

INVESTIGATING GENOMIC COPY NUMBER VARIATIONS IN SOUTH AFRICAN PATIENTS WITH MENTAL RETARDATION (MR)

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BACKGROUND

Mental retardation (MR) is a disability characterised by an IQ lower than 70 as well as a deficit in adaptive and learning abilities. The prevalence of MR is approximately 2-3% within the general population with a substantial proportion being attributable to genetic factors. It has been well established that gross chromosomal aberrations commonly underlie the etiology of the disorder, with prevalence estimates ranging from 12-24%. These aberrations have traditionally been detected by implementing a host of cytogenetic techniques. However, subtle chromosomal aberrations often go undetected owing to the limited resolution of these methods.

METHODS

In this pilot study 30 patients with MR and a range of additional clinical features were investigated for subtle chromosomal aberrations using microarray technologies. The platform used was the 250K Nsp Affymetrix SNP array and data analysis was performed using the CNAG software.

RESULTS

A total of 94 copy number variations (CNVs) were observed, clearly indicating the polymorphic nature of CNVs and the high incidence of these polymorphisms within the population. One known disease-causing deletion and two novel putative X chromosomal disease-causing aberrations (one deletion and one duplication) were identified. The novel 8Mb X-chromosomal deletion exhibits incomplete penetrance with the unaffected male sib of the male proband also carrying this deletion of 24 genes.

CONCLUSIONS

The finding of an 8Mb X chromosomal deletion exhibiting incomplete penetrance has important implications in the interpretation of the disease-causing nature of copy number variations. Additionally, this finding has ramifications in the genetic counselling of individuals who carry these aberrations. Finally, this pilot study demonstrates the superior capabilities of microarray technologies to detect subtle chromosomal rearrangements and highlights the importance of incorporating this technology within the diagnostic protocols offered to patients with MR.