EVOSIS
EVALUATION OF SLEEP IN SYNGAP1

accord
Academic and Clinical Central Office for Research and Development

THE UNIVERSITY of EDINBURGH

Evaluation of Sleep in SYNGAP1-related Intellectual Disability
Research Study Information Sheet

Your child/ward is being invited to take part in a research study. Before you decide if they should participate, it is important for you to understand why the research is being done and what it will involve for your child/ward. Please ask if there is anything that is not clear or if you would like more information. Your decision is completely voluntary. The decision you make will not affect your child's care in any way.

What are we trying to find out?

We are investigating how DNA changes (variants) in the *SYNGAP1* gene affect sleep. Sleep problems have been noted in 61.8% to 100% of participants in research studies who have SYNGAP1-related Intellectual Disability (ID) which is caused by *SYNGAP1* variants. Preliminary work from our research group also found sleep problems in all thirteen individuals whose parents completed a measure called the Children's Sleep Habits Questionnaire. Although it is clear that poor sleep is a significant issue for those with SYNGAP1-related ID, the nature of sleep patterns in affected individuals is yet to be fully evaluated.

We have neuroscience colleagues who are studying sleep in laboratory models of SYNGAP1-related ID. They have found certain types of seizure around the time of falling asleep and changes in the different stages of sleep. Laboratory researchers in the USA have also found seizure activity during sleep. Our aim is to identify any sleep changes or patterns that are specific to SYNGAP1-related ID by comparing sleep in children with the condition to children who don't have SYNGAP1-related ID. We will also be able to identify seizure activity or clinical sleep disorders that might require further evaluation or treatment by your child/ward's doctor.

Why is my child/ward being asked to join in?

We are asking your child/ward because they have a change in the gene *SYNGAP1* or know someone who does.

Does my child/ward have to join in?

No. It is up to you to decide whether they take part or not. If you decide they should take part you can keep this information sheet and will be asked to sign a consent form. You will have at least 24 hours to read and consider the information and ask questions before we seek consent. You are free to change your mind at any time without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that your child/ward receives, or their legal rights.

What will happen if my child/ward joins in?

We will meet you and your child/ward by video-link. If they are aged 12 years or over we will assess their ability to decide whether to take part or not. If they lack the ability to consent for themselves or if they are younger than 12 years old, we will seek consent from you if agree to them participating in the study. Legally, children younger than 12 cannot consent for themselves, but we will ask them how they feel about the study. We will do the same for young people over the age of 12 if they can't consent for themselves. If we are uncertain via video-link if your child/ward has capacity to consent, then a face-to-face appointment will be required to assess this further.

The person giving consent will be able to either sign and return the consent form by post or electronically sign it. When we use video-links during this study we will always use University of Edinburgh approved software/platforms.

If your child/ward has SYNGAP1-related intellectual disability, we will ask you for proof of this from something like a doctor's letter or genetic testing report.

We will ask you or someone of your choosing who knows your child/ward well to fill in some questionnaires about their health, quality of life and any sleep problems they may have. These questionnaires will take on average around 90 minutes to complete, but don't have to be filled in all at once. We will also ask for a diary of your child's sleep to be kept for 7 nights, which will take 5-10 minutes each morning, for 7 days in a row.

We will visit your child/ward's house to study their sleep for 2 nights using techniques similar to, but less invasive than those used in gold standard sleep evaluations in the NHS. Your child/ward will be asked to wear recording equipment similar to that shown in picture 1 for the overnight recordings. Researchers will visit to help to set up the equipment, but will not need to remain present overnight during data collection. The measurements recorded will include:

- Electroencephalography (EEG – measures electrical activity in the brain)
- Electrooculography (EOG – measures eye movements)
- Electrocardiography (ECG – measures electrical activity in the heart)
- Electromyography (EMG – measures electrical activity in muscle)
- Oxygen levels (SpO2)
- Video – for body position and movements
- Body movement
- Airflow (via nasal cannula)
- Pulse

During our visits researchers will wear appropriate PPE (which is highly likely to include face coverings) and social distancing will be maintained wherever possible. Government guidance and University of Edinburgh specific guidance regarding COVID-19 and other transmissible infections will be followed at all times. All non-invasive, reusable items will be disinfected with alcohol wipes prior to and after use.

As well as studying sleep itself, we are also researching circadian rhythm. This is the daily body rhythm that links to the sleep-wake cycle over roughly each 24 hour period. To measure this, we will ask your child/ward to wear a watch-like device called an actigraph (see picture 2) on a wrist or ankle continuously for a week; it measures activity levels. Our laboratory neuroscience colleagues are also now collecting circadian rhythm data.

Picture 2

Picture 2

What are the potential benefits of participating in the study?

If your child/ward takes part we will be able to tell you more about their sleep and circadian rhythm. We will also be able to tell you if we identify specific clinical sleep disorders, sleep-related seizures and/or circadian rhythm disorders which may require further investigation and treatment. We know that sleep disruption and circadian rhythm disorders can result in problems with learning, memory, behaviour, emotional functioning and quality of life. Therefore if any treatable cause of sleep disturbance is identified, successful management of it may improve various aspects of your child/ward's life. With your consent we will inform your child's doctor(s) about any seizures or sleep problems which may need treatment.

Although at present there is no specific treatment for SYNGAP1-related ID, trials of therapeutics in laboratory models are in progress. If your child/ward takes part in this study, their data will directly assist with the search for biomarkers (specific patterns) of sleep in SYNGAP1-related ID which hopefully will help assess how effective any new therapeutics are.

What are possible disadvantages and risks of taking part?

The risks of taking part are low, but there is a time commitment to the study. We know that some people can find new experiences or meeting new people anxiety provoking. We have tried to minimise any distress by planning the study so the sleep recordings will be in your child/ward's own home. This means they will be in a familiar place with the people who care for them. We will use as little equipment as possible and will send out some mock versions that will be a bit like the real recording devices so that your child/ward can acclimatise to them as much as possible. It is not a problem if they can only cope with some pieces of the equipment as we get slightly different valuable information from each sensor. We will show you how to remove anything that your child/ward finds too difficult to sleep with and although we hope not, we know it is possible that all of the equipment may have to be removed. Finally, although the study researchers will help set up the recording equipment they will not need to stay overnight and we will send pictures of us before we come. We hope all of this will help with any anxiety.

What do you do with my child/ward's information?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage. This study will be complying with the standards in the Data Protection Act 2018 in the UK.
We will need to collect the following personal data to conduct this research study:

- Name
- Date of birth
- Address
- Telephone number
- Email address
- Video recordings

The questionnaire information will be stored in paper form in locked cabinets and in electronic form in password protected files on secure computers and servers at the University of Edinburgh. We will allocate your child/ward a secret code number so that if anyone saw this information they would not recognise them (their information will be de-identified). The key to this code is kept separately from the data. If we use a video-link to contact your child/ward and those caring for them (which of course may well include you), it won't be recorded.

We will set up the sleep recording devices without entering any of your child/ward's identifiable information. The devices are encrypted and the data can only be decoded by someone with

access to the device docking station and the specific computer software provided by the manufacturer. The video will be transferred to a University of Edinburgh secure laptop prior to travelling back to Edinburgh so that the recording on the camera can be deleted.

If you agree for your child/ward to take part in a research study, the de-identified information about their health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad.
This information will not identify your child/ward and we will not combine it with other information in a way that could identify them. Specifically, we will not share names, contact details and dates of birth. We would seek separate consent from you if at any point we were thinking about sharing video recordings as we know the chance of identifying your child is higher from these even though we will blur/pixelate their face. Any information shared will only be used for the purpose of health and care research and cannot be used to contact your child/ward or to affect their care. It will not be used to make decisions about future services available to them, such as insurance. As the number of people diagnosed with SYNGAP1-related intellectual disability around the world is small, it may be easier to identify someone with the condition by piecing together information from different sources than it would be for someone without the condition. Hence there is a very small chance that if you have given information about your child to other parties it could be compared with our coded data in a way that allows people to recognise it as your child. It is important you are aware of this although we think the likelihood is very low.

Eighteen months following the completion of the study, anonymised data will be shared through the University of Edinburgh's DataShare open access data repository. It is possible that this data may be shared through other platforms in the future.

We will ask if you consent to us providing your child/ward's doctor with any relevant clinical findings from their sleep study, such as any sleep disorders or seizure activity identified. We will analyse the data as soon as possible after their sleep study to be able to provide this information. You can tell us which doctor or doctors you would like us to contact.

Audio-video recordings will be anonymised by pixelating your child/ward's face and removing any sounds that would allow them to be identified (such as saying their name) before being published or presented in any format. We will show you the videos and seek specific consent from you before using them in this way.

We will keep all the study data including the audio-visual recordings for 20 years and then it will be destroyed.

If you have any concerns about how we will use your information, please contact:

- Dr Mizen who is running the study: lmizen@ed.ac.uk
- Telephone Dr Mizen: 0131 537 6263
- Email The University of Edinburgh Data Protection Officer: dpo@ed.ac.uk

What if something goes wrong?

We don't expect your child/ward to suffer any health problems due to taking part in the study. The University has insurance so that anyone whose health does suffer as a result of being in the study can be compensated. You wouldn't have to prove it was anyone's fault.

What will happen if I withdraw my child/ward from the study?

You can withdraw consent to your child/ward's participation in the study at any time and without telling us why. If you do withdraw consent, we will keep the information we have already obtained. To safeguard your child/ward's rights, we will use the minimum personally-identifiable information possible. Withdrawal from the study will not change their right to healthcare or affect their legal rights.

Will we be paid for taking part?

We will refund all participants any expenses incurred as a result of being in the study. Participants will be asked to provide all relevant receipts so the refunds can be organised.

Do the researchers make any money from recruiting people to this study?

The study investigators are not paid anything for including your child/ward in the study other than their ordinary salary.

What will happen after the study has finished?

At the end of the study we will write to you with our results and specific information about your child/ward's sleep and circadian rhythm. We will also write reports for specialist scientific journals and the funders of the study. We will share our findings at conferences and public meetings where possible. Your child/ward's personal details will never appear in any report, lecture or talk without seeking your consent first.

After the end of the study we will keep the study data for 20 years so that we can use it to answer new or associated research questions. We will also ask you for permission to contact you or your child/ward in the future with information about other research studies.

If you would like to be kept up to date with Patrick Wild Centre work in the meantime, you can sign up to our database here: https://patrickwildcentre.com/join-the-pwc-database/. This is separate from giving consent for this EVOSIS sleep study.

Who is organising and paying for this research?

This study has been organised/sponsored by the University of Edinburgh. Funding comes from the University's Simons Initiative for the Developing Brain funded by the Simons Foundation Autism Research Initiative (www.sfari.org) and from The Patrick Wild Centre at the University of Edinburgh which conducts research into Autism, Fragile X Syndrome and Intellectual Disabilities (https://patrickwildcentre.com).

Who has reviewed the study?

The study proposal has been reviewed by the funders. The University of Edinburgh's Medical School Research Ethics Committee (EMREC) has also reviewed and approved the study.

If you have any questions you can contact

Dr Lindsay Mizen
She is running the study

Email: lmizen@ed.ac.uk
Telephone: 0131 537 6263

If you wish, you could contact Professor Stephen Lawrie who is not involved with this study and could give impartial information about it:

Professor Stephen Lawrie, Chair of Psychiatry and Neuro-Imaging & Head of the Division of Psychiatry, Telephone: 0131 537 6509 Email: s.lawrie@ed.ac.uk.

If you wish to make a complaint about the study and feel unable to discuss this with the study researchers, you can contact the Research Governance Team at the University of Edinburgh at researchgovernance@ed.ac.uk.

Privacy Notice

The University of Edinburgh is the sponsor for this study based in the United Kingdom. The Sponsor has overall responsibility for the running of the study. To follow the United Kingdom's data protection regulations we must inform you of how we will use and store your child/ward's personal data.

As a university, we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree for your child/ward to take part in a research study, we will use their data in the ways needed to conduct and analyse the research study.

We will use information from your child/ward in order to undertake this study. The sponsor will keep identifiable information about you for 20 years after the study has finished.

The University of Edinburgh will act as the data controller for this study. This means that they are responsible for looking after your information and using it properly.

Your rights to access, change or move your child/ward's information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw your child/ward from the study, we will keep the information about them that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Non-identifiable data from this project may be stored in a research data repository at the University of Edinburgh to allow knowledge sharing and learnings about this study. The University of Edinburgh provides its researchers (and their collaborators) two services for sharing and archiving of data which will be used for your information. There is an open access repository for anonymised data, which means that all non-identifiable data is freely available. For sensitive information a secure repository is used which can only be accessed by approved researchers who have undergone a rigorous application and review process.

Thank you for reading this information sheet.