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 received all final approvals and some new investigators have join the study team, which have greatly improved the likelihood of successful outcome. Recruitment has commenced at two sites and we will begin recruitment at a third once another investigator is approved. We have recruited 35 patients thus far, however this is below the target which is due to restrictions imposed as part of the Coronavirus pandemic. Recruitment was not possible for safety reasons as outlined by the HREC for about half of this year and as a result we have not expended the budget for the study as expected. We therefore request and extension of funding for a further 12 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.