Genotype-specific electrophysiological characteristics of the HSPs (Luger Schöls)

Hereditary spastic paraplegias (HSPs) are characterized by lower limb spasticity due to degeneration of the corticospinal tract. We set out for an electrophysiological characterization of motor and sensory tracts in patients with HSP. We clinically and electrophysiologically examined a large cohort of 128 patients with genetically confirmed or clinically probable HSP. Motor evoked potentials (MEPs) to arms and legs, somato-sensory evoked potentials of median and tibial nerves, and nerve conduction studies of tibial, ulnar, sural, and radial nerves were assessed. Whereas all patients showed clinical signs of spastic paraparesis, MEPs were normal in 27% of patients and revealed a broad spectrum with axonal or demyelinating features in the others. This heterogeneity can at least in part be explained by different underlying genotypes, hinting for distinct pathomechanisms in HSP subtypes. In the largest subgroup, SPG4, an axonal type of damage was evident. Comprehensive electrophysiological testing disclosed a more widespread affection of long fiber tracts involving peripheral nerves and the sensory system in 40%, respectively. Electrophysiological abnormalities correlated with the severity of clinical symptoms. Whereas HSP is primarily considered as an upper motor neuron disorder, our data suggest a more widespread affection of motor and sensory tracts in the central and peripheral nervous system as a common finding in HSP. The distribution patterns of electrophysiological abnormalities were associated with distinct HSP genotypes and could reflect different underlying pathomechanisms. Electrophysiological measures are independent of symptomatic treatment and may therefore serve as a reliable biomarker in upcoming HSP trials.