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## THE ROLE OF FAMILY PSYCHIATRIC HISTORY IN THE DEVELOPMENT OF PSYCHOPATHOLOGY IN PEOPLE WITH PWS

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**INTRODUCTION:** From a UK-wide study, we showed that psychotic illness was significantly more prevalent in those with the chromosome 15 uniparental maternal disomy (UPD) genetic subtype (62%) than in those with a 15q11-q13 deletion (17%). As a result, we initially hypothesised that the etiology of psychosis in those with UPD was the result of the specific arrangement of imprinted genes at 15q11-q13, whereas the etiology of psychosis in those with a deletion was influenced by the same bio-psycho-social factors that mediate psychosis in the general population. However, our finding that the phenomenology of psychotic illness was similar in both genetic subtypes suggested that the mechanisms of development of psychosis in both genetic subtypes might be the same. We investigated the presence of psychopathology in first-degree relatives (FDRs) of people with PWS and were able to develop hypothetical models that encompassed the above apparently conflicting findings. The clinical findings were supported and strengthened by genetic investigation.

**METHOD:** We recruited 119 individuals with genetically-confirmed PWS (85 deletion, 34 UPD). A full clinical and family psychiatric history was taken using a battery of tests including the Family History Research Diagnostic Criteria (using the Family history method). A blood sample was taken from each individual for genetic analysis.

**RESULTS:** Depressive illness is more common in FDRs of probands with a deletion with psychosis than probands with UPD with psychosis. Probands with a deletion with psychosis had a significantly greater rate of family history of depression than probands with a deletion without psychosis; this difference did not hold for probands with UPD. Where affective illness was present in parents of probands with a deletion with psychosis in this sample, that parent was inevitably the mother.

**DISCUSSION:** These findings suggest that the risk for developing psychosis in those with a deletion may be inherited via the maternal line. That is, depression in mothers may be caused by the over-expression of a paternally imprinted/maternally expressed gene, which when transmitted to their offspring with a 15q11-q13 deletion manifests as an affective psychotic disorder. Psychotic illness in those with UPD may also be the result of over-expression of a paternally imprinted/maternally expressed gene, but this abnormality is inherent in the UPD genotype and is not inherited.