Axonal Loss in a Rat Model of Optic Neuritis Is Closely Correlated with Visual Evoked Potential Amplitudes Using Electroencephalogram-based Scaling

It has been thought that the amplitude of the visual evoked potential (VEP), although quite variable, reflects the number of functional optic nerve fibers, and we have reported a structure/function relationship in postacute optic neuritis patients.[1] We have also shown and reported in this journal a positive relationship between VEP amplitude decrease and axonal loss in a rat model of optic neuritis.[2] However, the correlation between amplitude decrease and axonal damage was weaker than that observed between latency delay in VEP and demyelination, which may be due to the higher variability of the VEP amplitude.[2] We have developed modifications for rat VEP recording, and recently introduced an electroencephalogram (EEG)-based amplitude correction technique similar to that we reported for the human multifocal VEP,[3] which significantly improved the reproducibility of rat VEP amplitude measurement.[4]

Here, we reanalyzed our published data using this EEG-based VEP scaling methodology to investigate the potential of using VEP amplitude to assess axonal damage in vivo. Without signal correction, as described in the original IOVS article, a linear association was observed between axonal loss and N1-P2 amplitude decrease ($r = 0.681$, $P = 0.007$).[2] However, after EEG-based scaling,[4] the correlation between VEP amplitude and axonal loss became dramatically stronger ($r = 0.811$, $P < 0.001$, Fig. 1), which remained significant after controlling for demyelination (partial regression analysis, $r = 0.764$, $P = 0.002$).

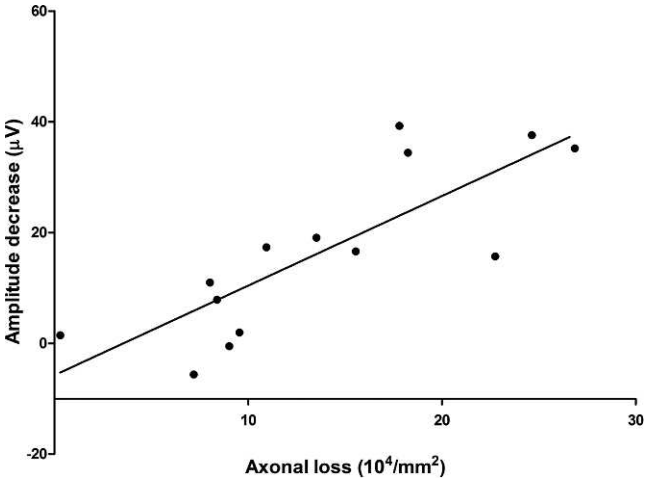

FIGURE 1. A strong linear correlation between axonal loss and VEP amplitude decrease (EEG-scaled) ($r = 0.811$, $P < 0.001$, $n = 14$).

This re-analysis supports the concept that VEP amplitudes reflect the number of functional optic nerve fibers. We recommend that background EEG levels should be considered in measuring VEP amplitudes. Our data-processing technique provides a useful tool for VEP amplitude analysis, and it could also be considered for clinical VEP interpretation in humans to evaluate the severity of axonal pathology in optic neuropathies.

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