

## Project title: Early DEvelopment in Neurofibromatosis Type 1 (EDEN)

### Overview Information Sheet

Dear Parent,

19<sup>th</sup> August 2016

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. You can ring us if there is anything that is not clear or if you would like more information.

#### **Purpose of the study**

Many children with NF1 can have difficulties such as Autism Spectrum Disorder (ASD) and Attention deficit Hyperactive Disorder (ADHD). But we don't understand how these conditions develop, what the early indicators of these difficulties might be or why some children with NF1 are protected from these difficulties. We hope that this research study will help us develop new tests that may in the long-term, help us with earlier diagnosis and developing new treatments for children with NF1.

#### **Taking part**

This study is for families who have an infant diagnosed with NF1 by your doctor. If you are pregnant and would like to know if your baby has NF1, you can ask your doctor for 'cord blood testing'. This means that your doctor can collect a blood sample from the umbilical cord (the cord connecting the baby to the mother) when the baby is born. Collecting blood samples in this way does not hurt the baby at all and is completely safe. Please discuss this with your doctor or get in touch with us if you would like more information. We can put you in touch with your regional genetic service who will be able to offer you this testing.

#### **What the research involves**

If you are interested in participating in the study, we will first collect background information about your family in order to determine whether this study is suitable for your child. This will occur over the phone. If the study is suitable for your family, we will invite you and your child to visit our research centre, the Babylab at the Centre for Brain and Cognitive Development in London. There are two starting points for this study, around 5 months and 10 months. Depending on your willingness and the age of your child when he/she is recruited, we will invite you to participate for a maximum of three visits until your child is 18 months. All expenses for your travel and accommodation are paid by the study. Later we will invite you for two follow-up visits, one at 2 and one at 3 years of age respectively which will take place in Manchester. A typical visit takes place over 5-6 hours, which includes time for meal and nap breaks. We aim to be flexible to you and your baby's needs and you can choose to split the visit over two days if that is more convenient for your family. We can provide a range of support to help you and your family participate in our study, and so please let us know if you have any additional needs.

#### **Questionnaires and Interviews**

We will give you a number of questionnaires about your child's behaviour to fill out at home or during your visit. These usually take 45 minutes to 1 hour to complete at each time-point. We will also ask you some questions on the phone or when you come into the lab. These will include questions about your child's motor abilities (such as whether they can grasp objects or crawl), vocalizations (for example the sounds your baby makes), as well as their behaviour in everyday settings. With your permission, we will also include information from your child's Personal Child Health Record (e.g. Red Book). This will help us to get information about how babies are in their everyday environment.

## **Activities for your child**

Your child will complete a number of short tasks and games, each examining a different area of development, and varying according to the age of your child. These may include watching animations on a screen or playing with you and the researcher. These tasks and games are designed to be fun and stimulating for babies. The details of the tasks are included in the appendix and will include:

1. What does baby look at: We are interested in how your baby uses their eyes to explore the world. We will use a small camera called the eyetracker to record baby's eye movements.
2. What is baby thinking: We want to find out how your baby's brain interprets information in the environment. To do this we will use two child-friendly techniques called Near-Infra Red Spectroscopy (NIRS) and Electroencephalography (EEG). You can find more information about these in the appendix.
3. How is baby feeling: We will record baby's heart rate, activity level and temperature to help us understand whether your baby feels calm or excited.

You will be present with your child throughout and are welcome to ask questions at any time. Some sessions will be tape recorded and viewed only by centre staff. You may decline to have your child's videotape retained for viewing by others if you wish. Participation in any part of the study is entirely voluntary, and you may choose to end the session at any time.

## **The 24 and 36m follow-ups**

These visits will take place at the Clinical Research Facility, Royal Manchester Children's Hospital. Prior to the visit, we will send you a few questionnaires to fill in and bring with you to the visit. During the visit the researcher will ask you a number of questions regarding your child's development and they will make observations during a structured play session with the researcher. The structured play session consists of several activities designed to elicit social and communicative behaviours such as eye contact and language.

Please note that we always adapt testing sessions to each child's individual needs. While the tasks we use target the development of specific abilities over time, each session is adapted for each child's specific age and individual needs. This means that we take as many breaks as the child needs to feed, rest, or play. We will do our best to make your visit as comfortable and enjoyable as possible.

After one of the sessions you will be kindly requested to fill in an anonymous feedback form, which will help us to improve our project in the future.

## **Data sharing and confidentiality**

We take confidentiality very seriously. We have a privacy policy that can be reviewed overleaf. In brief, we keep personal information (like names and addresses) separate from all study data but linked together by a 'study ID code'. Your personal information will only be accessed by members of the study team, or by appropriately trained members of regulatory authorities or our sponsoring organizations. With your consent, the study data we collect will be stored as per local policy at CBCD in London and Central Manchester University Hospital NHS Foundation trust for up to 30years. Personal information is kept in locked file cabinets or on password protected and/or encrypted computers.

Data is identified with the unique 'study ID' code that allows different pieces of data from your child to be associated with each other. Having one code for all your child's data helps us to get a complete picture of your child's development. Data coded in this way is called pseudonymised data. Personal and pseudonymised data are stored separately. All data is stored on password protected and/or encrypted computers and in locked file cabinets.

We will share pseudonymised data with other qualified researchers who are undertaking similar studies. Some of these researchers are in the UK, some in Europe and some in the US. Linking together with other qualified researchers helps us to use data from your baby to answer more questions about autism and ADHD risk.

## **Videotapes**

All lab visits of you and your child will be videotaped by research assistants. Videotapes in the study will be used for research purposes only. Only researchers involved in the study and our collaborators will watch these videotapes. No personal information (like names, addresses or diagnosis) will be shared with these videotapes. Videotapes will be kept securely in locked filing cabinets, in a locked room or on password protected and/or encrypted computers, and will be kept indefinitely. We will ask for your permission and consent to request using any photographs/short videos of your baby for publication.

**What if there is a problem?**

In the unlikely event that something does go wrong and you or your child are harmed during the research you may have grounds for legal action for compensation against the University of Manchester, Birbeck College or the NHS trust but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

If you have a minor complaint then you can contact the research team:

**Project Coordinator:** Dr Shruti Garg

**Tel:** 0161 3067967

**Email:** EDEN@manchester.ac.uk

If you wish to make a formal complaint or if you are not satisfied with the response you have gained from the researchers in the first instance, then please contact:

**Research Governance and Integrity Manager**

Research Office, Christie Building

University of Manchester

Oxford Road

Manchester

M13 9PL

**Email:** [research.complaints@manchester.ac.uk](mailto:research.complaints@manchester.ac.uk)

**Telephone:** 0161 275 2674 or 0161 275 2046

**Leaving the study**

You can choose to leave the study at any time. Whether or not you participate in our study does not affect your clinical care in any way. If you become unable to provide informed consent for your child's participation and no-one else can consent for your child, we will withdraw your child from the study. Any data collected up to the point of withdrawal will remain as part of the study for analysis.

**If you have any questions please contact:**

**Contact details of Project Coordinator:**

Dr Shruti Garg, Senior Lecturer in Translational Child Psychiatry

**Tel:** 01613067967

**Email:** EDEN@manchester.ac.uk

**Thank you**

## EDEN visits summary

**This study is for families who have a baby diagnosed with NF1**  
If you are pregnant and would like to know if your baby has NF1 then you can contact us and we can give you information about cord blood testing.

If you are unsure, please ring the research team on telephone  
01613067967

### VISIT 1, 2 & 3 SYNOPSIS

Two starting points for this study, when baby is 5 or 10 month olds  
There will be 3 visits – when baby is 5 month, 10 month and 14 months. These visits will take place at Birkbeck Babylab, Centre for Brain and Cognitive Development, London.

#### Typical visit times

5-6 hours which includes time for meal & nap breaks.  
Visit can be split over two days and we will pay for all expenses

#### Each visit will include:

Parent Questionnaires  
Activities for the child

We complete a number of short tasks and games with the child and use a number of child-friendly techniques such as EEG, NIRS and eye-tracking. The details of these techniques are in the appendix.

### Visits 4 & 5

Visit 4 will be when your baby is 24 months old and visit 5 when your baby is 36 months old. These visits will take place at Clinical Research Facility, Royal Manchester Children's Hospital. We will pay for all expenses.

#### Typical visit times

5-6 hours which includes time for meal & nap breaks.  
Visit can be split over two days and we will pay for all expenses

#### Each visit to include:

Parent Questionnaires  
Activities for the child

Will complete a number of short tasks and games and use number of child friendly techniques such as EEG, eye tracking and touchscreen games.

## **Early DEvelopment in Neurofibromatosis Type 1 (EDEN) Privacy Policy**

The EDEN study takes the protection of all personal information very seriously and complies with the Data Protection principles set out in the 1998 Data Protection Act. EDEN is affiliated with the British Autism Study of Infant Siblings (BASIS), a collaborative research network for the study of infants at-risk for autism in the UK.

### *Personal information*

Of fundamental importance within our data protection system is the security and confidentiality of your personal information. Personal data will be kept and processed securely and no unauthorised disclosures or transfers will take place to anyone either within or outside the EDEN Team.

You may contact us at the address overleaf to request that your personal data be removed at any time without having to give reasons or without affecting any of your rights.

To ensure that your information is kept secure, we will store all data in locked filing cabinets or on coded, encrypted or password protected computers.

Personal data will be disposed of in a way that protects the rights and privacy of data subjects. Manual records will be shredded or disposed of as "confidential waste". Hard drives of redundant PCs will be wiped clean by secure electronic deletion before disposal.

Any videotapes of sessions will be stored in locked filing cabinets within a locked building and separately from any personal data that may allow identification. When the data is no longer required, the videos will be destroyed by use of a robust and secure method.

### *Sharing Data*

Any data collected in the EDEN project will be coded and pseudonymised. This means that data will not be stored with names or personal information. At no time are personal details stored in the same database as test results. Data are stored with a unique code that allows different pieces of data collected from your child to be linked together, but not linked to any personal information (like names or addresses).

Once data has been pseudonymised, it will be shared with other qualified researchers who are asking similar questions about autism and/or ADHD risk. Some of the researchers we work with are located in the United States and in Europe. Sharing data allows us to ask additional scientific questions and increases the potential value of individual contributions to research. Sharing data across different countries helps us to benefit from the expertise of a wide network of researchers. We will only share your data with qualified researchers who sign up to our Confidentiality agreement and agree to store your data in line with our policies and procedures. No personal data will be shared with these researchers.

### *Child Protection*

Our organisation complies with government policy on child protection. In the event that any such issues arise we will follow local child safeguarding protocols. We will keep your child's information in confidence. This means we will only tell those who have a need or right to know.

## Appendix

### **Near Infra Red Spectroscopy**

We will use a brain imaging technique called near infrared spectroscopy (NIRS). Just like brain scanners that you may have seen in the media, this technique measures how the amount of oxygen changes in the blood supply to the brain, but this one is easy to use in research with babies. Such research is very important as it can teach us how the brain develops. It will also enable us to learn which areas of the brain are involved in different behaviours.

NIRS shines weak rays of light onto the head and measures the colour of the light reflected back. If your brain is busy responding to something and is using lots of oxygen, your blood will be red. If your blood has less oxygen it will be a more blue colour. By measuring these colour changes while your baby does an activity or watches something on the television, we can see which part of the brain is active. The fibres that carry the light to the head and back are embedded in a small hat that your baby can wear comfortably.



This technique is completely safe and has increasingly been used to study the infant brain all over the world. Although the hat may look like something from a science fiction film, there is no risk associated with measuring brain activity by this technique. Just like natural light does not change objects when it is reflected on them, the weak red light rays that we use do not have any effect on the brain.

If you are happy for us to proceed with the NIRS study, this is what will happen:

- You will be with your baby at all times during the study.
- First we measure your baby's head circumference with a soft tape measure so we can adjust the hat for your baby.
- Then we place the hat on your baby's head. While we do this, we play with your baby to keep him/her entertained, and then we can adjust the hat so that it fits your baby perfectly and comfortably. Generally babies are quite happy having the hat on and enjoy watching the screen, but if your baby becomes fussy at any point, we can take the hat off straight away.
- The fibers from the hat are then connected to the machine that generates the light rays and measures the light that comes back from the head.
- We will also give you a Polaroid photograph of your baby wearing the hat as a souvenir to take home.

## Recording Infant EEG Activity

For the past twelve years, researchers at the Centre for Brain and Cognitive Development have been carrying out research using equipment that allows us to measure the naturally occurring electrical activity of the human brain. Such research is very important as it can teach us how and when the brain develops. It will also enable us to learn which areas of the brain are involved in different behaviours.

Our brain cells communicate with each other using faint electric signals. We can eavesdrop on this communication by placing an array of sensors on the head that can pick up the natural activity of the person's brain (called electroencephalogram). The equipment we use is known as the Geodesic Sensor Net, specifically designed for babies. Using this net, researchers are able to achieve a detailed "map" of the working human brain.

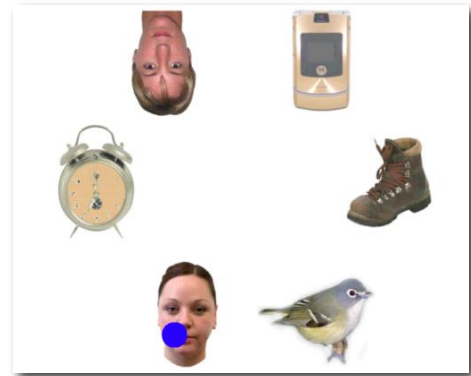
This technique is completely safe and has been used for studying how the brain works for many years without using expensive equipment. Although the sensor net may look like something from a science fiction film, there is no risk associated with measuring brain activity. Nothing comes out of the sensors. It is like a thermometer that takes your temperature but cannot change it.

If you are happy for us to proceed with the net study, this is what will happen:

- You will be with your baby at all times during the study.
- First we measure your baby's head circumference with a soft tape measure so we can choose the correct net size for your baby.
- Then we soak the net in warm, salty water with a bit of baby shampoo. This enables us to receive a good recording and also makes the sensors softer.
- Placing the net on a baby's head is quick and simple as it goes on just like a swimming cap. While we are putting the net on we will play with your baby to keep him/her from focusing on the net. Generally babies are quite happy having the net on (it's just like wearing a hat), but if your baby becomes fussy at any point, we can take the net off straight away.
- The net will be connected to a computer that records the brain's activity during the study. The net may leave pressure marks on your baby's head, which will go away in a couple of minutes after taking it off.
- We will also give you a Polaroid photograph of your baby wearing the net as a souvenir to take home.



## Infant Eye Tracking



*Baby in front of the eye-tracker and example of gaze data. The blue dot is where the baby was looking on the screen at a particular moment.*

Eye-tracking has been used for many years to understand attention and perception in infancy. The eye-tracker allows us to see exactly where the baby is attending on the screen.

The eye-tracker looks like a normal computer screen with the difference that it has incorporated a few light-emitting diodes. These emit infra-red light in a similar way to the light emitted by a camera in order to prevent the "red eyes", when using flash. The intensity of the light used is very small and is therefore harmless.

Once your baby is seated on your lap about 60 cm from the screen, we have to "calibrate" the eye-tracker. To do this, we present short animations on different parts of the screen and wait for your baby to look at them before taking a measurement. This will tell the machine the distance between baby's eyes (which varies from person to person). Sometimes we may need to do the calibration a few times, in case the baby has moved or not looked at one of the calibration points.

Once we have a good calibration, we're good to go! We will show your infant pictures or videos until the study is finished or your baby becomes bored or fussy. You can ask us to take a break or stop at any time.

Please do not hesitate to ask any questions you have about this method.



## Measures of Alertness

Researchers at the Centre for Brain and Cognitive Development are using equipment to measure arousal and activity levels. This includes measuring heart rate, movement, skin temperature and skin conductance. This helps us to understand how the body responds to particular events or types of information.

You may have seen doctors in hospitals or on television taking ECG (electrocardiography) readings of the electrical activity of the heart. The equipment we use is known as the Biopac system. We place sensors on the chest, back, arms, feet, hands or legs. These sensors can tell us about how different parts of the nervous system influence heart rate. We can also use these sensors to measure skin conductance.

We also use a wrist band called the Q-sensor to measure skin temperature, movement and skin conductance. This band has two sensors that sit against the skin and record skin conductance and skin temperature. Inside the band is an accelerometer that measures movement.

These techniques are completely safe and non-invasive. There is no risk associated with measuring these types of activity. For some types of measurement, a tiny current is passed between the sensors. This happens with some of the heart rate sensors, and the sensors on the wrist band. The charge is less than 1/1000000 of the power of a static charge you might receive when touching a door knob in a dry room.

If you are happy for us to proceed with the study, this is what will happen:

- You will be with your baby at all times during the study.
- We will also give you a Polaroid photograph of your baby wearing the stickers as a souvenir to take home.
- First we will stick on the heart rate sensors on your child's tummy, back, arms, hands, feet or legs.
- Then we will place wristbands around one or two of your child's wrists.
- While we are putting the sensors and wristband on we will play with your baby. Generally babies are quite happy having the sensors and wristband on, but if your baby becomes fussy at any point, we can take them off straight away.

Please ask if you have any questions.