47 - Frontotemporal dementia

Frontotemporal dementia

© SPMM Course ApoE status unknown (general population) 6.3% 12%

No Apo 4 4.6% 9.3% 0.75 times (less) Apo 4 heterozygote 12% 23% 3.2 times (up to 5 times in some studies) Apo 4 homozygote 35% 53% 14.9 times Modified from McGuffin et al. (ed) Psychiatric genetics and genomics. Oxford press: 2002

 An actually predicted risk of developing Alzheimer's disease in the first-degree relatives of probands with Alzheimer's disease is 15-19%, compared with 5% in controls. Thus, the risk to the first-degree relatives of patients with Alzheimer's disease who developed the disorder at any time up to the age of 85 years is increased some 3 – 4 times relative to the risk in controls. This translates to a risk of developing Alzheimer's disease of between one in five and one in six (from Liddell et al., 2001). In the case of patients with Alzheimer's disease who became demented late in old age, say by their 80s, relatives probably run the same 30-50% risk of developing dementia as anyone else who live to the age of 90 years and beyond (from Liddell et al., 2001). Like other disorders that reflect the combined action of several genes, the risk to relatives drops rapidly as the degree of genetic relatedness falls. Data are limited, but the risk to second-degree relatives, such as grandchildren, is probably less than twice the population levels (from Liddell et al., 2001) Probandwise concordance rates of about 40% for DZ and 84% for MZ twins are seen. Frontotemporal dementia Frontotemporal lobar degeneration (FTLD) refers to the 3 different syndromes of frontotemporal dementia (FTD), progressive non-fluent aphasia and semantic dementia. Some patients with FTLD show tau protein based pathological changes. In familial cases, mutations have been identified in the microtubule-associated protein tau gene (MAPT) on chromosome 17q21. Many cases are tau-negative but show ubiquitin-immunoreactive neuronal cytoplasmic inclusions. In some of these tau negative cases mutations have been identified in

progranulin (PGRN) gene, also on chromosome 17q21. Progranulin is a widely expressed growth factor that plays a role in wound repair and inflammation by activating signalling cascades in cell cycle. Progranulin has also been linked to tumorigenesis CADASIL CADASIL is a form of amyloid angiopathy that can present with Alzheimer’s like features. NOTCH3 is the only gene currently known to be associated with CADASIL. Most mutations in the NOTCH3 gene in individuals with CADASIL are located in exon 4. The mutation detection rate is up to 96% in individuals with well-defined or biopsy-proven CADASIL. The defective gene is identified as NOTCH3 in 19p13.1-13.2

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