



To whom it may concern.

My name is Mel Anderson.

I am the research liaison for the PURA Syndrome Foundation. The PURA Syndrome Foundation commenced a joint research collaboration with *Danish Epilepsy Research Hospital* (Denmark) and *Maastricht University Medical Center and Academic Centre for Epileptology* (The Netherlands) in 2018 to better understand epilepsy and general neurological issues occurring with PURA patients. The Foundation is supporting research by providing access to the study for PURA syndrome families and funding open access for research clinical papers resulting from the study.

In 2018, clinical data for a research paper on neurology genotype/phenotype correlations for PURA syndrome was collected. This manuscript is currently under draft.

For this next round of neurology research in 2019, researchers are collecting and studying EEG "raw data" (digital recordings of EEG waveforms) that have been previously recorded for PURA syndrome patients. For this study, patients who have been previously published may also be included. This collection of existing EEG reports and raw data from PURA patients may also include patients with and without diagnosed epilepsy.

We hope that in gaining a clearer understanding of the issues being faced by PURA patients, we can develop better care and treatment options long term for PURA syndrome.

The patient's mother/father put her/his child forward for the research involvement.

Child name:

DOB:

If patient is already published, please state paper:

The research contact for this EEG study is Katrine Johannesen MD, PhD stud.

EEG digital data can be posted to Katrine on CD, DVD or sent via an electronic dropbox.

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The Danish Epilepsy Hospital
Kolonivej 1 4293
Dianalund Denmark
Att: Katrine Johannesen*

Katrine can provide details regarding involvement in the study, consent and medical information required. Co-authorship will occur with publications involved in this EEG research.

I have attached the EEG study overview for you.

Could you please consider including your PURA patient in this EEG neurology research and making contact with me via email so I can formally connect you to Katrine and the research team.

Please do not hesitate to email me if you have any questions.

Kindest regards,
Mel

Mel Anderson

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PURA Syndrome Epilepsy Research Project – EEG study

In 2014, the first PURA patients were described in medical literature. Symptoms including severe neurodevelopmental delay, hypotonia, respiratory problems, feeding difficulties, hypothermia and seizures were reported in patients with PURA mutations. Epilepsy in particular is a concern in the development and treatment of patients, with seizure events reported in over 50% of diagnosed individuals.

An electroencephalogram (EEG) is a test used to find problems related to electrical activity of the brain, including seizure events. An EEG tracks and records brain wave patterns. Small metal discs with thin wires (electrodes) are placed on top of the scalp, and they send signals to a computer to record the results. Normal electrical activity in the brain makes a recognizable pattern (waveform). Through an EEG, researchers can look for abnormal patterns that indicate seizures from other non-epileptic movements. We hope to analyze existing EEG data from PURA patients, to identify what are standard waveform patterns for PURA syndrome, and what common patterns and occurrences we see when seizures are and aren't occurring.

While general clinical research has led to a greater understanding about the characteristics of PURA syndrome, there are still a lot of unanswered questions about how and why seizures and epilepsy develop, how they can best be treated and prevented. We hope that in gaining a clearer understanding of the epilepsy issues being faced by PURA patients, we can develop better care and treatment options long term for PURA syndrome children and adults.

Supporting Institutions/Groups in EEG research:

- Danish Epilepsy Research Hospital (Filadelfia), Denmark
- Maastricht University Medical Centre and Academic Centre for Epileptology (The Netherlands)
- Temple University Philadelphia, USA
- PURA Syndrome Foundation
- PURA syndrome families

This EEG research involves:

- Neurology studies of patients with PURA syndrome, known as clinical research.
- Collection of existing EEG (electroencephalography) reports and data from PURA patients – including patients with and without epilepsy.
- Comparison and analyses of existing EEG “raw data” (digital recordings of EEG waveforms).
- Studying how PURA seizures start, spread, and stop in both human and animal models.
- Studies of brain development and epilepsy for PURA syndrome.

This EEG research will also help support:

- Research using induced pluripotent stem cells (iPSC) of PURA patients.
- Brain imaging for viewing the structure and functioning of the brain (neuroimaging), such as magnetic resonance imaging (MRI) and positron emission tomography (PET).
- Use of PURA animal models (Zebrafish, Mice) to screen potential new treatments for PURA syndrome epilepsy.
- Development of an epilepsy treatment guide supporting both PURA syndrome families and their clinicians.

If you decide to take part in this study, patient data collected by the Danish Epilepsy Research Hospital (Filadelfia), Denmark, and Maastricht University Medical Centre and Academic Centre for Epileptology (The Netherlands), will be exchanged between them in an anonymised form as part of the study. Outcomes of this research may be shared in reports, publications and conferences. Questions regarding this research project can be emailed to the PURA Syndrome Foundation Research Liaison, Mel Anderson m.anderson@pura-syndrome.org