Index detects early signs of deviation from normal brain development

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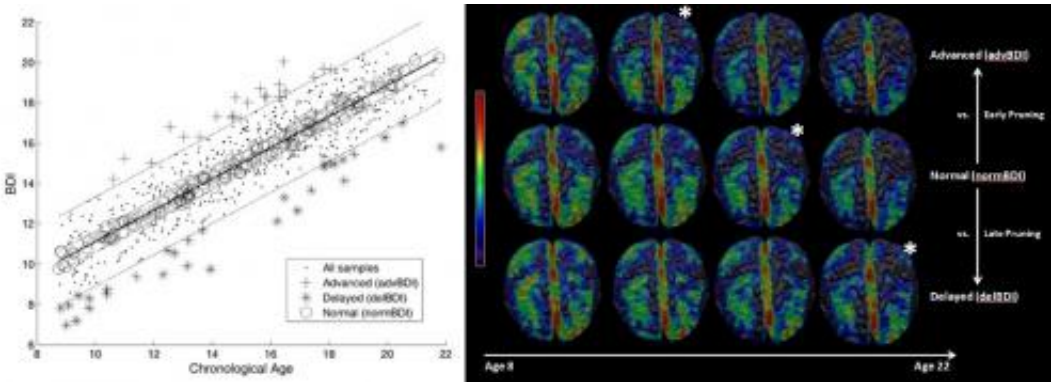

Left: Scatter plot of brain development indexes (BDIs) of 621 subjects calculated from MRI images, against their ages. The subjects with BDIs outside the 90 percent prediction interval have been labeled as outliers, i.e. advanced or delayed brain development. Right: The average gray matter tissue density maps in different ages for the advanced, delayed and normal subject groups indicate a consistent structural change in gray matter—with a developmental shift between the three groups. Credit: Guray Erus, PhD/*Cerebral Cortex*

(Medical Xpress)—Researchers at Penn Medicine have generated a brain development index from MRI scans that captures the complex patterns of maturation during normal brain development. This index will allow clinicians and researchers for the first time to detect subtle, yet potentially critical early signs of deviation from normal development during late childhood to early adult.

The study, published online in the journal *Cerebral Cortex*, shows a relationship between cognitive development and physical changes in the developing young brain (aged 8 to 21).

"Our findings suggest that brain imaging via sophisticated MRI scans may be a useful biomarker for the early detection of subtle developmental abnormalities," said Guray Erus, PhD, a research associate in the department of Radiology at the Perelman School of Medicine at the University of Pennsylvania, and the study's lead author. "The abnormalities may, in turn, be the first manifestations of subsequent neuropsychiatric problems."

Among its key findings is the consistency in healthy brain development of young people. The study examined cognitive performance of outliers – adolescents whose brains developed faster or slower than the normal rates. Early maturers performed significantly better than those with delayed brain development in the speed at which they completed certain tasks. The improved speed of performance indicates increased efficiency in neuronal organization and communication. Slower performance in such tests is a precursor to neuropsychiatric disorders, (the research suggests), including adolescent-onset psychosis.

The 14 tests used in the Penn study evaluate a broad range of cognitive functions including abstraction and mental flexibility, attention, working memory, verbal memory, face memory, spatial memory, language reasoning, nonverbal reasoning, spatial processing, emotion identification, and sensorimotor speed.

Penn's brain development index consolidates a number of complex visual maps derived from sophisticated analysis of MRI scans into a unified developmental template. By looking at an individual's brain maps in relation to the consolidated findings, researchers can estimate the age of the subject. Subjects whose brain development index was higher than

their chronological age had significantly superior cognitive processing speed as measured by the cognitive tests compared to subjects whose brain indices were lower than their actual age.

"This is analogous to producing growth charts used in pediatrics to screen for gross abnormalities of physical development," said Christos Davatzikos, PhD, professor of Radiology and Electrical and Systems Engineering at Penn and one of the study's co-senior authors. "We can assess individuals in terms of where they place in relation to the overall trends. While single image maps can be used for an accurate estimation of the age of the subject, the combination of all maps achieves a higher accuracy in age prediction than the accuracy of each map independently."

Previous studies have outlined normative trajectories of growth for individual brain regions across the lifespan; the Penn study is the first to present a comprehensive index for the entire brain during late childhood, adolescence, and young adulthood—periods when the healthy human brain maturates in a remarkably consistent way, deviations from which possibly signify later neuropsychiatric problems.

The Penn study used a sample of 621 participants in the Philadelphia Neurodevelopmental Cohort, a Grand Opportunity study funded by the National Institute of Mental Health, designed to understand how brain maturation mediates cognitive development and vulnerability to psychiatric illness and how genetics impacts this process.

"All of our young study participants have received a standardized neuropsychiatric evaluation at intake, and all agreed to be contacted for future studies. Some are followed up longitudinally," said Ruben C. Gur, PhD, director of the Brain Behavior Laboratory at Penn and the study's other co-senior author. "We can therefore follow those who score low on our index and examine whether interventions such as cognitive

remediation can mitigate potential symptoms."

More information: Guray Erus, Harsha Battapady, Theodore D. Satterthwaite, Hakon Hakonarson, Raquel E. Gur, Christos Davatzikos, and Ruben C. Gur. "Imaging Patterns of Brain Development and their Relationship to Cognition." *Cereb. Cortex* first published online January 12, 2014 DOI: 10.1093/cercor/bht425

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