

Final Report

Author: Dr Aicee Calma, MChD

Institution: Brain and Nerve Research Centre

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Title of Project: The Role of Clinical and Electrophysiological Biomarkers in Adult Motor Neuronopathies

Summary

This study investigated biomarkers for adult motor neuronopathies, particularly spinal muscular atrophy (SMA) and amyotrophic lateral sclerosis (ALS), with a focus on peripheral measures of lower motor neuron dysfunction.

In clinical practice, the compound motor action potential (CMAP) is commonly measured to assess lower motor neuron dysfunction. However, CMAP amplitude is influenced by both denervation and collateral reinnervation and therefore does not always provide a consistent estimate of axonal loss. Technical factors, such as electrode placement, may also affect recordings. In chronic denervation, CMAP amplitudes may remain preserved despite substantial motor unit loss due to collateral sprouting, as surviving axons reinnervate denervated muscle fibres.

Ulnar far-field potentials (FFPs) have emerged as a novel neurophysiological measure of lower motor neuron integrity. Previous studies suggest that these signals are more reproducible than conventional CMAP recordings and are associated with disease progression in ALS.

Hypothesis vs Findings

We hypothesised that ulnar far field potentials (FFP) have a role in assessing disease severity in SMA and as a complementary diagnostic tool in ALS.

SMA

FFP amplitude was lower in SMA participants compared to healthy controls and was similar to levels seen in ALS patients. In SMA, FFP amplitude showed a correlation with clinical assessments of upper-limb function, such as the Revised Upper Limb Module (RULM), upper-limb strength, and neurophysiological markers, including CMAP amplitude, NFP amplitude, and MUNIX. Additionally, we found that FFP amplitude could independently predict upper-limb functional performance.

ALS

In ALS participants, the FFP amplitude was lower than in individuals with ALS-mimicking neuromuscular disorders. FFP amplitude showed correlations with established neurophysiological markers, including CMAP amplitude, the split-hand index, the neurophysiological index, motor unit index (MUNIX), and MScanFit-MUNE. We also found that the FFP amplitude correlated with clinical measures of disease severity and progression, including upper limb strength, functional status (as measured by the ALSFRS-R), and the rate of decline in fine motor function. Additionally, our findings showed that FFP

amplitude reliably distinguished ALS from mimicking conditions, with consistent diagnostic performance across different ALS clinical phenotypes.

Unanswered Questions

n/a

What these research outcomes mean

These findings identify FFP amplitude as a promising marker of lower motor neuron dysfunction in both ALS and SMA. The results support its potential clinical value as a reproducible biomarker that may complement existing diagnostic tools and contribute to the assessment of disease severity and progression.

Future Directions

Future research will investigate additional biomarkers, including longitudinal measures of cortical excitability and fluid biomarkers like neurofilament levels.

Publications:

Calma AD, Pavey N, Silva CS, Tsuji Y, Van den Bos MAJ, Farrar MA, Menon P, Vucic S. Clinical Utility of Far-Field Potentials in Amyotrophic Lateral Sclerosis. *Muscle Nerve*. 2025 Oct;72(4):616-624. doi: 10.1002/mus.28480. Epub 2025 Jul 18. PMID: 40678914; PMCID: PMC12435138.