Examining a Controversial PPS Publication

Marcia Falconer, Ph.D.
Professor Edward Bollenbach

Recently a controversial article, "Electrophysiological findings in a cohort of old polio survivors" by Sorenson, Daube and Windebank was published in the Journal of the Peripheral Nervous System, volume 11, pages 241-246, September 2006. The findings in this article are the subject of heated discussion in the PPS world. Below we examine this article.

A scientific article usually is divided into parts; an abstract, which gives a brief overview of the article; the introduction, where related findings are discussed; the methods, which tell how the work was done; the results, which tell what was found in the study and the discussion in which the results are put into context with previous findings. In this final section the authors can speculate on wider implications of their findings.

The discussion section is often the source of intellectual debate. On occasion this debate can be vigorous, particularly when data from different studies point toward very different conclusions. Science would not be science if it was not exciting and controversial. We can expect scientists to have honest disagreements about methods, results and especially the discussion section of a paper. Unfortunately the debate is sometimes removed from the scientific arena to the public one when the popular press, or the internet, seizes upon an idea or a statement in the article.

This appears to be the case in the article by Sorenson et. al. In particular, one statement in the discussion section has been sensationalized. The statement is: *"This suggests that the most likely cause for the decline in our polio survivors is aging alone."* It is easy to understand why this sentence was highlighted. Taken out of context, this statement can infer that Post-Polio Syndrome (PPS) does not exist. It can even be interpreted, incorrectly, to mean that people with PPS are no worse off than their similarly aged peers with all this implies. Taken within the context of the reported data, the statement does not mean any of this.

This study is based upon two electrophysiological studies with the results explained using statistical methods and models. It is complex for the layperson to read and understand but it was not designed for the general reader. It is designed to pass specific data to people working in the field who are conversant with the methods and the interpretations of this data. We present here a less technical, but still scientifically accurate, summary of the main points in this paper.

In this study, the muscle strength and symptoms of 38 people with a history of prior paralytic polio were studied at 5 year intervals for 15 years. Innervation to two muscle groups, the thenar muscle at the base of the thumb and the digitorum brevis muscle on the sole of the foot, was examined using two electrophysiological measurements. One technique, CMAP (compound muscle action potential), examines the maximum amount of muscle contraction that can be achieved. The second technique, MUNE, (motor unit number estimate) provides information about the number of motor units in that muscle. A motor unit is a group of muscle fibers for which the message to contract is carried by a single neuron coming from the anterior horn of the spinal column. Both techniques indicate the functionality of the nerve that is tested.

The underlying cause of Post-Polio Syndrome remains unknown. Current theories include chronic inflammation of the spinal cord and die-back of recovered neurons from overuse. The "die-back hypothesis" suggests that fragile neuronal sprouts (which reinnervate muscles after the loss of neurons during acute polio) die because of metabolic stress caused by overuse. These two suggested origins for PPS are not necessarily contradictory but rather examples of different levels of observation; one at the tissue level, the other at the cellular level.

31 of the 38 people in the Sorenson study indicated they have PPS and experienced progressive muscle weakness during the 15 year period. 7 did not have PPS symptoms and did not experience this. It was found that the amount a muscle could contract (CMAP measurements) declined equally in people with PPS symptoms and people without symptoms. The number of motor units that could be activated (MUNE measurements) declined in both groups, but, oddly, there was a greater decline in people who did *not* report new muscle weakness! Since increasing weakness is associated with increasing loss of nerve connections to motor units, clarification or discussion of this unexpected result would be good.

A significant flaw in this article is the use of results derived from another study with different methods. It is acceptable to discuss and compare results from different studies. It is not acceptable to *use the results* of others to replace missing elements of your own study. This is particularly true when different methods were used to obtain the results. The authors did exactly this in the most provocative part of the publication. Because this study does not have a 'normal control group', the authors took the results from another, undefined study, with different methodology, to get data about people who did not have polio. They then compared the results from their electrophysiology study on polio survivors with the results from this undocumented study. By doing this, their comparison of the effects of aging in polio survivors and normal people is meaningless.

It is clear that the statements causing most concern to people with PPS are the ones least supported by the evidence. Unfortunately, these statements also are the ones most likely to be picked up and sensationalized. They are, in the authors' own words, "…the similarity of our results suggests that our polio cohort did not age any differently than a normal population. This suggests that the most likely cause for the decline in our polio survivors is aging alone." To make a statement with such import, the data that supports it must be impeccable. It is not. Without appropriate data the conclusion is unfounded and inflammatory.

Saying that "the most likely cause for the decline in our polio survivors is aging alone" invites many questions. For example, all polio survivors age, but not all polio survivors report an accelerated decline. What about them? What about young people, from the less developed world where polio is still endemic? They are reporting symptoms of PPS and they are not at the point where age causes loss of neurons. To ascribe aging as the main cause of PPS new muscle weakness ignores the other severe problem of PPS – central fatigue – which has no obvious connection to aging.

Indeed, to say that the decline is due to aging alone also suggests that the aging process is the root cause of PPS. This is a gigantic leap and ignores documented differences between similar aged polio survivors who have PPS and those who do not. Specifically, the profile of proinflammatory cytokines is significantly different in the two groups (Gonzalez et. al. *J. Neurol. Sci.* [2002] **205**: 9-13), as is the presence or absence of poliovirus fragments in cerebrospinal fluid (Leparc-Goffart et. al. *J Clin Microbiol* [1996] **34**: 2023-2026). Neither of these is typical of an aging population.

In addition, the Sorenson et. al. citation of work by McComas et. al. is perplexing. McComas disagrees about aging being the most likely cause of new weakness. Indeed, actually says the opposite. To quote from McComas et. al. "…denervation progresses in patients with prior poliomyelitis …and …this progression is more rapid than that occurring in normal aging." (McComas et. al. *Brain* [1977] **120,** 1415-1421).

The data in the current study shows that people with prior polio lost motor units at 3% per year. In the McComas article people with prior polio lost motor units at the rate of 6.7% per year and people without prior polio lost motor units at half this rate. Sorenson et. al. then say that "The rate of decline in our polio cohort was approximately the same as the normal population in the McComas study but about half that in their polio patients." It is not clear why this statement is included. It appears the authors are saying that the decline in the polio group in their study is the same as the decline in the normal population of the McComas study and this supports their contention that PPS weakness is due to normal aging. However they are comparing apples and oranges – results from two different studies. Moreover, the two studies came to diametrically opposed conclusions about PPS weakness and aging.

Another controversial part of the article is the suggestion by Sorenson et. al. that there are two models to explain new muscle weakness in PPS. One is "linear loss" where the loss of neurons (and hence of strength) is a constant rate of decline for everyone as happens in normal aging. The other model is "proportional decline" where the loss is related to the amount of damage from acute polio. In the discussion, the authors say that the proportional model best explains their findings. However the authors also say that neither model closely fits their data! This strongly suggests that neither model is correct. Therefore, the pattern for new muscle weakness is not related to a slow general loss (as is found in everybody with aging) and it is not (solely) related to the amount of original paralysis. There are other rate laws which could describe the way new muscle weakness is appearing. It might have been illustrative if these had been explored. It appears that the model preferred by the authors does not support their hypothesis that muscle weakness (loss) is related to normal aging (the first model).

Sorenson et. al. tell us that "The large degree of variation seen in both models may be a reflection of the underlying variation known to occur with most MUNE techniques available currently." This means that the method used to obtain this data may not be adequate for the job asked of it. In other words, be a bit skeptical about the results.

On a different topic, the authors say that *"There was no association between the magnitude of decline in either the summated CMAP amplitude or the summated MUNE and the presence of symptomatic progression."* One interpretation of this data is that a decline in the function of the two muscles they tested does not correlate with symptoms of new muscle weakness elsewhere in the body. If there is a significant relationship between the muscles tested and those generally reported as becoming weaker, this should be demonstrated or referenced.

This article is controversial not because of its actual findings, but because of the interpretation of its findings. The authors were poorly served by reviewers whose job was to point out all of the inconsistencies described above. This article has many statements that are not supported by the evidence. Unfortunately the popular press found a critical one and sensationalized it.

Address Correspondence to marcia.falconer@lincolnshirepostpolio.org.uk
PDF produced by the Lincolnshire Post-Polio Network.
Published August 27, 2006.
http://www.lincolnshirepostpolio.org.uk/downloads/extra/rebuttal.pdf

Marcia Falconer – Ph.D. in neuronal cell biology from University of Ottawa, Ottawa, Canada. Post-doctoral study in molecular biology at Massachusetts Institute of Technology, Cambridge, Mass. Led virology laboratory with biotechnology applications at the Centre for Food and Animal Research, Agriculture Canada, Ottawa. Also holds M.Sc. in cell biology from Carleton University, Ottawa, Canada and B.Sc. from Simmons College, Boston, Mass. Speaker at many PPS conferences and meetings in Canada, Australia and Britain. Now retired, she researches and writes about Post-Polio Syndrome. Has numerous publications in peer-reviewed journals and on the Web. She is currently writing a book about inflammation and PPS.

Contact information: marcia.falconer@lincolnshirepostpolio.org.uk

Edward Bollenbach – Emeritus Professor of Biology. Full Professor of Biology since the age of 39, won first Educational Excellence and Distinguished Service Award in the Connecticut Community College System, Specialized in the Teaching of Microbiology and Chemistry at Northwestern CT. Community College for 32 years. Holds a Master of Arts in Biology from the State University of New York at New Paltz, New York, and graduate certificates in Cryptogamic Botany, Origins of Life, and Holistic Health. He currently writes about and researches the Post-Polio Syndrome and has several articles in print and on the Web.

Contact information: edward.bollenbach@lincolnshirepostpolio.org.uk