New study tracks onset of schizophrenia in children: mapping changes in brain's white matter may open window to early diagnosis, treatment

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MONTREAL - Researchers have discovered a clue that may help explain why schizophrenia often does not develop until late adolescence. And, if further studies go well, physicians may eventually be able to identify children and teenagers at risk of developing the disease.

In the study, which was published in the March 19 issue of Science, MRIs were obtained from 111 normal subjects aged four to 17 at the National Institute of Mental Health in Bethesda, Md., and the results analysed at the Montreal Neurological Institute's brain imaging centre.

The investigators found that structural maturation of fibre tracts in the brain may play a role in cognitive development during childhood and adolescence. ``We were interested in looking for changes in white matter, which is made up of fibres that connect different parts of the brain,'' Dr. Tomas Paus (PhD), an assistant professor in the department of neurology and neurosurgery at the institute, said in an interview.

``We knew from post-mortem studies that myelination continues for a long period of time until the late 20s for certain fibre. What is new about it (the study) is that we could see such changes in the living brain.''

Among the MRI findings were significant age-related increases in white matter density in fibre tracts of the brain within the left and right internal capsule and the posterior portion of the left arcuate fasciculus.

The arcuate fasciculus contains fibres connecting frontal and temporal cortical regions involved in speech. ``It is therefore noteworthy that age-related white matter increases in this pathway reached significance only in the left but not the right hemisphere,'' the study noted. The left hemisphere is assumed to be dominant for speech in the majority of right-handed subjects.

This finding provides evidence for a gradual maturation, during late childhood and adolescence, of fibre pathways likely supporting motor and speech functions, the authors noted. ``That, very indirectly, made us think about schizophrenia,'' Dr. Paus said.

``What is neat about finding changes in that particular fibre tract is that it connects two speech regions,'' Dr. Paus said. ``Quite a few theories of schizophrenia now emphasize abnormalities in functional connections between different brain regions but also between, in fact, the two speech regions.''

In schizophrenia, miscommunication between the frontal and temporal speech regions--perhaps caused by an abnormal rate of myelin growth during childhood--might lead to the auditory hallucinations (such as hearing voices) that are characteristic of the disease.

Dr. Paus noted another study he was involved in found that when normal subjects speak--even when they don't hear themselves--the speech regions appear to send feedback to the brain, telling it: ``Now it's me that's speaking, you're not hearing

voices.'' In that study, patients were asked to whisper two syllables while their auditory input was masked. Even though they could not hear themselves, changes were detected in the left hemisphere in the region that normally processes speech sounds. This region is connected by the arcuate fasciculus.

It is theorized that this feedback does not work properly with schizophrenics. ``So when the (schizophrenic) patient speaks or even thinks silently, there is no feedback going back to the speech regions that process input.'' As a result, schizophrenics may explain that unusual experience by believing they're hearing voices.

Dr. Paus noted there is a lot of evidence to consider schizophrenia a developmental disorder. ``People think something happens in the developing brain of would-be schizophrenics in utero, whether it's environmental insult, perinatal injury, interaction of the environment with susceptibility genes, it doesn't really matter.''

If it is accepted that something happens that affects normal brain development and connectivity in the brain, it is puzzling that psychotic symptoms are not seen until late adolescence, Dr. Paus asked. What happens in the silent period between the insult and symptoms?

``Perhaps it's the maturation of the pathway that unlocks the symptoms,'' Dr. Paus said. To discover the answer, he is planning a followup study to determine whether the brain matures in a slightly different way in children or teenagers who are at risk for schizophrenia.

If the answer is yes, ``that may be an important window of opportunity to do something to prevent a full-blown disorder,'' Dr. Paus said. If early testing in children could determine who is at risk, it could change the way the mental disorder is treated, he suggested. ``If you could come up with a good rationale for a reasonable intervention before you have full-blown disease, that would be extremely helpful.''