive a bottle of capsules for the 2-3 week drug course, the first dose of which you will take at home in the evening or next morning. You will also receive instructions on how to use, and track side effects, via an app on your smartphone.

In the 2 to 3 weeks between the first and second behavioural sessions, you will take one capsule daily. On the eve or morning of the second behavioural session, you will take your last capsule. The capsules you receive will contain one of the following:
● 10 mg of escitalopram
● placebo

Whether you receive capsules containing escitalopram or placebo will be double-blind. That is, neither the researcher nor the participant will know which substance

(escitalopram/placebo) the capsules contain. This standard procedure is necessary to prevent expectations from influencing the study.

Step 4: Escitalopram/placebo course
At the end of the first behavioural session, you will receive a study information booklet containing all the information you need to complete the medication course, and for using the smartphone app to track side-effects (m-Path). During this phase of the study, you must take one capsule a day for the next 2 to 3 weeks (depending on your availability for the third appointment). Also, a member of the research team will contact you every 4 days to ask how you are doing. It is important to note that **if you are experiencing side effects, you will be advised not to drive a car** (see https://www.drugs.com/tips/escitalopram-patient-tips).

STEP 5: Behavioural session (DCC)
The evening or morning prior to the second behavioural session, you will take your last dose of escitalopram/placebo. On this second day of testing, you will again come to the DCC. You will again be asked to fill out some questionnaires and your blood pressure, heart rate, and body temperature will be measured. You will then perform various tasks on the computer, which will take about 4 hours, including breaks and including a longer break where we will offer you a snack.

What agreements do we make with you?
We want the study to go well. That is why we want to make the following agreements with you:

- You take the medicine in the way the investigator explained to you.
- You do not take part in any other medical research for the duration of this study.
- We expect you on time for each appointment unless prior notice is given.
- You contact the researcher in these situations:
    - o you suddenly experience problems with your health;
    - o you no longer want to participate in the study;
    - o your contact information has changed.
- You will avoid alcohol throughout the study, and not use narcotics or stimulants, or smoke cigarettes.

What side-effects, adverse effects, or discomforts could you experience?

ESCITALOPRAM:
In this study, you will receive 10 mg of escitalopram/placebo to take daily for up to 21 days. In previous studies, escitalopram has been given to healthy individuals without participants experiencing severe side effects. During clinical treatment with escitalopram, the most common side effects are:

- Drowsiness;
- Difficulty with sleeping;
- increased sweating;
- dry mouth;
- nausea;
- decreased appetite;
- nervousness/agitation;
- decreased sex drive.

Although such side effects are unlikely to occur from the tablets, we advise against driving if you experience drowsiness or dizziness, or other side effects that could affect your ability to do so safely. Contact details for a psychiatrist will be provided along with the medication

so that you can ask questions or discuss any negative side-effects that you may be experiencing. You will also receive contact information for the RadboudUMC psychiatry department, which you can contact if you feel very unwell. We will also contact you during the study to check how you are feeling. You can withdraw from the study at any time if you wish. We recommend that you read the package leaflets for escitalopram (see Appendix D) before you decide to take part in this study.
CAUTION: Because various drugs of abuse can interact dangerously with antidepressants, **it is important that you do not take illegal drugs during the study. DO NOT start any medications during the study without informing your doctor**, as they may be contraindicated for escitalopram. Please also inform us of any medication you take during participation in the study. Try to maintain a relatively regular diet and sleep pattern during the study.

What are the advantages and disadvantages if you participate in the study?

Participating in the study can have advantages and disadvantages. Below we list these. Think about these carefully, and talk about them with others.

Apart from the reward you receive for your participation, you yourself will not benefit from taking part in this study. But with your participation, you are helping researchers gain more insight into human behaviour and the brain.

Disadvantages may include:

- You may experience side effects from the drug/placebo.
- You may be bothered by the measurements during the study, for example, as already mentioned above, when applying electrodes for the ECG.
- You must keep the appointments and follow the instructions carefully that go with the study.

All procedures followed in this study are harmless. However, some procedures may be unpleasant. In one of the tasks you will perform on the computer, sounds will be played that may be perceived as annoying/irritating. In addition, participation will obviously cost you quite a lot of time, as you will have to come to the DCC for three days and take a capsule every day for 2-3 weeks and fill in data in an app on your phone.

INCIDENTAL MEDICAL FINDINGS
Even though we do not look at your date from a medical perspective it can be the case that in exceptional circumstances the research data may give indications concerning your health conditions (for instance within the heart signal we record). These findings are unrelated to our research question but may be relevant for your health and are called incidental findings. In case the finding appears relevant to your health you will be informed on this. In case you prefer not to be informed, you cannot participate in this study

When does the study end?
The researcher will let you know if and when there is any new information about the study that could be important or interesting to you. The researcher will then ask you if you want to continue with the study.
In these below situations, the study will immediately stop:

- All measurements according to the schedule are finished and/or the end of the whole study has been reached.

- You want to stop participating in the study yourself. You can stop at any time by informing the researcher immediately. You do not have to explain why you want to stop.
- The researcher decides it is better for you to stop
- One of the following national authorities decides that the study should stop:
    - The ethical committee that assessed the study
    - The research centre itself
    - A supervisory organization, such as an inspector who works for the researcher or sponsor or the Health and Youth Care Inspectorate.

What happens if you stop participating in the study before it ends?
The researchers use the data that have been collected up to the moment that you decide to stop participating in the study. If you wish, we will destroy the collected data. Please let the researcher know.

What happens after the study has ended?
You can ask the researcher to keep you informed about the research results. Since data analyses and publication are time consuming, it is not feasible for the researcher to agree on a notification term. In general, the researcher will ask you to get in touch over a certain length of time.

How will we process your data?
Are you participating in the study ?
You give permission to the researchers to collect, use and store your data. During our research you will also be asked to provide personal data. With personal data we mean information through which you can be identified directly (for instance name and mail address) or indirectly (for instance ID number of our SONA participation database). The collection of personal data serves two goals. First, it serves administrative purposes, and second, it serves to answer the research question. Below this is described in more detail.

Which personal data are stored for administrative reasons?
In order to be able to reimburse you for your participation, we will have to ask you to provide your name, address, date of birth, burgerservicenummer (BSN), bank account number and signature. No coupling will be made between your research data and this personal data. Your personal data is solely used for the payment procedure or to contact you in case of an incidental finding.
The financial department will save the financial personal data, according to their guidelines, for the duration of 7 years. The Radboud University is obliged to report the compensation that you receive for participation in this research to the Belastingdienst (dutch tax authorities; see also here (in dutch)). You should also declare this compensation in your income tax return (see also here (in dutch). We provide the following information to the Belastingdienst: the reimbursement you received, your name, address, date of birth and BSN. We do not disclose the reason for which you received this reimbursement. Hence, the Belastingdienst does not know that you participated in research nor in which specific study you took part.
Secondly, the researchers will store your contact details to inform you in case of incidental findings. These contact details and its coupling with the research data will be deleted 6 months after the measurements of these study have been ended.

Which (sensitive) personal data is stored to answer the research question?
In this research we won't collect any research data which can reveal your identity. In some cases it is required that we collect demographic information or sensitive personal data about your health, background of preferences to answer the scientific question and publish

about the results, for example gender, year of birth, handedness (left or right), language background or colour blindness. On the consent form you are asked to provide your consent for the collection of this data. If you do not want this, you cannot participate in this experiment.
Since we don't collect any research data that could be linked to your identity, we will share the research data including the specific personal data anonymously.

How do we protect your privacy during participation?
In order to protect your privacy we assign a code to all your data. We only use this code when processing your research data. In any reports and publications about the research, your identity will always remain concealed.
The key file, (the file in which the code is linked to your personal details and research data), is stored in a separate, secure place in our research centre and will be deleted 6 months after the measurements of this study have ended. Then the link between your identity and the research data has been removed.
In all cases we will handle your data confidentially.

Who is able to see your information?
Some people can not only see the code, but are also able to review your identifiable information. These are the members of the research team directly involved in the project. In addition, persons who check whether the researchers conduct the research in a proper way, are also authorized to access this information. These concern the following persons or authorities:

- Members of the committee for safe conduct of research.
- A monitor/supervisor who works for the researcher or sponsor (DCC).
- National regulatory affairs authorities, for instance the Health Care Inspectorate.

These people will keep your information confidential. We ask your consent for them to access your information.

How long will we retain and safeguard your research data?
We will keep your research data, including the (sensitive) personal data, that is used to answer the research question, for at least 15 years after study completion at secured locations of the Radboud University Nijmegen.
The personal data that are collected for the reimbursement (bank payment: name, address, date of birth, burgerservicenummer (BSN), bank account number and signature; participation credits: signature and ID number of the SONA participation database) are preserved at the financial department for 7 years.
Your contact information will be kept for a maximum of 6 months after the measurements of the study have ended.

Are we allowed to share your research data?
Your research data could be of potential interest for other scientific research of other interested organizations. Therefore research data are increasingly shared or made public. This is important to confirm the reliability of the results and inform the rest of the world on what kind of research is done within our scientific field. Sharing data can also increase the quality and efficiency of our own research and that of other organizations. Please therefore be aware that our research data are made public for the whole society. In principle anyone can get access to the research data, including the –in some cases sensitive- personal data, that are collected to answer the research question. Of course name, address, contact details are always kept confidential. Examples of these data which could be shared are information on age, gender, or data concerning your health.
Before we share research data with others, we will remove identifiable features from the data and mask your identity as much as possible (for example, we won't share your birth

date, but only your age). In this way it will be impossible or very difficult for other persons to trace the data back to your identity.
The personal data, that are collected for administrative purposes, such as reimbursement or your contact details, are not made public.

How about sharing my research data and my privacy?
Your data will be shared and processed under strict conditions and in compliance with the current Dutch and European data protection regulations (GDPR). Your name and contact information will never be shared with others.

Is it possible to withdraw your consent to use your research data?
Yes, you can withdraw your consent for us to use your data at any time. This concerns the present study and the use of your data in other research.
Please note: Are you withdrawing your consent after the researchers have completed the collection of the data for a study which took place more than one month before? In that case the research data won't be destroyed and researchers have the right to continue to use the already collected research data.

Would you like to know more about your privacy rights?
For more information with respect to compliance of your rights regarding processing your personal data, you may check https://www.ru.nl/privacy/english/ or the website of the authority personal data https://www.autoriteitpersoonsgegevens.nl/en. You can read the privacy statement of the Radboud University here.
Do you have a question about your rights? Or do you have a complaint about the processing of your personal information? The DCC is responsible for the processing of your personal information. In case of a complaint, we recommend to first discuss this with the researcher. You can also discuss this with the Local Privacy Officer of the faculty of Social Sciences (privacy.fsw@ru.nl, or see Appendix A). For general questions concerning privacy, you can contact the Data Protection Officer of the Radboud University (privacy@ru.nl; or see Appendix A). You can also submit a complaint to the Authority Personal Data.

Will you receive compensation if you participate in a study?
Participation in experiments is reimbursed. You will receive a financial reward via your bank account. To this end a reimbursement form has to be filled out. On this form you should fill out your name, address, date of birth, BSN, bank account number, and signature. After this, it takes about 3 to 4 weeks before the money is deposited on your bank account.

The financial compensation for participation in this study is as follows:

Component	Reimbursement	hours/units	Amount
Time investment lab	€15/hour	(3 + 5 + 5 hours)	€195
Time investment at home	€15/hour	1 hour	€15
Payment for medication intake	€10/dose	14–21 days, 1 dose/day	€140–€210
Bonus task performance	Max €15	-	Max €15
Total			Max €435

Are you insured during the study?
For everyone who takes part in a study at the DCC, as part of the Donders Institute, a liability insurance is in place. The insurance pays for damage caused by the study. This

concerns damage that surfaces during the experiment, or within four years after the experiment, see also Appendix B.

Do you have any questions?
You can ask questions about the study to the researcher or research team of your study. Would you like to get advice from someone who is independent from the study? Then contact Robbert-Jan Verkes, via robbert-jan.verkes@radboudumc.nl. He knows a lot about the study, but is not a part of this study.
You can share your experiences around participation with us. Are you satisfied or not at all and do you have a complaint? Share it with us via this webform enabling us to improve our research.

Would you like to participate in this study?
….

How do you give consent for the study?
Before you participate in the study you are asked to fill out a consent form (see Appendix C for an example). The researcher will hand out and discuss the form with you at the start of the intake session. By signing the consent form you confirm that you have been informed to your satisfaction and that are willing and able to voluntarily participate. In addition you can indicate whether you would like to be approached for future research. Naturally participation in future studies would also be completely voluntary.

Finally
If you, for some reason, are not able to attend the study in time, please inform the researcher as soon as possible.

Dr. Bertalan Polner, Donders Centre for Cognition, Nijmegen
Phone: +31 (0)6- 31670310 (Engels)
Email: serotonin.decisions@donders.ru.nl

Dr. Renée Koolschijn, Donders Centre for Cognition, Nijmegen
Phone: +31 (0)6-31132626 (Nederlands/Engels)
Email: serotonin.decisions@donders.ru.nl

Appendices
A. Contact information DCC
B. Information Insurance
C. Example informed consent form

Appendix A – Contact information DCC

Independent expert
Prof. Dr. Robbert-Jan Verkes
✉ robbert-jan.verkes@ru.nl
☏ +31 (0)24 3612185

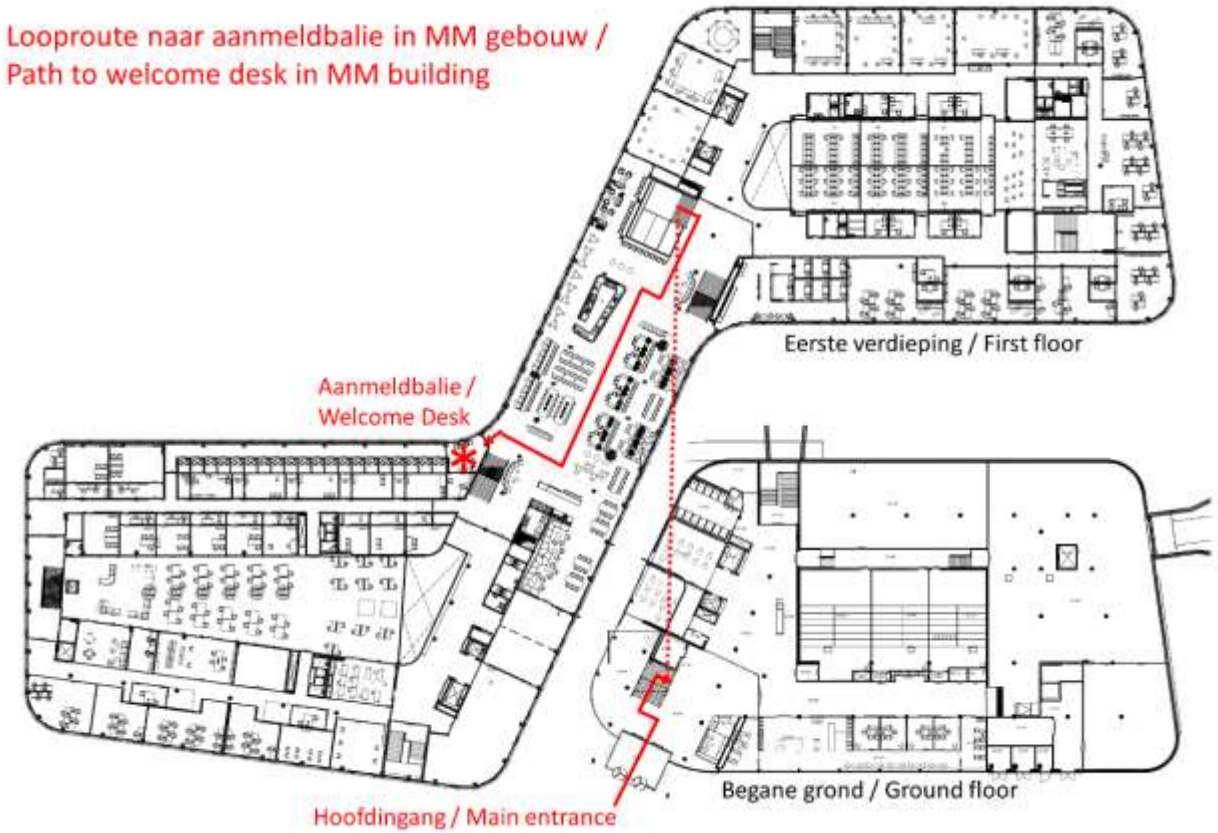
Local Privacy Officer of the faculty of Social Sciences
Enna Lujinovic or Aniek Wols
✉ privacy.fsw@ru.nl
☏ +31(0)631132640

Data Protection Officer of the Radboud University
✉ privacy@ru.nl

Want to provide us with feedback on your experience with research at the DCC?
🖇 https://www.ru.nl/donders/forms/feedback-webform-dcc-en/

Route Maria Montessori building

Follow the route below for waiting room 01.302:



Appendix B Participant Insurance

Centramed Deskundig in medische aansprakelijkheid

Insurance Certificate

Policy number	626.107.162
Type of insurance	Medical Liability Insurance
Policyholder	Stichting Radboud universitair medisch centrum
Insured	A: Medical Liability C: Product Liability
Sums insured	€ 5,000,000 as maximum per claim, with a maximum of € 15,000,000 per year
General wording	Polisvoorwaarden aansprakelijkheidsverzekering 2023 (General Conditions Liability Insurance Centramed 2023).
Policy period	From 2012/12/01 until 2026/01/01 with continuation for three-year terms.
Special rider	This certificate is subject to the terms, conditions, exclusions and limitations of the Dutch policy under no. 626.107.162 issued in Dutch and in the event of any discrepancies as to the translation, the Dutch wording of the original policy will prevail. This policy is in accordance with the Dutch law.

Onderlinge Waarborgmaatschappij Centramed B.A.

Zoetermeer, January 2023

drs. L. van Dijk RC
directievoorzitter

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postadres Postbus 7374, 2701 AJ Zoetermeer
t 070 301 70 70
e info@centramed.nl
KvK 08063107
IBAN NL83 INGB 0680 3235 46

Appendix C Example Consent form

CONSENT FORM

VERSION 3.0

DONDERS INSTITUTE

Donders Centre for Cognition

For participation in "THE ROLE OF SEROTONINE AND LEARNING AND DECISION MAKING: A BEHAVIOURAL STUDY

To be filled out by the PARTICIPANT:

- I was satisfactorily informed about the study both verbally and in writing, by means of the general information brochure (NL#####.###.##-v#.#).
- I was able to ask questions about the study which have been answered adequately. I had enough time to decide if I want to take part.
- I know that taking part in the study is voluntary. I also know that I can decide not to take part or stop taking part at any moment. I do not have to explain why.
- I give consent to the researchers to collect and use my research data for a minimum period of 15 years.
- I give consent to acquisition of personal data for administrative purposes.
- I give consent to collect demographic data (like gender or age) to answer the research question.

I understand that:

- I have the right to withdraw from the experiment at any time without having to give a reason.
- I will be contacted about accidental discoveries made during the study that are possibly important for my health. To this end my contact details are stored until maximally 6 months after finalization of the measurements.
- I have the right to request disposal of my research data that are potentially identifiable up to 1 month after finalization of the data collection.

Please tick yes or no in the below table and include the date.

I give my consent to participate in this experiment.	Yes	No*
I give my consent that sensitive personal data on my health, background or preferences is collected to answer the research question.	Yes	No*
For reviewing purposes some authorities will be able to see all of my data. These authorities are mentioned in the information brochure. I give consent to these to access and review my data.	Yes	No*
I give my consent that my not directly identifiable experimental data will be collected and stored.	Yes	No*
I give my consent that my not directly identifiable experimental data will be made public, e.g. the data are publicly shared with persons interested in the data, for instance for verification, re-use and/or replication.	Yes	No*

**If you answer one of the questions above with 'no', then you cannot participate in this experiment.*

I give my consent that some sensitive personal data on my health, background or preferences is made public, e.g. the data are publicly shared with persons world-wide who are interested in the data, for instance for verification, re-use and/or replication.	Yes	No**

**The answer to these questions does not affect participation in this research. Hence you can answer with 'no' and still participate.