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By reprogramming skin cells into brain cells, scientists gain new insights into mental disorders

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For many poorly understood mental disorders, such as schizophrenia or autism, scientists have wished they could uncover what goes wrong inside the brain before damage ensues.

Now in a significant advancement, researchers are using genetic engineering and growth factors to reprogram the skin cells of patients with schizophrenia, autism, and other neurological disorders and grow them into brain cells in the laboratory. There, under their careful watch, investigators can detect inherent defects in how neurons develop or function, or see what environmental toxins or other factors prod them to misbehave in the petri dish. With these "diseases in a dish" they can also test the effectiveness of drugs that can right missteps in development, or counter the harm of environmental insults.

"It's quite amazing that we can recapitulate a psychiatric disease in a petri dish," says neuroscientist Fred Gage, a professor of genetics at the Salk Institute for Biological Studies and member of the executive committee of the Kavli Institute for Brain and Mind (KIBM) at the University of California, San Diego. "This allows us to identify subtle changes in the functioning of neuronal circuits that we never had access to before."

Prior to this disease-in-a-dish approach, the only main avenue researchers had to study human brain disorders in detail was to look for

abnormalities in brain tissue removed from patients after their deaths. But such specimens were usually of poor quality, and often were taken from patients when they were in the end stages of a brain disorder. This made it difficult to assess what went awry earlier before much brain damage ensued and treatments would be more likely to be effective.

So there was great excitement when Gage reported this year that using this "disease in a dish" approach, he could see subtle anatomic differences between the neurons of normal and schizophrenic patients too small to be seen in imaging studies. When comparing the genes expressed in the neurons derived from schizophrenic patients to that of normal neurons, he also discovered altered expression of several genes that govern certain neuronal developmental pathways.

"The most amazing developments in the field over the last year or so are these examples where you can see differences in cells isolated from controls and patients," Anirvan Ghosh, a neurobiologist at the University of California at San Diego and executive committee member of KIBM. "It's something people have been speculating about for awhile, but to actually see the differences is very exciting from a scientific point of view."

The findings are helping explain the causes of mental disorders that have baffled researchers for generations because they couldn't peer inside the brains of patients. Drug companies are also excited about these models. "Now we can use cultures derived from individuals who are living to test drugs on their neurons to see their effectiveness and toxicity," Gage said, pointing out that this personalized approach for assessing treatment is more likely to be effective than standard drug tests, given the variability in what causes mental disorders and people's varied reactions to the same drugs.

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