WORKSHOP 2016

RESEARCH SUMMARIES

JANUARY 16 AND 17, 2016

CHELSEA HOTEL, TORONTO, ONTARIO

Contents

Welcome to our EpLink Workshop 2016 overview! Below are brief summaries of the research talks that took place on January 16-17, 2016 at our annual EpLink Workshop, organized by date and time of the presentations. To look for specific researchers or talk topics, please refer to the table of contents on pages 1 and 2. Also, if you come across any unfamiliar terminology **(in bold)**, please feel free to look at our terms and definitions outlined on page 17 onward.

DAY 1 – SATURDAY, JANUARY 16, 2016 – A.M. PRESENTATIONS

Dr. Asuri N. Prasad | Epilepsy & Comorbid Disorders in Canadian Children: Exploring National Longitudinal Survey of Children and Youth (NLSCY) Data

- Dr. Asuri N. Prasad is analyzing data gathered in the National Longitudinal Survey of Children and Youth (NLSCY). Run by Statistics Canada, this survey collected information on social and medical factors from a sample of 25,000 children ages 0-11 years, with each participant being surveyed every 2 years for a total of eight cycles (from 1994 to 2009). Of NLSCY survey data in cycle 3, collected from children ages 0-15, it was found that children with epilepsy accounted for 56.87%. Of these children:
    - 10.03% had at least 1 other neurological condition (known as a **co-morbidity**)
    - 23.57% had at least 2 other neurological conditions
    - 9.53% had three or more other neurological conditions
- In a recent EpLink-funded publication, Dr. Prasad found that children with epilepsy had a lower level of academic achievement on school readiness tests relative to their peers. Scores were likely to be lower than their peers when children had epilepsy and additional health or neurological conditions.
- IMPACT: This research demonstrates the need for the school system to screen children at risk early and allocate resources to support children with epilepsy and other neurological conditions.
- NEXT STEPS: Dr. Prasad plans a longitudinal study following 179 children who reported having epilepsy in the NLSCY survey to determine how the number of people with epilepsy changes with age, how long children typically have epilepsy, and what proportion experience recovery from their epilepsy.

Dr. Miguel Cortez | Monitoring Brain Activity to Prevent infantile Spasms (West's Syndrome)

- Previous studies have shown that changes in brain wave activity (known as **hypsarrhythmia**) may be seen before **infantile spasms** appear in **West's Syndrome**. **Hypsarrhythmia** is more frequently seen in children at risk for certain intellectual disabilities and may be predictive of cognitive outcomes.

- This study will record brain activity (using **electroencephalography** or **EEG**) in children who are at risk for developing **West's Syndrome** (e.g. before the appearance of **infantile spasms**).

- IMPACT: Early detection of **hypsarrhythmia** may allow for early intervention (e.g. with Vigabatrin or Adrenocorticotropic Hormone (ACTH)) to prevent **infantile spasms** and improve cognition.

- NEXT STEPS: Dr. Miguel Cortez and colleagues will conduct a clinical study to detect **hypsarrhythmia** in children prior to **infantile spasms** and study the impact of preventative therapy.

Dr. James Eubanks | A New Treatment for Rett Syndrome?

- Impairments in the function of **mitochondria** (the structures found within brain cells that are responsible for producing energy) have been seen in people with **Rett syndrome**. **Rett Syndrome** also shares several features with other **mitochondrial** diseases. Without properly functioning **mitochondria** in **Rett Syndrome**, there is a decrease in energy production and an increase in the production of toxic oxygen compounds within the brain.

- Dr. James Eubanks and colleagues found that anti-oxidant treatment assisted in improving locomotion (walking) and nesting behaviours (skills to build and maintain homes that are representative of social behaviours) in mice with **Rett Syndrome** symptoms.

- IMPACT: Anti-oxidants may be useful in the management of **Rett Syndrome** symptoms. Further research is required.

- NEXT STEPS: Dr. Eubanks will examine the clinical use and safety of anti-oxidants in children with **Rett Syndrome**.

Dr. Mac Burnham | Treating Epilepsy with a Medical Marijuana Extract

- Studies performed in animals suggest that the medical marijuana extract, **cannabidiol**, stops generalized seizures and may perhaps stop complex partial seizures.
- Dr. Mac Burnham is currently organizing a clinical trial to test the effectiveness of **cannabidiol** (with and without low levels of the marijuana extract **tetrahydrocannabinol**) for the management of uncontrolled seizures in adults.
- IMPACT: If **cannabidiol** is shown to stop seizures in adults with epilepsy, we hope it will lead to wider use of **cannabidiol** for treatment of **drug-resistant epilepsy** through a doctor's prescription.
- NEXT STEPS: Dr. Burnham will finalize the research study design and submit a clinical trials application to Health Canada in 2016.

DAY 1 – SATURDAY, JANUARY 16, 2016 – P.M. PRESENTATIONS

Dr. Sharon Whiting | Decreased Heath Care Utilization Post Initiation of the Ketogenic Diet in Ontario

- Dr. Sharon Whiting and her colleagues compared the healthcare usage of children with epilepsy before and after starting the **ketogenic diet** – a low carbohydrate, high fat and adequate protein diet that is effective for the management of **drug-resistant epilepsy**.
- Surveying children from 2000 to 2010, it was found that children used less healthcare resources after starting the diet. Also, the reduced healthcare usage resulted in reduced healthcare costs.
- IMPACT: This study highlights the benefits of starting children with **drug-resistant epilepsy** on the **ketogenic diet**. Not only will children benefit from better access to the diet, but the government could save in healthcare costs by making the diet more readily available.
- NEXT STEPS: EpLink would like to work with the Community Epilepsy Agencies to inform the Ministry of Health about the health and economic benefits of the **ketogenic diet**, and the need for more dietitians in Ontario.

Dr. Elizabeth Donner | Comparing the Effectiveness of Ketogenic Diets in Children

- In the classic **ketogenic diet**, fat makes up 90% of the calories. The classic **ketogenic diet** is highly restrictive and unpleasant for some children. An alternative to the **ketogenic diet**, the **MCT ketogenic diet** is less restrictive - fat makes up 70% of the calories and participants use medium chain triglyceride (MCT) oil. Both diets are known to be effective at treating seizures. While the exact mechanism is not known, it is believed that increasing levels of ketones in the body are important for seizure suppression; however, it has been observed that the **MCT ketogenic diet** does not produce as many ketones. Dr. Elizabeth Donner and colleagues are studying ketone levels and seizure control in different diet formulations.
- Dr. Donner's study found that despite ketone levels being lower on the **MCT ketogenic diet**, there was no significant difference in seizure control between the classic **ketogenic diet** and the **MCT ketogenic diet** at 6-month follow-up.
- IMPACT: These findings suggest MCT oil may have a beneficial effect on seizure control independent of ketone production.
- NEXT STEPS: Dr. Donner plans to examine other factors that may contribute to seizure control in children treated with **ketogenic diets**.

Dr. Mac Burnham | A Brief Comment: Can Adding Fish Oil to a Normal Diet Control Seizures?

- Fish oil is high in **omega-3 polyunsaturated fatty acids (PUFAs)** and these 'healthy fats' have been shown to reduce the likelihood of seizures (increasing seizure threshold) in animals.
- A clinical study for adults is currently taking place at Toronto Western Hospital - in collaboration with Dr. Peter Carlen and his colleagues - looking at the addition of fish oil to the diet for managing seizures.
- IMPACT: If **PUFAs** are linked to improved seizure control in humans, this study could highlight the usefulness of **omega-3** supplements in the management of seizures, and lead to its widespread use for **drug-resistant epilepsy**.
- NEXT STEPS: The study is currently in progress and preliminary results are expected this summer.

Dr. Tariqus Salam | Refining Brain Stimulation in Rodent Models of Epilepsy

- **Brain stimulation** experiments in rodent models have yielded optimal results in stopping seizure activity. Dr. Tariqus Salam and colleagues have found the following results:
    - **Closed-loop stimulation** allows stimulation to be administered only when needed.
    - Stimulation is most effective when it occurs in the early stages of the seizure.
    - Stimulation given at low frequency (5 Hz) and low current (150 µA) is most effective.
- IMPACT: This type of feedback stimulation could be a novel therapy for epilepsy as well as other neurological and psychiatric disorders.
- NEXT STEPS: Dr. Salam and colleagues plan to test the safety and effectiveness of this **brain stimulation** technique in humans. This on-demand stimulation is expected to have few or no side effects in patients with epilepsy.

Dr. Taufik Valiante | Understanding If Brain Stimulation Can Stop Seizures & Understanding How Brain Stimulation Starts/Stops Seizures

- A clinical study led by Dr. Taufik Valiante will take the **EEG** electrodes implanted within the brains of people with epilepsy and couple these electrodes to a new computer model that will (i) sense precisely *when* a seizure is starting, and (ii) use a new mathematical approach to determine *where* the seizure is starting. This will allow for more targeted **brain stimulation** to stop seizures.
- In another study using brain slices, Dr. Valiante and colleagues have shown that over-stimulating cells which typically decrease brain activity can trigger a seizure.
- IMPACT: These studies may help us to understand the mechanism of how seizures start, which is essential in learning how to stop them.
- NEXT STEPS: Upon receiving ethics approval, Dr. Valiante will begin recruitment for his clinical study using **EEG** to detect seizures and **brain stimulation** to stop them.

Dr. Berge Minassian | Moving Towards a Therapy for Lafora Disease

- In individuals with **Lafora disease**, **genetic mutations** cause an over-production of long sugar chains (known as glycogen, which normally does not form in the brain). Because of their structure, these sugar chains clump together in the brain and cause symptoms of **Lafora disease**.
- Blocking the enzyme that makes glycogen in the brain cured symptoms of **Lafora disease** in a rodent model.
- IMPACT: Drugs that block glycogen production may be effective in curing symptoms of **Lafora disease** not only in rodents but potentially in humans as well.
- NEXT STEPS: Dr. Berge Minassian will design a clinical trial examining the safety and effectiveness of a drug that blocks glycogen production in children with **Lafora disease**.

Dr. John Andrews | The Ketogenic Diet in a Pill

- Ketogen Pharma Inc. is creating new drugs based on the **ketogenic diet**, which increases ketone levels in the body. Ketones are anti-convulsant and can work to enhance the effectiveness of other anti-seizure medications.
- Ketogen Pharma Inc. is making 'the **ketogenic diet** in a pill' by using known anti-seizure medication structures and combining these drugs with different ketone groups.
- IMPACT: Creating new anti-seizure medications based on the **ketogenic diet** may reduce seizures in people with **drug-resistant epilepsy**.
- NEXT STEPS: Ketogen Pharma Inc. has the potential to develop and launch a compound within two years and additional compounds in about seven years.

Dr. Peter Carlen | A New Way to Treat Status Epilepticus at Home

- There is a need for improved, fast-acting, easy-to-administer therapeutics for **status epilepticus** – a medical emergency where an individual has a prolonged seizure and/or a series of seizures.
- EastGate BioTech Inc. is developing a new drug delivery system – a lorazepam anticonvulsant spray - that will make it possible to deliver small volumes of lorazepam in a form that easily crosses the mucous lining in the nose or mouth and then rapidly enters the bloodstream. This drug system will be delivered by a specialized oral device that can spray a small volume of lorazepam into the mouth or nose, or onto the lips, for rapid treatment of **status epilepticus** even when an individual's teeth are clenched in the midst of a seizure.
- IMPACT: This spray form of the anti-seizure medication lorazepam can be administered at home and may not require an emergency room visit, which would have both health and economic benefits.
- NEXT STEPS: Once development is complete, a clinical trial will be organized within the next year in Canada. Clinical trials will likely be expedited due to the large amount of pre-clinical and clinical data already available on lorazepam.

Dr. Malik Slassi | A New Drug for Epilepsy and Neuropathic Pain

- Fluorinov Pharm Inc. is developing a pill - which is chemically *unrelated* to current anti-seizure medications - for the management of epilepsy.
- Animal testing has shown that this compound has a superior safety profile to currently available anti-seizure medications and is effective for the treatment of complex partial seizures, inflammatory pain and **neuropathic pain**.
- IMPACT: Although more testing is needed, this compound could potentially be developed for use in humans to manage both seizures and **neuropathic pain**.
- NEXT STEPS: Dr. Malik Slassi plans to organize a clinical study examining the safety and effectiveness of this compound for people with epilepsy.

Dr. Ron Gonzalez | A SMART Headset for Portable Long-Term Monitoring of Brain Activity

- Avertus is developing the first commercial brain wave monitoring headset (using **EEG**), which when placed on the head, can be used to detect when a seizure starts.
- Ongoing improvements to the device include decreasing noise (background signals) during movements, improving signal quality and making it comfortable to wear during sleep.
- IMPACT: This project aims to create a practical, portable headset that can accurately detect when a seizure starts, which can be useful for diagnosis and for treatment when coupled with **brain stimulation**.
- NEXT STEPS: Avertus has received approvals for preliminary patient testing and plans to start selling commercial devices for clinical trial use and non-medical applications in late 2016.

Dr. Vera Nenadovic | Order from Chaos: Early Signs of Infantile Spasms

- BrainsView Inc. presented a new method to identify brain wave changes (known as **hypsarrhythmia**) associated with **infantile spasms**.
- IMPACT: This technology can be useful in diagnosing and monitoring **infantile spasms** in **West's Syndrome**.
- NEXT STEPS: This method will be applied to detect **hypsarrhythmia** in children at risk for developing **West's Syndrome** in a research study lead by Dr. Miguel Cortez and Dr. Blathnaid McCoy at SickKids.

Dr. Hossein Kassiri | A Battery-less and Wireless Implantable Microsystem for the Monitoring and Treatment of Seizures

- BrainCom Tech is developing a **closed-loop stimulation** system – either for implanting in the brain or for wearing on the scalp - that monitors, detects and can control seizures in patients with epilepsy. An implantable prototype of this system that is placed on the head has already been developed and tested in rodents with temporal-lobe epilepsy. It features:
    - An advanced computing method to detect and stop seizures before they start
    - Wireless power and data communication
    - High sensitivity (accurately detect when seizures start) and high specificity (minimizing the false detection of a seizure when none is present)
- IMPACT: The technology can be applied for both implantable and wearable headset devices, with the objective of detecting, diagnosing and treating seizures accurately and rapidly.
- NEXT STEPS: Dr. Hossein Kassiri and his team will continue developing the implantable device and test its safety and effectiveness in people with epilepsy.

DAY 2 – SUNDAY, JANUARY 17, 2016

Dr. Jorge Burneo | Why Don't Doctors Refer to Surgery?

- In Dr. Jorge Burneo's recent publication, a total of 10,661 patients identified as having **drug-resistant epilepsy** were followed for a two-year period and during this time, only 124 patients (1.2%) were referred for seizure surgery.
- Recently, Dr. David Steven did a study in which a survey was given to **general practitioners (GPs)** to understand why surgery referral rates were so low. The survey, completed by 201 **GPs**, found the following results:
    - 81% of **GPs** always refer (typically those with less than 20 years in practice); of these **GPs**, 89% refer to a general neurologist rather than an **epileptologist** (a neurologist who specializes in treating epilepsy)
    - 53% don't know what type of surgery is needed
    - 44% don't know the risks of surgery
    - 45% don't know the benefits of surgery
- IMPACT: This study demonstrates the need for more referrals to seizure surgery and better overall healthcare access, especially since it was found that 12% of people with **drug-resistant epilepsy** died within two years of diagnosis.
- NEXT STEPS: Dr. Burneo will focus on the role of neurologists, access to **epileptologists** and access to Epilepsy Monitoring Units as the source of the poor referral rates. EpLink would also like to work with the Community Epilepsy Agencies to increase awareness about epilepsy surgery as a treatment option for people living with seizures.

Dr. Ali Khan | Brain Imaging for Epilepsy

- Brain imaging using multiple **MRI** features (such as **tractography** to construct 3D models of neuron pathways in the brain) can help to accurately detect lesions for removal and reduce deficits in brain function after surgery.
- IMPACT: More precise imaging and lesion detection could improve targeted surgery outcomes and reduce side effects. It may also mean that more patients could be eligible for surgery.
- NEXT STEPS: Drs. Ali Khan and Terry Peters plan to conduct a clinical trial – in collaboration with Synaptive Medical - using **MRI tractography**. Their trial will specifically look at targeted removal of the anterior temporal lobe (located on the sides of the brain slightly above your ears), while avoiding neuron pathways related to vision.

Dr. Jorge Burneo | Using Advanced Imaging to Locate Where Seizures Start

- Brain imaging is essential for the localization of where seizures start, and whether surgery is appropriate. Advanced imaging (including **tractography**) can give crucial information:
    - 3-Tesla **MRI:** This standard **MRI** is important for assessing parts of the brain that did not form properly during development (e.g. differences in the cortex structure). These areas are typically responsible for starting a seizure and can also be used to identify areas that do not function properly.
    - 7-Tesla **MRI:** High-resolution **MRI** gives us a more detailed picture of the brain's structure.
- IMPACT: The use of advanced imaging can provide us with additional information needed to localize seizures and ensure surgeries are successful.
- NEXT STEPS: The goal of this project is to implement a standard imaging protocol across all EpLink centres so that a patient who is assessed for surgery in London will get the same assessment as someone who is seen in Toronto.

Dr. Mary Lou Smith | IQ Changes in Long-term Follow-Up After Epilepsy Surgery

- In previous studies, it has been shown that there is little to no change in intelligence measures (such as IQ) in short-term follow-up after epilepsy surgery in children.
- In Dr. Mary Lou Smith's study, participants who were seizure free at long-term follow-up (between 4-11 years), either from surgery or medication, eventually showed an improvement in general IQ. It was also found that participants who continued to have seizures had declines in various aspects of intelligence, whereas participants who were seizure-free had increases, resulting in a difference between the groups at long-term follow-up.
- IMPACT: This study shows that being seizure-free (either from surgery or medication) is related to improved intellectual function in the long term. Importantly, this also demonstrates the need for research into improved therapies for individuals with **drug-resistant epilepsy**, with the hopes that they can also experience the benefits of seizure freedom.
- NEXT STEPS: Dr. Smith plans to investigate whether other aspects of cognition (e.g., language, academic skills, memory) also improve with seizure freedom in long-term outcomes.

Dr. Kathryn Hum | The EpUp Study: Preliminary Analyses

- Distance-delivery of a group therapy program for people with epilepsy has been proven effective in reducing depressive symptoms. However, it is unclear how much the social support or the strategies learned with therapy contribute to these improvements.
- This study compares the efficacy of two distance-delivery programs - UPLIFT and EpINFO programs - which are designed for people with epilepsy and depression.
- Preliminary results have shown trends towards reduced depressive symptoms and improved **quality of life**, although further data collection and analyses are required.
- IMPACT: This study marks the first time these two intervention programs have been offered here in Canada.
- NEXT STEPS: Dr. Kathryn Hum and her colleagues plan to analyze whether treatment effects will be significant at long-term follow-up.

Dr. Gabriel Ronen | Patient Reported Outcomes (PROs) in Childhood Epilepsy

- **Patient Reported Outcomes (PROs)** are any report coming *directly* from patients, without interpretation, about how they are functioning or feeling. **PROs** are essential to understanding lived experience.
- A recent publication by Dr. Gabriel Ronen and colleagues (Epilepsy & Behavior, 2015) found that children with epilepsy feel as though they have the same **quality of life** as children from the general population, despite their condition. However, their parents believe that their children have a lower **quality of life** in the domains of 'mood and emotions' and 'bullying' compared to parents of children from the general population and parents of children with cerebral palsy.
- Another publication (Neurology, 2015) showed that 'mental health', 'parental and peer support' are closely associated with a child's self-reported **quality of life**. Interestingly, seizure severity had no influence on the **quality of life** of 480 Canadian children with epilepsy ages 8-14 years old.
- IMPACT: These studies highlight the importance of collecting information *directly* from children with epilepsy, and understanding the psychosocial factors that influence their **quality of life**.
- NEXT STEPS: Dr. Ronen will encourage clinicians and epilepsy programs to provide support for the psychosocial, mental health and **quality of life** needs of children with epilepsy.

Dr. Elizabeth Donner | Surveillance for SUDEP Among Canadian Children

- The risk of death for people with epilepsy is 2-3 times that of the average population, with some deaths attributed to **Sudden Unexpected Death in Epilepsy (SUDEP)**.
- Risk factors for **SUDEP** include having epilepsy for a long period of time, having **drug-resistant** generalized tonic-clonic seizures, and having seizures at night.
- Based on population studies, **SUDEP** is responsible for 1 death per 1000 patients per year but can be up to 9.3 per 1000 in patients with **drug-resistant epilepsy**. It is believed that **SUDEP** occurs less frequently in children (0.43 per 1000) but more studies need to be done on this topic.
- IMPACT: Studies on **SUDEP** in children need to be completed to understand which children are at risk and potential ways to prevent deaths in these children.
- NEXT STEPS: Dr. Elizabeth Donner has initiated a registry for **SUDEP** deaths in Canadian children. Also, in collaboration with the Ontario Forensic Pathology Service, Dr. Donner and colleagues are examining epilepsy-related deaths across the province.

Dr. Mac Burnham (presenting on behalf of Dr. Hiroshi Otsubo) | Who is at Risk for SUDEP?

- Dr. Hiroshi Otsubo has found that after tonic-clonic seizures, there is a period of time that brain activity is suppressed (seen as **EEG** flattening) and the person is unconscious. This is called **post-ictal generalized EEG suppression (PGES**).
- This decrease in brain activity may arise because of excess release of an inhibiting substance in the brain, known as **adenosine**.
- After a strong tonic-clonic seizure, marked by "all limb tonic posturing" or stiffness in all four limbs, excessive **adenosine** release and prolonged **PGES** could suppress the breathing centre in the brain stem, leading to **Sudden Unexpected Death in Epilepsy (SUDEP)**.
- IMPACT: This **SUDEP** theory – which reinforces the findings of Dr. Tariqus Salam and Dr. Jose Luis Perez Velazquez – may help to identify patients at risk for **SUDEP** and allow us to develop new intervention approaches.
- NEXT STEPS: Dr. Hiroshi Otsubo plans to use this knowledge to develop an approach that may prevent **SUDEP** cases related to excess **adenosine** release.

Dr. Berge Minassian | The EpLink Genetics Project

- The EpLink **Genetics** Project will conduct **whole genome sequencing (genetic testing)** of patients with epilepsy, which will help in the following areas:
    - Discovering genes underlying **drug-resistant epilepsy**
    - Developing and testing a resource that can help with diagnosis of **drug-resistant epilepsy**
    - Examining ethical issues and economic impact related to **genetic testing**
- This project is also leveraging a Genome Canada grant and partnering with groups in the European Union and United States.
- IMPACT: Through this project, we can better understand why people develop **drug-resistant epilepsy** and design therapies to target these genetic changes.
- NEXT STEPS: Dr. Berge Minassian plans to initiate **genetic testing** for people with epilepsy – both children and adults – to identify genes that may be responsible for putting certain individuals at higher risk for developing **drug-resistant epilepsy**.

TERMS & DEFINITIONS

Adenosine is a compound that is naturally found in all human cells, including in the brain. In addition to its role in transferring energy, adenosine promotes sleep and suppresses excitation in the brain.

Brain Stimulation is a technique that involves implanting electrodes in the brain to deliver electrical impulses to a specific brain area. This has been shown to be effective for the treatment of Parkinson's disease and depression, and it is now being tested in epilepsy. **Closed-Loop Stimulation**, also known as **Contingent Brain Stimulation**, is stimulation that is administered only when a seizure is about to start.

CBD or **cannabidiol** is an extract of marijuana that does not make you feel 'high.' CBD – potentially in combination with low levels of another marijuana extract **tetrahydrocannabinol** (**THC**) – may be useful in the management of **drug-resistant epilepsy**.

Co-morbidity or **co-morbid disorder** refers to an additional condition or disease that co-exists with a primary disorder. This additional condition may be independent of the primary disorder or they can be related, as is the case with depression and epilepsy. Individuals may have more than one co-morbidity.

Drug-Resistant Epilepsy can also be referred to as **intractable epilepsy** or **refractory epilepsy**. An individual is diagnosed with drug-resistant epilepsy when at least two drugs have failed to control seizures. EpLink's research is focused on improving health outcomes and **quality of life** for individuals with drug-resistant epilepsy.

EEG or **electroencephalography** records the brain's *electrical activity* using either non-invasive electrodes placed on the scalp or depth electrodes placed inside the brain.

Epileptologist is a neurologist that specializes in the diagnosis and treatment of seizures.

Genetics is the study of heredity – how specific traits or disorders can be passed from parents to their biological children. Today, it is possible to take a blood sample for **genetic testing (whole genome sequencing)**, where scientists read your genetic make-up like a book and identify changes in your DNA that put you at risk for certain disorders. The changes in a person's DNA that put them at risk or cause disease are **genetic mutations.**

GPs or **General Practitioners** are medical doctors who provide primary health care. GPs are also referred to as **Primary Care Physicians** or **Family Doctors**.

Infantile Spasms are uncontrolled body movements (known as convulsions) that are seen in infants with **West's Syndrome** - a childhood epilepsy syndrome. **West's syndrome** with infantile spasms has its onset around the first year of life, typically between 4-8 months of age.

Ketogenic Diet is a high fat, low carbohydrate and adequate protein diet that has been proven effective in managing seizures, specifically in people with **drug-resistant epilepsy**. In the classic ketogenic diet, fat makes up 90% of the calories.

Lafora Disease is a rare type of epilepsy that appears to be caused by **genetic mutations**. It is one of the most severe epilepsy syndromes, leading to a decline in intellectual functioning, seizures and eventually death. Typically, Lafora Disease has its onset in the teenage years.

MCT (Ketogenic) Diet is a less restrictive alternative to the classic ketogenic diet, where fat makes up 70% of the calories. As a requirement of the diet, participants use medium chain triglyceride (MCT) oil as a supplement to increase fat intake.

Mitochondria are structures found inside most human cells, including brain cells, which produce energy needed for the cell to function.

MRI or **Magnetic Resonance Imaging** is a medical imaging process used to visualize the structure of the brain.

Neuropathic Pain is a type of pain that occurs without any physical reason. It can cause localized or wide-spread pain that is highly resistant to pain medications. It may be caused by damage to the central nervous system (e.g. brain and spinal cord) and/or peripheral nerves.

Patient Reported Outcomes or **PROs** are reports coming *directly* from patients about how they are doing or feeling, without interpretation from a caregiver, doctor or other healthcare professional. PROs are essential to understanding lived experience.

Poly-Unsaturated Fatty Acids or **PUFAs** are 'healthy' fats that have been used in the treatment of cardiovascular issues and arthritis. **Omega-3 PUFAs**, which are found in fish oil, are currently being examined for their effectiveness in managing seizures in humans.

Post-Ictal Generalized EEG Suppression or **PGES** refers to the period of time following a tonic-clonic seizure where brain activity is suppressed or lowered (seen as 'flattening' of the **EEG** signal) and the individual is unconscious.

Quality of Life or **QoL** is a complex concept that describes the general health and well-being of an individual. This is a crucial aspect to consider when providing care for an individual.

Rett Syndrome is a disorder that most frequently occurs in females. Rett Syndrome causes intellectual disability, physical disabilities and is often associated with seizures.

Status Epilepticus is a medical emergency in which an individual has a continuous seizure lasting more than 5 minutes, or a series of seizures without full recovery of consciousness (awaking) between seizures.

Sudden Unexpected Death in Epilepsy or **SUDEP** is the unexpected death of an otherwise healthy individual with epilepsy that occurs either immediately after a seizure or sometimes when there is no evidence of seizure activity. Risk of SUDEP increases with having **drug-resistant epilepsy**, especially with tonic-clonic seizures.

THC or **tetrahydrocannabinol** is an extract of marijuana that makes you feel 'high.'

Tractography is a specialized **MRI** technique that allows 3D modeling of neuron pathways in the brain.

West's Syndrome is a childhood epilepsy syndrome that causes uncontrolled seizures (known as **infantile spasms**), changes in brain wave activity (known as **hypsarrhythmia**), and intellectual disability. It usually has its onset in the first year of life, and often occurs in children who have some sort of brain abnormality.