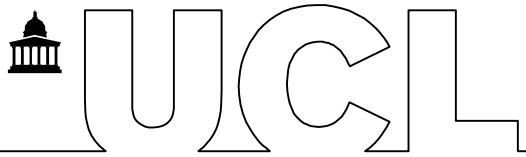

Bebbington, PE; (2014) The significance of copy number variations in schizophrenia. The British Journal of Psychiatry, 205 (1) 77 - 78. 10.1192/bjp.205.1.77a Downloaded from UCL Discovery: http://discovery.ucl.ac.uk/ 1434690

LETTER

The significance of copy number variations in schizophrenia

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Rees *et al'* seek to replicate the association with schizophrenia of copy number variants (CNVs) involving putative schizophrenia loci in a large case—control study. They conclude that 11 of the 15 previously implicated loci were strongly associated with schizophrenia. The odds ratios of these CNVs relative to schizophrenia range between around 2 and >90. The authors suggest that the findings now indicate a need for routine screening for CNVs.

However, I think there are grounds for reservations about the implication of these findings for the generality of cases of schizophrenia, both at the population level and in terms of public health initiatives. The authors report that one or more of the identified CNVs was present in 2.5% of the case group and in 0.9% of the control group. Let us assume that the prevalence of schizophrenia in the general population is around 0.5%, as reported in the British National Psychiatric Morbidity Surveys.'—' From this it is possible to calculate that, for every one person with schizophrenia who has one of these CNVs, there would be around 72 in the unaffected population. The positive predictive value (PPV) is the proportion of positive results of a test that are truly positive, and the PPV equivalent to these data can be calculated at 1.37%: in other words, this is the probability that someone with one of the identified CNVs has schizophrenia. If we change the assumed prevalence of schizophrenia to 1%, the PPV rises to 2.73%. The authors say: `[g]iven their frequency, these findings therefore suggest that routine screening for CNVs should be made available and that the results will have immediate implications for genetic counselling, and given their comorbidity with other medical disorders, for patient management as well'. However, in my view, these values for PPVs make this conclusion questionable.

It is also of interest to use the authors' data to calculate the population attributable fraction (PAF): this is the notional amount by which the prevalence of an outcome would be reduced if the particular exposure were completely removed from the population. It reflects both the frequency of the given exposure and the strength of its effect. Using these data and, as before, assuming a prevalence of 0.5%, the PAF is 0.618%. If we assume a prevalence for schizophrenia of 1%, this index changes very little, to 0.622%. This is not a large value: we found a PAF of 14% for the link between psychosis and non-consensual sexual intercourse before the age of 16,[5] whereas a meta-analysis by Varese *et* a)[6] suggests that the PAF for all forms of childhood adversity in schizophrenia is 33%.

The practical implications of CNVs in schizophrenia are thus in some doubt.

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