MUNE data review

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I am very concerned about the accuracy the article by *(Sorenson et al, 2006)* Electrophysiological findings in a cohort of old polio survivors Eric J. Sorenson, Jasper R. Daube, and Anthony J.Windebank published in Journal of the Peripheral Nervous System 11:241-246 (2006)

I've reviewed the article and if the math is done correctly, one gets entirely different results.

Page 242 bottom of first column to top of second column describes in detail the method for calculating the rate of decline. Dr. Sorenson's group describe using the first order kinetic formula. The one at the bottom of the page gives (ln MUNE(5)) = (ln MUNE(0)) (-kT) which is not right.

The change in P with respect to time, dP/dt = k*P is the first order kinetic formula.

Integrating, one gets P(t) = P(0)*e(to the power k*t) *(Stewart, 2003)* so

kt =ln (MUNE(t) /MUNE(0)) is the correct formula (Divide first then take the natural log)

Dividing by the time t gives us k = 1/t * [ln (MUNE(t) /MUNE(0))]

Using the study data, k = 1/5 * (ln (331/407)) = -.0413 using the 5 year data and

k = 1/15 * (ln (226/407)) = -.0392 using the 15 year data

k is the relative growth rate (a negative value indicates loss) and since t is in years, expressing k as a percentage gives MUNE declines at a rate of **4.13% per year** using the 5 year data or **3.92% per year** using the 15 year data.

The authors state "While neither model of loss (proportional or linear) closely matches the data, the stronger correlation and better coefficient of variation would favor the proportional model over the linear model." After concluding the loss was proportional, at the top of page 245, they give us "a rate of decline of 2.9% annually" (with no supporting calculations). Using the model they recommend and the given data, 2.9% is wrong. The rate of decline is **4.13% per year** using the 5 year data or **3.92% per year** using the 15 year data as show in the calculations above.

The study (*Doherty et al, 2003)* is cited as the source of "However, in a cross-sectional study of normal subjects, there was a decline in the thenar MUNE counts from a mean of 288 to 139 between the ages of 40 and 60 years *(Doherty et al., 2003)*. This represents approximately a 50% decline, or 2-3% per year." The study then compares 2.9% to the "normal" value calculated using the MUNE mean values from *(Doherty et al, 2003)* . If the authors used data other than their MUNE means to calculate their rate of decline, the data are not comparable.

I reviewed the study by Doherty et al. They very appropriately didn't even try to give a rate of decline per year. In their study, the two groups are described as "a group of younger (20 - 40 years) and older (60 to 80 years) healthy subjects." The two groups are better described in *(Doherty et al, 1993)* "In 37 trials from 17 younger subjects (20-40 years), the mean MUE was 288 +/- 95 SD based on negative peak area and, in 33 trials from 20 older subjects, mean

values were 139 +/- 68." These are the numbers used to calculate "normal MUNE losses" at the bottom of page 244 of *(Sorenson et al, 2006).*

Using the proportional model and (lacking more data), the middle of the age ranges instead of the upper extreme of one range and the lower extreme of the other, one gets a change from 288 to 139 from age 30 to 70. (40 years)

k = 1/40 ((ln (139/288)) = -0.018 or a decline of **1.8% per year.**

or, using the more general conclusion in *(Doherty et al, 2003)* that "on balance, average MUNE values in groups over 60 years of age show reduction of about 50% in comparison to younger controls" and the formula on page 242 of *(Sorenson et al, 2006).*

k = -0.693/(t =BD) = -0.693/(40) =-0.0172 or a decline of **1.72% per year.**

The data do not support the conclusion "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." *(Sorenson et al, 2006)* The polio survivors' MUNE losses of **4.13% per year** using the 5 year data or **3.92% per year** using the 15 year data were more than twice the rate of **1.72% per year** or **1.8% per year** in a "normal" population. This is what McComas found as stated on page 244. "McComas reported that the loss of motor units in their subjects was approximately twice that seen in their normal population *(McComas et al., 1997)*."

On page 243, *(Sorenson et al, 2006),* the authors state "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." and "There was a mean decline in MUNE of 229 (SD 43) for the asymptomatic group and a mean decline of 120 (SD 24) for the symptomatic group (p =BC 0.09)." Either this is wrong or Table 2 (on the same page) is wrong. Table 2 shows MUNE decline of 229 in the symptomatic group and 120 in the asymptomatic group. The numbers in Table 2 are internally consistent, but the 15 year MUNE values are switched in Table 2 and the paragraph on page 243 cited above.

Using MUNE values in Table 2 and the formula for proportional loss,

All subjects decline at 4.1% (5 years) and 3.9% (15 years)

Symptomatic at 3.5% (5 years) and 6.2% (15 years)

Asymptomatic at 2% (5 years) and 1.68% (15 years)

According to Table 2, over the 15 year period, the symptomatic group are losing motor units at **3.7 times the rate** of the asymptomatic group. The fact that "only seven subjects remained asymptomatic" probably means that this is not statistically significant so no conclusions can be drawn, not that no association exists. Either the table is wrong, or the conclusions are wrong.

I have only looked at the MUNE data in detail so I can not comment on the CMAP data.

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References

Doherty TJ, The estimated numbers and relative sizes of thenar motor units as selected by multiple point stimulation in young and older adults. Muscle & Nerve [Muscle Nerve], (1993) Apr; Vol. 16 (4), pp. 355-366.

Doherty TJ, Stashuk DW, Brown WF, MUNE measurement of age-related changes. J Clin Neurophysiol, (2003) 55:158-163.

McComas AJ, Quartly C, Griggs RC, Early and late losses of motor units after poliomyelitis Brain, (1997), 120, 1415-1421.

Stewart J, Exponential growth and decay. Calculus 5e, (2003), 10.4:647-655.

Sorenson EJ, Daube JR,Windebank AJ, A 15-year follow-up of neuromuscular function in patients with prior poliomyelitis. Neurology [Neurology], 2005 Mar 22; Vol. 64 (6), pp. 1070-1072.

Sorenson EJ, Daube JR,Windebank AJ, Electrophysiological findings in a cohort of old polio survivors Journal of the Peripheral Nervous System, (2006) 11:241-246.

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