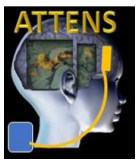
Information sheet for child (16 -18)

*The **ATTENS project (ADHD trial of external trigeminal nerve stimulation)***

A multi-centre, double-blind, randomized, parallel-group, phase IIb study to compare the efficacy of real versus sham external Trigeminal Nerve Stimulation (eTNS) on symptoms in youth with Attention Deficit/Hyperactivity Disorder (ADHD)



You are invited to take part in research at the Institute of Psychiatry, Psychology & Neuroscience at King's College London and at the University of Southampton. Before you decide to take part, you should understand why this research is being done and what we will ask you to do if you take part. Please take the time to read the information carefully and talk about it with your parents, carers, guardians or other people if you would like. Please do not hesitate to ask us if there is anything that is not clear. Please take your time in deciding if you would like to take part.

What is the ATTENS project about?

We are testing a new treatment for children with Attention Deficit/Hyperactivity Disorder (ADHD) because the typical treatment for children with ADHD is medication and this can have some side effects. We also do not know whether medication works in the longer run. We are testing a medical device called external Trigeminal Nerve Stimulation (eTNS) that is being applied when you are asleep. We will test two different devices, one with real stimulation and another one with fake stimulation (sham/fake or placebo). Some children will get the sham device (placebo), and some will get the real treatment but neither you, your parents or the researchers will know which device you will get. The device stimulates a nerve called the trigeminal nerve by putting a patch on your forehead which looks like a plaster. This patch stimulates the brain, in particular activity in the front parts of the brain.

The study will test whether eTNS can reduce symptoms of ADHD and other problems such as mood, concentration, memory, and sleep. We will ask you to do computer tasks, to test whether eTNS improves your ability to concentrate and your self-control. The questionnaires and computer tests will be done before using the eTNS device, after four weeks of using the eTNS device while sleeping and then again 6 months after the eTNS treatment to see whether any positive effects of eTNS are still there 6 months later.

What is the external Trigeminal Nerve Stimulation (eTNS)?

The eTNS device is shown in the picture below. It is a medical device that has a battery with some cables that lead small electrical stimulation to a patch which resembles a large plaster that is placed on the forehead. This patch stimulates the trigeminal nerve which is a nerve that sits on the forehead. In a study in the USA, this device has been shown to be very good for children with ADHD and we want to test this further. Because this is a research study, 50% of the children will receive a device with no stimulation which is called sham or fake stimulation or placebo. We cannot tell you whether you are in the sham or real eTNS treatment group, as you will be randomly allocated by a computerised system to one or the other treatment (like tossing a coin). The researcher who you will meet will not know either whether you will get the sham or real eTNS treatment. This means that both you and the researchers

are “blinded” or masked. We only expect the group who gets the real eTNS treatment to get improvements in their behaviour.

Why have I been invited?

You are invited because you have been diagnosed with ADHD. Or you have been contacted through a support group or seen a flyer.

Do I have to take part?

No. You can decide whether you want to participate or not and you will always be able to change your mind or drop out at any time. This will not have any influence on your usual medical treatment in any way. Please take at least 2 days, but no longer than 6 months to decide whether you want to take part or not.

What will I be asked to do if I take part in the ATTENS project?

To take part in this research you would be asked to:

- Be interviewed and asked to answer questions about your behaviour
- Have your IQ tested
- Use the eTNS device while you are sleeping for 7-9 hours every night for four weeks
- For four weeks during the eTNS treatment answer questions online (on zoom or similar) every week
- Wear a device on your wrist for 3-4 hours during research visits like a “fitbit”
- Come to the research centre four times and do some computer tests and answer some questions about your behaviour
- At the centre you will have your height, weight, and pupils measured (we can measure how alert you are in the pupils) when doing computer tasks
- **If you are on ADHD medication, we will ask you to take your usual dose, even on weekends and holidays during the 4 weeks of treatment**
  We would also like to record the interview but only if you are happy for us to do that.

We will ask your parents questions about you and would also like to ask your teacher what you are like in school. Also, we’ll send a letter to your GP and the doctor who gives you the medication (if applicable) to make sure that they know that you are taking part in this study.

Can I still take my usual medication during the eTNS treatment or what happens if I want to start taking medication treatment for the first time?

Yes, you can still take your usual medication, but we ask you to not change anything and not change the medication. We will also ask you to not take any breaks from your medication in the 4 weeks of the treatment. You can also stop taking your medication for 1 week before the treatment starts if you want to remain off medication while you use the eTNS treatment.

If you have never taken medication, we do not want you to start any new medication during the study. You will have to wait for the 4 weeks to be over before taking any new medication.

We will discuss this with your parents, carers or guardians and find out what is best for you.

How will I know if I can take part?

We will meet you and your parents online (like on Zoom) to discuss if you can take part. This visit includes an interview with your parents (about 2-3 hours). Then an interview with you (1 hour), and a test of IQ (20-40 min) at the research centre.

There are some reasons why you would not be able to take part in this project such as if you have some other disorders such as for example Autism Spectrum Disorders (ASD) or if your ADHD is mild. Also, we need to make sure that you do not have epilepsy or diabetes and check what medication you use as well as whether you regularly use alcohol or drugs. If you take some medications such as Atomoxetine (Strattera) and Guanfacine (Intuniv, Tenex) then you cannot take part.

Once the researcher has gathered all the information, they will confirm that you can take part, but they want to make sure that it is safe for you to do so first.

You can also do an optional part of the project which is doing two brain scans called Functional Magnetic Resonance Imaging (fMRI)

The brain scanner (MRI) is like a tunnel in which you must lie very still, you can see a picture of the MRI scanner below. The brain scan is perfectly safe, does not hurt and has no side effects but it is a bit noisy so you will have some headphones on. We will first show you on a test scanner what to do before doing the proper brain scan. Each scan takes about 60 minutes, and you will be asked to lie still the whole time and do some computer tests while you are lying in the scanner. There is a microphone inside the scanner so that you can talk to us and let us know if at any time you want the scan to stop. Your parent can be in the room with you the whole time if they have no counterindications to the MRI scanner. Once the scan is done, we can give you a picture of your brain.

We can talk about this part of the project if you are interested, and you can then ask any questions. We aim to include in the study mostly children who have never used stimulant medication or are currently not taking any stimulant medication. If you know that you are afraid of enclosed spaces, then you should not be doing this part of the study. The brain scan can only be done at the London research centre. You would need to go into the mock scanner. This is a fake scanner where you can get an impression on how it is to lie in the scanner and where we will show you the computer tests you will have to do in the scanner. This is to make sure that you are happy to take part in this part of the trial. The MRI scan would then be done on the following research visit to the research centre when you will also get the eTNS device and then again four weeks later after the treatment.

To do this part of the project you cannot have any metal in your body (e.g., braces, metallic tattoos, pacemaker). If you take part, then we will ask you to not have any new metal tattoos or metal piercings made in the four weeks when you are using the eTNS device.

What are the advantages in taking part?

Taking part in a project like this can be interesting and exciting. It is possible that it could help you with your ADHD. The study will help finding a new treatment for ADHD in the future.

What are the possible disadvantages and risk of taking part?

Possible discomfort: It is possible that it is a bit uncomfortable to sleep with the eTNS device at night. However, in the previous USA study, the sleep of the children who participated in the study became better and not worse.

Delay of medication treatment: If you are not taking medication, but are planning to start taking medication, you will have to wait until after the four weeks of the treatment.

Length of the assessment. You will have to come into the clinic at least three times. In addition, you and your parents will also have to fill in some questions every week during the treatment.

Personal information in assessments*:* Rarely some of the questions seem personal and can cause distress. These are similar to the questions asked when you were first diagnosed. We only ask questions that are important in gaining a full understanding of you, your family and your school situation. The assessment can take 1-2 hours, but we will give you frequent breaks if you want to.

Side effects: No serious side effects or adverse events have been reported in studies with eTNS and we do not expect any major side effects. However, we cannot guarantee that you will not have any side effects and some have complained about headache (that quickly goes away) or skin irritation (that goes away with cream). Other potential side effects could be fatigue and weight gain.

The National Institute for Health and Care Excellence (NICE) issued guidance regarding this treatment in January 2023 based on the USA trials. Their guidance mentions additional side effects such as negative effects on cognitive function and worsening of symptoms. However, it should be pointed out that this was reported more in the group with the sham device rather than the group with the real device. Given that the sham device is not doing anything, such side effects are then thought to be more likely to be related to ADHD itself rather than the device.

Worries about the scanner: MRI is a safe imaging method and there are no side effects. However, some people can sometimes be anxious about the scanner, which can be seen as noisy, unpleasant, and uncomfortable. We will stop all testing at the first sign that you feel uncomfortable or feel stressed. You are free to terminate the scanning session whenever you want to. There is a microphone in the scanner through which you can easily communicate with the radiographers. Also, the radiographers will constantly check that you are OK to remain in the scanner.

Unfortunately, this device is only available to you as part of this project, as it cannot be bought in the UK at the moment. However, it will be available to buy in the future. It will take some time until the study team can confirm if the device is beneficial, but they will let you know once they have analysed all the information gathered.

What happens when the research stops?

At the end of the study, we will send you a report about your response to the eTNS treatment. If you agree, we will also send it to your parents.

Who will access my medical records?

We will ask you for your permission that the research team can see your clinical records. This is important so that we can check if you can take part in the study.

Will the information that is collected about me in this research be kept secret?

All information you give us will be kept secret and your name will be removed and replaced by a number and only a few members of the research team will know who the numbers belong to.
In the data system where we will input all information about you and which we use to analyse the data,

we will use your initials and month and year of birth but nothing else that can identify you. Later this information will be removed and only a number will be kept.

However, in very rare cases it may be that we have discussed something with you that is making us concerned about your safety and wellbeing and of those around you. In that case, we are required by law to share that information.

The picture of your brain and all paper copies of information from you will be kept for 10 years, without your name on it.

Will I get anything for taking part?

To thank you for your participation we will give you:

- £50 for the first assessment (this may be done on more than one occasion and may be at the research centre)
- £50 for each of the three research visits (total of £150)
- £150 for the four weeks of sleeping with the device
- If you do the fMRI scan you will also get £50 for each scan (up to £100)

This will be given to you at different times. You will get £50 after the first assessment and then we will give you tokens for all your work until you are finished with the device. You will then be given £250 followed by a final payment of £50 after your last visit. Therefore, you can receive a total of £350 and an additional £100 if you also do the fMRI scans.

We will also give your parents, carers or guardians some money for travel expenses. However, we are not able to reimburse any hotel costs.

At the end of the research, we will write to you to let you know what we found out after looking at all the information we have collected.

Expected study results

We hope that this research will lead to a **new treatment for ADHD**, with no side effects. We hope that this treatment will help with the behavioural problems and attention skills of ADHD children. Also, we expect this treatment to have longer effects, lasting 6 months.

What if something goes wrong?

If you feel worried about something to do with this study, you should let your parents know and get in contact with us and we will do our best to help you further. Our contact details are at the bottom of this sheet.

What will happen to the results of this research?

The results of this study will appear as articles in special magazines that medical doctors and scientists read. However, your name will not be used in any of these articles. All data will be stored in anonymised form up to 10 years.

Who has reviewed the study?

To protect your interests, the West Midlands – Solihull NHS Research Ethics Committee (REC) (Ref:21/WM/0169) have reviewed the study and granted a favourable opinion.

Who is managing and paying for this project?

The Chief Investigator for the project is Prof Katya Rubia, Department of Child and Adolescent Psychiatry, Institute of Psychiatry, King's College London and she has received funds from the National Institute of Health Research (NIHR).

Is there insurance in place for this research?

King's College London and NHS have insurances in place for this study, to cover bodily injury.

Further information and contact details

If you want more information on anything to do with this study, please get in touch with the research team email:attens@kcl.ac.uk or telephone: 07923-881937.

You can also write to Dr Katya Rubia at the Department of Child and Adolescent Psychiatry, PO85, Institute of Psychiatry, Psychology and Neuroscience, De Crespigny Park, London, SE5 8AF for any more information or you can telephone: 020-7848 0463 or email: katya.rubia@kcl.ac.uk.

We would like to thank you for reading all this information.