

50 - Autism

Autism

© SPMM Course Lewy Body dementia No specific genetic associations have been established for Lewy Body Dementia. Certain mutations have been reported inconsistently at alpha-synuclein locus. DLB is considered as a part of 'synucleinopathies' where synuclein molecules aggregate in presynaptic terminals producing Lewy bodies. Other diseases included are Parkinson's and Multisystem atrophy. Parkinson's disease LOCUS POSITION/Protein Clinical features/inheritance PARK1, PARK4 4q21 Alpha-synuclein gene Dominant inheritance; not seen in sporadic cases. Onset in 40s. nigral degeneration with Lewy-bodies. PARK2 6q25 Parkin gene Recessive inheritance; nigral degeneration without Lewy-bodies. Onset 40 - 60. (most early onset cases, l-dopa responsive) PARK8 cen (pericentromeric) LRRK2 gene Dominant. Onset around 60. Variable - synuclein and tau pathology. PARK6 1p35-37 PTEN-INDuced Kinase (PINK1)

in mitochondria Autosomal recessive; onset 30-40 (12% of early-onset cases, l-dopa responsive) PARK7 1p38 DJ-1 Autosomal recessive; onset 30-40 α -synuclein is a protein that is expressed throughout the brain and has potential roles in learning, synaptic plasticity, vesicle dynamics and dopamine synthesis. E. Other disorders Autism □ The recurrence rate in siblings of autistic children is 2% to 8% (higher than the rate in the general population but lower than in single-gene disorders). This translates to 50 times (range: 30 - 120) relative risk in siblings. □ Risk of autistic disorder in a sibling of 2 autistic children: 25-30% (nearly 300 times higher) □ Twin studies reported 60% concordance for classic autism in monozygotic (MZ) twins versus 0 in dizygotic (DZ) twins. If a broader autistic phenotype that included communication, and social disorders is considered, the concordance increased remarkably from 60% to 92% in MZ twins and from 0% to 10% in DZ pairs. This translates to 90% heritability. □ The identity and number of genes involved remain unknown. Chromosomes 2, 7 and 15 are implicated. A segregation analysis in a series of multiplex families was consistent with autosomal recessive inheritance with sex-specific modifications □ The striking feature is the association of the genetics of autism with multiple single-gene disorders. The most clearly documented of these disorders is the fragile X syndrome. Perhaps 8% of autistic subjects have the cytogenetic fragile X; 16% of fragile X males are autistic. There are also probable associations between autism and tuberous sclerosis, neurofibromatosis, and phenylketonuria