NEWS

Large genome scan turns up new autism addresses

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An analysis of blood samples from nearly 17,000 individuals with autism points to new regions of

the genome likely to be involved in the disorder, researchers reported yesterday at a **conference at the Broad Institute** in Cambridge, Massachusetts. A study of about the same size highlights previously unknown genomic hotspots for attention deficit hyperactivity disorder (ADHD).

The unpublished work involves the largest sample to date for a study of its type in autism. As such, it boosts the promise of genome-wide association studies (GWAS), a method of unearthing genetic variants that contribute to a condition and are present in a broad swath of the general population. These common variants are likely to **account for the bulk of inherited risk** for autism[1].

The GWAS method compares the DNA of people with and without a disorder using thousands of markers scattered throughout their genomes. The approach has so far **failed to yield durable clear hits** in the case of autism, primarily because the sample sizes have not been big enough. That state of affairs may be about to change.

“The GWAS is working,” says **Benjamin Neale**, statistical geneticist at Massachusetts General Hospital, who presented the results. “It’s the first building block, that initial step that we can use to start to identify some of the biological influences.” Once scientists understand what is going on at a biological level, he says, they can begin to move toward therapies.

Numbers game:

The power of the new analysis comes from its large sample size. The sample represents the efforts of an international collaboration called the **Psychiatric Genomics Consortium,** in which more than 800 scientists from 38 countries collect and comb through genomic data.

“This international collaborative spirit is truly the lifeblood of genetics,” Neale says. “It is only through working together and drawing together these large sample sizes that we can make inroads into the genetic basis of these devilishly difficult phenotypes and disorders.”

By far the biggest **contribution to this dataset comes from Denmark**, where a national registry houses genetic, family and epidemiological information on the entire population. The researchers used about 70,000 blood samples that the State Serum Institute in Copenhagen has collected since 1981 from babies routinely screened at birth for metabolic diseases. They analyzed them using a technology called the **iPsych chip**. The chip includes 50,000 genetic markers — single-letter variations, or single nucleotide polymorphisms (SNPs) — that are associated with psychiatric disorders, scattered throughout the genome.

The new analysis is based on data from 16,966 individuals with autism, a huge bump from the approximately 6,000 total cases that others have studied so far, says **Mark Daly**, associate professor of medicine at Massachusetts General Hospital and a collaborator on the project. The researchers compared the pattern of markers in these samples with those in 26,732 controls.

So far, they have identified five new genetic regions as being significantly associated with autism, and two or three of those associations look particularly robust, says Neale. The findings are preliminary, and the team declined to reveal details because the analysis is unpublished. But Daly says there is significant genetic overlap with areas implicated in schizophrenia and a hint that immune genes play a role.

The team also scanned the genomes of about 18,000 individuals with ADHD and nearly 34,000 controls for the same set of SNPs. That analysis led them to eight new segments of the genome that are likely to contribute to the disorder, though the genes involved are still largely unknown. Here, too, there is overlap with schizophrenia, suggesting that the two disorders share a common biological mechanism.

The next challenge, Neale says, is to identify the mechanisms, and try to figure out the function of the genes implicated.

REFERENCES:

1. Gaugler T. *et al. Nat. Genet.* **46**, 881-885 (2014) **PubMed**