

Hearing deficits in schizophrenia tied to specific brain receptor

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The inability to hear subtle changes in pitch, a common and debilitating problem for people with schizophrenia, is due to dysfunctional N-methyl-D-aspartate (NMDA) brain receptors, according to a study by Columbia University Medical Center (CUMC) researchers. The study also shows that this hearing issue can be improved by combining auditory training exercises with a drug that targets NMDA receptors.

The findings were published online today in the journal *Brain*.

"Slight variations in our tone of voice are an important way of communicating emotions, such as happiness or sadness," said lead author

Joshua T. Kantrowitz, MD, assistant professor of clinical psychiatry at CUMC. "This inability to detect subtle changes in [pitch](#) can also make it difficult to "sound out" words while reading, with over 70 percent of patients meeting criteria for dyslexia and further exacerbating communication problems in social and work situations. But while psychiatrists have recommended medications for symptom control, these treatments have not addressed the underlying auditory deficits."

Dr. Kantrowitz and his colleagues compared auditory plasticity (the ability to learn from hearing tasks) in 40 stabilized [schizophrenia patients](#) and 42 healthy controls. Each subject listened to a series of tone pairs and was asked to indicate which tone was higher. Based on a subject's performance, the difficulty of the task was changed for the next pair of tones. When subjects correctly identified the higher tone, the pitch difference in subsequent tone pairs decreased; when subjects failed to identify the higher tone, the tones were moved further apart.

"People with normal auditory plasticity usually get better at discriminating between the two tones as the test progresses, reflecting the ability to learn," said Dr. Kantrowitz. "And that was the case with the healthy controls in our study."

At the start, there was a 50 percent difference in the pitch of the tones (e.g., 1,000 Hz and 1,500 Hz). On average, the healthy controls were able to discern between tones with a difference in pitch of as little as 3 percent. In contrast, the patients did not improve as much, detecting an average 16 percent difference in pitch.

EEG recordings, made while the subjects performed auditory brain exercises, revealed that the schizophrenia patients had lower brainwave activity than the controls. Lower brainwave activity is associated with impaired auditory sensory cortex functioning and a reduced response to the training exercises.

Dr. Kantrowitz and his colleagues suspected that schizophrenia patients' inability to improve their pitch discrimination is caused by dysfunction in their NMDA receptors, which are critical for learning and memory. If true, improving NMDA activity would improve their ability to discriminate between pitches.

To test this hypothesis, some schizophrenia patients in the study were given D-serine, an amino acid that activates NMDA receptors, once a week for up to three weeks, while others were given a placebo. The patients significantly improved their pitch detection with [auditory training](#), but only when D-serine was taken for two consecutive weeks. No improvement was seen in patients who took D-serine only once or in those who took a placebo.

"It remains to be seen whether D-serine or another NMDA-activating drug is best suited for this purpose," said Dr. Kantrowitz. "What's important is that we now know that people with schizophrenia can improve their pitch detection with a combination of auditory training exercises and repeated doses of a learning-enhancing drug that effects the NMDA receptor."

More information: Joshua T. Kantrowitz et al, Neurophysiological mechanisms of cortical plasticity impairments in schizophrenia and modulation by the NMDA receptor agonist D-serine, *Brain* (2016). [DOI: 10.1093/brain/aww262](https://doi.org/10.1093/brain/aww262)

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