COPY NUMBER VARIANTS IN ALZHEIMER’S DISEASE

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Introduction: Recent genome-wide association studies of Alzheimer’s disease (AD) have identified a number of new susceptibility genes. However, they only explain a proportion of the heritability of this disorder and other sources of variance need to be investigated. Copy number variants (CNVs) account for more genomic differences between individuals than single nucleotide polymorphisms (SNPs) and have been implicated in a number of brain disorders.

Aim: We aimed to carry out a large-scale study of CNVs in AD using data from our recent genome-wide association study.

Methods: We used intensity data from 2992 AD cases and 1186 age-matched controls genotyped on Illumina 610-quad arrays to identify CNVs using the PennCNV algorithm.

Results: CNVs previously implicated in neurodevelopmental disorders were not over-represented in patients. Burden analysis of rare (< 1%) and large (>100kb) CNVs did not find a significant excess of CNVs in cases. This analysis also indicated that there is a very low rate of such deletions >1Mb in our elderly controls.

Conclusions: We conclude that rare and large (>100kb) CNVs do not play a major role in the pathogenesis of AD, with the possible exception of duplications of the APP gene. Healthy elderly individuals might have a particularly low rate of the most pathogenic class of CNVs: rare deletions >1Mb