Author's response to reviews

Title: Diffusion Tensor Imaging in Neuropsychiatric Systemic Lupus Erythematosus

Authors:

Rex E Jung (rjung@mrn.org)
Arvind Caprihan (acaprihan@mrn.org)
Robert S Chavez (rchavez@mrn.org)
Ranee A Flores (rbarrow@mrn.org)
Janeen Sharrar (jsharrar@salud.unm.edu)
Clifford R Qualls (cquals@salud.unm.edu)
Wilmer Sibbitt (wsibbitt@salud.unm.edu)
Carlos A Roldan (croldan@salud.unm.edu)

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Letter to the Associate Editor of BMC Neurology:

We very much appreciate your compromise solution to our enquiry regarding the third revision of our manuscript entitled “Diffusion Tensor Imaging in Neuropsychiatric Systemic Lupus Erythematosus”. My co-authors and myself, Arvind Caprihan and Clifford Qualls have addressed the two remaining issues below. Dr. Caprihan is expert in diffusion tensor imaging techniques; Dr. Qualls is an outstanding and well recognized statistician [Qualls C. and Watanabe H. Asymptotic properties of Gaussian processes with a N dimensional parameter space. Trans. Amer. Math. Soc. 177, 155 171 (1973)]. My hope is that this manuscript can be published in your journal soon. You had indicated in your guidance the following:

“A detailed response to all the points raised by the reviewer 2 - equivalent in the context to a rejection of this original paper, from authors with an international expertise on the theme of this paper- may be not considered as a mandatory feature for publication.

However, I recommend before publication at least a shortened response to the reviewer 2 (who has a high expertise and carefully checked the manuscript); at least to the item 6 (potential error on a DF value only present in the revised version) and item 3 (a potentially not justified sentence, according to information only available in the revised version); correcting these points - or explaining why the authors disagree with the reviewer's comments - should not delay the publication nor overshad the focus of the manuscript.”

Our responses follow:

3. Since the two DTI sets were not averaged, but only concatenated, the
statement of “The DTI experiment was repeated twice to increase signal-to-noise ratio” may not be justified.

Response 3: We do not agree with the reviewer and an explanation follows. If calculations of apparent diffusion coefficients would have been linear, then not averaging but concatenating the data or calculating the average and then calculating the parameters would have been equivalent. Concatenation does not mean that we are not using the full data set. The SNR depends on the number of data points collected, provided it is properly analyzed. On the other hand if the calculations are non-linear then concatenating the data is better, because it weights the bad observations appropriately towards the final calculation. A trivial example is that if there is bad observation (motion artifact) then by concatenating and by examining the data we can detect and throw out the bad observations, while if the average was taken right from the start then this bad data would be part of the observation.

6. How had the df= 31 for “comparing NPSLE to SLE patients (df = 31)” of total 33 patients, after including age and gender covariates, been calculated?

The software package [TBSS] computes P-values based on Monte Carlo simulations at the voxel level so it is difficult to state what the degrees of freedom are for these simulations. Considering this issue at the subject level (the appropriate level), the denominator degrees of freedom for comparison of two groups would be the sum of the number of subjects minus 1 degree of freedom for 1) intercept 2) group 3) covariate age and 4) covariate gender. So we compute for NPSLE versus SLE for example, d.f. = n1 + n2 – 4, or 17 + 16 – 4 = 29. We have corrected this and the other d.f. calculations to reflect (now) all intercept, group, and covariate effects on degrees of freedom.

Thank you for your consideration,

Rex E. Jung, Ph.D.
Assistant Professor,
Department of Neurosurgery
University of New Mexico