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Early Cognitive Deficits, Developmental Delays, May Be a Harbinger for Adult-Onset Schizophrenia

Pam Harrison

January 11, 2010 — Children who develop schizophrenia as adults already show signs of cognitive deficits by the age of 7 years and lag behind their peers on measures of memory, attention, and processing speed as they mature, according to results of the 30-year Dunedin Multidisciplinary Health and Development Study.

In a study published online January 4 in the *American Journal of Psychiatry*, Abraham Reichenberg, PhD, Institute of Psychiatry, King's College, London, United Kingdom, and colleagues, found that children who developed schizophrenia as adults had signs of development deficits relative to their peers that emerged early and remained stable on cognitive tests assessing verbal and visual knowledge acquisition, reasoning, and conceptualization. The same children also lagged behind their peers on tests assessing processing speed, attention, visual-spatial problem solving, and working memory.

Neither one of these premorbid cognitive patterns were seen in children who later developed recurrent depression.

"The neurodevelopmental model of schizophrenia says many of these neurological deficits appear years before the disorder is diagnosed, and what we specifically wanted to do was learn more about the nature of these cognitive deficits and go beyond the IQ," study investigator Avshalom Caspi, PhD, told *Medscape Psychiatry*. "And I think these findings underscore the fact that what we think about as adult psychiatric disorders have their origins much earlier in life."

Longitudinal Investigation

The Dunedin Multidisciplinary Health and Development Study is a longitudinal investigation of the health and behavior of a complete cohort of children born in Dunedin, New Zealand, between 1972 and 1973.

A total of 1037 children from this birth cohort participated in the follow-up assessment at 3 years of age and formed the base sample for the study. The Wechsler Intelligence Scale for Children—Revised (WISC-R) was administered to participants within 1 month of their birthdays at ages 7, 9, 11, and 13 years. Participants were also given 8 subtests of the WISC-R. As previously reported, lower childhood IQ among the same cohort of children significantly predicted an increased risk of being diagnosed as having schizophrenia or depression as an adult, even after controlling for social class [*Am J Psychiatry*. 2009;166:50-57].

In the current analysis, children who developed schizophrenia as adults exhibited early cognitive deficits on 4 cognitive tests: information, similarities, vocabulary, and picture completion. "Calculated in terms of mental age, the extent of impairment on these tests ranged from 0.4 to 0.8 years," the study authors add.

Developmental deficits were also apparent, although less strikingly so, among children who developed recurrent depression as adults.

On tests measuring freedom from distractibility and visual-spatial problem solving, skills among children who would develop future schizophrenia were developmentally slower such that, on average, "for every year between the ages of 7 and 13, future schizophrenia case subjects fell behind healthy comparison subjects by an additional 0.17 to 0.26 mental age years," the investigators observe.

Again, developmental lags were less apparent among children who later developed recurrent depression.

Psychiatry's "Holy Grail"

Coinvestigator Richard Keefe, PhD, Duke University Medical Center, Durham, North Carolina, told *Medscape Psychiatry* that trying to establish which child will develop future schizophrenia is really the "Holy Grail" in psychiatry, but so far early

identification of future schizophrenia is more complex than simply identifying children with lower IQs.

Indeed, the study authors stress that they do not recommend testing IQ in children for the early identification of those at potential risk for schizophrenia because there is simply too much change in cognitive development over time in all children, and a single test at a single age will not be helpful.

"We've known for a while that cognitive deficits make an individual vulnerable to progression to psychoses, and what these data show are that vulnerable children perform worse on certain tasks than their peers, and these deficits make them vulnerable to worsening over time, and the combination of early deficit and worsening over time appears to be the most sensitive index we have of vulnerability to psychosis at this point in time," said Dr. Keefe.

Accumulating Evidence

Peter Jones, MD, PhD, University of Cambridge, United Kingdom, said the study adds to accumulating evidence for the developmental aspect of schizophrenia.

"The fact that there were early cognitive and developmental abnormalities in schizophrenia has really been known for more than 15 years from similar studies," he told *Medscape Psychiatry*. This study, however, "takes it a bit further because it examines cognitive function from a more dynamic point of view — in other words, the way things change over time rather than the fact that children are different from anyone at any one point in time."

He also suggests that it is "no surprise" that there are these sorts of deficits and development lags in children who develop schizophrenia as adults.

"We know that different parts of the brain subserve different cognitive function, so if those different parts of the brain develop in different ways, then you would expect that abnormalities that develop would be expressed in different ways," he said. Dr. Jones added that the "really important goal" in this sort of research is to understand the neurobiology of these deficits, which, once better understood, "may suggest new interventions."

The study was supported by a United Kingdom Medical Research Council grant. National Institute of Mental Health grants, a National Institute on Aging grant, funding for the Dunedin Multidisciplinary Health and Development Research Unit from the New Zealand Health Research Council, and the Royal Society-Wolfson Merit Award. Dr. Reichenberg has received speaker's honoraria from AstraZeneca. Dr. Keefe has served as a consultant to Cortex, Schering-Plough, Abbott, Acadia, AstraZeneca, BiolineRx, Bristol-Myers Squibb, Cephalon, Dainippon Sumitoma Pharma, Eli Lilly, Johnson and Johnson, Lundbeck, Memory Pharmaceuticals, Merck, NeuroSearch, Orexigen, Orion, Otsuka, Pfizer, Roche, Sanofi/Aventis, Targacept, Wyeth, and Xenoport. Dr. Caspi has disclosed no relevant financial relationships. Dr. Jones has received honoraria from Bristol-Myers-Squibb, Otsuka, and Eli Lilly for lectures and has received a research grant from GlaxoSmithKline within the previous year.

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Authors and Disclosures

Journalist

Pam G. Harrison

Pam G. Harrison is a freelance writer for Medscape.

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