NEWS

Genetics: Spontaneous mutations play role in schizophrenia

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Harmful spontaneous mutations may account for up to half the cases of non-inherited schizophrenia, according to a study published 7 August in *Nature Genetics*[1].

The results support a role for *de novo* mutations — those not inherited from either parent — in schizophrenia and autism. Studies have linked a high rate of *de novo* copy number variations — duplications or deletions of genetic regions — to both autism and schizophrenia. A study published in May also suggests a role for ***de novo* point mutations**, which change, insert or delete a single DNA base, in autism[2].

Researchers sequenced the exomes, the entire protein-coding regions, of 20 individuals from simplex families, which have one child with autism, but unaffected parents and siblings. They found

21 *de novo* point mutations, four of which appear highly likely to lead to disease.

Researchers generally believe that insults to genetic regions underlie most cases of schizophrenia. However, only 50 percent of these mutations are likely to be inherited.

In the new study, researchers sequenced the exomes of 53 individuals with non-inherited schizophrenia and 22 controls, and their parents. They found 40 *de novo* point mutations in the individuals with non-inherited schizophrenia. Each of the 40 mutations is in a different gene, and none of them are present in any of the controls or parents, or in 679 control individuals from the **1000 Genomes Project**.

Of the 40 mutations, 38 alter the corresponding protein code. Based on predictive software, 19 of these are highly likely to affect protein function. By contrast, among controls, the study identified seven *de novo* point mutations, four of which change the corresponding protein code.

The *de novo* point mutations in the individuals with schizophrenia are also ten times more likely to affect protein function than are rare inherited gene variants in the same group of people. This suggests that the *de novo* mutations are more likely to be causative than the inherited variants.

Only one of the identified 40 mutations is in a region associated with schizophrenia, **22q11.2**. Specifically, the researchers found a mutation in **DiGeorge syndrome critical region gene 2** (DGCR2).

References:

1: Xu B. *et al. Nat. Genet.* Epub ahead of print (2011) **PubMed**

2: O'Roak B.J. *et al. Nat. Genet.* **43**, 585-589 (2011) **Abstract**