Brain asymmetry and schizophrenia in the post-genomic age

How a symptom-based approach might help uncovering the genetic link

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SCHIZOPHRENIA & LATERALIZATION ARE LINKED...

Most people are right-handed and show left-hemispheric language lateralization, but a minority exhibits left-handedness and right-hemispheric language lateralization. This atypical lateralization pattern is observed significantly more often in schizophrenia patients than in the general population.

...PRESUMABLY GENETICALLY...

Since both schizophrenia and lateralization have a substantial hereditary component, several authors concluded that there is a genetic link between lateralization and schizophrenia. It has even been suggested that a failure in the lateralization process, orchestrated by genes, could be the primary cause of schizophrenia. However, the molecular genetic evidence for a link between lateralization and schizophrenia is weak. Recent genetic evidence indicates that schizophrenia is not a single disorder but a group of heritable disorders caused by different genotypic networks leading to distinct clinical symptoms.

...BUT HOW?...

To uncover the link between schizophrenia and lateralization we therefore suggest a paradigm shift where genetics are not mapped on schizophrenia as a whole but on discrete schizophrenia symptoms. For instance, some lateralized functions, like language, can be directly linked to certain symptoms (e.g., auditory verbal hallucinations, disorganized speech) because both pertain to the same cognitive system (i.e., language). Other symptoms, such as catatonic behavior, for example, may not show such a clear-cut association with atypical lateralization.

...TOWARDS A SYMPTOM-BASED APPROACH

Specifically, we propose that each major schizophrenia symptom should be assessed with detailed and specialized questionnaires. Moreover, since different lateralized functions seem to have partly independent genetic determinants, we would suggest to always assessing hand preference, hand skill, and a behavioral measure of language lateralization (e.g., with dichotic listening) as basic asymmetry phenotypes. In addition, behavioral markers of other lateralized functions (e.g., emotional or spatial processing) and markers of structural brain asymmetries (e.g., measured with voxel-based morphometry of diffusion tensor imaging) might be of interest. The same phenotypes need to be examined in patients with schizophrenia and healthy controls.

Taken together, we hope that such a symptom-driven approach, in which specific schizophrenia symptoms are assessed with specific lateralized functions, may help to stimulate new research that might help to finally disentangle the riddle of how lateralization and schizophrenia are associated.


References