PARTICIPANT INFORMATION SHEET

Are cognitive deficits associated with tobacco abstinence mediated by dopamine depletion?

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You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it would involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part and remember that your participation is voluntary.

What is the purpose of the study?

The purpose of this study is to understand how apomorphine influences computer-based cognitive measures in abstinent smokers. Understanding how cognition is affected by apomorphine can help us to develop novel smoking cessation methods.

Why have I been invited?

You have been chosen because you have enquired about our studies and requested to receive this further information following reading the summary version described in the letter of invitation or in a study advertisement.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part, you would be given this information sheet to keep and be asked to sign a consent form prior to any further procedures. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, would not affect your future or be held against you in any way.
Am I eligible to take part?

Please note you must be aged over 18 to volunteer and may be asked to provide identification as proof of age.

In order to take part you should:

- Be 18-50 years old;
- Smoke at least 5 cigarettes per day;
- Smoke first cigarette within one hour of waking;
- Smoke for at least 6 months;
- Have English as first language (or equivalent level of fluency);
- Have normal or corrected-to-normal vision;
- Be willing to abstain from smoking for about 20 hrs on three occasions and use nasal spray containing varying doses of apomorphine (0.0 mg, 0.5 mg and 1.0 mg), without being made aware of the order of the conditions at any point in the study.

You would not be able to take part in the study if you:

- Are currently taking any psychoactive medication, including nicotine substitution;
- Used any medication (except local treatment, aspirin, paracetamol, birth control) within past 2 weeks;
- Recently used illicit drugs;
- Consumed alcohol less than 36 hours prior to each study session;
- Have/had significant current or past medical or psychiatric illness (specifically, history of cardiac or respiratory problems, including asthma, history of sleep disorder, dementia);
- Had acute coronary syndrome or a stroke;
- Have a personal or strong family history of mood disorder, including panic disorder;
- Are not registered with a general practitioner;
- Are actively trying to give up smoking;
- Have a history of substance/alcohol misuse or dependence (other than nicotine or cannabis);
- If female: are pregnant, breast feeding or trying to conceive;
- Have systolic or diastolic blood pressure lower than 90/60 mmHg or higher than 140/90 mmHg;
- Have a heart rate lower than 50 beats per minute (bpm) or higher than 90 bpm;
- Have a body mass index (BMI) less than 17 kg/m² or greater than 30 kg/m²;
- Have a personal history of migraine headaches;
- Are prone to fainting;
- Are allergic to any of the drug-ingredients (specifically sulphites);
- Are drinking more than 35 alcoholic units*/week for females or 50 alcoholic units*/week for males;

* One unit equals one 25 ml single measure of spirit (ABV 40%), or a third of a pint of beer (ABV 5-6%), or half a standard (175 ml) glass of red wine (ABV 12%).

Expenses and reimbursement

You will be reimbursed £120 for your time and expenses after completion of all three sessions.
**What will I have to do?**

You would be required to come to the School of Experimental Psychology on three separate days (at least 1 week apart) in the morning, between 8 am and 11 am.

On each day, you would be asked to use a nasal spray (either low dose apomorphine, high dose apomorphine or placebo). Then, you would be asked to spend about two hours at the testing site, completing four computerised tasks. After that, you would be provided with a mobile phone and asked to indicate how you are currently feeling using the phone, throughout the afternoon. This should only take a minute or so each time, and you would be asked to do so about once per hour. You will be free to leave the testing site during that time. At the end of this period, you would be asked to bring the mobile phone back to the testing site between 4-6 pm in the afternoon.

At the end of the third session, you would be fully debriefed as to the purpose of the study.

**What does the study involve?**

This study involves testing on three separate days. Furthermore, you would be asked to abstain from smoking on all of the days from midnight before the testing day until about 6 pm of the following day. You would have to come in 3 times in total: using two doses of 0.5 mg apomorphine nasal spray on one day, using two doses of 1 mg apomorphine nasal spray on one day and two doses of placebo apomorphine nasal spray on one day. You would not be made aware at any point of the order in which you receive placebo or active spray.

The nasal spray would contain apomorphine hydrochloride, propylene glycol, glycerin, ascorbic acid, sodium metabisulphite, di-sodium edetate, benzyl alcohol, citric acid, sodium citrate and purified water.

Testing at the site would involve completing four computer-based tasks. One of the tasks would use equipment to measure your eye-movements whilst doing a reaction time task. Furthermore, you will be required to complete a memory task, a decision-making task and another reaction time task. After testing, you would be equipped with a mobile device and will be shown how to use it. You would then be free to leave the testing site. You would be required to answer several questions about your tobacco cravings on the device, which you should answer as soon as possible after receiving a prompt to do so.

**What are the possible disadvantages and risks of taking part?**

You might experience discomfort due to the cigarette abstinence. This will be comparable to any discomfort experienced in a regular attempt to stop smoking for a similar period.

Pregnant women should not take part in this study, and neither should women who are currently planning on becoming pregnant. All women will be asked to take a pregnancy test before taking part, to exclude the possibility of pregnancy. If the pregnancy test indicates a positive result, we will inform you of this outcome. If we find any clinical abnormality or medical condition during the screening process, if deemed appropriate, we shall inform your GP who will advise any relevant further tests or treatment. Your life insurance or private medical insurance could be affected by taking part and if you have private medical insurance you should check with the company before agreeing to participate.
**What are the side effects of any treatment received when taking part?**

Many of the known side effects of apomorphine have been reported in patient samples (i.e., people suffering from disease) and with other forms of administration (such as under the skin) and at higher doses than are given in the current study.

The most common side effects include:
- Dizziness/syncope (i.e., fainting)
- Headache
- Nausea/vomiting

More serious but less common side effects include:
- Anaphylaxis and bronchospasm
- Breathing difficulties

This study recruits healthy participants, uses low doses of apomorphine and uses intranasal administration (i.e., drug is taken through the nose). Taken in this way, side effects are not expected to be very common, and if experienced are not expected to be serious or long-lasting. However, if you have any concerns you should speak to your GP/doctor before taking part. If you experience any symptoms during the study, you should inform the researcher. We advise that you do not take part if you suffer from low blood pressure as this may make the common symptoms noted above more likely.

**What are the possible benefits of taking part?**

You would not directly benefit from taking part in this research study and your participation is voluntary. However, the information we get from this study may help us to understand the underlying mechanisms of tobacco withdrawal. This is important in order to develop novel treatments to aid smoking cessation.

**What if there is a problem?**

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed.

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action but you may have to pay for it. Regardless of this, if you wish to complain or have any concerns about any aspect of the way you've been approached or treated during the course of this study, please contact Liam McKervey (liam.mckervey@bristol.ac.uk).

**Will my taking part in this study be kept confidential?**

Yes. Personal information that could identify you (e.g., name, email address) will be kept securely by the study team and will not be shared publicly or with other research groups. On occasion this information may be made available to university staff, funders or government bodies which monitor whether research studies are performed properly. However, this information will not be used to contact you or to make your participation in this study known.

**What would happen to the results of the research study?**

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During the study, we will collect two types of data: screening data and study data. Both types of data are anonymised. This means we give the data a unique identification number and your personal information (e.g., name, email address) will be removed, so that you cannot be identified by this information.

Screening data are collected before you are fully enrolled onto the study. They identify whether you are eligible for the study, but they are not part of the study data. We keep these data securely within our research group but do not share them.

Study data refer to the information gathered once you are enrolled onto the study. These data are collected to answer our research questions.

When the study has been completed, we analyse the study data we have collected and report the findings. This will be reported in an appropriate scientific journal or presented at a scientific meeting. If you would like a copy of the final paper, you may request this. As your study data are anonymised, it will not possible to identify you by name from any aspect of documentation or reporting for this research study.

At the end of the study your data will become “open data”. This means that it will be stored in an online database so that it is publicly available. Your screening data will not be shared.

**What is open data?**

Open data means that study data are made available, free of charge, to anyone interested in the research, or who wishes to conduct their own analysis of the data. We will therefore have no control over how these data are used. However, all data will be anonymised before being made available and therefore there will be no way to identify you from the research data.

**Why open data?**

Sharing research data and findings is considered best scientific practice and is a requirement of many funding bodies and scientific journals. As a large proportion of research is publicly funded, the outcomes of the research should be made publicly available. Sharing data helps to maximise the impact of investment through wider use, and encourages new avenues of research.

**Can I withdraw my study data after I have participated in the study?**

Yes. If you decide that you do not want your data to be used you can contact the study team and request that your data are withdrawn. You can do this up to one year after the study ends or until the point the data are shared as “open data” (whichever comes first). At this point, links between your identify and your anonymised data set will be destroyed, and therefore we will no longer be able to withdraw your data as we will no longer be able to identify which data set is yours.

**Who is organising and funding the research?**

This research funded from Rusan Pharma Ltd, who are also providing and manufacturing the apomorphine spray and matching placebo.
Who has reviewed the study?

This study has been reviewed and approved by the Faculty of Science Research Ethics Committee at the University of Bristol (ethics approval code: 06101642002).

Who can I contact for further information?

For further information please contact Olivia Abrams (olivia.abrams.2016@my.bristol.ac.uk) or tel: +44 (0) 117 331 7493.

If you participate in this study you would be given a copy of this information sheet and a signed consent form to keep.