Two unique studies indentify three genetic regions associated with schizophrenia

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(Medical Xpress) -- Two new independent research groups looking to find the genetic roots of schizophrenia and bipolar disorder have found evidence of variations in regions of the human genome that appear to be associated with either or both neurological disorders. In the first study, a Chinese group led by Wei Huang, found variations in chromosome region 11 -- 11p11.2. The second group, led by Lin He and Yongyong Shi and comprised of an international team of researchers from both Asian and Western countries, found variations in two chromosome regions 8p12 and 1q24.2. Both teams have published their results in *Nature Genetics*.

What is most unusual about both studies is that both were carried out using Chinese populations as the study group. Until now, virtually all genome-wide association studies (GWAS) have been carried out using western populations. In the first study, 746 people diagnosed with schizophrenia were compared with a control group composed of 1,599 people. In the second 3,750 schizophrenic patients were compared against a 6,468 person control group. To verify their results, both groups repeated their studies with a second group of patients and control groups.

In both studies the variants in the chromosome regions were unexpected as they had never before been connected with either schizophrenia or bipolar disorders. Though previous research had suggested a region associated with chromosome 6 had some connection with the immune system, which is relevant because it is commonly believed by researchers that autoimmunity is involved in schizophrenia.

Schizophrenia and bipolar disorders for that matter are believed to be caused by genetic variations that cause people to become particularly sensitive to unknown environmental factors that lead to neurological problems that can cause hallucinations in the case of schizophrenia and emotional problems in those with a bipolar disorder. Because of this, research has focused on finding which chromosomal regions are at play. The problems thus far though have centered around discerning which regions are in fact contributing to the problem and which aren't and which might in fact overlap.

The two studies together comprise one of the largest psychiatry projects ever undertaken, with over 5000 people tested and studied by a combined group of over 250 people; the work involved a colossal amount of planning, coordination and work. And while the results themselves are interesting, they don't by themselves mark a breakthrough in treating either ailment. What they have found though, will almost certainly lead to many more research projects that use what has been discovered in these studies to reach farther into the unknown. Research that will hopefully one day solve many of the mysteries of neurological disorders and offer relief to those afflicted.

More information: 1. Genome-wide association study identifies a susceptibility locus for schizophrenia in Han Chinese at 11p11.2, *Nature Genetics* (2011) doi:10.1038/ng.979

Abstract

To identify susceptibility loci for schizophrenia, we performed a two-stage genome-wide association study (GWAS) of schizophrenia in the Han Chinese population (GWAS: 746 individuals with schizophrenia and 1,599 healthy controls; validation: 4,027 individuals with schizophrenia and 5,603 healthy controls). We identified two susceptibility loci for schizophrenia at 6p21-p22.1 (rs1233710 in an intron of ZKSCAN4, Pcombined = 4.76 × 10−11, odds ratio (OR) = 0.79; rs1635 in an exon

of NKAPL, Pcombined = 6.91 × 10−12, OR = 0.78; rs2142731 in an intron of PGBD1, Pcombined = 5.14 × 10−10, OR = 0.79) and 11p11.2 (rs11038167 near the 5′ UTR of TSPAN18, Pcombined = 1.09 × 10−11, OR = 1.29; rs11038172, Pcombined = 7.21 × 10−10, OR = 1.25; rs835784, Pcombined = 2.73 × 10−11, OR = 1.27). These results add to previous evidence of susceptibility loci for schizophrenia at 6p21-p22.1 in the Han Chinese population. We found that NKAPL and ZKSCAN4 were expressed in postnatal day 0 (P0) mouse brain. These findings may lead to new insights into the pathogenesis of schizophrenia.

2. Common variants on 8p12 and 1q24.2 confer risk of schizophrenia, *Nature Genetics* (2011) doi:10.1038/ng.980

Abstract
Schizophrenia is a severe mental disorder affecting ~1% of the world population, with heritability of up to 80%. To identify new common genetic risk factors, we performed a genome-wide association study (GWAS) in the Han Chinese population. The discovery sample set consisted of 3,750 individuals with schizophrenia and 6,468 healthy controls (1,578 cases and 1,592 controls from northern Han Chinese, 1,238 cases and 2,856 controls from central Han Chinese, and 934 cases and 2,020 controls from the southern Han Chinese). We further analyzed the strongest association signals in an additional independent cohort of 4,383 cases and 4,539 controls from the Han Chinese population. Meta-analysis identified common SNPs that associated with schizophrenia with genome-wide significance on 8p12 (rs16887244, P = 1.27 × 10−10) and 1q24.2 (rs10489202, P = 9.50 × 10−9). Our findings provide new insights into the pathogenesis of schizophrenia.