Introduction: APOE is the only risk gene for sporadic AD. Recent large GWAS found links with CLU, CR1 involved in clearance of Aβ, and PICALM affecting synaptic neurotransmitter release and intracellular trafficking.

Aims: We aimed to investigate whether SP and NFT are associated with any of the recently identified GWAS SNPs; CLU, CR1 and PICALM.

Methods: We investigated the association of SP and NFT with the risk genes, along with APOE, in the Tampere Autopsy Study (TASTY) series comprising 603 cases, representing a sample of the general population (0-97 yrs), who died out-of-hospital. Only 32 (5.3%) had memory problems or clinical AD, although 31.1% had SP and 42.1% NFT (both with age dependence).

Results: There was a relationship (OR 4.4, p=0.004) between burnt out SP and CLU C allele carriers compared to the common TT carriership. The oldest (80+ years) PICALM TT genotype carriers less often (OR 0.18, p=0.025) had SP compared to common CC carriers. CR1 CC genotype carriers were more likely (OR 2.1, p=0.048) to have sparse than no SP (compared to AA carriers). APOEε4 carriers more often had primitive (OR 2.5, p=0.010), classic (OR 2.5, p< 0.0001) and burnt out SP (OR 2.8, p=0.014) compared to ε3-ε3 carriers, as expected. There were no correlations with NFT and the SNPs.

Conclusions: Along with age and APOEε4, the genetic variants of CLU, PICALM and CR1 genes were associated with SP in this population sample that died outside institutions.