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Movement disorders in adults with 22q11 deletion syndrome

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Dear Sir,

I read with great interest the recent review article by Boot et al on Parkinson's disease in 22q11 deletion syndrome[1]. There is evidence to suggest an increased risk of Parkinson's disease among people with 22q11 deletion syndrome. In our study of 50 adults with 22q11 deletion syndrome, we identified an increased prevalence of potential clinical markers of prodromal neurodegeneration (e.g. hyposmia)[2]. We fully agree with Boot's argument that the core clinical features of 22q11 deletion syndrome may account for the presence of some of these apparent prodromal markers. We also identified a significantly increased prevalence of symptoms of REM sleep behaviour disorder in our cohort. Formal sleep studies in people with 22q11 deletion should be performed to try and identify the prevalence and significance of REM sleep disorder in 22q11. The 22q11 deletion syndrome offers a genetically defined group in which to study prodromal PD and development of the motor features of PD. However, we need to consider which clinical features to use as prodromal markers to make sure we are not simply detecting core clinical features of 22q11 (e.g. hyposmia associated with upper airways malformation).

Chromosome microdeletions frequently cause disease through hapolinsufficiency for genes in the deletion region (or deletion of genes at the breakpoint)[3,4]. There are several interesting candidates within the 22q11 deletion; involved in dopamine metabolism, mitochondrial function or microRNA processing. No single nucleotide variants in any of these candidate genes have been reported in PD cases to my knowledge. The deletion is due to non-allelic homologous recombination (NAHR) and therefore is of a consistent size, precluding identification of a critical region. The molecular mechanisms explaining increased PD risk in 22q11 remain open for exploration. Once again it will be crucial to disentangle mechanisms which are core to the 22q11 deletion phenotype from those which might explain increased PD risk.

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**Author Roles**

Alisdair McNeill 1) Research project: A. Conception, B. Organization, C. Execution;
3) Manuscript: A. Writing of the first draft, B. Review and Critique.

**Ethical Compliance Statement:**

The authors confirm that the approval of an institutional review board was not required for this work. Informed consent was not obtained as no patients are described in this manuscript. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.