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HUNTING FOR THE OBESITY GENES: Medications that switch off the obesity genes can become a reality in the future, if Professor Pål Rasmus Njølstad's research can find the underlying causes of obesity in infants and children.



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Solving diabetes

What roles do diets and genetics play in the development of obesity and diabetes?

TEXT **SOLRUN DREGELID**

This is one of the questions Professor Pål Rasmus Njølstad and his colleagues at the Department of Paediatrics at Haukeland University Hospital are working on. It is for his studies of diet and genetics among mothers and children in Norway that Njølstad has been awarded a European Research Council (ERC) Advanced Grant.

Obesity is #1 killer

Njølstad wants you to imagine a future, in which, by a simple gene test, you can predict if your children are at risk of obesity. A future where there is a way of stopping those extra

kilos piling on. In which case, you will also see a future with fewer cases of diabetes, cardiovascular disease and cancer.

Through his research, Professor Njølstad hopes to solve these problems. His goal is to find what genes, combined with environmental factors, cause six per cent of the world's pre-school children, or 44 million, to be overweight or obese.

"We know from previous research that infants with a high birth weight, and who experience weight increase in early childhood, are more at risk of becoming overweight or obese later in life than children of aver-

age weight," says Njølstad about the theses underpinning his research.

"However, we do not know why this happens. I believe that genetic factors, combined with early childhood weight gain, play an essential part. Previously, we have found that diabetes genes may be associated with changes in birth weight."

Obese children often become obese adults, underlining the case for treating obesity early in life. Today more than half the adult population of Europe is overweight or obese, according to numbers from the World Health Organization (WHO). WHO's numbers show that, world-

wide, more people die of obesity than from hunger.

"If we know the mechanisms behind child obesity, it is easier to do something about the problem," says Njølstad.

Norway's unique archives

In the hunt for the obesity genes, the University of Bergen (UiB) researchers have a powerful tool in the Norwegian Mother and Child Cohort Study (MoBa), in which more than 90,000 pregnant women participated between 1999 and 2008. In the study, both biological samples and survey data were collected as early as week

“ We have found that diabetes genes may be associated with changes in birth weight. ”

17 of pregnancy. More than 70,000 budding fathers also participated in the survey.

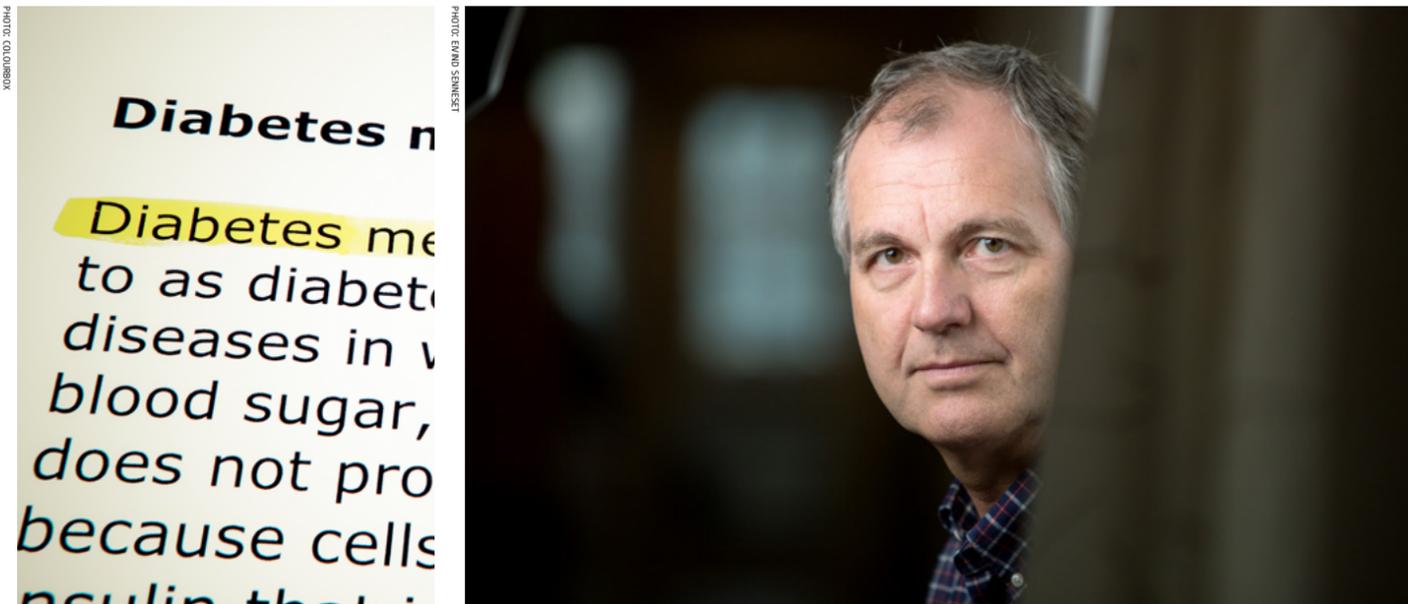
"Norway's material is unique. While American studies can be socially selective, studies such as ours are based on a population with a much smaller degree of selection. The surveys are also carefully done," says Njølstad.

From this extensive database, the researchers have picked 33,000 participants for further study: 11,000 children, 11,000 mothers, and 11,000 fathers.

"The infants are divided into two groups. The first group consists of

infants with high birth weight and high growth rate in the first year of life. The second group consists of infants with low birth weight and low growth rate in the first year of life. The participants are then weighed again when they are five years old," explains Njølstad. "By comparing genetic profiles of the two groups, we hope to find what genetic changes recur in the obese group and what sets them apart from the second group."

"With information across generations, about both genes and environment, we can study what genes the child gets from the mother and what genes from the father, and if these



LOOKING FOR CLUES: Professor Rolv Terje Lie is responsible for the trio analysis of the diabetes research project, where genetic material from mother, father and child is collected and analysed.



PHOTO: OLOMBERX

44 If we know the mechanisms behind child obesity, it is easier to solve the problem. 45

- ▶ have a different impact on the child," says Head of UiB's Department of Global Public Health and Primary Care, Professor Rolv Terje Lie.

Fat-busting medication

Lie is involved in the epigenetics work at UiB. Epigenetics is the study of heritable changes in gene activity that are not caused by changes in the DNA sequence. Or, in layman's terms, how environmental factors impact on child obesity.

"To find what environmental factors have an impact on whether obesity genes are active or not; we want to study the whole trio of mother, father and child. This way we can examine whether conditions in pregnancy influence the child's genetics or if the parents' dietary habits influence the child's food preferences," says Njølstad.

If Njølstad and Lie's research is successful, it is not inconceivable that the future will bring medication that can switch off the obesity genes.

"If we can prevent children, in particular those predisposed to obesity, from becoming overweight, this is not only cost-efficient for society," Njølstad says, "but also important for children, who will not suffer life as obese, with all the medical and social problems this may cause for them."

Child + mother + father = trio analysis

Lie is responsible for the trio analysis in the project. Trio analysis is a term used to describe genetic studies where material is collected from mother, father and child.

"Trio analysis provides us with more reliable results than traditional case-control studies," says Lie. A case-control study is a type of observational study in which two existing groups differing in outcome are identified and compared on the basis of a supposed causal attribute.

"Another advantage is that trio analysis enables us to separate be-

tween different genetic mechanisms. In short, the result from trio analysis is both highly credible and may provide us with an entirely new type of knowledge," Lie points out.

Trio analysis is a complex research method, and combined with environmental factors and epigenetics brings new challenges.

International collaborations

"No one has found a technical solution to use the full potential of trio analysis yet. New methods need to be developed. In order to do this, we need to work internationally to find the solutions," says Rolv Terje Lie.

This is why Njølstad, Lie and the other UiB researchers work closely with researchers from, amongst others, Lund University in Sweden and Boston's Broad Institute, which grew out of research environments at Harvard and the Massachusetts Institute of Technology (MIT). This is one of the world's leading research environments in genetics, diabetes, and common diseases. ●

FACTS

Diabetes research at UiB

- Professor Pål Rasmus Njølstad of UiB's Department of Clinical Science was awarded a European Research Council (ERC) Advanced Grant in October 2011.
- Njølstad receives NOK 17.6 million (EUR 2.15 million) from the ERC for a five-year period.
- Njølstad leads the KG Jebsen Centre for Diabetes Research at UiB.
- The centre's vision is to uncover the causes of diabetes and to develop treatment methods by integrating findings from large-scale genetics investigations and model systems with clinical research.
- The diabetes group at UiB was set up in 1997, and in 2001, an article was published in the *New England Journal of Medicine* on glucokinase deficiency, a particular type of diabetes that affects newborns.
- The group has charted a new diabetes syndrome and published the findings in the journal *Nature Genetics*.
- The group has also demonstrated that a certain type of childhood diabetes can be treated with tablets rather than insulin, and published the finding in *Diabetes and New England Journal of Medicine*.
- For more information on diabetes research at UiB, visit: uib.no/en/diabetes

ERC grants at UiB

Advanced Grants from the European Research Council (ERC) are awarded to researchers working on projects that are highly ambitious, pioneering, and unconventional. In addition to Pål Rasmus Njølstad, six other UiB researchers are currently recipients of ERC Advanced Grants.

Organisms in the ocean

There are millions of viruses and other organisms in a litre of water, and the interaction between them is complex. The research group Marine microbiology, headed by Professor Frede Thingstad, want to get a better understanding of the complexity of how organisms in the ocean interact.

Hearing voices

Schizophrenia can make you hear voices in your head, but where do these voices come from? That is one of the questions Professor Kenneth Hugdahl and the Bergen fMRI Group are trying to answer. fMRI is short for functional Magnetic Resonance Imaging, and a particular focus for the group is the study of auditory hallucinations in schizophrenia, and so-called dichotic listening studies of cognitive control.

Early man's symbols

The TRACSYMBOLS project, headed by Professor Christopher Henshilwood, looks at how environmental changes influenced key behavioural features of Neanderthals and early Homo sapiens in Europe and southern parts of Africa. Henshilwood's archaeological finds in South Africa have shed new light on early humans' abilities to adapt to climate change; research that may hold value as modern man faces climate change challenges of his own.

Space is the place

One of the main tasks for Professor Nikolai Østgaard and his colleagues at the Birkeland Centre for Space Science is to look at how earth connects electrically to space. They also study so-called gamma-ray bursts (GRBs) that occur during thunderstorms, and are believed to affect the climate. The centre is also one of UiB's Centres of Excellence (SFF), and you can [read a report on their work in Svalbard on pages 10-13](#).

Advanced algorithms

Using an Internet search engine to find the hottest restaurant in town? Letting your car's GPS tell you where to turn left to reach the parking house? Worrying if your money is safe when you use online banking? Looking for the love of your life on an Internet dating site? Then most certainly, an algorithm has helped you. Professor Fedor Fomin and the Algorithms Research Group at UiB develop new mathematical theories to provide better algorithms.

Equality in crisis

Professor Bruce Kapferer is the most recent addition to UiB's ERC stable, being awarded Advanced Grant status in August 2013. How does greater inequality create divisions in society? That is one of the central issues of his new research project *Egalitarianism: Forms, Processes, Comparisons*. His project aims to study egalitarian structures and processes and the underlying values that inform these.