

An investigation into psychiatric illness in people with Prader-Willi syndrome: evidence for a genetic basis for psychosis

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Summary

A recent population-based study found that people with the uniparental maternal disomy (UPD) genetic subtype of Prader-Willi syndrome (PWS) inevitably developed a psychotic illness with increasing age, whereas people with the deletion genetic subtype were at a similar risk of developing psychosis as those in the learning disability population in general. This finding implicated a direct relationship between a specific genetic abnormality and psychotic illness and led to the hypothesis that the etiology of psychosis in those with UPD is fundamentally genetic whereas the etiology of psychosis in those with a deletion is the result of the same biologically and socially mediated factors that lead to psychosis in the general population.

To test this hypothesis, the profile of psychiatric illness in people with PWS was explored from three main aspects. First the above finding was investigated in a UK-wide sample. Second the type of illness was fully characterised in terms of diagnosis, phenomenology, characteristics of the clinical course of illness and etiologic factors in three groups: those with PWS caused by UPD, those with PWS caused by a deletion, and an IQ-matched comparison group without PWS but with a history of psychotic illness. Finally, a longitudinal follow-up of the sample was undertaken examining the course of psychiatric illness over time with specific reference to medication.

The findings of this study confirmed that psychotic illness is more prevalent in those with UPD than those with a deletion, but contrary to the previous finding, is not inevitable. Furthermore, the original hypotheses were not supported inasmuch as the nature of illness in both genetic subtypes was similar and resembled an atypical affective disorder with the few differences between the subtypes possibly pertaining to severity of illness. These findings suggested that the fundamental etiology of psychosis is similar for both genetic subtypes. Putative models for the development of psychotic illness in PWS are presented with reference to genetic, neurobiological and environmental etiologic factors. The clinical and genetic implications of this research are discussed, with suggestions for future work, including the possibility that these findings may indicate a genetic cause for psychosis in the general population.