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## In Schizophrenia Patients, Auditory Cues Sound Bigger Problems

Researchers at the University of California, San Diego School of Medicine and the VA San Diego Healthcare System have found that deficiencies in the neural processing of simple auditory tones can evolve into a cascade of dysfunctional information processing across wide swaths of the brain in patients with schizophrenia.

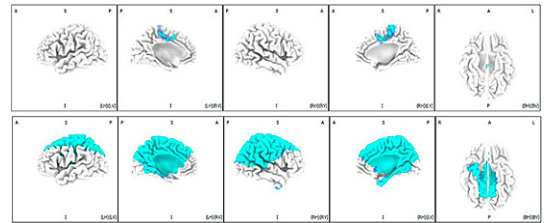
The findings are published in the current online edition of the journal *Neuroimage*.

Schizophrenia is a mental disorder characterized by disturbed thought processes and difficulty in discerning real from unreal perceptions. Common symptoms include auditory hallucinations and unfounded suspicious ideas. The disorder affects about 1 percent of the U.S. population, or roughly 3 million people.

“Impairments in the early stages of sensory information processing are associated with a constellation of abnormalities in schizophrenia patients,” said Gregory Light, PhD, associate professor of psychiatry at UC San Diego and senior author of the study.

These impairments, according to Light, may explain how schizophrenia patients develop clinical symptoms such as hearing voices that others cannot hear and difficulty with cognitive tasks involving attention, learning and recalling information. “If someone’s brain is unable to efficiently detect subtle changes in sounds despite normal hearing, they may not be able to automatically direct their attention and rapidly encode new information as it is being presented.”

Light and colleagues used electroencephalography – a technique that records patterns of electrical brain activity using electrodes positioned on the scalp – on 410 schizophrenia patients and 247 nonpsychiatric comparison subjects. The researchers employed novel



*In this schematic, reduced activation in discrete medial prefrontal brain regions is depicted (in blue) in schizophrenia patients, occurring 0.2 seconds after sound changes (top panel), cascading forward to widespread brain regions associated with the automatic activation of attentional networks 0.1 second later (bottom panel).*

computational imaging approaches to deconstruct the brain dynamics that underlie two leading neurobiological markers used in schizophrenia research: mismatch negativity (MMN) and P3a event-related potentials.

In healthy volunteers, a specific pattern of EEG responses across a complex network of brain structures is elicited within a fraction of a second in response to changes in auditory tones. In patients with schizophrenia, the researchers found that this normal process is disrupted. Reduced activity in specific areas of the medial frontal lobe quickly propagated to other regions of the brain that support activation of attentional networks.

“Changes in the tone of speech convey complex information including nuances of emotional meaning and content,” said Light, who is also associate director of the VISN-22 Mental Illness, Research, Education and Clinical Center (MIRECC) at the San Diego VA Medical Center. “If a patient’s brain is not processing auditory information optimally, he or she may miss out on important-but-subtle social cues and other critical information. They may not properly recognize sarcasm or humor that is carried by pitch changes in speech. This can be a major barrier to achieving better functioning in social relationships, school or job performance, and ultimately limit their overall quality of life.”

In research published earlier this year, Light and colleagues established that MMN and P3a showed promise for unlocking the elusive brain and molecular dysfunctions of schizophrenia patients. “These brain-based biomarkers may eventually prove to be useful for assisting clinicians with diagnosis, guiding treatment decisions, and tracking therapeutic response over time. These measures may also predict which individuals are at risk for developing a serious mental illness and are most likely to benefit from course-altering early interventions.”

According to Stephen R. Marder, MD, VISN-22 MIRECC director and a professor at UCLA’s Semel Institute for Neuroscience and Human Behavior, “this study makes a valuable contribution to our understanding of how impairments in the very early processing of sensory information in schizophrenia can explain the complex symptoms of the illness. This new knowledge may also be useful in developing better pharmacological and non-pharmacological treatments for schizophrenia.”

Co-authors of this study are Hidetoshi Takahashi, UCSD Department of Psychiatry and National Center of Neurology and Psychiatry, Japan; Anthony J. Rissling, Kenji Kirihara, Marlina Pela, and Joyce Sprock, UCSD Department of Psychiatry; Robert Pascual-Marqui, Key Institute for Brain-Mind Research, University Hospital of Psychiatry, Switzerland; and David Braff, UCSD Schizophrenia Research Program.

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