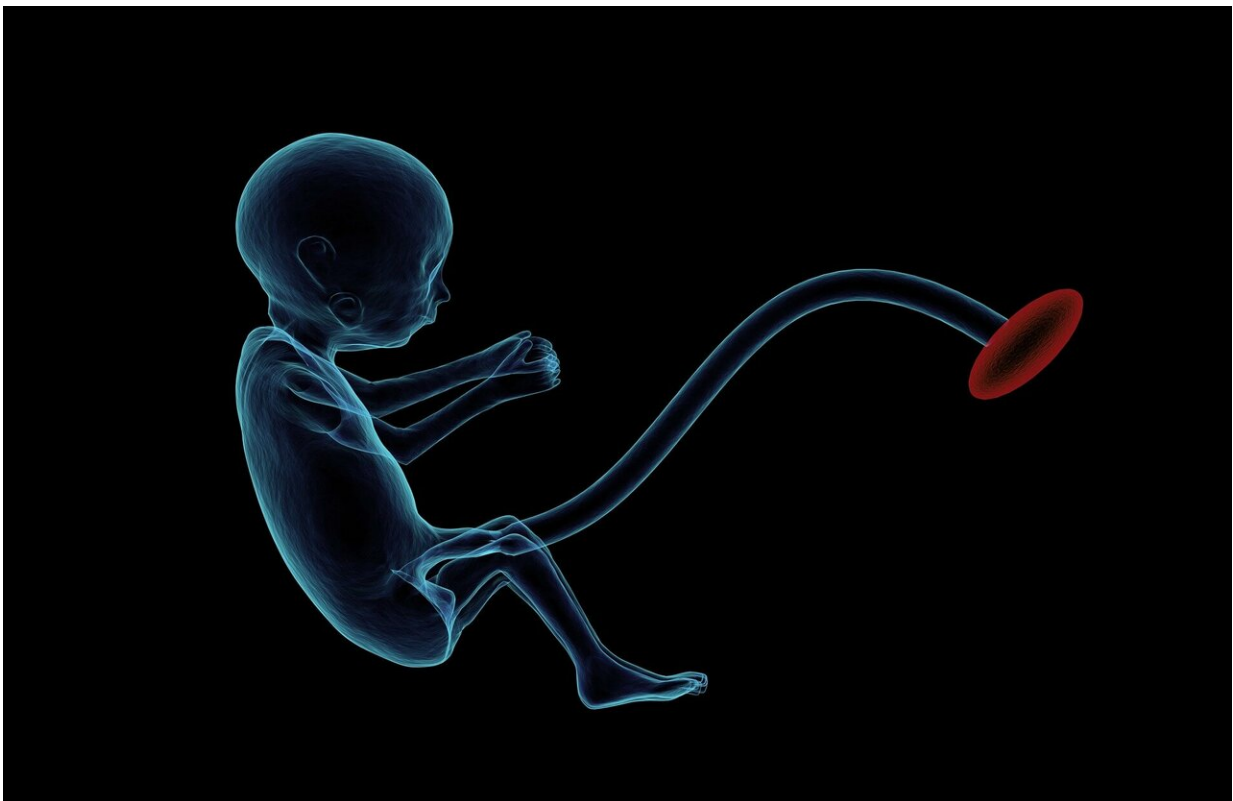


A correlation found between psychiatric disorders and events during the prenatal stage

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Particular genetic variants in the human genome that are important for the development of the brain early in the life of the foetus are frequently

found in psychiatric disorders. This is shown by a study carried out by iPSYCH.

Researchers studied a total of 8 million genetic variants and found that some of them occur particularly often in people who have one of more of the following psychiatric disorders: schizophrenia, depression, bipolar disorder, autism and ADHD.

This background is provided by Professor Thomas Werge from the Mental Health Services & University of Copenhagen and the Lundbeck Foundation's Initiative for Integrated Psychiatric Research, commonly referred to as iPSYCH, which has received a total of DKK 361 million in funding from the Lundbeck Foundation. He explains:

"When we take a closer look at these genetic variants, one of the things we can ascertain is that they are tied to genes that are active in connection with the establishing of synapses in the brain during the prenatal stage—that is to say, the formation of the wiring that runs from nerve cell to nerve cell. And this means that the causes of mental disorders may actually originate all the way back from the point during pregnancy when the brain of the foetus was being formed."

Thomas Werge headed the study, which has just been published in the scientific journal *Nature Neuroscience*. The Danish contribution involved researchers from Aarhus University, Statens Serum Institut (SSI) and the Technical University of Denmark. Researchers from Australia, Switzerland and USA also took part.

Enormous battery of blood tests

Researchers who study psychiatric disorders have long held an assumption that across psychiatric diagnoses, there will be common characteristics in the form of specific genetic variants. This assumption

also builds on the fact that a range of psychiatric disorders can often be seen to appear at the same time—both in families and individuals.

Whether or not this is the case has been tested in a range of studies, but never in a way that actually involves an entire population, explains Thomas Werge: "And that is exactly what we have done, because we have looked at a whole population in Denmark. By doing things in this way, you can achieve the highest possible degree of statistical certainty, as it's now possible to exclude a long list of biases and thus chance findings, which have to do with factors such as the selection of material for the study. At the same time, we get a very detailed picture of all the forms of mental disorders that can affect a person."

The study behind the article in *Nature Neuroscience* is based on the [blood samples](#) that are taken from nearly all newborn babies in Denmark with parental consent. These heel prick samples, or PKU tests as they are known, are accessible for research work, but only in anonymised form.

The PKU archive is the only one of its kind in the world and by looking at the DNA profiles from all samples taken during the period between 1980 and 2005, Thomas Werge and his colleagues were able to carry out a unique study:

The samples were correlated with the Danish healthcare system's CPR (civil registration number) registrations, which is to say that the database behind the individual PKU samples—in addition to containing the DNA of the person in question—would also contain in anonymised form much of the [health information](#) of the same person that is stored in the Danish public healthcare system, including information on psychiatric diagnoses.

"In 2012, when we looked at the registers holding detailed information on all of the PKU samples taken in the period

1980-2005—approximately 1.5 million in total—we could see that 46,000 people from this group had, during that time, received one or more major psychiatric diagnoses. We then compared their DNA with the DNA from a sufficiently large number of persons in the register who had not received a psychiatric diagnosis," says Professor Thomas Werge.

A question of vulnerability

What do these discoveries mean? Is it the case that the genetic variants in the study that were shown to appear especially frequently in people diagnosed with one of the five major [psychiatric disorders](#) will necessarily trigger the disease?

"No, it's not that simple," says Professor Thomas Werge. "But knowledge of specific predisposing processes enables us to carry out a qualified search for matching environmental factors that are active in the same time period during foetal brain development, and that may make particularly vulnerable people ill, but have little effect on less liable individuals."

Andrew Schork from iPSYCH says, "Our study shows that the foundation for both early and late-stage mental disorders is in part located in the foetal stage; that is to say, very, very early in life, and long before the [disorders](#) present clinically."

According to Thomas Werge, it ought to be possible to utilise knowledge of the correlation between mental vulnerability and genetics in preventative contexts: "Hopefully, this knowledge can help us to identify damaging or protective environmental factors enabling us to provide improved guideline on dos and don'ts during pregnancy.

More information: Andrew J. Schork et al. A genome-wide association study of shared risk across psychiatric disorders implicates

gene regulation during fetal neurodevelopment, *Nature Neuroscience* (2019). [DOI: 10.1038/s41593-018-0320-0](https://doi.org/10.1038/s41593-018-0320-0)

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