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Romanian Prader-Willi Association

ASOCIACIÓN MADRILEÑA
PARA EL SÍNDROME DE
PRADER-WILLI



AFFECTIVE PSYCHOSIS IN PEOPLE WITH PRADER-WILLI SYNDROME

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Affective psychosis associated with PWS occurs mainly in people with UPD(15)mat rather than those with 15q11q13del. This suggests that it is related to the presence of two active copies of a gene(s) located in the distal half of the PWS/ASCR (Prader-Willi/Angelman syndrome critical region) where some genes are paternally imprinted but maternally active and whose loss of expression results in Angelman syndrome (AS).

A large population study of PWS within the UK identified 12 people with a deletion in 15q11q13 who had suffered a psychotic episode and four people over 30 years of age with UPD(15)mat who so far had not.

These people were investigated using a series of microsatellite markers located within the PWS/ASCR.

It was found that the 12 people with 15q11q13del who had suffered psychotic episodes, despite having the same deletion breakpoints as the remainder of the study participants with 15q11q13del, demonstrated two maternally derived copies at loci lying between D15S975 and D15S661 making them effectively disomic for this small region of the ASCR. When a series of 25 people with 15q11q13del who were not psychotic were studied with the same microsatellite markers, they all demonstrated a single allele at each of these loci. So, with only the four exceptions mentioned previously, all of the people with PWS accompanied by psychotic episodes had two active copies of any putative imprinted genes or transcripts lying within this small region while non-psychotic people, including a series of control individuals, had only one. The four people with PWS due to UPD(15)mat but without affective psychosis were also found to have two maternally derived alleles at loci between D15S975 and D15S661 with no paternal copy, so segmental UPD had not occurred in them.

As D15S975 is located within IVS3-4 of the *GABRG3* gene and D15S661 lies within the 5'UTR of the *OCA2* gene, neither of which is believed to be imprinted, real-time expression studies were carried out on six ESTs (expressed sequence tags) and three possible scan genes (theoretical genes) identified from database searches of the region. The results obtained suggest that it may not be simple over-expression of a causative imprinted gene present in two active copies that permits the manifestation of psychotic symptoms in PWS people with UPD(15)mat, but an epigenetic dysregulation of gene expression.