Better prediction for effectiveness of paroxetine

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A third of patients with depression do not respond to the first antidepressant medication prescribed. Currently, the only approach available is one of trial and error. In this study, Max Planck scientists have identified a biosignature able to distinguish patients who will and will not respond to treatment with the antidepressant paroxetine. This study is an important step forward in personalised medicine.

The therapeutic response to antidepressants varies considerably between patients with depression. About one third of the patients do not respond to the first prescribed antidepressant, an outcome only known after four to six weeks of continuous medication. It is not uncommon for these patients to have to undergo several rounds of treatment with different antidepressants in order to find a suitable drug and dose. Aside from the associated costs, this situation results in lengthy suffering and an elevated risk of suicide for the patient.

Biosignatures able to predict the antidepressant treatment outcome for each patient would provide a precise medical approach to replace the current trial and error medication regimen. Biosignatures are objective biological measurements that are already used in other areas of medicine, but are absent in psychiatry. Such biosignatures would be of great value, allowing the treating psychiatrist to predict whether a patient will respond favourably to an antidepressant drug at the outset or during the early course of treatment.

Pathways in the neurons of the hippocampus as biosignature

Scientists around Chris Turck at the Max Planck Institute of Psychiatry in Munich, in collaboration with Marianne Müller at the University of Mainz, have used mice to delineate relevant molecular pathways characteristic for the response or non-response to the antidepressant paroxetine. In this study, the scientists profiled proteins and metabolites present in the hippocampus. They found that glutamate and ubiquitin-proteasome pathways are associated with the response to antidepressants. Glutamate is one of the major neurotransmitters and plays a central role in various brain functions. Ubiquitination is a quality control process critical for the removal of damaged proteins.

The suitable drug from the beginning

The scientists then looked to see if these pathways could be used to identify which patients would and would not respond to treatment. They took blood samples from patients with Major Depressive Disorder and found that the biosignature profiles were capable of stratifying the clinical antidepressant response. Importantly, they were able to distinguish antidepressant responder and non-responder patients prior to starting medication. "Predictive biosignatures for the antidepressant treatment response will reduce lengthy treatment ordeals for the patient because we will know the most suitable antidepressant drug from the get go. This is a great step forward in the personalised medicine approach in psychiatry" concludes Dongik Park, the paper's first author. According to Chris Turck, "Biosignatures will also help in drug development by providing new target information. Additionally, they will be useful for clinical trials of novel antidepressants for patients suffering from treatment resistant depression."

More information: D I Park et al. Delineation of molecular pathway activities of the chronic antidepressant treatment response suggests important roles for glutamatergic and ubiquitin–proteasome systems, *Translational Psychiatry* (2017). DOI: 10.1038/tp.2017.39