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News about the etiology and pathogenesis of ALS

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For the most frequent adult motor neuron disorder (MND), i.e. amyotrophic lateral sclerosis (ALS), the concept is nowadays generally accepted that frontal deficits / frontotemporal dementia (FTD) are a part of its phenotype. Genetic studies in TDP-43 as a molecular signature of FTD and ALS and also in mutations of the FUS protein have brought further evidence for this concept. In addition, the current status of knowledge is presented concerning a new gene described in 2011, that is a hexanucleotide repeat expansion in *C9ORF72* as the cause of chromosome 9p21-linked ALS-FTD, together with an assessment of its frequency (*C9ORF72* > Cu/Zn SOD > FUS = TDP-43 > optineurin). It has to be considered that all mutations are also found in sALS patients and that *C9ORF72*, FUS and TDP-43 are not restricted to the „Charcot“ motor phenotype so that ALS is probably a di- / polygenetic disease. From the view of neuropathology, ALS and FTD are clinicopathologically related so that TDP-43 and FUS pathology led to a reclassification of ALS and FTD, in association with the above-named disease-causing mutations. Beyond these pathogenetic aspects, new and ongoing epidemiological studies and the results of recent clinical studies are presented.