# LEARNING FROM 87,000 TWINS

Dorret Boomsma is a leading scientist in twin and genetic studies of behavior, health and psychopathology. Studies in Dutch twins revealed for example that ADHD in children is a genetic disorder, that is not the "fault" of the parents. The work of her research group has provided a wealth of information on how genes influences health and behaviour.

As with every success story, there's a measure of luck involved. For example, the fact that the focus of her research – twins – intrigues almost everyone. Not to mention the general fascination with intelligence, depression and susceptibility to addiction and the question of how genetic they these traits are. Another stroke of good fortune presented itself once she had completed her PhD research on cardiovascular risk factors in twin families in Amsterdam and decided that a larger scale twin register would be useful. As it turned out, her supervising professor lived next door to the CEO of a prominent marketing company that visits families when a baby is born. The researchers included their brochure in the company's package, inviting parents to sign up their newborn twins to the register. In addition, a diligent graduate student asked municipal authorities whether the researchers would be allowed to approach twins in their area. In 1987, these initiatives led to the founding of the Netherlands Twin Register (NTR). Now, 25 years on, this database contains over 87,000 twins and multiple births and is famous around the world. In total, including multiples and their families, the NTR contains the details of almost 178,000 people. Each year, they complete a number of questionnaires about their behaviour and health.


## HISTORY

Dorret Boomsma is Professor of Biological Psychology at VU University Amsterdam since 1998 and head of the department of the same name. "I graduated in the middle of an economic downturn, which had an impact on opportunities to try to make a career in science. I spent a year working in dentistry, then a PhD position in biological psychology came up, with funding for two days a week. Because my husband had a good salary, I could afford to take it."

The initial research involved building up the infratructure, with few means at her disposal: "We had to use discarded envelopes from other departments when mailing out surveys to collect data. Family members and volunteers did a lot of work for us. That's true to this day but we still have omissions in our database because in the early days we sometime lacked the resources to keep up the longitudinal data collection. Yet Boomsma has come a long way from these humble beginnings. In 2002, she was awarded the Spinoza Prize (sometimes referred to as the 'Dutch Nobel Prize') and in the same year the James Shield Award (awarded by the International Society for the Study of Twins). In 2011 she won the KNAW Merian Award, the highest Dutch honour for women in science. Internationally, she is regarded as a leading light in the field of twin studies and behavioural genetics. When she received the Spinoza Prize, the jury praised her courage, rigour and cognitive prowess. She feels truly at home in her interdisciplinary field. "I enjoy the combination of the hard science of genetics and statistics on the one hand and the complexities of psychology and epidemiology on the other hand."

## TWINS AS A PHENOMENON

Twins make valuable subjects for genetic research because they can be either monozygotic (from the same fertilized egg) or dizygotic (from two different eggs). This phenomenon gives rise to two groups of subjects that are ideal for scientists: all conditions are the same, except for one. It enables one to conclude with a high degree of certainty that this one condition is responsible for any differences in trait resemblance that is observed between the two groups. Dizygotic twins share their age, background and environment. But genetically they are no more closely related than any other set of siblings. Monozygotic twins, which occur when a single embryo splits, have the same genes. The essence of twin research is to find out in what respects monozygotic twins are more alike than dizygotic twins. For example, monozygotic twins look more alike than dizygotic twins. This tells us that appearance is strongly genetic, a factor on which environmental conditions have little influence.

## INTELLIGENCE: THE OLDER YOU ARE, THE MORE GENETIC IT BECOMES

One important discovery made by Professor Boomsma and her department is the heritability of intelligence. The older you get, the more your genes determine how intelligent you are. The scores achieved by dizygotic twins on intelligence tests are more alike at the age of five than at twelve. That shift occurs less among identical twins, who continue to be very much alike throughout their lives. If intelligence is genetically determined, you would expect to see different intelligence test scores in dizygotic twins, because they partly inherit different genes. But this only happens later in life, which suggests that, in your early life, your environment – in particular your family environment – is a strong determinant of how intelligent you are. For example, if you are given plenty of encouragement to learn at home, you are likely to score well on intelligence tests, regardless of what is 'written' in your genes. As you age, your genetic predisposition plays an increasingly important role. This may be because you are increasingly free to decide for yourself what you do and have the opportunity to pursue your own interests. In terms of intelligence, your 'true self' therefore only develops later in life, in this case around the age of twelve.
It's a difficult situation to decipher: intelligent parents are not only more likely to encourage their children, but will also pass on relatively more 'high-IQ genes'. It's a compelling illustration of how much thought and statistical expertise go into this type of research. You have to think very precisely about the questions you ask, and what conclusions may be drawn from the answers.

## ONE BREAKTHROUGH AFTER ANOTHER

Professor Boomsma describes this as a boom time to be working in genetics. "We are living in an age when genes can actually be identified. We're experiencing one breakthrough after another." Nowadays, she herself is more involved in supervising the next generation of researchers as opposed to carrying out her own analyses or interacting with twins. Yet she remains in contact with her data providers: "In the evening, I still write many letters to twins. They often approach us with complex questions about serious topics, such as 'My identical twin brother has a brain tumour. Does that mean I'll get one?' Or sometimes the parents of twins have a particular worry or want to know whether their children should or should not be placed in separate classes at school." For clinical questions, her department recently joined VU University Medical Center in setting up TWIN, an information centre for twins. "Twins give us such an enormous amount of help, so we have a duty to help them if they are concerned about something."

## SENSITIVITY TO ADDICTION

Other intriguing outcomes of the work by Professor Boomsma and her department includes addiction. Whether your take your first drink or smoke your first cigarette depends mainly on your environmental circumstances; on whether you are encouraged by your friends, for example. A religious environment often prevents people – especially women – from starting to drink alcohol. But whether you become an chronic smoker after you take your first puffs, and even how many cigarettes you smoke a day, is genetic. The same applies to drinking alcohol for example.

## LIBERATING KNOWLEDGE

What exactly happens with all that knowledge about the origins of our behaviour and our health? Is it changing the society in which we live? Professor Boomsma explains "We are now so familiar with the idea of biological vulnerability due to heredity, that we are almost unable to imagine the ideas people used to have about psychiatric disorders, such as ADHD, thirty years ago. 'It's caused by the mother,' was a common view at the time. We now know that such notions of culpability apply just as little to ADHD and depression as they do to diabetes and heart disease. This knowledge is very liberating for patients." And for their mothers.
But surely diabetes and heart disease are still caused by environmental risk factors? After all, people can influence their chances of developing diabetes and heart disease by what they eat and how much exercise they take. Professor Boomsma reminds us "This is a complex issue. We probably all know people who suffer from these conditions because of their genetic predisposition, even though they lead a healthy lifestyle. And we are just as likely to know someone who breaks every rule of healthy living and yet lives to a ripe old age. It shows that risk factors, whether genetic or environmental, are not predictors but contribute to the probability of a particular disorder. The way in which genetic risks translate into disease is also a complex process. Part of that mechanism can be channelled through behaviour: today people's sensibilities are constantly under psychological attack. Just look at the racks of sweets at the checkout of almost every store." Some people succumb to this kind of temptation more easily than others. It is perhaps less a matter of conscious choice than you might think. One thing is certain: Professor Boomsma, her colleagues and her successors have plenty of work ahead of them, unravelling the great mystery of our health and behaviour.

### GENES + ENVIRONMENT ≠ THE WHOLE STORY

Some time ago, an unusual pair of monozygotic twin girls were born in the Netherlands: one was healthy while the other had a severe abnormality of the spine. It was an abnormality caused by a genetic mutation, so why wasn't her sister affected too? It turned out that the sick girl did not have the mutation either, but that the gene in question had simply been 'deactivated' as it were, in her system. Even in conditions with a strong genetic determinant, such as schizophrenia, asthma or autism, differences between monozygotic twins do occur.
The explanation for these differences – same genes, but different outcome – lies in epigenetics, a discipline that focuses on the on and off switches of genes. Your genes may or may not have an effect depending on whether they are activated or deactivated. In essence, your brain cells contain the same genes as the extremely different cells that make up your intestinal wall but in each case, different genes have been activated. This ensures that each cell develops according to plan and functions appropriately.
Epigenetics adds a whole new dimension of complexity to Professor Boomsma's research. We are still a long way from understanding the mechanisms that switch genes on and off.

You can read more about Professor Boomsma's work in an article from Psychologie Magazine, March 2012."Upbringing has no effect on the occurrence of ADHD. I'd never have thought that 25 years ago."