

Exercise May Increase Hippocampal Volume for Patients With Schizophrenia

Deborah Brauser, **Medscape Medical News - Psychiatry**

February 18, 2010 — Aerobic exercise can significantly increase the relative hippocampal volume in patients with schizophrenia, as well as in healthy controls, a small, randomized study suggests. In fact, the volume increased by 12% in those with schizophrenia and by 16% in those without and was associated with improvements in short-term memory test scores.

"These results indicate that in [these patients], hippocampal volume is plastic in response to aerobic exercise," write Frank-Gerald Pajonk, MD, Dr. K. Fontheim's Hospital for Mental Health, Liedenburg, Germany, and colleagues.

"To provide a context, the magnitude of these changes in volume was similar to that observed for other subcortical structures when patients were switched from typical to atypical antipsychotic drug therapy," they add.

"To be honest, we've been surprised that we found these results," Dr. Pajonk told *Medscape Psychiatry*. "We double and triple checked it, but the results were always confirmed. To our knowledge, this is the first time that it has been shown that the hippocampus is growing in patients with schizophrenia with a suitable method.

"As the hippocampus is one of the core structures in schizophrenia, we were thinking that if there was an increase in volume, it could give some improvement in cognition. And that's what we found, at least to a small extent," he added. This study is published in the February issue of *Archives of General Psychiatry*.

Assessing Neuroplasticity

Previous research has shown that schizophrenia is associated with reduced hippocampal volume with impaired neuroplasticity or "mechanisms of reorganizing brain function in response to a challenge," the study authors write. The formation of new neurons is 1 component of plasticity.

Although other studies have shown that "adult neurogenesis in the hippocampus in healthy humans can be stimulated by exercise," Dr. Pajonk and his team sought to assess

changes in hippocampal volume after exercise in people both with and without schizophrenia.

The study authors also investigated whether exercise-induced changes may be associated with clinical or cognitive improvement and a possible increase of *N*-acetylaspartate, a neuronal marker.

"The therapeutic options for schizophrenia are not really good, and we're convinced that schizophrenia is a brain disease [characterized by] a lack of neuroplasticity," said Dr. Pajonk. "So we wanted to look at solutions that could possibly improve this deficit."

The study included 16 male patients with chronic schizophrenia and 8 matched healthy controls (mean age for all, 35.0 years). Participants were enrolled in the study from June 2005 to September 2006. Those with schizophrenia were randomized to participate in an exercise program consisting of 30 minutes of supervised cycling 3 times per week for 3 months or were assigned to play tabletop football for the same amount of time. All of the healthy controls took part in the cycling program.

All participants underwent magnetic resonance imaging (MRI) of the hippocampus, as well as magnetic resonance spectroscopy (MRS), neuropsychological measures with the Rey Auditory Verbal Learning Test and Corsi block-tapping test, and clinical measures with the Positive and Negative Syndrome scale. All subjects also underwent fitness testing. The overall relative hippocampal volume was 4% smaller before exercise training in all patients with schizophrenia compared with the healthy controls, but this finding was not statistically significant.

Increases in Volume, Memory

Results showed that although the relative hippocampal volume increased significantly in all of the patients who completed exercise training ($P < .001$), there was no significant change in volume found in the group that played tabletop football (-1%).

The mean amount of enlargement between the 2 exercise training groups was not statistically significant ($P = .09$). However, a change in hippocampal volume in the schizophrenia exercise group was associated with "a 35% increase in the *N*-acetylaspartate to creatine ratio in the hippocampus" — a finding that was not seen in the healthy controls.

In addition, the volume changes in both exercise groups "were correlated with improvements in aerobic fitness measured by change in maximum oxygen consumption ($P = .003$)," report the study authors.

Finally, test scores for short-term memory in the combined schizophrenia groups were significantly correlated with change in hippocampal volume ($P < .05$). The patients in the schizophrenia exercise group showed a 34% improvement in short-term memory score compared with a 17% lower score in the healthy controls.

"We've done this same study in other brain structures and did not find any volume increases," said Dr. Pajonk. "So this really seems to be a result that is specific to the hippocampus. That means it's not just a question of blood flow or unspecific factors, but maybe it's really specific for development of neurons in terms of increase in synapses or even neurogenesis." However, he added, it may be too soon to draw any clinical conclusions.

The investigators hope to continue to follow up these patients and are awaiting funding for a new study comparing the effects of exercise with cognitive training.

"Although I can't prove it right now, I'm positive that exercise is doing good in the treatment of schizophrenia," said Dr. Pajonk. "Many of the schizophrenia patients from the sporting groups were able to go on and develop a life of their own, moving to a new apartment, taking up a job again, etc. It's a bit early and we just had a small sample size, but with this small number of patients, we were really surprised and amazed at what has happened to them."

Clear Brain Abnormalities

"This was an interesting study," Christopher A. Ross, MD, PhD, director of the Division of Neurobiology and professor of psychiatry, neurology, pharmacology, and neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland, told *Medscape Psychiatry*.

"However, it's not really a study about schizophrenia. It's more about exercise and increases in hippocampal volume," said Dr. Ross, who was not involved with this study. "Also, the study is based on the assumption that schizophrenia has a lower [hippocampal] volume, and I don't know that that's really been proven yet."

"For clinicians, I think the message continues to be that there are clear brain abnormalities in schizophrenia. We're beginning to understand much more about the biology of those abnormalities, and they may involve problems with neurogenesis or other issues of neural connectivity," he added.

"The good news is that the brain is much more plastic than we had previously appreciated. Just something like exercising may alter a significant feature of brain structure. If we can get a better handle on what interventions to make, I think that gives us hope that we can do more for schizophrenia than we've been able to do so far."

He noted that he would like to see more research examining whether there really is a difference in schizophrenic individuals' response to exercise. "If there is, that would suggest something about impaired plasticity in the schizophrenia brain. I'd also be very interested in seeing the effects of other interventions and some more functional brain measures, such as functional MRI and more extensive MRS studies."

"Overall, in a sense, this was more a study about the brain and plasticity than schizophrenia per se. But it does have implications for how to think about and potentially treat schizophrenia in the future," Dr. Ross concluded.

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