Leukodystrophies are a group of rare genetic disorders affecting the white matter of the brain. Disease onset may be at any age, mostly in childhood. There is only a limited understanding of the mechanisms underlying leukodystrophies and most of these disorders are not curable at this point. Clinicians are challenged by a deficit of knowledge of phenotypic characteristics and disease course. In this thesis, we delineate the clinical and genetic properties of four different leukodystrophies, aimed at improved patient counseling, enhanced understanding of underlying disease mechanisms and providing natural history data for the planning and evaluation of future therapeutic trials.