Abstract

Psychotic illness is strongly associated with the maternal uniparental disomy (mUPD) genetic subtype of Prader-Willi syndrome (PWS), but not the deletion subtype (delPWS). This study investigates the clinical features of psychiatric illness associated with PWS. We consider possible genetic and other mechanisms that may be responsible for the development of psychotic illness, predominantly in those with mUPD. The study sample comprised 119 individuals with genetically confirmed PWS, of whom 46 had a history of psychiatric illness. A detailed clinical and family psychiatric history was obtained from these 46 using the PAS-ADD, OPCRIT, Family History and Life Events Questionnaires. Individuals with mUPD had a higher rate of psychiatric illness than those with delPWS (22/34 v. 24/85, $p<0.001$). The profile of psychiatric illness in both genetic subtypes resembled an atypical affective disorder with or without psychotic symptoms. Those with delPWS were more likely to have developed a non-psychotic depressive illness ($p=0.005$) and those with mUPD a bipolar disorder with psychotic symptoms ($p=0.00005$). Individuals with delPWS and psychotic illness had an increased family history of affective disorder. This was confined exclusively to their mothers. Psychiatric illness in PWS is predominately affective with atypical features. The prevalence and possibly the severity of illness are greater in those with mUPD. We present a 'two-hit' hypothesis, involving imprinted genes on chromosome 15, for the development of affective psychosis in people with PWS, regardless of genetic subtype.