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Evaluation of sleep in the genetic condition known as SYNGAP1, in children who have SYNGAP1-related intellectual disability

Submission date 12/01/2022	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 16/02/2022	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 20/08/2025	**Condition category** Genetic Diseases	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims

We are investigating how DNA changes (variants) in the SYNGAP1 gene affect sleep. The SYNGAP1 gene provides instructions for making a protein, called SynGAP, that plays an important role in nerve cells in the brain. SynGAP is found at the junctions between nerve cells (synapses) where cell-to-cell communication takes place. 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 participants doctor.

Who can participate?

Children (<16 years) with a confirmed SYNGAP1 gene variant, who live in the UK, and can consent, or have a parent or someone with parental responsibility who can consent on their behalf, study partners (siblings, family members, other matched controls).

What does the study involve?

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.

What are the possible benefits and risks of participating?
We will be able to tell you more about the sleep and circadian rhythm of participants. We will also be able to tell 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 the participant's life. With consent, we will inform the participant's doctor(s) about any seizures or sleep problems that 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.

The risks of taking part are low, but there is a time commitment to the study. We don't expect participants to suffer any health problems due to taking part in the study. Some participants might find wearing the equipment overnight uncomfortable, it can be removed at any time by themselves or their care-givers. We know that some people can find new experiences or meeting new people anxiety provoking.

Where is the study run from?
University of Edinburgh (UK)

When is the study starting and how long is it expected to run for?
May 2021 to July 2023

Who is funding the study?
This study has been organised/sponsored by the University of Edinburgh (UK). 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 is the main contact?
Dr Lindsay Mizen, lmizen@ed.ac.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Protocol serial number
Version 1.0, 09.06.2021. 21-EMREC-020

Study information

Scientific Title
A case-control observational study of sleep patterns (using actigraphy and video-polysomnography) of children (≤15 years old) with SYNGAP1-related intellectual disability (n=15 participants, with matched controls), to evaluate any differences in sleep pattern, sleep stages, and disorders of sleep.

Acronym
EVOSIS

Study objectives
Differences in brain electrical activity in rats with Syngap1 mutations during sleep are also present in people with SYNGAP1-related ID and biomarkers in the sleep patterns of rats and people with SYNGAP1 variants which can in future be used as markers of treatment response.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/07/2021, Edinburgh Medical School Research Ethics Committee (EMREC) (Edinburgh BioQuarter, 47 Little France Crescent, Edinburgh, EH16 4TJ, UK; +44(0)131 650 1000, emrec@ed.ac.uk), ref: 21-EMREC-020

Primary study design
Observational

Study design
This is a case-control observational study lasting 15 months. Sleep patterns of participants with SYNGAP1-related ID and unaffected controls (typically siblings) will be measured in their own homes.

Study type(s)
Other

Health condition(s) or problem(s) studied
Children with SYNGAP1 gene mutation

Interventions
Observational trial performing polysomnography and actigraphy on children (<18) with SYNGAP1 gene mutation compared to controls.

Once consent has been obtained to enrol a participant in the trial, they will be sent a clinical history questionnaire as well as the standardised Childhood Sleep Habits questionnaire and

Pediatric Quality of Life Inventory to complete. The participant will wear an actigraph watch-like device (similar to a FitBit) 24 hours a day for a week. This measures activity levels to collect information about the participant's sleep-wake cycle (circadian rhythm). At the same time, the participant will be asked to keep a 7 night sleep diary. The last 2 nights wearing the actigraph and recording the sleep diary will correspond with the study team visiting. The team will conduct two consecutive nights of a standardised, non-invasive procedure known as polysomnography. Polysomnography involves attaching a number of sensors to the participant’s head, face, fingertip, legs and body, to measure brain activity, eye movement, muscle tone, pulse rate, oxygen level, limb movements and respiration, used to quantify the participant’s sleep. The sensors are either attached via mild, easily removable adhesive stickers or wax, or clips and can be removed in a matter of minutes by the participant or caregiver, either in the morning, or whenever the participant wants them to be removed.

No follow up assessments will be scheduled as part of this research study unless there is a need to repeat the polysomnography or actigraphy due to technical difficulties with the equipment.

Intervention Type
Not Specified

Primary outcome(s)
1. Childhood Sleep Habits questionnaire - Provided once consent has been given, to be completed at participants' convenience prior to the home visits
2. Paediatric Quality of Life Inventory - Provided once consent has been given, to be completed at participants' convenience prior to the home visits
3. Sleep diary – Provided once consent has been given, to be completed at the same time as actigraphy
4. Rest/activity cycle measured using actigraphy – 7 consecutive days/nights, commencing 5 days before polysomnography, and continuing during 2 nights of polysomnography
5. Electrical activity during sleep measured using Overnight Simplified Polysomnography – days 6 and 7 of actigraphy

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
31/07/2023

Eligibility

Key inclusion criteria
1. Have a confirmed SYNGAP1 gene variant
2. Be 15 years of age or younger
3. Live in the UK (Scotland, England, Wales or Northern Ireland)
4. Be able to consent to participation themselves or have a parent or someone with parental responsibility to consent on their behalf
5. Have a study partner who can complete questionnaires about them

Participant type(s)
Mixed

Healthy volunteers allowed

No

Age group
Child

Upper age limit
15 Years

Sex
All

Total final enrolment
30

Key exclusion criteria
1. Living outwith the UK
2. Lacking capacity to consent to participation themselves and lacking a parent or someone with parental responsibility to consent on their behalf
3. Aged 16 years or over
4. Lacking a study partner who can complete questionnaires

Date of first enrolment
12/10/2021

Date of final enrolment
22/07/2022

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
The University of Edinburgh
Patrick Wild Centre
Kennedy Tower
Royal Edinburgh Hospital
Edinburgh
United Kingdom
EH10 5HF

Sponsor information

Organisation
Accord (United Kingdom)

ROR
https://ror.org/01x6s1m65

Funder(s)

Funder type
Research organisation

Funder Name
Simons Initiative for the Developing Brain

Alternative Name(s)
SIDB

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Funder Name
The Patrick Wild Centre

Results and Publications

Individual participant data (IPD) sharing plan
Eighteen months following the completion of the study, anonymised data will be shared through the University of Edinburgh's DataShare open access data repository.

Repository name/weblink: Edinburgh DataShare https://datashare.ed.ac.uk/
The data will be open for any member of the public to download them from the publically visible dataset page.
The data will be open for any member of the public to download them from the publically visible dataset page.
The data will be released on DataShare under the default licence, a Creative Commons

Attribution licence, so that those who download the data have clear information that they're free to use the data for any purpose, on condition that they give credit by citing the dataset, for example in any journal publications.

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Basic version 1.0	09/06/2021	18/01/2022	No	Yes
Participant information sheet	Detailed information sheet version 3.0	22/07/2021	18/01/2022	No	Yes
Participant information sheet	For parents/guardians version 3.0	22/07/2021	18/01/2022	No	Yes
Participant information sheet	Moderate detail version 2.0	07/07/2021	18/01/2022	No	Yes
Protocol file	version 2.0	07/07/2021	18/01/2022	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes