Irmhild Altmann-Schneider, physician researcher at the Department of Radiology about her research into brain structures

Does the brain reflect a long and healthy life?

Do members of the families who participate in the Leiden Longevity Study have a different brain from their partners? An answer to that question can teach us a lot about how and why our brains age, as well as the consequences of this. In her quest for the answer, research physician Irmhild Altmann-Schneider has spent the past 18 months imaging the brains of about 400 participants in the Leiden Longevity Study.

Structures in the brain change as we get older. The quantity of fluid in the brain increases and its size decreases: it shrinks. Abnormalities develop in the white matter, where the wiring of the brain runs. And over the years iron accumulates in the brain. These changes appear to be associated with cognitive deterioration such as memory problems or difficulty with planning. Yet we still know very little about the causes and the exact consequences. The research into the brains of participants in the Leiden Longevity Study, who have been specially selected because 'ageing healthily' is in their genes, is a unique opportunity to change that. Altmann: "The research group is ideal. It has been demonstrated that in view of their familial background, the now adult children from the long-living families have an increased chance of becoming old as well. Their partners form the ideal control group because they have shared their lives with these children for many years. They live in the same environment, eat the same, et cetera but for the rest, they represent the general population. The average age of the study subjects is 66. That is also favourable. At this age, people are still fit enough to participate in the study but changes associated with ageing are already taking place in their brains."

Shape and structure

Altmann spent the first 18 months of her research making many different MRI scans. She mostly made structural scans: scans that image the shape and structure of the brain tissue. "Our main reason for doing this was to see the differences between children from the long-living families and their partners," explains Altmann. "The question is whether by looking at their brains, we can deduce their secret to becoming old."

Now that all of the scans have been made it is time for the analysis. Altmann: "I combine all of the data and try to make hypotheses on the basis of this information. That is the purpose of my research." If Altmann finds structural differences then a subsequent study can take place to test the hypothesis. In that case, the first step is to make scans that image the function of a certain area of the brain. One functional scan has been performed already. This examined the brain activity of the two groups during rest.

Altmann has only just started to analyse the data that she has collected in recent years. During the comparison and analysis, she starts with what we know already: "We know that as people get older, changes occur in the volume of the brain, the number of lesions in the white matter increases, and more iron accumulates in the brain. Changes also occur in the subcortical nuclei." Little can be said about the results yet. "However, it is already clear that there are differences between the shape of the brain in children from long-living families and those of their partners. One such example is a subcortical structure that plays a role in the forming and storage of memories of emotional events." The enormous natural variation present in the brain makes it difficult to analyse the scans. "We try to take this natural variation into account by using various computer programs that calculate 'average scans'. This makes it possible for us to compare groups with each other."

Magnetic field

Altmann's research is unique. It is the first time that so many people with a genetic similarity, and the ideal control group, namely their partners, have been put in an MRI scanner. An MRI

scan was chosen because it can be used to image the structures of the brain with a minimum of inconvenience to the study subjects. The MRI scan is a non-invasive investigation: the researcher obtains knowledge about the inside of the body without having to enter it. An MRI scan does not use X-rays and to the best of our knowledge it is not harmful. “At least as long as you don’t have any metal in your body such as a pacemaker or an insulin pump,” explains Altmann. This is because the MRI scanner works with a magnetic field. This field changes the energy state of the hydrogen molecules found in the human body. The hydrogen content differs per tissue type. If the magnetic field is switched on, then with the help of radio waves the MRI scanner can calculate how much hydrogen is present in a certain piece of tissue. The structure of the different tissues is then imaged in various shades of grey. Dependent on the measurement technique used (sequence) various abnormalities of the brain are imaged. For example, on the one scan you can clearly see accumulated iron, whereas on another scan you can see structures in the white matter or possible haemorrhages.

There are various types of MRI scanners. The 3-Tesla scanner was chosen for this research. Altmann: “This gives us a good quality image. The 7-Tesla scanner, which has an even stronger magnetic field, provides an even more detailed result. However, there are more contraindications due to the strength of the magnetic field: For example, dental bridges and crowns are not a problem for a brain scan in the 3-Tesla scanner, but can give problems in the 7-Tesla scanner.”

Most of the people asked wanted to participate in the study. “Some were anxious about the procedure beforehand,” says Altmann. “But after a brief explanation almost everybody was enthusiastic. Participants lay with their head in the head coil, which has the shape of a birdcage and is important for the reception of the radio waves. And then they went into the tunnel for 30 minutes.” Unfortunately not everybody could participate in the MRI study. “This age group contains a significant number of people who have a pacemaker or who have undergone an operation which makes participation impossible due to the introduction of metal objects to their bodies.”

Dementia

“We expect that the children from the long-living families will have fewer signs of ageing than their partners,” says Altmann. “However, that has yet to be established. For example, we had expected that the partners would suffer more from atrophy: shrinking brains. However, that proved not to be the case. It could also be that the differences only develop later. Our study subjects are, on average, 66 years old, and they might be just too young to demonstrate a difference.” The aim of Altmann’s research is to generate hypotheses. “We decided in advance to take a broad view. Only if we find something will we zoom in, for example, on a disease such as dementia.”

In a society where people are becoming increasingly older and where there is a growing number of elderly people, old age diseases of the brain will become an ever greater problem. Altmann: “We are now investigating a group of very healthy people. If we find out what makes them healthy, what their favourable factors are, then this information might well benefit the ‘ordinary’ population. Yet achieving that ideal requires a lot of further research. It is simply not enough to know which areas of the brain in people from long-living families differ from those of the general population. We must also know what is really important. Which differences count and which not?”

Room for research

Altmann comes from Germany and studied in Tübingen. During her final year of study, she did an internship at the Department of Oncology and Radiotherapy at the LUMC, which was organised through the Erasmus Exchange Programme of the EU. “I had always wanted to work abroad,” she says. “A big difference between Germany and the Netherlands is that it is far less hierarchal here. Another big plus is that I am given far more room for research!”

Altmann was looking for a research project that would directly benefit society. “Research into ageing satisfies that requirement. I opted for radiology because I like images and image creation. What I really like about this subject is its broad scope and the fact that you are helping to find a diagnosis.”

Altmann hopes that she can find a few structures in the brains of the children from the long-living families that we know are associated with longevity. “And, of course, the icing on the cake would be finding out how the brains of the partners could be influenced such that they gain this benefit as well. However, that’s still a long way off.”