26th August, 2015



Vitamin D is mainly synthesised in the skin in response to ultraviolet radiation, with a smaller proportion of our daily vitamin D requirements coming from our diet. It plays a crucial role in many biological processes, including bone health, and is known to play a key role in regulating the immune system.

Vitamin D insufficiency is thought to play a role in MS since geographical

areas of lower levels of UV radiation, and hence lower vitamin D synthesis in the skin, have higher incidences of MS (known as 'the latitude effect'). Variations in genes involved in the vitamin D metabolism pathway have been implicated in a person's risk of developing MS, and vitamin D deficiency has also been shown to be associated with a higher rate of relapses in people with established MS.

However, this clear observational data is not conclusive proof that low vitamin D levels play a role in causing MS. It could simply be a marker of something else that people with MS have in common, including the possibility that having MS causes low vitamin D levels (reverse causation).

For doctors to be able to provide accurate advice on whether taking vitamin D supplements can help prevent or treat MS, further evidence is required that low vitamin D is a contributing cause of MS.

Canadian researchers have now helped to provide strong evidence that low vitamin D levels play a causal role in MS, by looking at the link between a genetically determined low vitamin D level and the risk of developing MS. The study was published this week in the journal <u>*PLoS One*</u>.

There are a number of genes that are involved in processing vitamin D in the body, and the Canadian researchers used a huge study of vitamin D levels in the general population to identify a number of variations in those genes that are linked to low vitamin D levels.

After confirming that these genetic variations were linked to lower levels of vitamin D in a population of people with osteoporosis, the team then moved on to examine the link between genetically determined low vitamin D levels and MS risk. They utilised the large International Multiple Sclerosis Genetics Consortium study, the largest genetic association study to date for MS (with over 14,000 individuals with MS, including many contributed via the Australian New Zealand <u>ANZgene</u> MS genetics consortium).

By using this particular approach to analyse the data, the researchers were able to largely rule out any confounding factors such as environmental effects, and could also rule out reverse causation as having MS does not change your genes. They were

indeed able to show that in this population of people with MS, all of European ancestry, having a larger number of genetic variations that contribute to a lower circulating vitamin D level was associated with an increased risk of developing MS.

The results greatly strengthen the evidence that low vitamin D plays a causal role in the development of MS. However, it still remains to be seen whether supplementing with vitamin D can prevent the development of MS in people at high risk. This is exactly what MS Research Australia and our colleagues around Australia and New Zealand are studying in the PrevANZ MS Prevention clinical trial with people who have experienced a first clinical episode suggestive of MS.