Progress Report

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Title of Project: Defining the clinical phenotype of autoimmune epilepsy
Study ID: HREC/18/MHS/97

Summary:
In the last 12 months, the project has increased recruitment substantially which has been aided by the easing of Covid related restrictions. Currently, there are 91 participants recruited into the study. Furthermore, several new investigators have joined the project and recruitment has expanded to include 4 sites across Queensland, greatly improving the likelihood of meeting the recruitment target of 300 participants in the next 18 months. In addition, PI Gillinder has received further funding for the project (Betty McGrath Seeing Grant) which has enabled the addition of a second study coordinator to the team. Therefore, while recruitment to the study was significantly affected by the restrictions imposed as part of the Coronavirus pandemic, we expect the study to reach target. Due to the delayed recruitment, we have not expended the Brain Foundation budget for the study (allocated for antibody testing) as expected in the previously allocated time. We therefore kindly request and extension of funding for a further 18 months to enable us to complete the project.

Hypothesis vs Findings
Our hypotheses remain unchanged:

1. *There is a defined clinical phenotype associated with neuronal autoantibodies in chronic epilepsy and that this will be identifiable by a clinical syndrome of perisylvian seizure semiology and low amplitude mid temporal electrographic changes.*
2. *The prevalence of autoantibody-associated epilepsy is higher than currently reported.*
3. *Autoantibody positive epileptics will have detectable inflammation using advanced imaging techniques.*
4. *Mental health disorders are more common than in other epilepsy subtypes.*

Unanswered Questions

What these research outcomes mean

This will be the first study to extensively analyse clinical features and define a clinical phenotype in neuronal autoantibody associated epilepsy which is an important, yet under-recognised condition. Our results will vastly change clinical approach of epileptologists and neurologists both in Australia and internationally, and lead to this condition being included in the differential diagnosis of chronic epilepsy. It will change the lives of many people with refractory debilitating seizures and could offer a cure (ie: seizure freedom) for this epilepsy subgroup.

The data gathered from this study will enable us to create diagnostic criteria, similar to what exists for autoimmune encephalitis. Therefore, in the future these patients will be more readily identifiable, so the condition is less likely to be missed. As a result, many patients will be correctly diagnosed and receive more effective treatments. This means many patients who were previously told they had exhausted all therapeutic options will have a new possibility for seizure freedom. It will also ensure that patients are managed in a holistic manner and their mental health issues are adequately addressed. When these patients are easier to identify, it will be possible to recruit enough participants for future research.

The results of this study will also inform our understanding of the underlying pathophysiology of this condition and strongly guide the direction of further studies. Storage of serum and CSF will enable evaluation of immune activation in these patients by way of cytokine analysis, immunophenotyping and cytogenetics. This will inform treatment choices and assist in the design of, and choice of agents for an RCT to adequately analyse therapeutic options. It will also set the foundation for the creation of an animal model and eventually allow us to understand the aetiology of this condition and determine if this association represents true CNS autoimmunity.