Brain Foundation Research Grant
FINAL REPORT

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Project: Nerve and muscle excitability in inclusion body myositis

Background
Sporadic inclusion body myositis (sIBM) is the most common acquired myopathy in people over the age of 50 years with an estimated prevalence of 51.3 per million in Australia. It is a disease of adulthood and affects more males than females. It is characterized by both proximal and distal muscle weakness and dysphagia. It is a slowly progressive, but rather variable, disorder with the most severe patients becoming wheelchair bound.

Despite this, the cause of this disease is poorly understood. It causes degeneration and inflammation of muscles, but why this occurs is unknown. At present, there is no known effective treatment for sIBM. Despite the evidence of inflammation in disease, immunosuppressive therapies are not effective.

A key feature of sIBM is the accumulation of intracellular amyoid-related proteins. There is some evidence from animal models that intracellular amyloid accumulation alters membrane potential and therefore excitability. Whether this occurs in humans with sIBM is unknown.

Early involvement of distal muscle, the presence of neurogenic changes on electromyography and presence of distal sensory symptoms in some patients has long led to debate regarding the presence, relevance and aetiology of neuropathy in patients with sIBM.

Hypothesis
This project aims to use recently developed computerized neurophysiological techniques to study nerve and muscle excitability in subjects with sIBM. We hypothesise that there are differences in the electrical properties of nerve and muscle cell membranes between healthy people and people with sIBM.

Using these techniques, we can infer whether cell membrane dysfunction is occurring in sIBM and, if so, gather clues as to where the problem is arising. In doing so, we hope to contribute to the understanding of the mechanisms by which sIBM causes symptoms which in turn could lead to development of more effective therapies.

Findings
This project is ongoing. Regarding nerve excitability studies, thus far we have recruited, consented and studied 39 healthy controls (18 over 50 years old) and 13 subjects with sIBM. Our preliminary results for motor and sensory studies are

shown below (Figure 1 & 2 respectively). At this stage, we have found no significant difference between healthy controls and subjects with sIBM. The trends seens in the motor data are not replicated in the sensory data. However, our sample size is too small and further recruitment and data is required for us to reliably detect differences in nerve excitability properties.

Additional data pertaining to the presence and relevance of neuropathy has been gathered for all studied sIBM subjects including thermal thresholds, routine nerve conduction studies, needle electromyography and autonomic nerve studies. This data has not yet been analysed.

Suitable normative data for healthy controls in thermal threshold studies was lacking and we have collected, analysed and published normative values for thermal threshold studies as part of our project. Details of the resulting publication are included below.

Unfortunately, clinical studies to assess muscle excitability have been technically very challenging and we have been unable to collect data from controls or subjects with sIBM to this point. We have been liaising with experts in the technique in the United Kingdom to refine our methods and hope that we will be able to collect this data in the future.

What research outcomes mean
As detailed above, sufficient data to draw meaningful conclusions has not yet been gathered. Further work is required to confirm or refute our hypothesis.

FIGURES

Figure 1: Preliminary results for motor nerve excitability studies of the median nerve to the abductor pollicis brevis (healthy controls – unfilled circles; sIBM subjects – filled circles). No significant differences detected.

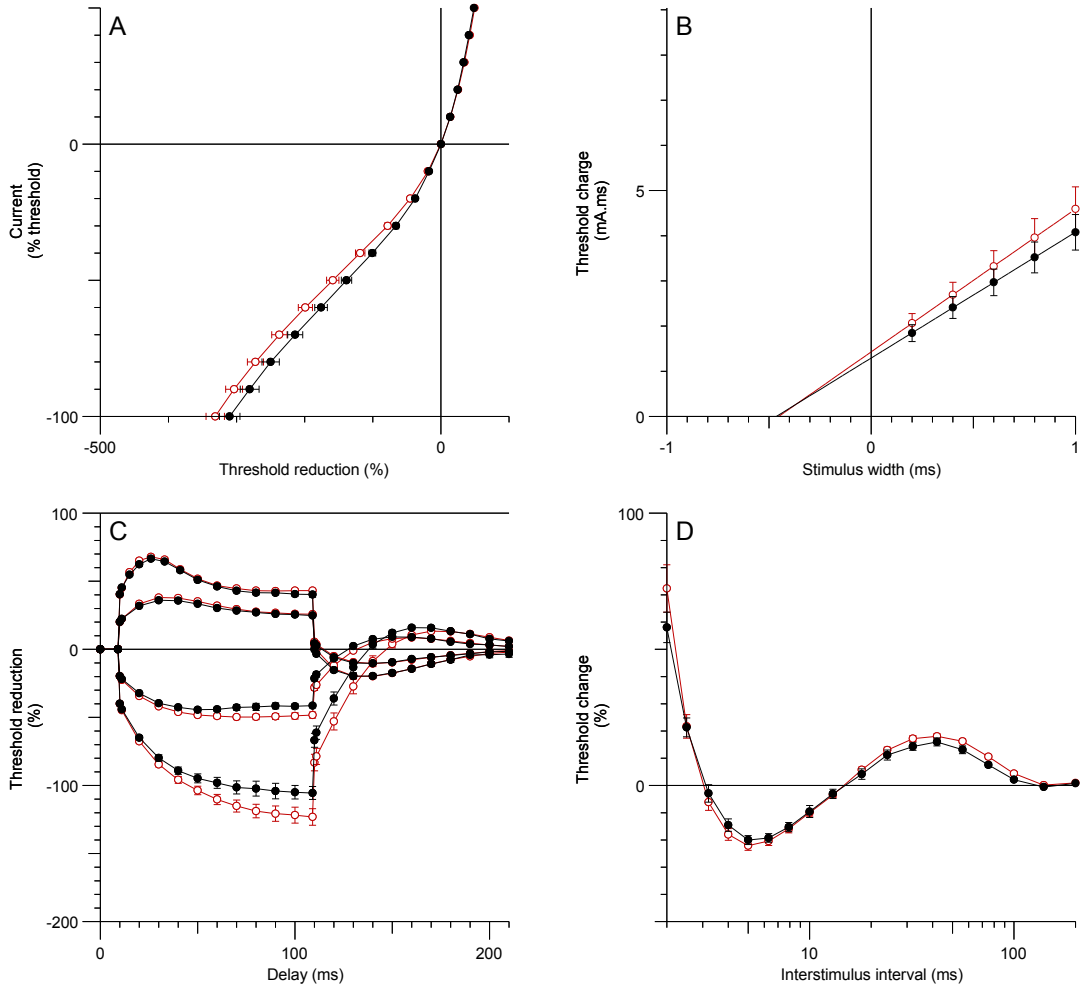
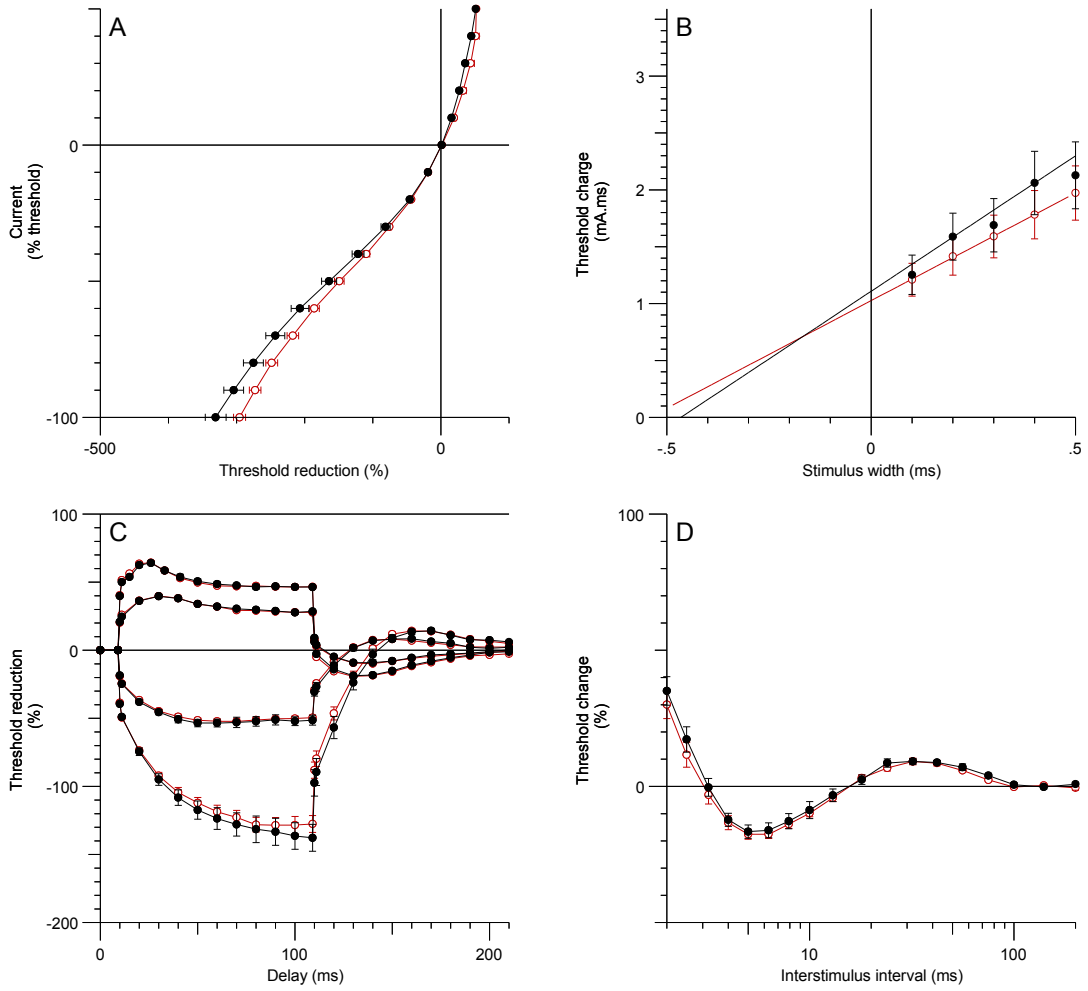


Figure 2: Preliminary results for sensory nerve excitability studies of the median nerve to the index finger (healthy controls – unfilled circles; sIBM subjects – filled circles). No significant differences detected.



Publications

1. Hafner J, Lee G, Joester J, Lynch M, Barnes EH, Wrigley PJ, et al. Thermal quantitative sensory testing: a study of 101 control subjects. Journal of clinical neuroscience. 2015 Mar;22(3):588-91. PubMed PMID: 25624058. Epub 2015/01/28. eng.