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Large 3Mb deletions at 22q11.2 locus in Parkinson's disease and Schizophrenia

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22q11.2 microdeletions are among the most common deletions found in humans.

While most cases present in early childhood, a large fraction remain undetected into adulthood. Adult carriers are at increased risk of developing schizophrenia¹. More recently, these deletions have also been associated with Parkinson's disease (PD). Butcher et al reported that a small proportion of 22q11.2 deletion carriers aged above 35 years have developed early-onset PD², although the diagnosis was delayed in individuals undergoing antipsychotic treatment for schizophrenia. Subsequently, Mok et al screened for the deletion in 9,387 PD cases and 13,863 controls³ and identified eight carriers amongst cases but none in controls. This deletion was particularly enriched among early-onset cases. Most of these studies were conducted in samples of European ancestry, but the prevalence in Asian samples is unknown.

To evaluate the frequency of this deletion in the Chinese population, we analysed log R ratios (LRR) and B-allele frequency (BAF) across 900,015 SNPs genotyped on the Illumina HumanOmniZhongHua-8v1_A array in 773 PD cases (446 males, 327 females, age 68.0 ± 10.1 years, age of onset 63.7 ± 10.3 years), 829 schizophrenia cases (380 males, 318 females, 131 missing info, age 39.2 ± 9.9 years) and 1020 healthy controls (536 males, 477 females, 7 missing info, age 37.6 ± 12.7 years) (Supplementary Material). All are of Chinese ethnicity, confirmed using principal components analysis. All subjects gave informed consent and the study received approval from the respective institutional ethics committee. Only samples with genotyping call rates $>95\%$ were analysed. We used PennCNV for copy number variant (CNV) calling⁴, and filtered for calls larger than 500kb that overlap the interval chr22:18.9-20.4Mb (Hg19).

We identified one PD case hemizygous for the large 3Mb deletion (1 out of 773 PD cases, 0.13%). This carrier is female with age of onset 51 years (recruitment age 56 years) – within the range reported by Mok et al³, and has a history of mental deficiency since young

(see Supplementary Material for clinical notes). This gives a higher frequency of 0.81% (1 out of 124) in the subset of PD cases with onset below 55 years (86 males, 38 females, age 53.1 ± 7.4 years, age of onset 47.8 ± 5.3 years).

We also identified two schizophrenia cases (2 of 829 schizophrenia cases, 0.24%) with the same 3Mb deletion, consistent with previous observations⁵⁻⁶. We did not observe duplications or the smaller 1.5 Mb deletion in any of our samples. Both schizophrenia carriers are females, with age of onset 20 and 35 years (recruitment ages 25 and 45 years respectively). Further follow-up of these subjects will provide additional insights into the clinical spectrum of 22q11.2 deletion carriers of Chinese ethnicity.

In summary, we have identified large 3Mb deletions at the 22q11.2 locus at similar frequency in Chinese PD and schizophrenia patients. None was observed in 1020 healthy controls. We conclude that the 22q11.2 deletion should be taken into account as a risk factor in Asian PD patients, especially the early-onset cases. Moreover, 22q11.2 carriers should be monitored for PD symptoms.

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