University of Pittsburgh

Transduction of Psychological Stress Into Systematic Inflammation by Mitochondrial DNA Signaling

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APPROVED CONSENT FORM. Most recent version revised 02-23-2021 and approved by the IRB 03/01/2021

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CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: BIOLOGICAL RESPONSE TO BRIEF PSYCHOLOGICAL CHALLENGE

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If you have any questions about your rights as a research subject or wish to talk to someone other the research team, please call the University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668. You can contact the study investigator if you have any questions about the study, concerns or complaints. Contact Principal Investigator, Dr. Marsland at 412 624 2434 or the Study coordinator, Dr. Katie Stanko, at 412 383 5038.

SOURCE OF SUPPORT: National Institutes of Health

FINANCIAL CONFLICT OF INTEREST: None of the study investigators have a significant financial conflict of interest with the proposed study.

KEY INFORMATION: You are being asked to take part in a research study. Research Studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision.

The purpose of this research study is to explore bodily responses to a brief laboratory task designed to mimic a daily stressor. If you decide to participate, you will be asked to attend two laboratory visits scheduled in the afternoon. The first visit will last 4 hours and the second visit 3.5 hours. At these visits, we will measure changes in your heart rate and rhythm, blood pressure, and markers in your blood in response to (1) a laboratory challenge task, (2) watching a wildlife film and (3) resting quietly. Discomforts of participation include the use of an intravenous catheter (a thin flexible tube) for collecting blood samples. Risks of this procedure include bruising, feeling faint or dizzy, and rarely, an infection at the needle site. There will be no direct benefit to you from participating in the study. However, this study will help doctors learn more about how stress can impact physical health.

Why is this study being done?

Individuals who report high levels of psychological stress are at increased risk for health problems. However, the pathways linking stress to health risk remain unclear. You are being

invited to participate in a research study that will explore bodily responses to a brief laboratory task designed to mimic a daily stressor. We will also investigate factors in people's lives that may contribute to differences in stress responses.

Who is being asked to take part in this research study?
You are being invited to take part in this research study because you are between the ages of 20 and 50 years, are generally healthy, are a non-smoker, weigh more than 110lbs, and have a body mass index less than 30. If you are female, you are also premenopausal and not pregnant or nursing. The study is being performed on a total of 60 (30 male and 30 female) volunteers at the University of Pittsburgh.

What procedures will be performed for research purposes?
If you decide to take part in this research study, you will be asked to attend two study visits scheduled more than one month apart, but within a three-month period. The first study visit will last approximately 4 hours and the second visit 3.5 hours. Both visits will be scheduled in the afternoon starting between 1-2pm. They will take place in the Behavioral Physiology Laboratory on the 5th and 6th floors of Old Engineering Hall, University of Pittsburgh.

Before both visits you will be asked to not eat or drink (except water) after 12pm and to avoid alcohol and intense exercise (such as a cardiovascular workout, going to the gym, or jogging) for 24 hours. We will also ask you not to take non-prescription medications for 2 days before each visit. The visits will be rescheduled if you have a cold, flu or symptoms of infection on the date of the visit or if you have received a vaccination, taken antibiotics or had an infection in the prior 2 weeks. If you are female, your visit will be scheduled during the second half of your menstrual cycle.

At visit 1, consent will be obtained and then the research nurse will conduct a past medical history and medication use interview, measure your height and weight, and take your blood pressure to confirm that you are eligible to participate (generally health, not taking medications that influence the biological pathways being investigated, weight > 110 lbs, BMI < 30, and have resting blood pressure < 140/90 mmHg). If you are not eligible, you will be thanked for your time.

If you are eligible, at both visits you will undergo the following procedures:

- Measurement of your height, weight, percentage body fat, waist-to-hip ratio and blood pressure. Percentage body fat will be measured using Tanita Body Composition Scales, which use bioelectrical impedance to estimate body fat.
- Complete standardized questionnaires at the computer assessing your demographic characteristics, current levels of stress, exposure to challenging life circumstances, lifestyle, and mood. Questionnaires will take ~ 30 minutes to complete.
- A blood pressure cuff will be placed on your arm for the assessment of blood pressure throughout the visit.
- Eleven spot electrodes will be put on the back of your neck, your chest, shoulders, and calf to provide a continuous measure of your heart rhythm throughout the visit.

- The nurse will insert a sterile intravenous catheter (a thin flexible tube) into a vein in your arm for collecting blood samples.
- You will be seated and rest for a 30-minute period before answering questions about your mood.
- Following this rest period, you will complete one of two tasks: At one visit, you will be asked to prepare (2 minutes) and give a short (3 minutes) speech, recorded by a video camera and watched by two study staff to assess non-verbal behaviors. At the other visit, you will rest quietly for 5 minutes. At the end of the task period, your mood will be reassessed.
- After the task period, you will be asked to sit quietly and watch a wildlife documentary and complete questionnaires for 120 minutes before answering questions about your mood.
- Samples of blood will be drawn from the IV catheter at 10 different timepoints across the laboratory session at each visit. A total of 11 tablespoons of blood will be collected at each visit.

What are the possible risks, side effects, and discomforts of this research study?
Venipuncture (pricking a vein to draw blood) may cause some minor pain, bleeding, possible black and blue mark, blood clot, feeling faint or dizzy, or rarely, an infection at the needle site. Attachment of the spot electrodes used to assess heart rate may cause skin irritation. The blood pressure cuff may cause discomfort. Giving a speech may cause physical arousal (e.g. increased heart rate, breathing, blood pressure, and muscle tension) or mild psychological arousal (e.g. frustration, irritation). The degree of stress is similar to that experienced in everyday life. Cardiovascular responses to the task are monitored closely by the research nurse and in the unlikely event that your blood pressure rises above 200 mmHg (systolic) and/or 120 mmHg (diastolic) the task will be discontinued and your blood pressure will be monitored closely until it is in the normal range. There is a slight chance that some people may find the computer questionnaires frustrating, upsetting, insensitive, or objectionable in some other way. You are not obligated to answer any questions that make you uncomfortable.

What are possible benefits from taking part in this study?
There is no direct benefit to participating in this research study.

Will anyone know that I am taking part in this study?
We will do our best to keep your personal information private, but confidentiality cannot be guaranteed. You will not be identified by name or other identifiable information in any publication or presentation at a scientific meeting. All records related to involvement in this research study will be stored in a locked file room. Your identity on these records will be indicated by a number rather than by name, and the information linking these case numbers with your identity will be kept in a separate, secure location. All computerized records will be password protected. All biological samples will be labelled by number only, and staff processing these samples will not have access to your identity. A portion of the blood that we collect will be sent to a laboratory at Columbia University for analysis of stress hormones. These samples will be labelled by number only and no information about your identity will be shared with this laboratory. It is also possible that we will share de-identified data or blood samples with other colleagues in the future.

Are there any limits on the confidentiality?
With your permission, we will utilize text messaging for scheduling and appointment reminders.

- **Risk**. Text Messages can be inadvertently misdirected by the sender or intentionally intercepted by third parties. The University of Pittsburgh cannot and does not guarantee the confidentiality of text messages, nor is it responsible for text messages that are lost due to technical failure during composition, transmission and/or storage.
- **Privacy and Confidentiality**. Text messages are an insecure method of communication. The content of a text message may be viewed by any person who has access to your phone. Text messages that you send us may be viewed by other staff depending on the nature and timing of your messages, and may be monitored by the University to ensure appropriate use. Text messages may be viewed by your employer if you are using a work phone. Different University staff may view and process text messages depending on the time of day you send them, or when your typical point of contact is not available. Communication by phone, postal mail, and e-mail are considered secure. You should consider using these forms of communication for sensitive information.
- **Content**. Text messages should be used only for non-sensitive and non-urgent issues. You should limit the amount of health information in your text messages to us to the minimum necessary.

Data from this study will be submitted to the National Institute of Mental Health Data Archive (NDA) at the National Institutes of Health (NIH). NDA is a large database where deidentified study data from many National Institute of Mental Health (NIMH) studies is stored and managed. Deidentified study data means that all personal information about you (such as name, address, birthdate and phone number) is removed and replaced with a code number. Sharing your deidentified study data helps researchers learn new and important things about mental health and substance use more quickly than before.

During and after the study, the study researchers will send deidentified study data about your health and behavior to the NDA. Other researchers across the world can then request your deidentified study data for other research. Every researcher (and institutions to which they belong) who requests your deidentified study data must promise to keep your data safe and promise not to try to learn your identity.

Each participant will receive a Global Unique Identifier (GUID). A GUID is a computer-generated alphanumeric code that is unique to each research participant. In order to generate the GUID, study staff will enter 4 pieces of your personal information into a “GUID generator”, your birth name, birth date, gender and city of birth, which will generate a unique code. Experts at the NIH who know how to keep your data safe will review each request carefully to reduce risks to your privacy. Sharing your study data does have some risks, although these risks are rare. Your study data could be accidentally shared with an unauthorized person who may attempt to learn your identity. The study researchers will make every attempt to protect your identity.

You may not benefit directly from allowing your study data to be shared with NDA. The study data provided to NDA may help researchers around the world learn more about mental

health and substance use and how to help others who have problems with mental health and substance use. NIMH will also report to Congress and on its website about the different studies using NDA data. You will not be contacted directly about the study data you contributed to NDA.

You may decide now or later that you do not want your study data to be added to the NDA. You can still participate in this research study even if you decide that you do not want your data to be added to the NDA. If you know now that you do not want your data in the NDA, please tell the study researcher before leaving the clinic today. If you decide any time after today that you do not want your data to be added to the NDA, call or email the study staff who conducted this study, and they will tell NDA to stop sharing your study data. Once your data is part of the NDA, the study researchers cannot take back the study data that was shared before they were notified that you changed your mind. If you would like more information about NDA, this is available on-line at http://nda.nih.gov.

We understand the importance of maintaining your privacy and the confidentiality of your records, as described in this document, but cannot guarantee the confidentiality of your research records once your personal information is disclosed to others outside the University. In addition to the investigators listed on the first page of this consent form and their research staff, authorized officials from the following groups may have access to information obtained during this research study, for the purpose of monitoring the study.

- University of Pittsburgh Research Conduct and Compliance Office
- Study sponsor: National Institutes of Health

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally-funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. The Certificate of Confidentiality will not be used to prevent disclosure to state or local authorities of abuse and neglect, or harm to self or others.

University of Pittsburgh policy requires that research records be kept for a period of not less than seven years following completion of a project. The investigators may continue to use information collected for the purposes described above for an indefinite period of time.

Can I withdraw from this research study?

You can withdraw from this research study at any time. Any identifiable research information obtained as part of this study prior to the date that you withdrew your consent will continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw from this research study, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form. Your decision to withdraw from this study will have no effect on your current or future relationship with the University of Pittsburgh.

It is possible that you may be removed from the research study by the researchers if, for example, you do not attend study sessions.

Will I or my insurance provider be charged for the costs of any procedures performed as part of this research study?
There are no costs to you or your insurance provider for participating in this study. All assessments will be paid for by the research grant.

Will I be paid if I take part in this research study?
You will receive $150.00 for completing both study visits. If you only complete the first visit, you will receive $50. Also, your parking fees or public transportation costs to the University will be paid. If you have agreed to be an on-call participant, you will receive an additional $25 compensation. Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the University of Pittsburgh Accounting Office. If the total reimbursement for your participation in research at the University of Pittsburgh is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income.

Who will pay if I am injured during this study?
If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You do not, however, waive any legal rights by signing this form.

Is my participation in this study voluntary?
Your participation in this research study is entirely voluntary. You may want to discuss this study with your family and friends and your personal physician before agreeing to participate. If there are any words you do not understand, feel free to ask us. The investigators will be available to answer your current and future questions. Whether or not you provide your consent for participation in this research study will have no effect on your

current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

CONSENT TO PARTICIPATE:
The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research during the course of the study and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigators listed on the first page of this consent document at the telephone numbers given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that occurred during my participation. By signing this form I agree to participate in this research study. A copy of this consent form will be given to me.

_____ _____
Participant's Signature Date

INVESTIGATOR CERTIFICATION:
I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual had about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____
Printed Name of Person Obtaining Consent Role in Research Study

_____ _____
Signature of Person Obtaining Consent Date