Version Date: 10/19/2018

CONSENT FOR RESEARCH
Penn State College of Medicine
The Milton S. Hershey Medical Center

Title of Project: Neurophysiological Markers of Pediatric Irritability and its Response to Intervention
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Telephone Numbers: Weekdays: 8:00 a.m. to 5:00 p.m. (717) 531-0003 ext. 285968

After hours call (717) 531-8521. Ask for the operator to page Drs. Raman Baweja and James Waxmonsky or the child psychiatrist on 24-hour call.

Subject's Printed Name: _____

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

Some of the people who are eligible to take part in this research study may not be able to give consent because they are less than 18 years of age (a minor). Instead we will ask their parent(s)/guardian(s) to give permission for their participation in the study, and we may ask them to agree (give assent) to take part.

1. Why is this research study being done?

We are asking you and your child to be in this research study because your child is between the ages of 5 and 12, has been diagnosed with Attention Deficit Hyperactivity Disorder (ADHD; defined as problems with paying attention or controlling impulsive behavior), and has problems with irritability or anger.

Many children with ADHD are persistently irritable and have problems with frequent temper outbursts. Many children with ADHD take Methylphenidate based medication like Concerta, Metadate, Ritalin, Focalin, OR amphetamine based medication like Vyvanse or Adderall to help them listen and focus better and to help them control their behavior. For many children, medication for ADHD also improves their levels of irritability and anger but some children are more irritable when they take medication for ADHD, especially as it wears off at the end of the day. Right now, we have no way of predicting which children will become less irritable and which children will become more irritable when taking medication for ADHD. The purpose of the study is to examine the impact of ADHD medications on irritability to see if we can learn how to predict which children will show reduced irritability or anger and which will experience increasing levels.

Approximately 47 child/parent pairs will take part in this research study at Hershey Medical Center.

2. What will happen in this research study?

Participating families will receive an assessment of their child's behavior problems by a mental health specialist that evaluates whether their child meets criteria for ADHD and/or other related disorders that commonly occur with ADHD (i.e.: depression, anxiety, oppositional defiant disorder, conduct disorder). Children will also have their ADHD medication reviewed by experts in the management of ADHD and irritability. Your child will be given a prescription for ADHD medication if he/she is not currently taking medication for ADHD.

Visit 1 (Intake)

If you decide to participate in this study with your child, we will first interview you and your child at our office at Penn State Hershey Medical Center at 22 Northeast Drive, Hershey. This appointment would take about two hours and would be used to determine whether your child is potentially eligible for the study. The parent or legal guardian would complete a series of rating scales as well as computerized diagnostic interview focusing on their child's behavior. Ratings will also be sent to your child's teacher in order to assess the level of ADHD symptoms, behaviors, and impairment in school.

Visit 2 (Testing)

Your child will come to our center within 1- 4 weeks after visit 1 (as per family preference about date and time, which will be less disruptive to school for the child) to complete two computer tasks that measure his/her response to reward and loss and his/her ability to pay attention and resist impulses. On the testing day they should not take their medication for ADHD if it is a CNS Stimulant. Please ask the study staff and they will notify you if your child should skip their medication dose for the day. For the first task, your child will have to guess, by keypress, if there is a prize behind one of two doors presented on the computer screen. For the second task, your child will be asked to press a key when a specific image is presented on the computer screen. For both tasks, we will be measuring his/her electrical activity (brain waves) using electroencephalography (EEG)- the same type of tests doctors use to diagnose seizure disorders. An EEG measures the electrical activity in the brain and provides the researchers with a "picture" of brain activity (brain waves). Your child will wear a snug fitting cap, similar to a swim cap, with electrodes (small metal discs or sensors), which will be placed on the head with gel. Your child can earn a prize for trying their best. These tasks should take no more than 90 minutes to complete.

Baseline Assessment (1 week duration)

You will be asked to monitor your child's mood and behavior for the next week. We will ask you to complete a rating of your child's behavior twice a day using a survey application that can be downloaded to your own smartphone or tablet. Each rating should take less than 5 minutes to complete.

Visits 3-8 (Open label medication trial)

Your child will come to our center within 1- 2 weeks after baseline assessment for medication trial. You would meet with study doctors once every 1-2 weeks to adjust your child's ADHD medication. Children not currently taking ADHD medication will be required to start an ADHD medication that the study doctor will prescribe. You will meet with study doctors every 1 or 2 weeks for up to 12 weeks to adjust the ADHD medication. While there would be no charge for

these visits, you will be responsible for the cost of filling any prescriptions just like you would when you see your child's other doctors. This study would not use placebos or fake medication. Study doctors will work with to select a medication option that is affordable. Your child would need to come to each visit, as we need to check how well he/she is tolerating the medication without any concerning side effects. During our treatment program, only our study doctors should prescribe medication for ADHD or other emotional or behavioral problems for your child. Your child's weight, blood pressure and pulse will be measured at each visit. You will also be asked to fill out some rating scales at each visit.

Endpoint Assessment (1 week duration)
Once your child's medication is adjusted, you will complete twice a day ratings of your child's behavior at home for the next 7 days using the same survey application on your smartphone or tablet. The dose of your child's ADHD medication will only be changed if a side effect concern arises.

Visit 9 (Final visit)
You will come to our center within 1- 2 weeks after endpoint assessment, to complete the final rating scales for the side effects of medication and to return the study material including study provided rating scales. Rating scales will also be sent to your child's teacher in order to assess the level of ADHD symptoms, behaviors, and impairment in school.

If you/ your child withdraw or are withdrawn from the study prior to the completion of the study, research staff will contact you and schedule a follow-up visit for assessment of safety and to collect and obtain any possible data that may be available such as rating scales or your study provided cellphone.

What are my responsibilities if I take part in this research?
If your child takes part in this research, his/her major responsibilities will include:

- Attend and complete the intake and testing visits
- Take study medication as prescribed by the doctor
- Attend medication check visits (3-8)
- Attend the final visit (visit 9)

Your responsibilities include:

- Attend and complete the intake visit
- Complete rating scales through an app on your smartphone or tablet at designated time points during baseline assessment
- Fill your child's prescription medication as prescribed by the study doctor
- Attend medication check visits (3-8) and complete any rating scales necessary for the visit
- Complete rating scales through and app on your smartphone or tablet at designated time points during endpoint assessment
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3. What are the risks and possible discomforts from being in this research study?

You and your child may be stressed due to time commitment needed to attend sessions and complete the necessary ratings. We will try to schedule meetings at the time that works best for you and are collecting some ratings over the internet (using a free application that can be accessed from your smart phone or tablet) to reduce how many times you have to come to the clinic.

You and your child may become distressed or uncomfortable by the sensitive nature of some of the questions being asked. However, you and your child do you not need to answer any questions that you do not want to for any reason.

Participants (children or family) may become distressed as a result of not taking current CNS stimulant treatment for one day during the testing visit. This could lead to an increase in symptoms of ADHD (problems with paying attention or controlling impulses) and oppositional behavior. Many children do not take these medications 7 days a week and there is no medical risk from stopping the medication for a day. They will start to work again as soon as the next day. We will try to schedule this visit on a day that it is most convenient for your child to be off their ADHD medication. Participants using other nonstimulant ADHD medications (atomoxetine and alpha agonists – clonidine or guanfacine) can continue their medications as these may take several days to start working again after stopping them.

All medications can cause side effects so it is possible adjusting your child's ADHD medication could cause side effects. We will only use medications that have been well studied for the treatment of ADHD in children. Common side effects of ADHD medications include decreased appetite and weight loss, problems falling asleep, headaches, stomachaches, repetitive movements of the head or neck or repetitive noises (called tics) or being too quiet or dulled. CNS stimulant use during pregnancy may increase the risk for fetal preterm birth, low birth weight, and possibility of birth defects.

ADHD medication can also increase blood pressure and heart rate. Long term use of ADHD Medication can affect a child's growth rate. We also know that some children can become irritable or even aggressive with ADHD medication, especially as it wears off. One of the goals of the study is to determine how to predict which children might have these types of bad reactions to ADHD medication.

Rare side effects include visual disturbances, heart palpitations, mania or psychotic symptoms, or seizures. Children with seizures or serious heart problems could experience an increase in these problems if prescribed CNS stimulants so they should not enroll in this study. In addition, children with other forms of serious mental health problems, such as Bipolar Disorder or schizophrenia, could experience an increase in symptoms with methylphenidate so they should not participate in this study.

Your child will be closely monitored by study doctors for side effects. The dose can be changed or stopped at any time to address any concerns about side effects. You can always reach a psychiatrist 24 hours of the day should any adverse reactions occur. The risks of side effects from medication should be no different if you were to get ADHD medication from your child's pediatrician.

There are minimal risks associated with participating in the EEG assessment. Your child might experience boredom or fatigue while completing the computer tasks. There is a possibility of mild skin redness where the EEG electrodes and gel contact the skin; however, this is rare and generally temporary. Participants are assured that they can withdraw from the study at any time if they do not wish to complete the tasks, and participants are given breaks between EEG tasks to reduce fatigue.

There is a risk of loss of confidentiality if you or your child's information or identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. All information will be kept private and coded without identifying information and only study staff will have access to this information. Some data is not protected (mandated reporting of child abuse, clear imminent risk to self, others, subpoenaed records etc.) and that confidentiality cannot be 100% guaranteed despite the procedures described herein to protect their identity.

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to me?

There is no guarantee that your child will benefit from this research. The possible benefits your child may experience from this research study include an improvement in your child's ADHD and other behavior problems.

4b. What are the possible benefits to others?

The results of this research may guide the future treatment of children with ADHD.

5. What other options are available instead of being in this research study?

Your child does not need to participate in this research study to obtain treatment for his or her ADHD symptoms or problems with irritability or anger. Instead of participating in this research, your child could:

- Receive commercially available treatments for irritability. All medications prescribed by study doctors can also be obtained from doctors who are not part of the study. ADHD and irritability can also be treated with counseling services.
- Be part of a different research study if one is available
- Choose not to be treated for his/her irritability/ medical condition.

Before you decide if you want your child to be in this research, we will discuss the other choices that are available to your child. We will tell you about the possible benefits and risks of these choices.

6. How long will I take part in this research study?

If you and your child agree to take part, participation in the study will last approximately five to nine weeks, which includes 2 weeks for data collection over the application accessed from your smart phone or tablet and up to 12 weeks of medication trial.

7. How will you protect my privacy and confidentiality if I decide to take part in this research study?

7a. What happens to the information collected for the research?

Efforts will be made to limit the use and sharing of you and your child's personal research information. In our research files at The Milton S. Hershey Medical Center (HMC) and Penn State College of Medicine (PSU) we will include these identifiers: your and your child's name, address, phone number, medical record number, email address, date of birth, and a study ID.

- A list that matches your/ your child's name with a code number will be kept in secure data file in in a secure site at our research center.
- Your child's research records will be labeled with your child's study ID code and will be kept in a separate safe area in research offices of the Attention and Behavior Clinic.
- A copy of this signed consent form will be included in your HMC medial record. This means that other HMC healthcare providers will know you are in this study.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

7b. How will my identifiable health information be used?

If you and your child give consent, health information that can be traced to you or your child will be collected for this research study. In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so. We will use and disclose your information only as described in this form and in the HMC Privacy Notice.

The research team may use the following health information:

- Past, present, and future medical records
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

The following people/groups may see, use, and share your identifiable health information:

- HMC/PSU research staff involved in this study
- The HMC/PSU Institutional Review Board (IRB), a group of people who review the research study to protect subjects' rights and welfare
- The HMC/PSU Human Subjects Protection Office
- The HMC/PSU Research Quality Assurance Office
- Researchers from other campuses of Penn State University who are part of this study
- Non-research staff within HMC/PSU who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- Federal and state agencies (such as the U.S. Food and Drug Administration, the Office for Human Research Protections, the Department of Health and Human Services, the National Institutes of Health, and other U.S. or foreign government bodies that oversee or review research)
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- The sponsor(s) of this study (Children's Miracle Network) and the people or groups it hires to help perform this research
- A group that oversees the data (study information) and safety of this research
- Organizations that provide independent accreditation and oversight of hospitals and research

- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)

These groups may also review and/or copy your child's original PSU/HMC records while looking at the results of the research study. It is possible that some of the other people/groups who receive your health information may not be required by Federal privacy laws to protect your information. We share your child's information only when we must, and we ask anyone who receives it from us to protect your privacy.

Because research is an ongoing process, your permission for the use, storage and sharing of you and your child's health information will continue indefinitely.

Your privacy rights:

- The free application used to collect ratings directly from your smart phone or tablet is called LifeData, LLC. LifeData, LLC keeps your information private and does not share or sell your information. LifeData, LLC does not use your information for their own purposes except in certain circumstances such as a court subpoena or if you make your own information public.
- Data collected from the free LifeData, LLC application is stored on servers located in the United States. This storage process happens automatically when surveys are completed over WiFi. If completed surveys occur through your data plan, the data is stored on the device until the device is connected to WiFi.
- LifeData, LLC collects geographic location from the device you choose to use to access the app. However, you have the option of allowing or disallowing this information to be collected. Additionally, if you allow LifeData, LLC to collect your geographic location, you may change your mind and disallow the information to be shared by going into your device's settings.
- LifeData, LLC collects your mobile device's unique identification number and stores it on their server. This means LifeData, LLC and the research team can tell if you are using an android or iOS (Apple) product when completing surveys through the LifeData, LLC application. This also allows the LifeData, LLC application server to send you notifications to your smart phone or tablet to alert you that you have a survey to complete. LifeData, LLC cannot access your personal information through the collection of your mobile device's unique identification number.
- You have the right to refuse to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you will not be able to take part in this research study.
- You have the right to withdraw your permission for us to use or share you or your child's health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing using the address on the front of this form. Once permission is withdrawn, your child cannot continue to take part in the study.
- If you withdraw your permission, we will stop collecting health information about your child for this study; we may continue to use and share your child's health information that we already have if it is necessary for safety and scientific soundness of the research study; and we will not be able to take back information that has already been used or shared with others.

You have the right to see and get a copy of your child's health information that is used or shared for treatment or for payment. However, you may not be allowed to see or copy certain health information that is a part of this research study. This is only for the period of the study. You will be allowed to see that information when the entire research study is complete.

8. What are the costs of taking part in this research study?

8a. What will I have to pay for if I take part in this research study?

For costs of tests and procedures that are only being done for the research study:

- You and/or your insurance company will not be charged for the cost of any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your condition.
- The research-related tests and procedures that will be provided at no cost to you include:
  - All study visits
  - Computer tasks with measurement of brain waive activity
  - A free application download directly onto your smart phone or tablet.

For costs of medical services for care you would receive even if you were not in this research study:

- You and/or your insurance company will be responsible for the cost of prescribed study medications. Study doctors will work with the family to select medication options that are affordable. Most FDA approved ADHD medications come in generic forms or have brand names that are on most major local formularies.
- Neither you or your child or your child's insurance company will be charged for the cost of any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your child's condition.
- All research-related tests and procedures will be provided at no cost.
- The study does not pay for services that are not directly provided by research staff.

If you have any questions about costs and insurance, ask the research study doctor or a member of the research team.

8b. What happens if I am injured as a result of taking part in this research study?

It is possible that your child could develop complications or injuries as a result of being in this research study. If your child experiences a side effect or injury and emergency medical treatment is required, seek treatment immediately at any medical facility. If your child experiences a side effect or injury and you believe that emergency treatment is not necessary, you should contact the principal investigator listed on the first page of this consent form as soon as possible and he/she will arrange for medical treatment.

HMC/PSU compensation for injury

- There are no plans for HMC/PSU to provide financial compensation or free medical treatment for research-related injury.
- If an injury occurs, medical treatment is available at the usual charge.
- Costs will be charged to your or your child's insurance carrier or to you/ your child.
- Some insurance companies may not cover costs associated with research injuries.
- If these costs are not covered by your insurance, they will be your responsibility

When you sign this form you are not giving up any legal right to seek compensation for injury.

9. Will I be paid to take part in this research study?

Families will be provided with a $10 gift card and prize to your child for completing the single lab-testing day and $20 gift cards for each week that the smart phone/ tablet ratings are completed. Standard data rates apply for download and use of the survey application. Surveys through the app may be completed over WiFi or through your data plan. Any data costs incurred will not be reimbursed. All services at our office will be provided at no charge. Parking is free at the HMC campus and the 22 Northeast Drive Clinic. Families will not be reimbursed for travel.

10. Who is paying for this research study?

The institution and investigators are receiving a grant from Children's Miracle Network to support this research.

11. What are my rights if I take part in this research study?

Taking part in this research study is voluntary.

- You or your child do not have to be in this research.
- If you and your child choose to be in this research, you and your child have the right to stop at any time.
- If you and your child decide not to be in this research or if you and your child decide to stop at a later date, there will be no penalty or loss of benefits to which you and your child are entitled.

If you or your child stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect medical information from your child's routine medical care. If you agree, this data will be handled the same as research data. If you withdraw completely from the research study, no further information will be collected and you and your child's participation will end. You and your child may discontinue taking part at any time without penalty or loss of benefits to which you and your child are otherwise entitled.

The research doctor may take your child out of the research study without your permission.

- Some possible reasons for this are: your child's condition has become worse, you did not follow the instructions of the study doctor, or you repeatedly miss appointments
- If your participation ends early, you and your child may be asked to visit the research doctor for a final visit.

During the course of the research you will be provided with any new information that may affect your child's health, welfare or your decision to continue participating in this research.

12. If I have questions or concerns about this research study, whom should I call?

Please call the head of the research study (principal investigator), Raman Baweja M.D. at 717-531-0003 ext. 285968 if you:

- Have questions, complaints or concerns about the research.
- Want to speak with a study clinician about your child's behavioral problems
- Believe you or your child may have been harmed by being in the research study.

For after hours, please call 717-531-8521 and ask the operator to page Dr. Baweja or Dr. Waxmonsky, or the child psychiatrist on call.

You may also contact the research protection advocate in the HMC Human Subjects Protection Office (HSPO) at 717-531-5687 if you:

- Have questions regarding your and your child's rights as a person in a research study.
- Have concerns or general questions about the research.
- Have questions about your and your child's privacy and the use of your child's personal health information.

  You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

You may visit the Penn State College of Medicine's Clinical Research web site at http://med.psu.edu/clinical-research/faqs for:

- Information about your rights when you are in a research study;
- Information about the Institutional Review Board (IRB), a group of people who review the research to protect your rights; and
- Links to the federal regulations and information about the protection of people who are in research studies. If you do not have access to the internet, copies of these federal regulations are available by calling the HSPO at (717) 531-5687.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you or your child. At most, the web site will include a summary of the results. You can search this web site at any time.

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INFORMED CONSENT AND AUTHORIZATION TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative and have answered any questions he/she has about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent and Authorization

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Parent(s)/Guardian for Child

By signing this consent form, you indicate that you permit your child to be in this research and agree to allow his/her information to be used and shared as described above.

_____	_____	_____	_____
Signature of Parent/Guardian	Date	Time	Printed Name

ASSENT FOR RESEARCH

The research study has been explained to you. You have had a chance to ask questions to help you understand what will happen in this research.

You Do Not have to be in the research study. If you agree to participate and later change your mind, you can tell the researchers, and the research will be stopped.

You have decided: **(Initial one)**

___ To take part in the research.
___NOT to take part in the research.

_____	_____	_____
Signature of subject	Date	Printed Name