Faculty of Health & Life Sciences

**PARTICIPANT INFORMATION**

**TITLE OF PROJECT:** The acute and chronic effects of Resveratrol supplementation on cognitive function, gastrointestinal microbiota and cerebral blood flow: a double-blind, placebo-controlled parallel-groups study in healthy, overweight humans.

Lead Researcher: Ellen Smith (ellen.smith@northumbria.ac.uk)
Principal Supervisor: Dr Emma Wightman (emma.l.wightman@northumbria.ac.uk)

This project is funded by: Evolva
The study code is: 52P6
Number of participant points / payment: £140/£160 (qNIRS)

**INFORMATION TO POTENTIAL PARTICIPANTS**

**What is the purpose of the project?**

Research shows that a diet high in fat has harmful effects on gut health. This increases the chance of developing obesity-related diseases (such as type 2 diabetes) and causes problems with cognition and mood.

Research has suggested that gut health can be improved by taking certain supplements. Resveratrol is found in red grape skin and has been shown to improve gut health; brain blood flow and possibly improve brain function. However, there has been little research studying this.

This study aims to measure the effects consuming resveratrol for 12 weeks has on gut health, brain function and brain blood flow. Blood, urine and stool samples will be taken to measure markers relating to gut health.

**2. Why have I been selected to take part?**

You have indicated that you are:

- Interested in taking part in the study
- Healthy
- Aged 35-60 years (inclusive)
- Have a BMI of between 25-39.9
- Willing to consume your normal diet during the 12 week supplementation period

See **Section 4** for exclusion criteria.

**3. What will I have to do?**

You will be required to attend the laboratory on 4 occasions:

**Appointment 1: Introductory/training (approx. 3 hours)**

I**nstructions for this appointment: There are no restrictions on food, drink or medication use prior to this appointment. Please bring with you any medications that you are currently taking so we can document details about them (name, dosage etc.). NOTE: You are encouraged to check with the research team that these do not exclude you from the study prior to attending this appointment.**

The first appointment is a screening appointment, during which you will be asked to give your informed consent to participate. Once you have completed the consent form you will be asked to provide lifestyle and demographic data. You will also be screened with regards to your physical health (including measurement of height, weight, blood pressure and waist to hip ratio). You will then be trained on the cognitive and mood tasks. Please note that you do not need any prior experience of a computer to complete these tasks. The screening appointment will last approximately 3 hours and will take place at an agreed time. At the end of the appointment you will be provided with a food diary, which you must complete during the four days prior to your next visit. You will also be provided with a stool sample collection kit and instructions on its use. You will be asked to bring the sample with you to your next appointment.

**Appointment 2: Study Day 1 (approx. 7hr 30 mins)**

**Instructions for this appointment: You must have fasted from 8pm the previous evening, avoided caffeinated products for 18 hours, alcohol and over the counter medication for 24 hours and oral antihistamines for 48 hours prior to the session commencing.**

This appointment will take place within 14 days of your screening visit. You will bring your completed stool sample with you to this appointment. The sample should be collected within the previous 16 hours or on the morning of the testing visit. Your completed food diary should also be returned.

You will attend the laboratory at 8:00am in the morning, having been fasted from 8:00pm the previous evening. You will have avoided caffeinated products for 18 hours and alcohol for 24 hours prior to the session. In addition, oral antihistamines should be avoided for 48 hours and over the counter medication for 24 hours prior to the session commencing. Any breaches of these criteria will result in the session being rescheduled.

On arrival, we will check your eligibility to continue with the study, you will then provide a blood sample. Following this you will be given a standardised breakfast of x2 slices of white toast with butter and a decaffeinated tea or coffee. You will then complete a computerised cognitive assessment (~1 hour in length), followed by measurements of blood-pressure and heart rate. If you would like to be part of the sub-sample of participants who also provide brain (cerebral) blood flow data, then here you will have the quantitative near-infrared spectroscopy (qNIRS) headband fitted across the forehead and a 5 min baseline measure of cerebral blood flow (CBF) will be recorded. At some point during the morning, you will provide a urine sample to the researcher, this can be

completed at any time prior to taking your treatment, however it must not be your first urination of the day. Following this, you will consume your treatment for that day (~10:00am). After a break, at approximately 10:45am you will complete a 2nd cognitive assessment and a break will follow where those qNIRS participants will again provide brain blood flow data. You will be given a standardised lunch in the lab which consists of a cheese sandwich, ready salted crisps and a custard pot at approximately 01:10pm. At approximately 2:00pm you will complete your final cognitive assessment of the day, you will then provide a second blood sample and the testing day should end at ~3.30pm.

At the end of the study day you will be provided with your treatment and treatment diary to take home with you. You will be given either Resveratrol or a Placebo, but neither you or the researcher will know what you have received. You will take one capsule, twice a day; detailed instructions will be provided to you in the treatment diary.

**Appointment 3: Treatment Exchange (approx. 10 minutes)**

You will report to the laboratory during Week 6 to collect the second batch of capsules, there are no restrictions to this appointment. You will need to bring with you your completed diary and empty treatment containers. You will also be provided with a stool sample collection kit and 4 day food diary to be completed prior to your next appointment.

**Appointment 4: Study Day 2 (approx. 7hr 30 mins)**

**Instructions for this appointment: You must have fasted from 8pm the previous evening, avoided caffeinated products for 18 hours, alcohol and over the counter medication for 24 hours and oral antihistamines for 48 hours prior to the session commencing. You should NOT consume your treatment on the morning of your appointment, as you will consume it in the laboratory.**

This appointment will take place 84 days (+/- 5 days) following your Appointment 2. The procedure during appointment 4 will be identical to appointment 2. The same dietary and medication restrictions apply as with the previous study day.

**Throughout participation (from training session onwards)**

Participants will be requested not to change their dietary habits during their whole participation, medications should not be changed throughout the participation period (including starting new medications or stopping current medications) without contacting the researcher.

**4. What are the exclusion criteria (i.e. are there any reasons why I should not take part)?**

You should not take part if you:

- Are aged under 35 or over 60
- Have a Body Mass Index (BMI) lower than 25 or higher than 39.9. If you are unsure of your BMI you can use the following link to calculate it based on your height and weight. http://www.nhs.uk/Tools/Pages/Healthyweightcalculator.aspx
- Have taken antibiotics (including pre- and pro-biotic supplements/drinks e.g. Yakult or Actimel) during the previous 8 weeks

- Have irregular bowel movements (less than 1 per day)
- Have any pre-existing medical conditions/illness with some exceptions – **please check with the researcher**
- Have type 1 or type 2 diabetes
- Are currently taking prescription medications with some exceptions- **please check with the researcher**
- Have a visual impairment that cannot be corrected by glasses or contact lenses, including colour blindness.
- English is not your first language or your English proficiency is not equivalent to IELTS band 6 or above
- Have any learning difficulties or dyslexia
- Currently suffer from frequent migraines that require medication (>1 per month)
- Have any food allergies, intolerances or sensitivities
- Have high blood pressure (systolic over 159 mm Hg or diastolic over 99 mm Hg)
- Smoke
- Have a history of alcohol or drug abuse
- Are pregnant, seeking to become pregnant or lactating
- Are unable to complete all of the study assessments
- Are currently participating in any other clinical or nutritional intervention study, or have done within the past 4 weeks
- Have any health condition that would prevent fulfilment of the study requirements
- Have habitually used supplements within the last month (defined as more than 3 consecutive days or 4 days in total)
- Have an excessive caffeine intake (>500mg per day) – equivalent to 5/6 cups of coffee/8 cups of tea per day or equivalent from other sources
- Consume more than 5 portions of fruit or vegetables per day
- Any sleep disturbances or take sleep aid medication
- Have any known active infections
- You have or may think you are at risk of having syphilis, hepatitis, the Human T - lymphotropic virus or the Human Immunodeficiency Virus?
- You have ever had breast cancer and/or a mastectomy
- You have haemophilia or any similar clotting disorder
- Do not have a bank account (required for payment)

**If you are unsure about your eligibility, then please contact the research team and we can discuss any issues or ambiguity.**

We cannot list every individual medical condition and medication in the exclusion criteria; if you have any health issues or are taking any medications (prescribed or over the counter) you are encouraged to check with the research team that these do not exclude you from the study before you attend the lab. These criteria are study specific, so whilst one study may allow certain conditions, another may not.

**5. Will my participation involve any physical discomfort?**

Venous blood samples may cause you some minor physical discomfort and possibly minor bruising. These samples are taken using standard techniques with minimal discomfort and will only be carried out by trained phlebotomists. You are advised to avoid heavy lifting or strenuous exercise after taking part to minimise bruising.

You will be required to remain seated at a desk for the duration of the cognitive and mood assessments which will each (x3 per day) last for approximately 60 minutes. Prolonged computer testing may cause some minor discomfort and you may feel tired at times. It is therefore important that the correct eyewear is brought along to the testing session and that you inform the researcher of any back/arm/wrist problems you may have. If at any point during the testing session you wish to discontinue, please inform the investigator and your session can be re-scheduled, if desired.

The subsample of qNIRS participants will be required to wear a headband to measure brain blood flow. The headband needs to be fastened securely and you may experience temporary marks on your forehead following the test sessions from where the optical sensors have been resting on your skin. Any discomfort from this should be temporary and minimal.

You will have your blood pressure taken at all appointments using a standard battery operated monitor and cuff. You may find the pressure of the cuff tightening on your arm uncomfortable during this procedure.

There are no known side-effects of the experimental product when taken as directed. In addition, prior to your participation in this test the sponsor has determined that consumption of any such ingredient(s) is safe and appropriate under these test conditions. However, in the unlikely event of any perceived adverse response following participation, you should contact a member of the research team immediately at 0191 2437012 and reference the study title and study code (Study Code: 52P6) referenced on the front page of this packet. Both the University and the sponsor possess adequate third-party insurance covering this type of research and this includes provisions for any trial related injury.

In the event that you seek advice from a medical practitioner during the study, you should inform them that you are participating in the study.

If any irregularities are discovered during the course of this study, you will be advised to consult your G.P.

**6. Will my participation involve any psychological discomfort or embarrassment?**

Completion of the mood measures may cause some discomfort or embarrassment. However, this is likely to be minimal and you are free to leave any questions that you do not wish to answer blank. Providing stool and urine samples may also cause embarrassment to some participants. There will be a box in the toilets for participants to deposit urine and stool samples on study days, rather than giving to the researcher face to face.

**7. Will my participation result in any benefits to me?**

Participation in this study will have no direct benefit to you. However, the study results are intended to extend knowledge on the relationship between gut health, brain function and blood flow and the effect that resveratrol supplementation can have on these factors, which could benefit others in the future.

**8. Will I have to provide any bodily samples (i.e. blood, saliva)?**

Yes, you will be required to provide a urine sample and two venous blood samples on each of the two study days. Stool samples will also need to be collected prior to both of the study days, you will be provided a kit at your first and third appointment in order to complete these.

Your stool samples must be collected a maximum of 16 hours prior to attending the laboratory or the morning of the testing sessions. These samples should be brought with you to the laboratory on the day of your testing appointment. All the equipment needed to collect the samples will be dispensed to you by the researcher with clear instructions and labelled with your Subject ID No. and should be dropped off into boxes provided in the unisex bathroom on the 4$^{th}$ floor of Northumberland Building when you arrive for your study visits.

Urine samples will be collected upon arrival to the research centre (as it must not be your first urination of the day). You will be provided with a kit to collect the sample and you will be instructed to leave the sample in a box within the unisex bathroom.

Venous blood samples will be collected at the start and end of each study visit (four in total, over the study), by trained phlebotomists.

You must also be willing to have your blood pressure and pulse rate taken. Should the tests reveal an abnormality (where recognised clinical guidelines regarding test results exist) the researcher will recommend to you that you seek further medical advice from your GP, bear in mind though that a single test may not always provide an accurate reflection of your health status.

**9. How will confidentiality be assured?**

You will be assigned a number that will be used for identification purposes throughout the study. Only the research team will have access to any identifiable information; paper records will be stored in a locked filing cabinet and electronic information will be stored on a password-protected computer. Any personal details will be kept separate from data and will be treated in accordance with the Data Protection Act.

**10. Who will have access to the information that I provide?**

Only the lead researcher (Ellen Smith), her supervisory team, the BPNRC research team and the industrial sponsors (Evolva) will have access to the information that you provide. However, any data that leaves the site will only be identifiable by an identification number and it will not be possible for anybody outside of the investigational site to identify you.

**11. How will my information be stored / used in the future?**

The data from this study will be used in a Postgraduate thesis. It is also a possibly that the results of the study will eventually be published in a peer-reviewed journal. After the final report has been completed, all study related materials will be archived in accordance with the Good Clinical Practice (GCP) guidelines, for a minimum of 15 years. At no time will you personally be identified as having taken part.

**12. Has this investigation received appropriate ethical clearance?**

Yes, this study has received ethical approval from the Faculty of Health and Life Sciences Ethics committee. If you require confirmation of this please contact the Chair of this Committee, stating the title of the research project and the name of the principal investigator:

Chair of Faculty of Health and Life Sciences Ethics Committee, Northumberland Building, Northumbria University, Newcastle upon Tyne, NE1 8ST

**13. Will I receive any financial rewards / travel expenses for taking part?**

You will receive £140 or £160 (for the qNIRS subsample) for completing the study to cover your out of pocket expenses and potential loss of earnings. You will be paid by BACS transfer into your bank account after you have completed the study. It may take a few weeks for this payment to reach you after you have finished the study due to university procedures; we apologise for any inconvenience this may cause.

**14. How can I withdraw from the project?**

You are free to withdraw from the study at any time. If you choose to withdraw from the study, the investigators will attempt to follow-up with you, check how you are feeling and request your reason for withdrawing for their records, however you do not have to disclose this reason. The investigator also has the right to terminate your participation in the study. Your right to withdraw at any time is not affected by the receipt or offer of any financial compensation or other inducements for participation. If you wish to withdraw, simply contact the researcher or her supervisor.

**15. If I require further information who should I contact and how?**

If you need more information, would like to discuss your participation, or experience any problems as a consequence of taking part in the study you should contact Ellen Smith (**ellen.smith@northumbria.ac.uk**) on **0191 243 7012** (Office hours).