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Understanding The Genetics Of Schizophrenia

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Abstract

Schizophrenia has been considered heritable for a long time, but only with the advent of new technologies such as whole-genome sequencing and genome-wide association studies can we begin to identify specific molecular causes of schizophrenia. This poster will review some of the genetic variants that research groups have associated with schizophrenia. Current research has indicated that schizophrenia is a polygenic disease and has been linked to many genes. Some of these common risk variants are in protein coding sections of the DNA. These proteins are often linked to neurological development or immune system function. Other variants that have been associated with schizophrenia are copy number variants(CNV's), DNA repeats that vary in length. Certain changes to the length of these CNV's, either through deletion, insertion, duplication or translocation have been associated with schizophrenia. These associations may help researchers identify new protein coding regions of DNA that have been changed. Identifying these genes can help us better understand how schizophrenia is inherited and it may also allow us to detect and monitor high risk patients or lead to new treatment options that enable regular function of these proteins.

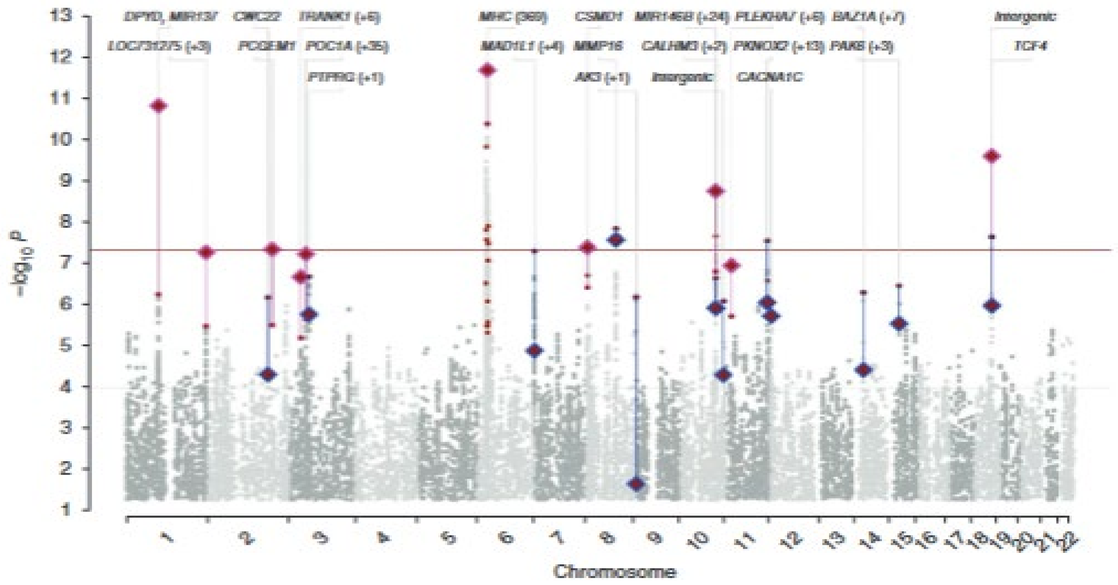


Fig.1: Shows a Manhattan plot of different regions affected by SNP's. Regions more closely associated with schizophrenia are highlighted in pink and regions less associated with schizophrenia are highlighted in blue. (above)

This table shows many different genes that were associated with schizophrenia by using genome wide association studies. These studies helped researchers find many new genes that had not been associated with schizophrenia before. Genes with a high association are highlighted in pink whereas genes highlighted in blue have a lower association. One of these genes is MIR137 which codes for a micro-RNA which regulates the expression of many genes which are important in neuronal development and maturation. Variations in the MIR137 gene and the genes it regulates have all been associated with schizophrenia. Other genes that code for intermembrane proteins such as CACNA1C(Codes for a calcium channel) and ANK3 (A anchor like protein which helps bind other proteins to the cytoskeleton) have also been associated with schizophrenia and other mental illnesses such as bipolar. There is no doubt that as research continues new gene variations and proteins will be associated with schizophrenia.

The two figures at the right show parts of the genome called copy-number variants(CNVs). These copy-number variants are long repeated sections of the DNA and in everyone these repeated sections are different lengths. In some cases, and at some specific high-risk locations on the genome these CNVs can overlap coding parts of the genome. This overlapping can result in genetic variation and can affect protein function. Some of these CNVs have long been associated with certain diseases been only with new technology such as whole-genome sequencing have these CNVs been associated with schizophrenia and some other mental illnesses and intellectual disabilities The first picture shows three CNVs(1q21.1, 15q11.2, 15q13.3) which were associated with schizophrenia by researchers. The second picture on the right is an easy-to-understand example of how these variations occur.

Fig 2. Shows the genomic architecture of the 1q21.1, 15q11.2, and 15q13.3 deletions.(below)

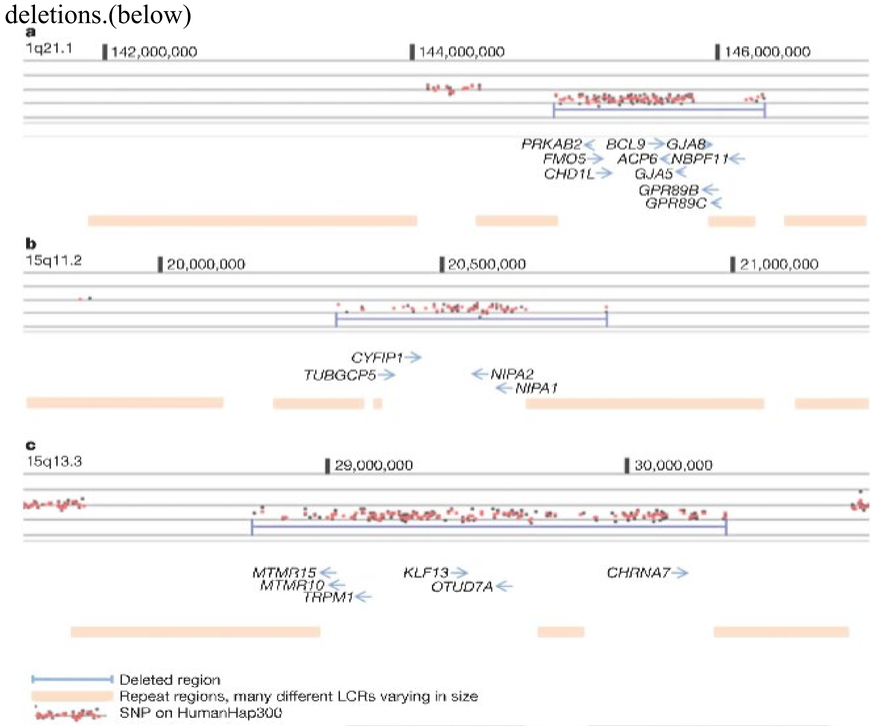
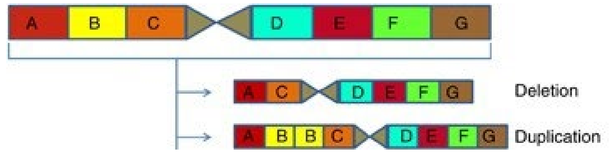


Fig 3. Illustration of a copy number variant and the different mechanisms which change the length of the CNV.(right)



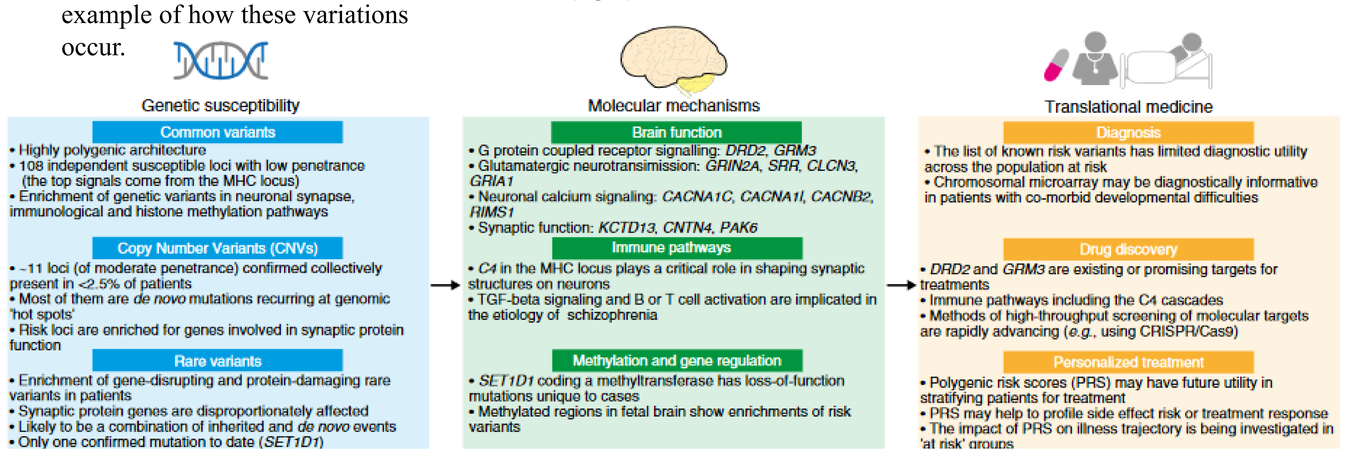


Fig. 4: schematic flow of translational research. Diagrams show a pipeline from genetic discoveries via biological insights to potential applications for translational medicine.(above)

The flow chart above shows how new technologies that allow us to identify genetic variations that increase the risk of developing disease can lead to new medicine and treatment. This gives researchers the information they need to start working on and identifying the mechanisms that cause diseases such as schizophrenia and allows them to begin working on developing new treatments. Furthermore, as these technologies become more accessible, treatment will become more personalized and will be more effective for patients. Moreover, it will also allow patients to be diagnosed and monitored for their risk before showing signs of illness.

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