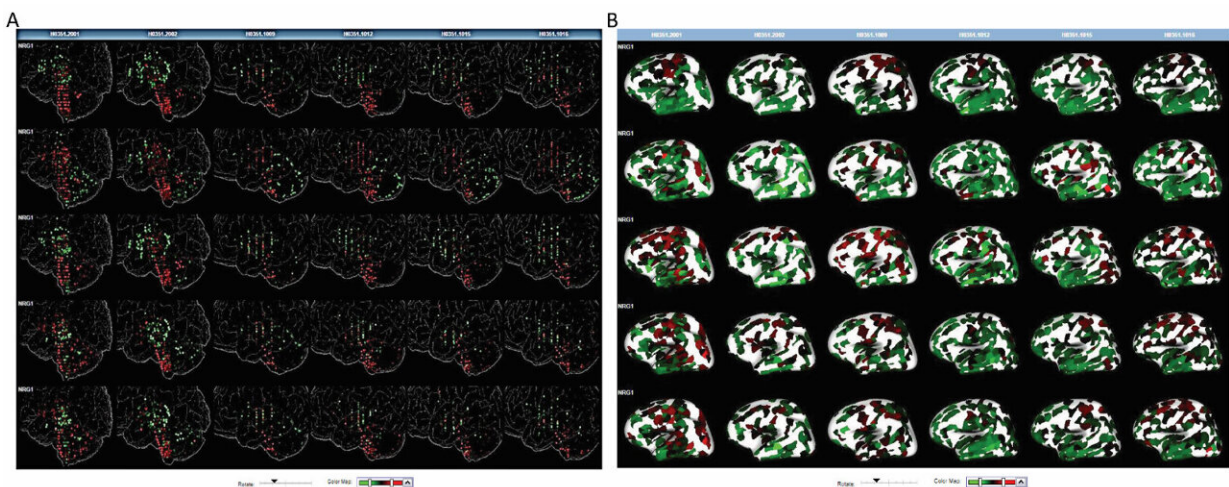


# New study uses machine learning to unveil non-invasive biomarkers for clinical depression

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Expression of significant genes in areas of the human brain. Credit: Neurobiology of Stress

Researchers from Skoltech, the University of Sharjah, and Al-Farabi Kazakh National University have discovered biological markers for clinical depression that will make diagnostic criteria more objective. Their study is published in the journal *Neurobiology of Stress*.

Clinical depression, or [major depressive disorder](#), is the second most popular reason for disability after oncology. It is expected that in 2030 it

will be the leading cause. Although the WHO reports that [clinical depression](#) afflicts 280 million people across the world, it is still difficult to diagnose.

"Currently, mental disorders are diagnosed through talks with the patient, questionnaires, and assessment scales. Different practitioners can interpret the results in various ways, which makes them subjective. There are still no reliable biomarkers—objective indicators of a predisposition to mental disorders or their progression."

"We intended to find such biomarkers that would be reliable and accessible. An MRI examination, for example, is not always possible to carry out, while blood tests are often avoided by patients," said study co-author, Assistant Professor, Head of Research Group at the Applied AI Center Maxim Sharaev.

In collaboration with the University of Sharjah, researchers used multimodal data, which characterize the patient from different perspectives. They include MRI examination, electroencephalography, blood tests, genotyping and transcriptome analysis.

"We assume that the era of simple biomarkers is coming to an end. Now, one criterion is not enough to diagnose a disease. We need a combination of markers that are easier to find through [machine learning](#). We obtained comprehensive data and made [machine-learning models](#) which can reveal integrative biomarkers based on these different types of data. But before bringing these types together, we studied each of them separately to realize where to pay closer attention," Sharaev comments.

This study explores one type of data—transcriptome analysis. Transcriptomics deals with the expression of genes in the cells that can predict the phenotype, which in this case is clinical depression.

Some biomarkers were discovered through machine learning methods and open datasets by comparing indicators for patients of different ethnicities. The transcriptome analysis involved 170 patients with clinical depression and 121 healthy controls that were studied using common bioinformatics and machine learning methods.

"Traditional methods of bioinformatics help deal with multimodal data and a small sample imposing limitations to it. These are common methods based on statistics, but they have some deficiencies. For example, they generate [false positives](#), take a long time to converge, and may exclude some biomarkers. In Skoltech, we added machine learning to these methods. Using the same data, we set up models, ensured the high quality of classifications, and obtained significant features in the form of genes, the expression of which impacted the result," Sharaev adds.

Researchers identified the most important genes after comparing the results of two analyses. This approach increased their objectiveness because the methods are based on different models and were used concurrently. The results were validated through a separate new sample and lab tests using saliva samples of 12 patients with clinical depression and eight healthy participants. With the help of the Allen Brain Atlas, scientists proved that these genes are expressed in different areas of the human brain.

"In the future, we aim to expand and specify the set of genes for screening and rapid diagnostic procedures. To that end, we only need saliva tests, without blood analysis or any complicated examinations. For the preliminary analysis, that would be enough to draw conclusions," Sharaev says.

"This research highlights the importance of using AI in combination with bioinformatic analytics to gain a deeper understanding of some

molecular mechanisms involved in such complex diseases as major depressive disorder. Also, identifying putative diagnostic non-invasive biomarkers in the process is of huge benefit to both the patients and the clinical psychiatrists," concludes the study lead author Rifat Hamoudi.

The research is part of the collaborative project pursued by Skoltech and the University of Sharjah and entitled Interpretable Artificial Intelligence and Deep Learning Models based on Integrative Neuroimaging and Genetics Data for predicting abnormal emotional development.

**More information:** Amal Bouzid et al, Integrative bioinformatics and artificial intelligence analyses of transcriptomics data identified genes associated with major depressive disorders including NRG1, *Neurobiology of Stress* (2023). [DOI: 10.1016/j.ynstr.2023.100555](https://doi.org/10.1016/j.ynstr.2023.100555).

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