A brain signal for psychosis risk

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Only one third of individuals identified as being at clinical high risk for psychosis actually convert to a psychotic disorder within a 3 year follow-up period. This risk assessment is based on the presence of sub-threshold psychotic-like symptoms.

Thus, clinical symptom criteria alone do not predict future psychosis risk with sufficient accuracy to justify aggressive early intervention, especially with medications such as antipsychotics that produce significant side effects.

Accordingly, there is a strong imperative to develop biomarkers of psychosis risk that can improve the ability to predict which individuals are most likely to transition to a psychotic disorder.

A study published in the current issue of *Biological Psychiatry* provides evidence that mismatch negativity (MMN), an event-related brain potential component derived from scalp electroencephalography (EEG) recordings, may be such a biomarker.

Mismatch negativity is an EEG signal that is elicited automatically from auditory cortex and frontal lobe regions of the brain in response to sounds that deviate from preceding sounds in pitch, duration, or other auditory features, even when one is not paying attention to the sounds. This electrophysiological measure of auditory deviance detection is thought to reflect short term plasticity in the brain, since it depends on the formation of a short term memory of recently heard sounds in order to detect a deviant sound.

Mismatch negativity is known to be reduced in patients with full-blown schizophrenia. So, to conduct this study, researchers assessed MMN in patients with schizophrenia, patients at clinical high risk for psychosis, and healthy control subjects. Compared to the healthy subjects, MMN was reduced in the patients with schizophrenia, as expected, but was also reduced in the high-risk patients. Analyses showed that MMN did not differ between the two patient groups.

"Our study results show that mismatch negativity deficits precede the onset of psychosis in clinical high risk individuals, and further shows that the larger the deficit, the more imminent the risk for conversion to a psychotic disorder," said Dr. Daniel Mathalon, Professor of Psychiatry at the University of California, San Francisco and senior author on the paper.

In addition, they also followed the clinical high-risk group for over twelve months and compared those who converted to a psychotic disorder with those who did not. MMN was reduced in those individuals who ultimately developed a psychotic disorder, compared to those who remained only in the clinical high risk category.

Mathalon added, "Importantly, our study results converge with those reported by several other studies from researchers in Europe and Asia. This remarkable convergence of findings points to the mismatch negativity as a promising EEG-based biomarker of psychosis risk that, with further development, could enhance our ability to identify which individuals are at greatest risk for psychosis and in greatest need of early treatment, particularly if the treatment is associated with potential adverse effects (such as antipsychotic medication)."

Indeed, there is substantial interest in developing diagnostic and prognostic tests for psychiatric disorders. "We do not currently use tests to help us make diagnoses or to inform patients about the likely long-

term course of their illness," commented Dr. John Krystal, Editor of *Biological Psychiatry*. "However, this study suggests that one day it may be possible to develop this type of test."

More information: The article is "Automatic Auditory Processing Deficits in Schizophrenia and Clinical High-Risk Patients: Forecasting Psychosis Risk with Mismatch Negativity" by Veronica B. Perez, Scott W. Woods, Brian J. Roach, Judith M. Ford, Thomas H. McGlashan, Vinod H. Srihari, and Daniel H. Mathalon (DOI: 10.1016/j.biopsych.2013.07.038). The article appears in *Biological Psychiatry*, Volume 75, Issue 6 (March 15, 2014)

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