NEWS

Genetics: Spontaneous mutation links dopamine to autism

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Structural shift: A genetic mutation that changes one amino acid on the dopamine transporter protein from threonine (green) to methionine (gray) alters its interaction with dopamine.

A newly discovered spontaneous mutation, described 27 August in *Molecular Psychiatry*, links autism to changes in the regulation of the chemical messenger dopamine[1].

Dopamine, a **neurotransmitter**, has been implicated in a range of psychiatric conditions, including attention deficit hyperactivity disorder (ADHD), schizophrenia, **Rett syndrome** and **Angelman syndrome**.

This study is the first to link a spontaneous, or *de novo*, mutation in the dopamine transporter gene SLC6A3, which codes for a protein that helps regulate dopamine levels in the brain, to autism. Individuals with autism are known to have an **elevated rate of harmful *de novo* mutations**.

The researchers discovered the mutation in a child with autism who had been recruited as part of the **Autism Consortium**, a Boston-area collaboration of 15 institutions. The child's parents and sibling are unaffected and do not carry the mutation.

The mutation, dubbed T356M, leads to a single amino acid change in the resulting protein. This mutant version no longer functions correctly, the researchers found: Instead of ferrying dopamine into the cell, the transporter pushes it out.

To examine the behavioral effects of the mutation, the researchers injected fruit fly embryos lacking the dopamine transporter with either the normal version of the gene or the T356Mvariant. They then assessed behavior in the adult fruit flies by tracking how much they flew around a tube over three days.

Flies with the T356M variant, they found, are hyperactive compared with those that carry the normal version of the transporter. This suggests that the *de novo* mutation plays a role in hyperactivity, a common feature of autism.

References:

1: Hamilton P.J. *et al*. *Mol. Psychiatry* Epub ahead of print (2013) **PubMed**