

Invited Commentaries

Association of severity of spinal muscular atrophy with the loss of NAIP gene

Spinal muscular atrophy (SMA) is a devastating genetic disorder of children and infants. Based on the onset and severity of disease, SMA patients are grouped into three types. SMA type I is the most severe and the most frequently occurring form in which patients die before the age of two years. SMA type II is of intermediate severity in which patients survive longer than two years, but may die before they reach the age five years. SMA type III is less frequent disease in which patients may live well into their adulthood. All three forms of SMAs are associated with the deletion of or mutation within the *Survival Motor Neuron 1* (SMN1) gene, which produces SMN, an essential protein for survival of all cell types. A nearly identical copy of gene, SMN2, fails to compensate for the loss of SMN1 due to skipping of exon 7 during pre-mRNA splicing. Other than abnormal skipping of exon 7, SMN2 is a normal gene. Thus, it is hoped that compounds that increase SMN2 exon 7 inclusion will eventually hold the promise for cure.^[1] Despite a huge progress in our understanding of SMN function, the exact role of SMN in motor neurons (the most affected cells in SMA) remains elusive. The fact that SMA has different phenotypes suggests that factors other than SMN also contribute towards the severity of SMA. In this issue of “Neurology India”, authors have analyzed 39 Indian SMA patients and have found a surprisingly high correlation between severity of SMA and the loss of both SMN1 and NAIP gene.^[2] Interestingly, this report comes at a time when another report suggests that patients with high copy-number of SMN2 are likely to have a less severe form of SMA.^[3] Further, severity of SMA will also depend upon the nature of mutations within SMN2 because deletions/mutations within SMN2 are capable of correcting SMN2.^[4,5] Hence, effect of absence of NAIP on severity of SMA

should be interpreted with caution. Further confirmation of the above report with a larger sample size would be important for both, providing the correct prognosis of disease, as well as for arriving at the proper treatment strategies. To a broader significance, this report is likely to invoke an interest in finding the exact mechanism by which loss of NAIP protein causes a much severe form of SMA.

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