Vanishing white matter (VWM; also termed childhood ataxia with central hypo-myelination or CACH) is an often severe inherited neurological disorder. It involves substantial loss of myelin. The cells that make myelin, oligodendrocytes, are preserved, although they display an unusual ‘foamy’ cytoplasm. The phenotype associated with VWM is very variable in onset, severity and its non-neurological effects. VWM is caused by mutations in the genes for the 5 subunits of an mRNA translation factor, eukaryotic initiation factor (eIF) 2B. Mutations in any subunit can cause VWM. eIF2B plays an essential role in the mechanism by which ribosomes find the start codon in mRNAs. eIF2B is also crucial in controlling protein synthesis and is subject to numerous regulatory inputs. mRNA translation is a key node in controlling gene expression and plays important roles, e.g., in learning and memory. We have studied the effects of mutations in the human eIF2B subunits on the properties of eIF2B including the assembly of the pentameric eIF2B complex and its activity in catalysing guanine nucleotide-exchange on eIF2. Our data reveal that many VWM mutations impair the function and/or the assembly of eIF2B but exert diverse effects both in quantitative and qualitative terms. There is no simple relationship between the type/degree of impairment and the observed severity of the disease, as exemplified e.g., by two mutations in eIF2B4 that both cause very severe disease but have very different effects upon eIF2B activity. The implications of our data for understanding the etiology of VWM will be discussed.