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RACP Foundation Research Awards

FINAL REPORT

Project / Program Title		
Name		Dr Nimeshan Geevasinga
Award Received		2016 Sir Roy McCaughey Research Establishment Fellowship
Report Date		28 March 2017
Chief Investigator / Supervisor		Dr Nimeshan Geevasinga / Professor Steve Vucic
Administering Institution		The University of Sydney
Funding Period	Start Date:	1 January 2016
	Finish Date:	1 January 2017

PROJECT SUMMARY

Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease, is a rapidly progressive neurodegenerative disorder of motor neurons in the spinal cord, brainstem, and motor cortex, for which there is no cure. The prevalence of ALS in Australia is estimated to be 4-6 per 100 000 with a median survival of 3-5 year. Cortical dysfunction, or dysfunction at the level of the brain is thought to play an important role in the disease process. We have shown that a sensitive neurophysiological test, utilising transcranial magnetic stimulation, helps to identify early brain changes in ALS. This technique could be an ideal biomarker to monitor disease progression and hopefully identify changes early in Familial ALS.

PROJECT AIMS / OBJECTIVES

1. To determine the site of disease onset in Amyotrophic Lateral Sclerosis (ALS) – Work that we have undertaken suggests that cortical dysfunction precedes the development of lower motor neuron degeneration in familial ALS patients (caused by the C9ORF72 expansion). This was ellucidated after longitudinal assessment by utilising novel central and peripheral neurophysiological techniques, exploring cortical and peripheral nerve function.
2. To develop quantifiable neurophysiological biomarkers that can be used to facilitate an earlier diagnosis of ALS – We have shown that the threshold tracking TMS technique is a reliable biomarker in the diagnosis of ALS.
3. To develop robust biomarkers which could be employed longitudinally over time. With the goal of then utilising these biomarkers for future clinical trials and monitoring disease progression - We hope to use the threshold tracking TMS in ongoing clinical trials and research studies to further understand individual patient progression.

SIGNIFICANCE AND OUTCOMES

Our research work has shown that cortical changes occur early in the disease process in ALS. A unique neurophysiological tool, threshold tracking TMS may enable earlier diagnosis in ALS and also aid in understanding the complex pathophysiological process in ALS. This study has now recruited one of the largest genetic cohorts of familial ALS patients worldwide, and will over time result in more significant publications.

Moving forward we hope to utilise MRI imaging to further understand early changes in ALS, correlating these findings with our established threshold tracking TMS technique. We also hope to start proteomic analysis in our ALS cohort, which will further add to aid in the understanding of ALS pathophysiology.

PUBLICATIONS / PRESENTATIONS

Pathophysiological and diagnostic implications of cortical dysfunction in ALS. Geevasinga N, Menon P, Özdinler PH, Kiernan MC, Vucic S. Nat Rev Neurol. 2016 Nov;12(11):651-661

Diagnostic criteria in amyotrophic lateral sclerosis: A multicenter prospective study. Geevasinga N, Menon P, Scherman DB, Simon N, Yiannikas C, Henderson RD, Kiernan MC, Vucic S. Neurology. 2016 Aug 16;87(7):684-90.

Awaji criteria improves the diagnostic sensitivity in amyotrophic lateral sclerosis: A systematic review using individual patient data. Geevasinga N, Loy CT, Menon P, de Carvalho M, Swash M, Schrooten M, Van Damme P, Gawel M, Sonoo M, Higashihara M, Noto Y, Kuwabara S, Kiernan MC, Macaskill P, Vucic S. Clin Neurophysiol. 2016 Jul;127(7):2684-91.

Oral presentation at the International ALS symposium in Orlando – December 2016