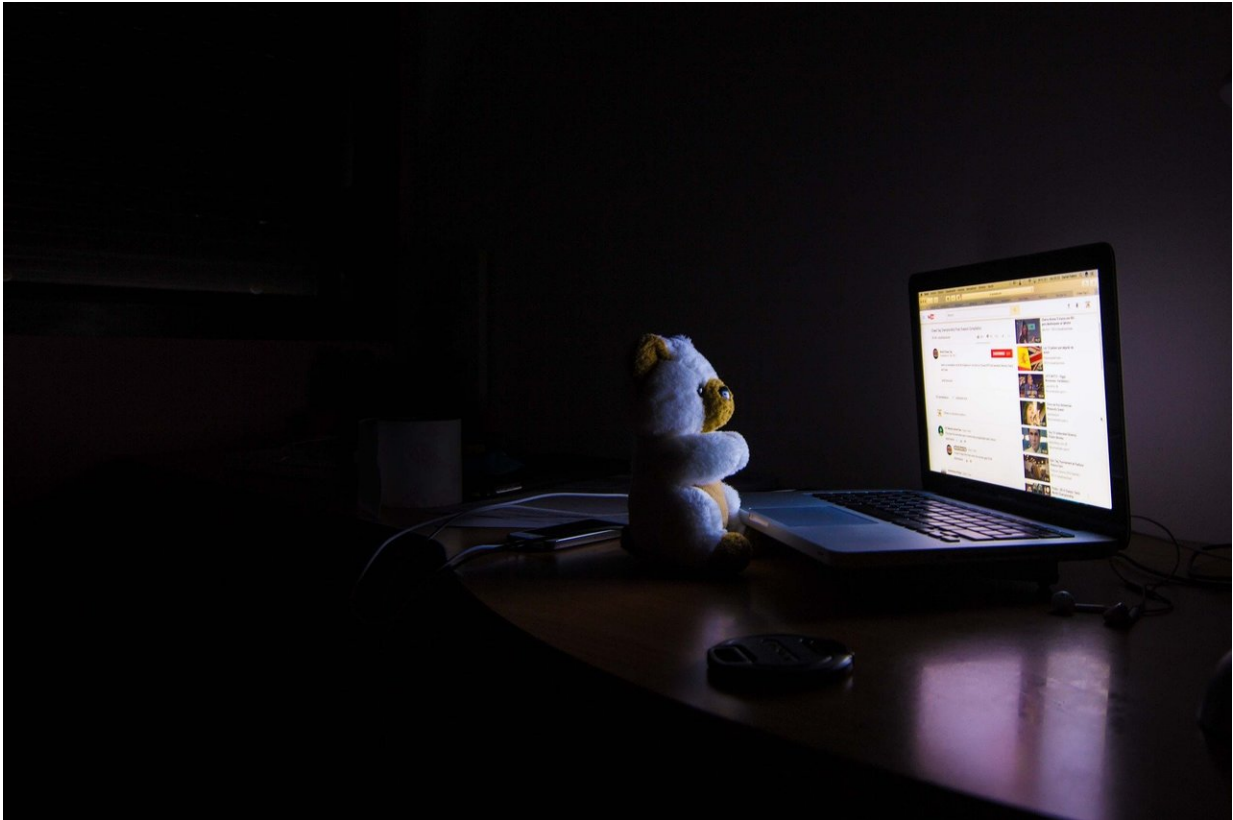


# Brain cells involved in insomnia identified

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An international team of researchers has identified, for the first time, the cell types, areas and biological processes in the brain that mediate the genetic risk of insomnia. This was made possible by assessing DNA and sleep features in no less than 1.3 million people. The findings are a major step toward getting a grip on the biological mechanisms that cause

insomnia. Today, *Nature Genetics* publishes the results of this research.

Insomnia is one of the most common disorders. Many people occasionally have a bad night of sleep. One out of 10 people chronically experience poor sleep and suffer severely from the daytime consequences. Worldwide, 770 million people have chronic insomnia.

## **Vulnerability is rooted in the brain**

While treatment alleviates symptoms, most sufferers feel that they remain vulnerable to experiencing poor nights of sleep. The vulnerability to insomnia runs in families and seems hard-wired in the brain. So far, researchers have only identified a few genes involved in the vulnerability. Researchers are also unsure where in the brain insomnia risk genes exert their influence. This knowledge is crucial to develop better treatments.

Amsterdam Statistical Genetics professor Danielle Posthuma (VU Amsterdam/ Amsterdam UMC) and Neurophysiology professor Eus Van Someren (Netherlands Institute for Neuroscience) assembled a large group of scientists and cohorts, including the UKBiobank and US-based company 23andMe, to find out where in the brain insomnia risk genes exert their effect. Together, they were the first to assemble DNA and sleep data provided by no less than 1.3 million people—the largest genetic dataset ever

The researchers identified 956 genes in which variants contributed to the risk of insomnia. They then extensively investigated which [biological processes](#), [cell types](#) and brain areas utilize these genes. They found that part of these genes had an important role in the functionality of axons, which are the long protrusions of brain cells that allow them to communicate with each other. Another significant part of the insomnia risk genes was active in specific cell types of parts of the frontal cortex

and the subcortical nuclei of the brain. These brain areas had also recently been marked as suspect in brain imaging studies of people suffering from insomnia. The findings thus seem consistent.

## **Specific cell types involved in insomnia**

"Our study shows that insomnia, like so many other neuropsychiatric disorders, is influenced by hundreds of genes of small effect. These genes by themselves are not that interesting to look at. What counts is their combined effect on the risk of insomnia. We investigated that with a new method that enabled us to identify specific types of brain cells, like the so-called medium spiny neurons," says Danielle Posthuma.

"These findings are a breakthrough, since we can now for the first time start searching for underlying mechanisms in individual brain cells in the laboratory," says Guus Smit, a VU-University neurobiologist involved in the study. Postgraduate student Philip Jansen, first author of the paper, continues: "It is fascinating that we can nowadays start to understand what happens at the micro-level of molecules and cells in the brain, just because we can assemble so many data at the macro-level, worldwide."

## **Insomnia is genetically more related to psychiatric disorders than to other sleep traits**

The researchers compared risk genes of insomnia with those of other traits and disorders. Surprisingly, they found little overlap with [genes](#) involved in individual differences in other sleep traits, like being a morning person or a night owl. Instead, there was a strong genetic similarity with depression and anxiety.

"This is a very important finding, because we have always searched for causes of insomnia in the [brain](#) circuits that regulate sleep. We have to

shift our attention to the circuits that regulate emotion, stress and tension. Our first results in that direction are already spectacular," says Van Someren. "This study is an immense step forward in understanding the genetic background of insomnia. The findings emphasize that [insomnia](#) is a serious condition, because of the shared [genetic risk](#) of psychiatric disorders and metabolic disturbances involved in obesity and diabetes," says Vladimir Vacic, senior scientist in computational biology at 23andMe.

**More information:** Genome-wide analysis of insomnia in 1,331,010 individuals identifies new risk loci and functional pathways , *Nature Genetics* (2019). [DOI: 10.1038/s41588-018-0333-3](https://doi.org/10.1038/s41588-018-0333-3) , [www.nature.com/articles/s41588-018-0333-3](https://www.nature.com/articles/s41588-018-0333-3)

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