

Specific genes increase the risk of bedwetting

January 19 2021



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In a large-scale study of Danish children and young people, researchers from Aarhus University have for the first time found genetic variants that increase the risk of nocturnal enuresis—commonly known as bedwetting or nighttime incontinence. The findings provide completely new insights into the processes in the body causing this widespread

phenomenon.

Researchers have long known that nighttime incontinence is a highly heritable condition. Children who wet the bed at night often have siblings or parents who either suffer from or have suffered from the same condition. But until now, science has been unable to pinpoint the genes concerned.

In collaboration with the Danish research project iPSYCH and a team of international colleagues, researchers from Aarhus University have for the first time identified genetic variants that increase the risk of bedwetting. The results have just been published in the scientific journal *The Lancet Child & Adolescent Health*.

"As many as sixteen per cent of all seven-year-olds suffer from nocturnal enuresis and although many of them grow out of it, one to two per cent of all young adults still have this problem. It is a serious condition, which can negatively affect children's self-esteem and well-being. For example, the children may be afraid of being bullied, and often opt out of events that involve overnight stays," says Jane Hvarregaard Christensen, who is one of the researchers behind the study.

Regulates urine production

In the study, the researchers studied the genes of 3,900 Danish children and young people, who had either been diagnosed with nocturnal enuresis or had taken medication for it. This group was subsequently compared to 31,000 children and [young people](#) who did not suffer from the problem.

"We identified two locations in the genome where specific genetic variants increase the risk of bedwetting. The potential causal genes which we point to play roles in relation to ensuring that our brain

develops the ability to keep urine production down at night, that the bladder's activity is regulated and registered, and that we sleep in an appropriate way, among other things," explains first author of the study, Cecilie Siggaard Jørgensen.

The study also shows that commonly occurring genetic variants can explain up to one-third of the genetic risk of bedwetting. This means that genetic variants which all of us have may lead to involuntary nocturnal enuresis, when they occur in a certain combination.

"But you can still also have all the variants without wetting the bed at night, because there are other risk factors in play that we haven't mapped yet—both genetic and environmental. So it's clear that this is very complex and that it's not possible to talk about a single gene that causes nocturnal enuresis," says Jane Hvarregaard Christensen.

Particularly vulnerable

The study also shows that children with many genetic variants that increase the risk of ADHD are particularly vulnerable to developing bedwetting.

"Our findings don't mean that ADHD causes bedwetting in a child, or vice versa, but just that the two conditions have common genetic causes. More research in this area will be able to clarify the details in the biological differences and similarities between the two disorders," she emphasizes.

As the study is a first-time study, the researchers also examined more than 5,500 people from Iceland, where they found that the same genetic variants also appear to increase the risk of nocturnal enuresis.

"This means that we can be more certain that our findings are not

coincidental. In the future, we wish to find out whether the same genetic variants increase the risk of bedwetting in children in other parts of the world. Bedwetting is not just an issue in northern European but affects millions of [children](#) all over the world," she says.

The researchers hope to be able to further clarify the causes of [nocturnal enuresis](#). It is very likely that it will be possible to identify even more genes and thereby gain a deeper understanding of what is required for a child to become dry at night.

"At present we still can't use a child's genetic profile to predict, for example, whether the child will grow out of its condition or whether a particular treatment works. Perhaps this will be possible in the future when more [detailed studies](#) have been conducted," says Jane Hvarregaard Christensen.

Behind the results

The study is a so-called genome-wide association study (GWAS). By examining thousands of genetic variants spread out in the [entire genome](#), a GWAS makes it possible to point to statistically significant correlations between specific genetic variants and nighttime incontinence in the persons who are examined.

More information: Cecilie S Jørgensen et al, Identification of genetic loci associated with nocturnal enuresis: a genome-wide association study, *The Lancet Child & Adolescent Health* (2021). [DOI: 10.1016/S2352-4642\(20\)30350-3](#)

Provided by Aarhus University

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