

EDITORIAL

Motor Neurone Disease: bringing New Zealand patients onto the world stage

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Motor neurone disease (MND) is the umbrella term for a group of degenerative diseases of the motor neurons, of which amyotrophic lateral sclerosis is the most common form. The incidence of MND is around 2 per 100,000 globally and median survival time is approximately 3 years from symptom onset.¹

MND may be either familial or sporadic, with the vast majority of cases (95%) being sporadic.² Genetic characterisation of international cohorts shows this to be a somewhat artificial distinction—at least 1 in 10 sporadic cases carry a heritable genetic mutation.³ However New Zealand MND patients are yet to be represented in those cohorts. Indeed, there is a woeful lack of publicly available data on the demographics, aetiology (including genetics) and provision of care of MND patients in New Zealand thus far.

Outside of New Zealand, there have been significant recent advances in the genetic characterisation of both sporadic and familial MND. This has been made possible by massively parallel DNA sequencing technology which can process more samples for a fraction of the time and cost of previous methods.

To date, 33 disease-causing genes have been identified,⁴ accounting for around 15% of all ALS cases.³ Notably, the same genetic mutations are present in both sporadic and inherited forms of MND, dispelling previous notions that these were distinct diseases. Furthermore, many of these genes can also cause frontotemporal dementia, consolidating the clinical and neuropathological picture of MND and frontotemporal dementia as a spectrum of overlapping diseases.

Disease-causing genes implicate dysfunction of gene expression (RNA processing), protein degradation, and cargo trafficking in the degeneration of motor neurons which causes MND. It is likely that the genetic profile of MND in New Zealand will largely resemble that of the UK and Europe, given the ancestry of New Zealand Europeans, however the genetics of Māori and Pacifica MND is currently a black box.

Although a rare disease, MND is certainly under-studied in New Zealand when compared to the likes of Huntington's disease, which has similar prevalence. This is surprising given that the MND studies conducted here have yielded findings worthy of follow-up.

A "cluster" of six port workers in the Nelson area developed MND within a 10-year reporting period (1995–2005), five of them within a 4-year period (2002–2005).⁵ The estimated population of port workers in the Nelson area at the time was 150. This led to postulation that these MND cases were linked to the use of methyl bromide gas as a fumigant for cargo.⁶ The small numbers involved mean that the cluster could simply have been due to chance⁵ and that continued reporting is needed.

In 2006 a larger, prospective longitudinal study in Christchurch reported the highest incidence of MND in the world thus far, finding a steady increase in incidence over a 22-year period from 1985, the cause of which is yet to be determined.⁷ When included in large international meta-analyses (and considered to represent the national average), these two studies paint New Zealand as having extraordinary disease rates¹ not attributable to higher numbers of familial cases.²

There is a clear need for both regional and nationwide studies of MND incidence, prevalence and mortality rates in New Zealand, whether remarkable or unremarkable compared to international averages.

The article⁸ by Dayal et al in this edition of the *Journal* provides important and timely new information on the demographics of MND patients in the greater Wellington area, and on the provision of healthcare to those patients. The 40 MND patients identified would have represented around 15% of all MND cases in New Zealand at that time, based on a predicted prevalence of 300 MND patients in New Zealand at any point in time.⁹ It is of interest therefore that this study reports rates of incidence and other disease demographics (male to female ratio, median survival time) that align closely to international averages. Dayal et al. also provide some of the only available information on the ethnic makeup of MND patients in New Zealand.

The authors detail useful statistics on the provision of care of MND patients in New Zealand. Non-invasive ventilation, speech language therapy, and provision for percutaneous feeding can significantly improve quality of life for MND patients. Their complex and rapidly changing needs can be challenging for non-specialist MND care providers, such as hospice,¹⁰ so this report provides valuable information on the whether patients are receiving the needed services within the hospital setting. Before this can occur however, patients must be diagnosed with definitive or probable MND by a specialist neurologist. The median delay to diagnosis of MND according to international studies is about 14 months due to its heterogeneity and similarities to other diseases,¹¹ and these delays are a major concern in a disease with relentless and rapid progression.

The aetiology of MND has been scrutinised for nearly 150 years since it was first described by Charcot in 1869, and yet only in the last decade has real progress been made in identifying causal factors. Although analyses of disease clusters (temporal, geographical or both) have failed to confirm or refute the role of any one environmental factor, genetic studies have been illuminating.

The ultimate goal will be to examine the interplay between all gene variants and environmental factors which increase risk, in order to best design therapeutic and prevention strategies. New Zealand must keep up with (and be included in) these analyses so that our unique profile of genetic and environmental factors can be understood.

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