Lay Summary

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Understanding the mechanisms contributing to epileptogenesis in Alpers' disease

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Alpers' syndrome is a rare progressive disorder which typically affects young children (6 months to 3 years) and is characterised by severe epilepsy, loss of developmental skills and liver failure. Alpers' syndrome may develop when the cellular batteries, known as mitochondria, do not work properly. More specifically, Alpers' is caused by a fault in Polymerase Gamma, an enzyme that allows the mitochondrion to make its own DNA (mtDNA). This defect was not discovered until 2004 when researchers found faults in a gene called POLG, which contains the genetic code for Polymerase Gamma. In Alpers' syndrome the faulty Polymerase Gamma does not make sufficient mtDNA in brain or liver and so these organs become depleted of mtDNA. This loss of mtDNA contributes to fatal neurodegeneration and liver failure however there is limited understanding of the precise mechanisms underpinning these changes. Since the onset of symptoms is rapid, and there are no cures for Alpers' disease, this project aims to further our understanding about disease pathogenesis in order to explore potential avenues for the development of targeted therapies. We are specifically interested in exploring the link between the devastating seizures, brain pathology and mitochondrial dysfunction in post mortem tissues from patients with Alpers' syndrome.