NORTHWESTERN UNIVERSITY
Department of Physiology

Consent Form For Reflex Sympathetic Dystrophy Patients
CORTICAL PATHOPHYSIOLOGY OF PAIN

INVESTIGATOR: Dr. A. Vania Apkarian
SPONSOR: National Institute of Health

Introduction/Purpose: You are being asked to participate in a research study because you have the condition known as Reflex Sympathetic Dystrophy (RSD), and are over the age of 18. The purpose of this study is to answer basic questions regarding the organization of pain in the human brain, as well as the biochemistry of the brain. Your brain activity will be monitored using functional magnetic resonance imaging (fMRI, which makes pictures of brain activity) during painful stimulation of your hand or foot, or using magnetic resonance spectroscopy (MRS which makes pictures of brain chemistry) to measure the concentration of different biochemicals in your brain while you are in your usual pain state. The fMRI study is comprised of two sessions. In the first session we check the characteristics of your pain. In the second session we do brain scans. The MRS study is a single brain scan session.

Procedure:
Just before the brain scans you will fill out a general medical history, mood and anxiety, depression, handedness and pain questionnaires. This will take about twenty minutes.

In order to make sure that it is safe for you to have an MRI procedure, you will first be asked to fill out a screening form prior to participating in this study. It is important that you tell the experimenters if you have any history of:

Metal fragments in your eyes or face.
Implantation of any electronic devices such as (but not limited to) cardiac pacemakers, cardiac defibrillators, cochlea implants or nerve stimulators.
Surgery on the blood vessels of your brain
Claustrophobia (fear of enclosed places)

fMRI is a type of brain scan that uses magnetic fields and radio waves to take measurements of your brain. Specifically we are able to measure blood flow throughout your brain without the injection of contrast material. MRS is a type of MRI scan that is able to detect the chemical composition of the brain. Both of these procedures involve lying on a bed and placing your head inside a comfortable head holder (a bean bag pillow). The MRI scanner makes loud banging noises while performing a measurement, so earplugs will be placed in your ears before you enter the scanner. The experimenters will be in constant communication with you through an intercom system to inform you of the progress of the study. The earplugs should not interfere with your communication with the experimenters or your performance in the study.

You will be encouraged to tell the experimenters if you are at all uncomfortable or anxious at any time during the scanning procedure. The bed will then slide into the scanner. You will be asked to lie quietly while the imaging is done for about one and a half hours. The information obtained from the MRI scanner is only useful if you are able to complete the entire imaging session, and hold your head very still the entire time. fMRI scan participants will be imaged while resting in the scanner and during painful stimuli. MRS scan participants will be imaged while resting in the scanner.

It is possible that the pain may be too unbearable or that your body position is too uncomfortable. If at anytime during a brain scan, and for any reason, you decide to stop the study you can simply say so by talking to the experimenter.

The total duration of time that you are required to lie still is one hour.

You may be asked to return for further brain scans a few weeks after the initial scan. These scans will repeat the procedures used in the initial sessions, and are designed to monitor changes in your brain responses to therapy or simply to test the reproducibility of the results.

Session 1: fMRI scans participants only

During this session (lasting one and a half hours) you will be instructed to verbally evaluate the sensations you experience when various painful and non-painful stimuli (air-puff, digit movement, vibratory, chemical, mechanical pressure probe or heat) are applied to your hand or foot, on the normal and RSD side. A range of temperatures you can tolerate with minimal discomfort will be presented for the heat stimuli.

Chemical painful stimulus is the topical application of 1% capsaicin. Mechanical painful stimuli are spatially varying pins (the specifics of this stimulator are still in development). Vibratory stimuli are applied either through a pneumatically activated unbalanced wheel or through a piezo-electric device, or through a toothbrush applied by hand. All three methods are tested and work. In specific cases we may choose between them. Painful stimuli are also applied electrically (electrodes attached to the skin). Thermal painful stimuli are applied through thermodes that are either heated electrically or by circulating water (both methods have been tested), depending on the number and size of stimuli needed.

You will also fill out a general medical history, mood and anxiety, depression, handedness and pain questionnaire, which requires twenty minutes.

Session 2: fMRI and MRS scan participants

FMRI: The purpose of this session is to study the activity of your brain in response to painful stimuli during fMRI scans. The stimulus will have been determined during session 1.

During the first twenty minutes of the fMRI session you need to lie quietly in the scanner while we collect images of your brain. Then we will perform either four 7-minute fMRI scans or eight 3.5-minute fMRI scans. In these scans you will be rating your pain either with no stimulus or during painful stimuli applied to the body part with RSD, or to a body region that feels normal. The painful stimuli depend on the type of symptoms that you have. For example if you have sensitivity to touch or cold we will use these as stimuli. The painful stimuli are applied for 35 seconds and removed for 35 seconds.

MRS: You will fill the questionnaires (a general medical history, mood and anxiety, depression, handedness and pain questionnaires) just before the brain scans. The purpose of this session is to measure the concentration of different biochemicals in your brain.

During an MRS session we first collect images of your brain for twenty minutes. Then we collect images of chemistry for different portions of your brain. Each such image takes about seven minutes. We will collect 4-6 such images.

Risks: You will be asked to tolerate an increase in your level of chronic pain. The stimuli will increase your pain for at least 35 seconds. This pain should subside minutes after the brain scan ends. The increased pain will have no long lasting effects and will not harm you. The chemical stimulus is Capsaicin. This is injected under the skin. The injection will sting and the chemical will cause a burning sensation that would last for about 15 minutes. You will always be attended by a researcher who can be alerted in case of any

discomfort, and if necessary the session will be terminated. There are no known risks associated with the MRI, fMRI or MRS procedures, although some subjects experience mild discomfort from trying to keep still during the study, and some subjects feel anxious or claustrophobic in the scanner.

Benefits: This study is designed to answer basic questions regarding the organization of the senses, specifically regarding pain, in the human brain, as well as the biochemistry of the brain. This understanding might result in the development of new diagnostic techniques for the treatment of patients suffering from unbearable pain.

Alternatives: You have the alternative to choose not to participate in this research study.

Confidentiality: Participation is this study is confidential. Subjects will be identified by number, not by name. If the results of the study are published, you will not be personally identified. The study sponsor and the Food and Drug Administration reserve the right to inspect study records, which may identify subjects

Financial Information: Participation in this research study is at no cost to you. You will receive $20 per session in cash upon completion of each session. If you withdraw from the study, the payment will be pro-rated, depending upon the time which you participated.

Subjects' Rights: Participation is voluntary, and you are free to withdraw your consent and to discontinue participation in this study at any time. Participation or withdrawal will not affect your present or future medical treatment.

Contact Persons: The Office for the Protection of Research Subjects of Northwestern University (312) 503-9338 can provide additional information about your rights as a research subject. Further information regarding this stud may be obtained from the project director, Dr. A. Vania Apkarian at (312) 503-0404.

Consent

I agree to participate in the research study described above and will receive a copy of this consent form.

_____ _____

Subject's signature Date

_____ _____

Investigator's signature Date

Northwestern University
Institutional Review Board
Approval Date 8-10-00
Approval Expires 8-4-01

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