NCT4414930: Pharmacologic augmentation of targeted cognitive training in schizophrenia

Approved: May 02, 2022

University of California, San Diego
Consent to Act as a Research Subject
Pharmacologic augmentation of targeted cognitive training in schizophrenia

Introduction
Neal R. Swerdlow, M.D., Ph.D., and his colleagues are conducting this research and asking for your consent to participate. This section provides a summary of important information. The rest of the form provides additional details.

- Research is voluntary - whether or not you join is your decision. You can discuss your decision with others (such as family, friends or another physician).
- You can say yes but change your mind later.
- If you say no, we will not hold your decision against you.
- Your decision will not affect your health care or any other benefits you may be entitled to.
- You can say no even if the person inviting you is part of your healthcare team.
- Please ask questions or mention concerns before, during or after the research.
- It is important that you continue to take your prescribed medications, including your antipsychotics, throughout the duration of the study.

We are conducting a research study to determine the effects of specific drugs on the way the brain processes information. You have been asked to participate because you have been diagnosed with schizophrenia or schizoaffective disorder, depressed type. Participation in the study may or may not benefit you directly and may result in new knowledge that may help others.

You will first undergo several procedures to determine if you are eligible for the study. The first visit is a screening session to determine eligibility. If you are eligible, you will participate in 2 test days, where you will receive either the study drug or placebo (an inactive substance). Then, you will be assigned to receive the study drug or placebo over a period of about approximately 10 weeks. During these 10 weeks, you will visit our clinic 3-4 times weekly for training session procedures designed to monitor your safety and measure the effect of the study drug. 30 of those visits will last up to 3 hours, 2 of those visits will last up to 2 hours, and 1 of those visits will last up to 4 hours. You will also be asked to come back approximately 22 weeks after your first visit. The most commonly expected risks of the study are fatigue, boredom or irritation.

The most serious risks of the study may include side effects from amphetamine. The active dose used in this study is one-half the recommended starting dose for adults with narcolepsy (5 mg). A higher, 20 mg oral dose of amphetamine is used commonly in published literature in studies of healthy volunteers without adverse reaction. Since amphetamine is a stimulant, it may cause physical side effects of over stimulation, palpitations, rapid heartbeat, or increased blood pressure. In some individuals, it might also cause stomach upset, restlessness, dizziness, tremor, headache, or abnormal movements. These side effects are most likely to be experienced in individuals taking higher doses than will be used in this study, and in individuals who are using amphetamine on a regular, sustained basis. Thus, the likelihood that you will experience medically significant side effects from amphetamine is low. Additional, detailed information about this research is provided below. Please feel free to ask questions before signing this consent.

Who is conducting the study, why you have been asked to participate, how you were selected, and what is the approximate number of participants in the study?
Neal R. Swerdlow, M.D., Ph.D., and his colleagues, located at the Clinical Teaching Facilities on the Hillcrest campus of UCSD, are conducting a research study to determine the effects of specific drugs on the way the brain processes information. You have been asked to participate because you have been diagnosed with schizophrenia or schizoaffective disorder, depressed type. There will be 70 people participating in the study.

What will happen to you in this study and which procedures are standard of care and which are experimental? How much time will each study procedure take and how long will the study last?
Here is a quick summary of the Study Calendar, with details of each type of visit below:

Screening Session	**Test Day 1 and 2**	**Training Sessions**	**Assessment**	**Post-Treatment**	**Durability**
Week 1	Week 2 and 3	Weeks 4-15*	2 times during Weeks 4-15*	After 30th training session*	Week 22*
7 hours*	8 hours*	3 days/week*, 3 hours each visit	2 hours each visit *#	4 hours*	4 hours*

* schedule is approximate, and may fluctuate due to laboratory closures, or your availability
# these visits occur after the 10th and 20th Training Session visit

SCREENING SESSION
The screening session will be approximately 7 hours. You will be given a physical and psychiatric examination, which includes medical, psychiatric, social and drug histories, which takes approximately 2 hours, as well as an electrical recording of your heart (EKG) and urine test, each procedure taking approximately 10 minutes. In the physical examination, Dr. Swerdlow, or one of the covering physicians for this study, will test some of your reflexes, and your arm and leg strength, will listen to your heart and lungs with a stethoscope, and will press on your upper abdomen to assess your liver size. At your request, a female assistant to a male physician, or a male assistant to a female physician, may be present at the physical exam. You will be excluded from the study if the urine test is positive for any illicit substances, and for any medical conditions that are identified that Dr. Swerdlow and colleagues feel would make it unsafe for you to complete this study. You will be asked to fill out several questionnaires, which take approximately 30 minutes to complete. You can skip any questions you do not want to answer.

You will then complete a series of tests that include the following procedures:

a) "TONE TESTS": You will be asked to complete various computer tasks, which can be completed in approximately 1 hour and 30 minutes. You will hear tones and will be asked to respond to each tone using buttons on a computer keyboard.
b) "EEG": You may be asked to participate in a test where an electrode will be placed on your head so that your brain waves (EEG) can be measured, which can be completed in approximately less than 1 hour. Additional sensors will be placed next to each eye, above and below your left eye and on your nose. You will be asked to listen to a series of brief clicks or tones while watching a silent film for approximately 20 minutes, and you will be asked to listen

to additional series of brief clicks or tones for a total of approximately 45 minutes. Foam Insert earphones are placed within each ear to deliver sounds. Breaks will be given every 20 – 30 minutes, or sooner, if needed.

TEST DAYS
After completing the Screening Session, you will be scheduled to return to the laboratory for Test Day 1 (approximately 7 days after the Screening Session) and Test Day 2 (approximately 7 days after Test Day 1). Each of these visits will take no longer than 8 hours each. You will be completing "Tone Tests" and "EEG tests (as described above) as well as questionnaires, like you did during the Screening Session. You will receive a either an oral dosage of amphetamine or placebo. You will not know if you are receiving amphetamine or placebo. Only the pharmacist knows which capsules contain amphetamine and which contain placebo, however, the investigators will be able to find out this information in case of an emergency.

TRAINING SESSIONS
After completing the Test Days, you will be scheduled to return to the laboratory approximately 3 days a week for the following 10-15 weeks. Each of these visits will take no longer than 3 hours,.

You will be assigned by chance to a study group. Your chance of being assigned to each group is 50%. At each of these visits, you will receive either an oral dosage of amphetamine or placebo. You will not know if you are receiving amphetamine or placebo. Only the pharmacist knows which capsules contain amphetamine and which contain placebo, however, the investigators will be able to find out this information in case of an emergency.

ASSESSMENT, POST-TREATMENT AND DURIBILITY VISITS,
During the course of your training session visits, you will be asked to return to the lab between your 10^{th} and 11^{th} training sessions and between your 20^{th} and 21^{st} training sessions (Assessment). These visits will take approximately 2 hours. You will also be asked to return after your 30^{th} training session (Post-Training). This visit will take approximately 4 hours. You will also be asked to return once more, approximately 22 weeks after your first visit (Durability).

During these visits, you may be asked to complete the following:
a) "TONE TESTS", as described above;
b) "EEG", as described above;
c) You will be asked to evaluate your present mood state in a questionnaire.

To insure your own safety in this study, you will be asked to tell the investigators about any past and current medical or psychiatric symptoms or conditions you have had, about your past and current use of medications, drugs, or other substances, and to keep them informed of any changes in your condition. Also, you will be asked not to use alcohol, over-the-counter cough syrups such as "Robitussin", or other substances for at least 72 hours before and during participation in this study. Study staff will arrange for transportation. The research study pays for all transportation costs to and from the lab.

During some or all of these tests your performance may be monitored with the use of a camera. This is to help ensure your safety, and to ensure that you are awake and performing the task as instructed. Only the investigator running the test session will be able to see you. The camera will not record your session.

A urine test will be required at your first 3 visits and may be requested during every visit during your participation; at minimum, a urine test will be required once per week after your first 3 visits. Your study participation will be terminated if the urine test is positive for illicit substances.

During your first 3 visits, your heart rate, blood pressure, weight and other symptoms will be recorded. These will continue to be recorded at minimum once per week but may be recorded at every visit.

It is very important that you continue to take your prescribed medications. We will ask you to verify that you are taking your prescribed medications at the start of every visit. If there are any changes in your medications, we may have to reschedule your appointment or terminate your participation in the study.

If you are female: the urine test will also test for evidence of pregnancy. Your study participation will be terminated if the urine test is positive for pregnancy. Details about this subject are discussed in the next section.

UCSD Institutional Review Board will have access to review all the study data.

You will not be asked to complete more than 5 hours of actual testing (not counting meals and rest periods) on each test day.

What risks are associated with this study?

Participation in this study may involve some added risks or discomforts. In addition to the risks briefly described at the beginning of this form, you may experience:

- Amphetamine effects: Amphetamine is a medication used to treat Attention Deficit Disorder in children and adults. It is also used to treat narcolepsy (a sleep disorder) in children and adults. The active doses to be used in this study is one -half the recommended starting dose for adults with narcolepsy (5 mg). A higher, 20 mg oral dose of amphetamine is used commonly in published literature in studies of normal, healthy volunteers without adverse reaction. This has also been the case in Dr. Swerdlow's studies of over 100 healthy adult subjects. Amphetamines should not be used by individuals with severe heart disease, including moderate to severe hypertension, or by individuals with hyperthyroidism, glaucoma, a history of drug abuse, or individuals who have taken a monoamine oxidase inhibitor (some types of antidepressants or St. John's Wort) during the past 14 days. Since amphetamine is a stimulant, it may cause physical side effects of over stimulation, palpitations, rapid heartbeat, or increased blood pressure. In some individuals, it might also cause gastrointestinal (stomach) upset, restlessness, dizziness, tremor, headache, or abnormal movements. These side effects are most likely to be experienced in individuals taking higher doses than will be used in this study, and in individuals who are using amphetamine on a regular, sustained basis. Thus, the likelihood that you will experience medically significant side effects from amphetamine is low. Due to amphetamine's possible effects it is important prior to each TRAINING SESSION not to use over-the-counter medications such as cough syrups, allergy medications and appetite suppressants. Driving, drinking or the operation of machinery should not occur within 12 hours of drug administration. Because you will receive amphetamine in this study, in the event that you would take a urine or

blood test to screen for drugs, amphetamine or its byproducts will be detectable in these tests for 4-5 days after you take your last active dose in this study.

- An alcohol swab is used to clean the skin before electrodes are applied and some minor skin irritation and redness may occur.
- Some participants might experience fatigue, boredom or irritation during the test session.
- Some participants may be embarrassed or feel uncomfortable by some of the questions asked in the questionnaires.
- During the study, your blood pressure and pulse will be regularly monitored.
- There is the risk of loss of confidentiality of information regarding positive drug screen results. Positive drug screen results, if they became known outside the research, could reasonably place the participants at risk of criminal civil liability or be damaging to the participants' financial standing or employability.
- Individuals with certain disorders sometimes experience symptoms that make them concerned that they may be at risk of hurting themselves or others. Should you experience such symptoms, please inform our staff, and our licensed staff physician will speak with you about your concerns. Should the physician determine that you are in need of further evaluation, we will escort you to the UCSD Medical Center Emergency Room for additional evaluation. For safety reasons, should the evaluating physician be concerned that your symptoms pose a threat to another person, they will need to inform that person of the situation; under such circumstances, your identity would no longer be considered confidential information.

None of the psychological tests or tests used to evaluate your body's response to the drugs are of any potential harm to you, except the inconvenience of time they take to perform.

Because this is a research study, there may be some unknown risks that are currently unforeseeable. You will be informed of any significant new findings.

Are there risks to the reproductive system or a developing fetus?

The effects of the treatment procedures may pose some unforeseeable risks on the reproductive system (sperm, eggs) or to the developing fetus. For this reason, participants in this investigational study should not become pregnant or father a child. We require that all participants agree to either abstain from sexual intercourse or use a reliable, effective contraception for this period, such as hormonal contraceptive, intrauterine device (IUD), diaphragm with spermicide, contraceptive sponge or use of condom by the partner.

After you have been enrolled in this study and during the research, pregnancy testing will be performed. If you have a positive pregnancy test, we may withdraw you from the study. If you (or your partner) become pregnant or if there is any chance of pregnancy (e.g., late menstrual period), please contact the study personnel immediately so that we may provide medical assistance and counseling.

What are the alternatives to participating in this study?

The alternative to participation in the study is to not participate.

What benefits can be reasonably expected?

In addition to the benefits listed at the beginning of this form, the investigator's understanding of how the brain processes information may be improved. Results of the tests are used entirely for

research purposes. As such, results will not be made available to you or your family members, and only to their primary physician when the participants sign a release of information form.

You will be told if any important new information is found during the course of this study that may affect your wanting to continue participation.

There may be no benefit to you from your participation.

What happens if you change your mind about participating?
Participation in this research is entirely voluntary. You may refuse to participate or withdraw any time without jeopardy to the medical care you will receive at this institution. Please inform anyone in the study team if at any time during the research study you want to withdraw. If you choose to withdraw from study participation after ingesting a test pill, we recommend that you choose to remain in our facility for monitoring one hour and 30 minutes after pill ingestion. Should you choose to leave our facility for any reason prior to that time, you are doing so at your own risk; we ask that you write a signed letter acknowledging that you have decided to leave prior to one hour and 30 minutes after pill administration at your own risk. We will provide transportation from our lab.

You will be told if any important new information is found during the course of this study that may affect your wanting to continue.

Can you be withdrawn from the study without your consent?
You may be withdrawn from the study if Dr. Swerdlow or his assistants believe that it is in your best interest. You may also be withdrawn from the study if you do not follow the instructions given to you by the study personnel.

Will you be compensated for participating in this study?
After the screening day, there will be 35 total visits over about 12 weeks - generally about 3 visits per week. Two visits will be about 8 hours long, one week apart, but all other visits will last between 2 and 4 hours. We'll also ask you to return for visit about 10 weeks after the study ends. You will be paid after each visit. In total, including the screening day, maximum payment in this study is $1875 for completing all visits. The breakdown is as follows:

Screening Session	**Test Day 1 and 2**	**Training Sessions**	**Assessment**	**Post-Treatment Assessment**	**Durability Assessment**
$15 per hour, up to $105*	A maximum of $120* for each visit	A maximum of $45* for each visit	A maximum of $30* for each visit	A maximum of $60*	A maximum of $60*
Maximum total compensation for completion of all visits listed above is $1905.					

* if your participation is terminated before the completion of your visit, you will be paid $15 per hour

If you fail to pass the tests in the SCREENING SESSION, you will be paid $15.00 per hour for your time and will be asked not to complete the other sessions.

It is very important that you can complete ALL visits.

If you are receiving Supplemental Security Income (SSI), you are responsible for reporting compensation from this study over $85 in one month needs to be reported to the Social Security Administration. One-half of any amount over $85 would then be deducted from the next SSI payment.

In order for us to pay you, you may need to give us private information like your home address or social security number. Payment received as compensation for participation in research is considered taxable income for a research subject. If payments are more than $600 in any one calendar year, UCSD is required to report this information to the Internal Revenue Service (IRS). Research subject payments exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to you and a copy will be sent to the IRS.

Are there any costs associated with participating in this study?
There will be no cost to you for participating in this study.

What if you are injured as a direct result of being in this study?
If you are injured as a direct result of participation in this research, the University of California will provide any medical care you need to treat those injuries. The University will not provide any other form of compensation to you if you are injured. You may call the Human Research Protections Program Office at 858-246-HRPP (858-246-4777) for more information about this, to inquire about your rights as a research subject or to report research-related problems.

What about your confidentiality?
Research records will be kept confidential to the extent allowed by law Your privacy will be protected by the assignment of coded numbers to each participant in the study. The database that relates the participants to a specific study number will be maintained using initials. Any database file will be encrypted on a password-protected computer. Paper copies of your files will in a locked storage cabinet. Only Dr. Swerdlow and those immediately involved with the study will have access to information collected as part of this study. Research records may be reviewed by the UCSD Institutional Review Board and the NIMH.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this website at any time.

Data from this study may 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. 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 laboratory 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. Please check YES or NO if it is ok to share your data to the NDA:

- ❑ Yes, you agree to share your data to the NDA.
- ❑ No, you do not want to share your data to the NDA.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

Will you be contacted in the future?
Dr. Swerdlow or his assistants would like to contact you regarding future studies. If you agree, we will contact you using the information you provided for this study. Please check YES or NO if it is ok to contact you about these studies:

- ❑ Yes, you agree to be contacted for future studies.
- ❑ No, you do not want to be contacted for future studies.

Will you receive any results from participating in this study?
Results of the tests are used entirely for research purposes. As such, results will not be made available to you or your family members, and only to their primary physician when the participants sign a release of information form.

Who can you call if you have questions?
This study has been explained to you and your questions have been answered. If you have other questions or research-related problems, you may reach Neal Swerdlow, M.D., Ph.D., at 619-543-6270. Dr. Swerdlow may also be reached after hours by contacting the UCSD operator at (619) 543-6222 and having them page Dr. Swerdlow.

You may call the Human Research Protections Program Office at 858-246-HRPP (858-246-4777) to inquire about your rights as a research subject or to report research-related problems.

What if I feel sick and think I have COVID-19 (also known as coronavirus)?
If you report feeling symptoms that may be due to COVID-19, we will ask you to stay home until you are symptom free, and follow guidelines as set by the CDC (Centers for Disease Control and Prevention). We provide COVID-19 testing for participants who report symptoms, at no cost to you. You do not have to be tested. If you are tested, the study physician would like to access the results of your COVID-19 test. Please check YES or NO if it is ok for the study physician to view the results of your COVID-19 test:

- ❑ Yes, you agree to let the study physician check the results of your COVID-19 test.
- ❑ No, you do not want the study physician to check the results of your COVID-19 test.

Your Signature and Consent
You have received a copy of this consent document and a copy of the "Experimental Subject's Bill of Rights" to keep.

You agree to participate.

_____ _____
Subject's signature Date

_____ _____
Signature of the person conducting the informed consent discussion Date