

## Project Title: Neuroanatomical, Cognitive and Behavioural Phenotypes in Intellectual Disability of Genetic Origin

### INFORMATION SHEET FOR PARENTS

Thank you for your interest in this project. Your child is being invited to take part in a research study. Before you decide whether you wish them to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please contact us if there is anything that is not clear and if you would like more information. Take time to decide whether or not you wish your child to take part.

#### ***What is BINGO?***

BINGO stands for **B**rain and **B**ehaviour **I**n **N**eurodevelopmental disorders of **G**enetic **O**origin. BINGO is a research project involving researchers from the MRC Cognition and Brain Sciences Unit, University of Cambridge (MRC CBU) and the University of Oxford. We want to find out the different ways that genes can affect the brain, and want to understand the different problems that this can cause for individuals with ID.

#### ***What is the purpose of this study?***

Until recent years, it has been very difficult to discover the genetic cause of Intellectual Disability (ID), unless it was a common cause such as Down Syndrome (Trisomy 21). Now geneticists are able to study the genetic code in detail for each individual, making it possible to find genetic problems in many more individuals.

For the first time, this project will bring together developments in genetics and in brain science, to find out how specific gene differences have affected the brain in patients with ID.

We want to find out much more about how the brain develops and functions differently in individuals with ID, where a possible genetic cause has been found. We are also interested in creating new methods of assessments which are more appropriate for individuals with ID. In future, the information we gather might make it easier to support people with ID, because we will have a better understanding of why the specific pattern of problems has occurred for each person.

#### ***Why has my child been invited to participate?***

Your child has been invited to participate because they have been diagnosed with Intellectual Disability (ID) and they have previously had some genetic tests to look for a cause of their ID. If you decide that they could participate in this project, you and your child will be helping our research into ID by informing us about how different genes affect the brain to cause ID.

#### ***Does my child have to take part?***

No. It is up to you to decide whether or not your son or daughter could take part. If you decide that they can be included, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. Your decision will have no effect on the medical care that your child receives now or in the future.

### ***How is the study to be done?***

The project involves four separate research activities. Each of the different activities described below is entirely optional, and you and your child can choose which (if any) of the activities to take part in.

#### **Activity 1: Parent / carer questionnaires**

We will ask you to fill in some questionnaires about your child. You can complete these using pen and paper (we will send these to you by post) or online, according to your preference. If you choose to complete the questionnaires online, we will talk through the procedure beforehand over the telephone. This activity typically lasts about one and a half hours.

#### **Activity 2: Parent / carer interviews**

For this activity, a member of the project team will arrange to visit you at home or at another appropriate location, at a time that suits you. This a chance for us to find out more about your child's health and behaviour. We will ask you about their medical history and any treatment or therapies they are receiving or have received in the past. We will also ask you about some of your child's everyday behaviour. This activity typically lasts about two to three hours.

#### **Activity 3: Child cognitive and behavioural tasks**

This activity will also take place at home at a time that suits you and your family. Your child will be asked to try out some language tasks and simple puzzles. There will also be some tasks on a computer, and we would like to record a short (10-minute video of your child interacting with a familiar adult, i.e. a parent). We will always describe what we will be doing before starting the activities and give clear instructions. During this activity, your child can take breaks or stop at any time. This activity will last about two hours.

Afterwards, if you like, your child will be left with a touchscreen-enabled tablet computer. A number of interactive, user-friendly games will be available on the tablet which the participant can play and data stored from them will be downloaded by the research team when the tablet is returned. We will also leave you with a video camera, as we would like you to record your child interacting with an adult during everyday activities. We will arrange for the iPad and video camera to be returned to the MRC CBU after a period of 6 to 12 weeks.

#### **Activity 4: Brain scanning session**

For the final activity, we would like to organise a special MRI (magnetic resonance imaging) brain scan and MEG (magnetoencephalography) assessment for your child, if they are able to travel to Cambridge and if these activities are appropriate for them. This takes place at the MRC CBU in Cambridge. We will arrange transport (and if needed, accommodation) for your child and an accompanying adult.

### ***What is the MRI brain scan like?***

The MRI scanner is a large box with an open-ended tunnel through its middle. When you arrive at the MRI Centre, we will show you around the scanner and spend time making sure your child is comfortable. For the scan, your child lies on a comfortable, padded table that is moved into the opening of the scanner. Usually people bring some music with them that they like, which helps them to relax. During the MRI scan, your child has to lie still. You can stay in the scan room with your child. MRI uses a harmless magnetic field to obtain images of the brain, and information about blood flow in different parts of the brain. During the first part of the MRI session, we will use the scanner to take some very detailed pictures of the brain. After that, we may ask your child to do some very simple tasks in the scanner such as looking at pictures or listening to words. This is called functional MRI, and is a way of looking at activity in different part of the brain, almost like a video. We will practice the tasks outside the scanner until your

child is comfortable with them. The MRI scanning session lasts up to 45 minutes (usually less than this), and your child can ask to stop at any time.

### ***Are there risks and discomforts?***

MRI does not involve X-rays or radioactivity, and there are no known health risks.

The scanner does use powerful magnetic fields, and so all metallic items (coins, jewellery, keys, etc.), must be left in lockers outside the scanning area, and we will ask you to tell us if they have any magnetic metal in their body, for example surgical clips or heart valves, as these can be affected by the magnet. If they do have a heart valve or heart pacemaker, or other metal implants, and your child goes inside the scanner, it could be very serious (normal metal fillings in teeth are not affected by the magnet though, so are safe). If you are not certain about any aspects of the MRI safety checklist, scanning will not proceed until the researcher can obtain accurate information.

Most people find the scan easy to tolerate although some people can find it slightly confined and noisy initially. Your child will be provided with earplugs to cut down the noise, and they will be able to communicate with the researchers through a microphone at all times during scanning. We will ask you to tell us if they suffer significantly from claustrophobia. If they do not like the feeling of being inside the scanner for too long, they can ring a bell and we will take them out of the scanner immediately.

Like faces, brains come in all shapes and sizes, so that there are many normal variations of what the scan shows. There is a chance of less than 1 in 100 that your child's MRI scan may show a significant abnormality of which you are unaware. In such circumstances, you will be appropriately counselled. You would be offered a clinical appointment with a senior clinician, and, if appropriate, your child would be referred to the appropriate specialist in consultation with your GP in this circumstance. Such early detection has the benefit of starting treatment early but, in a small number of cases, may have implications for future employment and insurance.

### ***What is the MEG session like?***

MEG is a special type of non-invasive brain scanner. An MEG scanner simply sits over your child's head and measures naturally occurring brain activity. The MEG scanner is not noisy or enclosed and is generally not a difficult or intimidating experience. It will take around 30 minutes to set your child up for the scan. Metal in or on the body can interfere with the scan, so any metal will need to be removed e.g. coins, watches, underwire bras, hair clips etc. If your child has fixed braces, it will not be possible to take part in this particular study. Once comfortably seated, your child can watch a cartoon whilst the scan takes place. A relative/carer can be present throughout the scan.

### ***What will happen if my child doesn't want to carry on with the study?***

If you decide that your child can take part, you or your child are still free to withdraw from the study at any time without having to explain why. Any information collected that can still be identified will be destroyed if you wish. This will not affect any medical care that your child receives.

### ***What are the potential benefits of taking part?***

This research project will not bring any immediate medical benefits to you or your child. If this research leads to the development of new assessment methods, the participation of industry and commercial companies may be included, however you and your child will not benefit financially from this. However we hope that the information we collect from this research project will help other people with ID in future.

### ***Will information collected in the study be kept confidential?***

All information which is collected during the course of the research will be kept strictly confidential. The normal principles of confidentiality apply (just as when you visit your doctor) and there are very rare occasions, relating to potential serious harm to self or others, when doctors and researchers are obliged to break confidentiality. Clinical information and behavioural data will be anonymized and physically stored in locked filing cabinets, and electronically stored on secure servers at the MRC CBU, and only members of the research team working on this project will be able to access it.

MRI and MEG\_data will be stored on a secure network and only members of the MRC CBU and members of the research group will have access to the data. If you have previously taken part in other studies at the MRC CBU, or if in future you decide to take part in additional studies at the MRC CBU, then it is possible that the brain imaging data that we collect in this study may be also be used by researchers in those other studies to which you consent; the same standards of confidentiality will apply. If (and only if) you agree, then anonymised data may also be disclosed to other research teams, when those teams are working in close collaboration with the MRC CBU. This may include sharing the data with researchers outside the European Union, where different data protection laws apply, such as in the USA, for example. In these cases, those other researchers will have signed a Code of Conduct guaranteeing that the data will be kept confidential and securely. Consent to this data-sharing is an optional part of the research.

All enquiries concerning access to data held by the MRC Cognition and Brain Sciences Unit should be addressed to the Unit Research Governance Officer (Dr Tom Manly) at the Unit in the first instance. The researcher with whom you have contact will be able to tell you the name and address of this officer.

### ***Information collected online***

If you choose to complete the questionnaires online, the data that we record during the session will be sent back to a server at the MRC Cognition and Brain Sciences Unit (CBSU) through an encrypted (secure) connection. After the study is finished, the data will be moved to an offline secure storage area. Only certain members of the CBSU and members of the research group will have access to the data. In addition to the information you provide through your responses during the study, we collect information about the device, operating system and web browser that you're using. This information is essential for ensuring that the study runs properly for you, and allows us to investigate problems that might be due to device or software incompatibility. We may report summary statistics from this data, which may then be made public, but such reports will not include any information that would identify individuals who participated in the study. Cookies are information packets sent by the web server to the browser, and stored by the browser. This information is sent back to the server each time the browser makes a request. This enables the server to keep track of multiple requests that come from the same individual. The use of session cookies, which are cleared when you close your browser tab/window, is necessary in order for the study to run properly.

### ***What will happen to the information collected and the study results?***

They will be kept securely for a minimum of 10 years and possibly indefinitely. All data will be stored at the MRC Cognition and Brain Sciences Unit data archive in accordance with good research practice. We will analyse and write up the anonymised results and present them at scientific conferences, and we also plan to publish in scientific journals in order that the results will be available to other researchers and clinical teams. We will also provide a lay summary of the results of the study so the findings are available to all.

### ***How will I find out about the results of the study?***

When the study is completed a report will be sent to you, to inform you about the conclusions of the project. This will report the results of the project, but not individual test scores.

### ***Who is organising and funding the research?***

The study is being carried out by researchers at the MRC Cognition and Brain Sciences Unit (MRC CBU), University of Cambridge and University of Oxford. This project is funded by the Wellcome Trust/ Academy of Medical Sciences, The Newlife Foundation for Disabled Children, and the Baily Thomas Charitable Fund.

### ***Who has reviewed the study?***

This study has been reviewed by the Wellcome Trust / Academy of Medical Sciences, who then awarded Dr Baker, in collaboration with Dr Raymond, a research grant to pursue the study. The study has also been reviewed by the Newlife Foundation and the Baily Thomas Charitable Fund, both of which subsequently awarded Dr Duncan Astle, Dr Kate Baker, Professor Lucy Raymond and Professor Gaia Scerif a grant to continue the study. This study has been reviewed by the Cambridge Central Research Ethics Committee and given a favourable opinion. Research ethics reference: 11/EE/0330, substantial amendment 5, approval dated: 29/05/2019.

### ***What if there is a problem?***

If you are unhappy about the conduct of the study, and you wish to make a complaint about any aspect of the study, please contact Dr Kate Baker on the number below, or, if you prefer, you can contact the Study Sponsor:

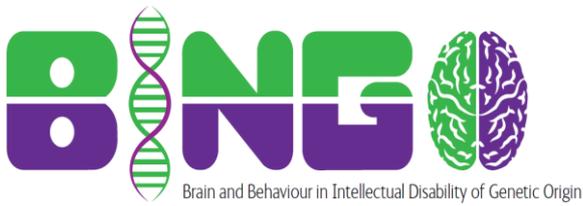
Research and Development Manager,  
Cambridge University Hospitals NHS Foundation Trust,  
Box 277 Addenbrooke's Hospital,  
Cambridge CB2 0QQ  
r&denquiries@addenbrookes.nhs.uk

### ***Are there compensation arrangements if something goes wrong?***

If you have a concern about any aspect of this study, you should first ask to speak to a member of the research team - their contact details are at the bottom of this letter. In the unlikely event of anything untoward happening, insurance has been arranged through the University and NHS. Specifically, this research will be covered, through University of Cambridge, by Newline policy B0823Q31000177, which has a £10,000,000 limit of indemnity. This provides cover for negligent and non-negligent harm. NHS indemnity also applies. Additional cover is in place for the unlikely event of negligent harm incurred during research activities on site at the MRC Cognition and Brain Sciences Unit. In addition, the MRC may offer, on a voluntary basis, an ex-gratia payment in the event of non-negligent harm.

### ***If you would like more information***

For an independent opinion about being involved in research in general, you can, if you wish, contact the Patient Advice and Liaison Service:



**MRC Cognition and Brain Sciences Unit,**  
15 Chaucer Road,  
Cambridge,  
CB2 7EF  
**bingo@mrc-cbu.cam.ac.uk**

Box 53,  
Cambridge University Hospitals NHS Foundation Trust,  
Cambridge  
CB2 0QQ.  
Tel: 01223 216756.  
Email: pals@addenbrookes.nhs.uk

We encourage you to think about the points made on this information sheet. It is up to you to decide whether or not your child should take part. If you do decide that they should take part you will be given this information sheet to keep and asked to sign a consent form. Your child can also sign this form if they understand the information about the project and wish to confirm that they assent to participation. You may have some questions and we would be very happy to discuss these with you. If you wish to discuss this study with someone outside the research team, you could contact the study sponsor, Cambridge University Hospitals NHS Foundation Trust, via the Research and Development Manager at the above address.

If you have questions, please contact **Dr Kate Baker** for specific details:

Tel: **01223 769433**  
Email: **bingo@mrc-cbu.cam.ac.uk**

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