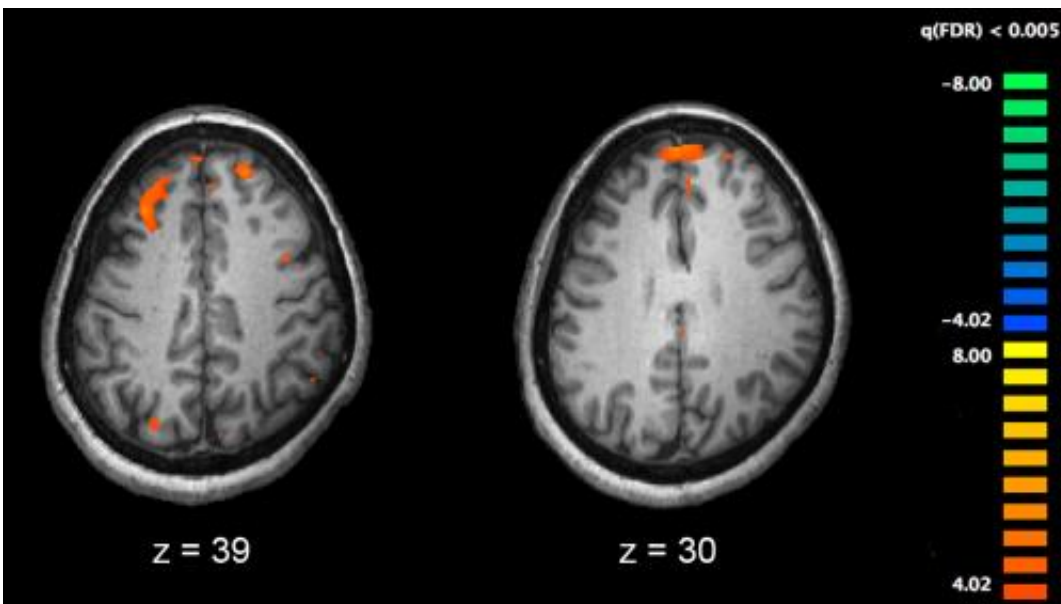


Lipidomics research provides clues for drug resistance in schizophrenia

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Functional magnetic resonance imaging (fMRI) and other brain imaging technologies allow for the study of differences in brain activity in people diagnosed with schizophrenia. The image shows two levels of the brain, with areas that were more active in healthy controls than in schizophrenia patients shown in orange, during an fMRI study of working memory. Credit: Kim J, Matthews NL, Park S./PLoS One.

Researchers from Skoltech and the Mental Health Research Center have found 22 lipids in the blood plasma of people with schizophrenia that were associated with lower symptom improvement over time during treatment. These can help track resistance to medication that affects

over a third of patients. The paper was published in the journal *Biomolecules*.

Studies suggest that up to 34% of people living with schizophrenia can be resistant to two or more antipsychotic medications used to treat the disorder. Individual responses vary greatly, and there are no satisfactory biomarkers of treatment response yet, which can often turn finding the right medication into a painful and protracted guessing game.

Recently researchers have turned to studying lipids and the important function they are now known to play in both the properties and functionality of the brain, such as membrane fluidity and permeability, retrograde signaling, neural plasticity, and neurotransmitter release modulation. "Lipidomics is a growing field, and a lot remains unknown about [lipid metabolism](#) and its alteration in disease, which makes lipidomics a promising field for new discoveries," the paper's lead author, Anna Tkachev of the Skoltech Center for Neurobiology and Brain Restoration (CNBR), says.

Anna Tkachev and her colleagues measured the blood lipid abundances for 322 blood plasma lipids in 92 individuals diagnosed with schizophrenia and undergoing treatment in a hospital. They studied the associations between symptom improvement and individual changes in blood plasma [lipid levels](#) by collecting blood plasma at two distinct time points: at the beginning and at the end of a hospital stay that lasted for 37 days on average.

Doctors used the Positive and Negative Syndrome Scale (PANSS) to assess the condition of the patients; a higher score corresponds to more severe symptoms, so researchers were looking for a drop in PANSS score over time. All but one patient showed improvement, but the extent was different. "We found that, for patients with the least improvement in symptom severity, 22 lipids, including 20 triglyceride species, were

increased at the second time point, while patients with most improvement did not demonstrate the same increase in lipid levels," the authors write.

Anna Tkachev notes that a lot remains uncertain about the role of lipids in disease, and the role of lipids in schizophrenia in particular.

"Typically, in a clinical setting, only total triglycerides are measured in the blood. In our study, we assessed lipids at a more detailed level of individual triglyceride species. The lipids we find significant in our study (shorter chain triglycerides) are not among the most abundant triglycerides, and any variation in their levels would probably remain undetected at the level of total triglyceride measurement. Because many studies in the past have focused on total triglyceride levels and not detailed level of individual lipid species, it is difficult to say for now what these alterations signify," she says.

The lipids the team found seem to be related to metabolic alterations: they have been reported to be affected in diabetes and non-alcohol fatty liver disease. "Metabolic abnormalities are, unfortunately, common in patients suffering from schizophrenia, and managing these metabolic abnormalities is an important part of managing the psychiatric disorder. However, there seems to be a complex interplay between metabolic abnormalities and psychiatric health. The role these metabolic abnormalities play in schizophrenia is not well understood, and the cause-effect relationship between the two is unclear as well," Tkachev explains.

Since the researchers were looking at individual changes in lipid levels and not the levels of lipids at baseline, their results cannot be used for a predictive model of treatment response. "Our results show that different levels of symptom improvement are associated with different alterations in [lipid](#) levels. Rather than providing a predictive biomarker, we hope that our results can help further the understanding of the underlying

mechanisms of disease manifestation and treatment response," Tkachev says.

More information: Anna Tkachev et al, Shorter Chain Triglycerides Are Negatively Associated with Symptom Improvement in Schizophrenia, *Biomolecules* (2021). [DOI: 10.3390/biom11050720](https://doi.org/10.3390/biom11050720)

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