

## **The Mayo Clinic haunts postpolio patients again**

Sorenson E. J., Daube J.R. and Windebank A. J. (2006) Electrophysiological findings in a cohort of old polio survivors. *Journal of the Peripheral Nervous System*, 11: 241-6

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In 1996, the Lancet published a news article called 'Study casts doubt on postpolio syndrome'. This was based on a Mayo Clinic 5-year follow-up study of 50 postpolio patients, 30 (60%) of whom had new symptoms. (McCarthy 1996). The authors of the study concluded that as their tests showed no neuromuscular decline, the patients' new weakness, fatigue and pain should be explained by other diagnoses such as arthritis and fibromyalgia (Windebank et al 1996).

In 2005, the Mayo Clinic team completed a 15-year follow-up of 38 of the 50 patients, finding that 31 (82%) had new weakness and there was a decline in strength, neuromuscular function and the number of motor units in both those with and without new weakness (Sorenson et al 2005). A motor unit is the motor neuron (nerve cell), the axon (nerve) and its sprouts, and the muscle fibres maintained by the unit. The authors commented that as there was no control group, the effects could not be compared with normal ageing. However, a recent article by Sorenson et al (2006) again 'casts doubt on postpolio syndrome' by arguing that the decline in neuromuscular measurements, particularly the estimated number of motor units (MUNE), was equal to normal ageing. Not having used controls themselves, the authors compare their study to other studies on motor units and ageing. It must be remembered that the results of a study and the interpretation of the results depend, to some extent, on the intentions and original design of the study. These influence the sample chosen, how terms are defined, the results that are emphasised in the final discussion, the studies that are used as references and how those references are interpreted.

### **Creating a sample**

The Mayo Clinic sample of 50 patients, selected from a population of 286 paralytic polio patients, was chosen because they lived close to the clinic and could be followed more easily. This is problematical because it is not a random sample and cannot be the basis for generalisations. The sample was selected from a slightly larger group of 58 in order to try and match the original population sample, but the group of 50 had a higher level of initial polio severity, were older when they had polio (13 versus 9) and were not matched in relation to postpolio symptoms. In the recent cohort of 38, the average polio age has risen to 15. Polio age differences are important because even though research has found that those who were older had more severe polio and were more likely to develop PPS, those who had polio at a younger age, often with better recovery, have a relatively high risk of developing PPS and may have more symptoms such as fatigue and pain. As the sample had such a high polio age it may not be representative of polio populations in general.

### **Testing for weakness and muscle fatigue**

Rather than looking at postpolio symptoms and the problems they cause for patients, the Mayo study team has concentrated solely on one postpolio symptom, weakness, and the tests to measure it. These tests, such as the manual muscle test, have been shown to be of limited use and

unreliable for polio patients as muscles compensate for each other (Perry et al 1988, Nollet et al 2003). Several studies have also shown that what is thought to be weakness in polio patients is sometimes the rapid fatigue of muscles, for which there are no reliable tests (Nollet et al 1999, Willen and Grimby 1998). It is often this rapid fatigability that has the biggest impact on daily activities. Recent definitions of postpolio syndrome have included both muscle weakness and endurance problems as major symptoms (Jubelt and Agre 2000).

### **Ageing and PPS**

The main conclusion of the recent Mayo Clinic article is that "the most likely cause for the decline in our polio survivors is ageing alone." The statement is based on the loss of motor units in selected muscles of the whole group, which was 44.5% over 15 years or 3% per year. However, this involved combining patients with and without new weakness, which was justified by the lack of statistical significance between the differences of the two groups. But as the entire group was quite small (38) and the group without weakness was extremely small (7), it would have been difficult to ever obtain a statistically significant difference. In actuality, over the 15 years, the group with weakness lost 61% or 4.1% per year and the group without weakness lost 22% or 1.5% per year. Even if not statistically significant, this is a substantial difference which requires some explanation.

After many years of researching the loss of motor units through ageing, the consensus of the major research teams in this field is that "motor unit numbers are well maintained until the seventh decade and then begin to decline precipitously thereafter" (Doherty 2003: 1722) and that "subjects in their seventh and eighth decades of life had about 50% fewer than MUUs than younger subjects between 20 and 40 years of age" (Doherty and Brown 1993: 364). A study by Galea (1996) found approximately a 1% per year loss until age 70 when the average loss rose to nearly 2%. In contrast, the Mayo Clinic researchers suggest that normal subjects have a 50% decline between ages 40-60, a 2-3% decline per year. Using the figure of 1% per year below age 70, it would appear that the polio group with weakness was losing motor units at about 4 times the normal rate and those without weakness were declining at slightly above the normal rate.

### **PPS symptoms and physical performance**

Sorenson et al justify their result of only modest progression in weakness by comparing their study to a Dutch study by Nollet et al (2003) who found little decline in physical functioning over six years, using younger people (46 years), who had polio at a younger age (2.9 years). Unlike the Mayo Clinic study, the Dutch team explored not only weakness but other PPS symptoms and daily function, selecting a group who showed a steeper decline in performance (27% of the cohort) in order to try to understand the cause of postpolio syndrome. Results showed that it was not muscle weakness but a higher number of PPS symptoms, such as fatigue and pain, that predicted mobility decline. The authors suggest that in these cases performance was at the upper end of muscle capacity causing overuse. They also found that how widespread the weakness was predicted decline rather than the severity of weakness, as there are fewer strong muscles to compensate for weaker ones.

The Dutch study indicates that in order to understand postpolio syndrome it is necessary to look at the whole constellation of symptoms, performance of daily activities, the amount of initial recovery, and the extent of weakness and muscle fatigue. By choosing to concentrate on only one

aspect of postpolio syndrome, weakness, in a limited sample, the Mayo Clinic study has overlooked the complexity of the changes, and how muscle fatigability may have major effects on patients' daily lives.

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