A fast-paced life

Silvia Cappello's life is all about movement: at the **Max Planck Institute of Psychiatry**, she performs research into the way in which different types of neurons migrate to the correct position in the cerebral cortex, during embryonic development of the brain. In her free time, the passionate athlete rarely stands still either.

TEXT **ELKE MAIER**

Walking up the stairs with Silvia Cappello to her fourth floor office in the Max Planck Institute of Psychiatry, you may well get out of breath. "I like to use this walk for exercise," the scientist explains. Since April 2015 she has been the leader of an independent Max Planck Research Group in the field of "Developmental Neurobiology".

Already when looking at the Institute's website, it is obvious that she is very sporty. There is one picture of hear astride a wooden sled wearing an anorak, a woolen hat and a big smile. Another picture shows her just after a running competition. The caption reads: "Silvia Cappello, who is now officially the third fastest female boss in Munich!" Talking to her it soon becomes apparent that she enjoys a wide range of sporting disciplines: the list includes running, cycling, climbing, swimming, skiing, snowboarding and surfing, and she also used to do boxing and judo. "I am kind of hyperactive," she says, "and I use exercise to compensate for that. I rarely sit still, except when I am working on the computer. I also tend to try and do too many things at the same time!"

FINDING THE RIGHT PLACE AMONG BILLIONS OF CELLS

Silvia Cappello's office is colorful and homey: a bright yellow sofa is paired with a black rug with white dots. The walls are decorated with radiantly colored images of neurons. There is a shelf filled with a harmonious mix of specialist literature, an Asian lucky cat, children's artwork and photos of family and friends. By the window there are houseplants she has adopted from former doctoral students: "They always remind me of them. I like being surrounded by everyone I care about!"

In our meeting, the scientist comes across as easy-going and approachable. The kind of person you may like to go out with to have a beer. Or to go on a mountain hike at the weekend. Wearing jeans, a t-shirt and trainers, she leans back in her desk chair as she talks about science as well as her personal life. She speaks English with a hint of a Mediterranean accent, and she talks at the fast pace you would expect from her: taking notes of our conversation soon becomes a challenge, owing to my lack of shorthand skills.

Silvia Cappello's area of expertise is the embryonic development of the brain. With her team of seven researchers, she examines the processes that ensure that each individual cell takes the correct place in which it is able to fulfill its function, within the complex network that consists of billions of cells.

The scientist pulls a sheet of paper showing two magnetic resonance images of human brains from a stack of documents, to illustrate her research topic. Using a pen she points out an area in the picture on the right: "This gray layer should normally not be here," she explains, "these cells should have moved further on to the outside, towards the edge."

The outer cerebral cortex of around three percent of all human beings features malformations, caused by incorrectly positioned neurons. The effects of

Photo: Axel Griesch

Thinking on the run: running not only keeps Silvia Cappello physically fit, it also helps her to put her thoughts in order. The scientist often has new ideas during her runs.

this vary, depending on the cells and the area affected: "Some people are completely unaware of it, others suffer from severe epilepsy," says Silvia Cappello. "There may also be links to autism."

WHY CELLS SOMETIMES GO ASTRAY

But why do brain cells migrate in the first place? "During embryonic development, neurons are formed from neural stem cells in the neural tube," the researcher explains. "From here they migrate to their respective destinations in the different layers of the cerebral cortex."

Along the way, the young neurons specialize, developing for example into visual or olfactory cells. However, sometimes cells settle in the wrong place – researchers refer to this as heterotopia. The electrical signals they fire from there can disrupt the complex circuits in the brain and as a result cause conditions such as epilepsy. Silvia Cappello and her team would like to find out, why it is that neurons sometimes go astray.

The scientist speaks about her work passionately: "Just try to imagine this: each cell has to move to one particular place to be able to carry out its function. How does this work? How do the cells know where they need to go? It is a great mystery. And even the smallest of mistakes may have disastrous consequences!" However, what Cappello is

A strong position in science: Silvia Cappello has been a Research Group Leader at the Max Planck Institute of Psychiatry in Munich since 2015. She appreciates not only the working environment, but also the close proximity to the Alps and her home country Italy.

Photo: Axel Griesch

» Each cell has to move to one particular place to be able to carry out its function. It is a great mystery, how the cells know where to go.

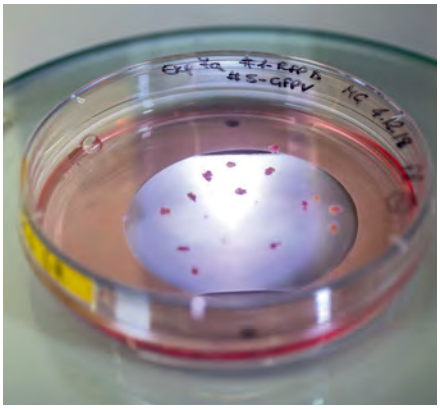
fascinated by the most, is that in most cases everything goes well, despite the high degree of complexity: "This doesn't only require precise spatial coordination, but also temporal coordination, as the stem cells that give rise to the different cell types divide at varying times."

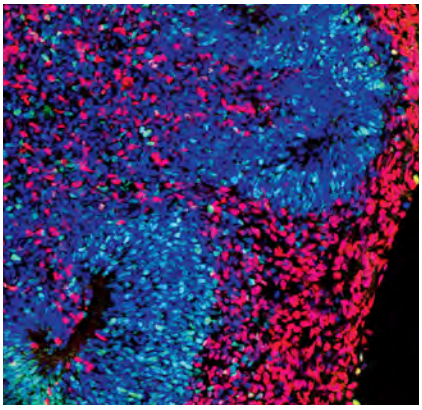
So far, researchers have only begun to understand how all of this is coordinated: "We know that young neurons are guided by chemical signals, but also by the appearance of cells in their environment." Silvia Cappello and her team are conducting research into the migration of cells using a range of different model systems, such as neurons in petri dishes and the brains of mice.

They also work with brain organoids – pinhead sized cell clusters (see MaxPlanckResearch 3/18, p. 54) that are grown from human neural stem cells.

This method is still relatively new: "The first publications about brain organoids came out in 2013. We tried the protocols right away and we were lucky: it worked right from the start!" The unremarkable looking cell clusters live in a reddish nutrient solution and they thrive in culture dishes in the incubator at a pleasant temperature of 37 degree Celsius. A slow vibrator keeps the organoids in constant motion. This prevents them from sticking to the bottom, and it ensures that they receive an ideal supply of oxygen and nutrients. After about ten days, the young organoids are ready for the researchers to start working with them. The cell clusters can survive in the laboratory for up to a year.

"The organoids represent a revolution for research," says Silvia Cappello. "They resemble a human brain at a very early stage of development. This means that we have access to a cell culture system in which we are able to watch cells in three-dimensional tissue." The researchers are able to monitor the movement of individual cells under the microscope. Organoids featuring mutations in their genetic material provide clues of the effects that these genetic changes have on cell migration.





Small yet revolutionary: to study cell migration, Silvia Cappello and her team use pinhead sized brain organoids that they grow in the laboratory (left). Fluorescent dyes enable the researchers to make the different types of cells visible (right): the cores of all cells are marked in blue, the neural stem cells are green, and particular neurons are highlighted in red.

MIGRATION IS DISRUPTED DUE TO GENETIC CHANGES

In the first step it is important to identify mutations that have an impact on migration. "There are a wide range of different genetic causes for malformations of the cerebral cortex," the scientist explains. "In order to find a starting point for future treatments, we need to find out what the various disease patterns have in common."

To this end, Silvia Cappello cooperates with peers from Germany and abroad, such as Barbara Treutlein from the Max Planck Institute for Evolutionary Anthropology in Leipzig. Stephen Robertson, human geneticist at the University of Otago in New Zealand is another important cooperation partner. The scientists work together, searching the genetic material of patients for tiny changes. Meanwhile they are aware of quite a few mutations that affect migration behavior of neurons, and they continue to examine their effects.

After all those years Silvia Cappello still thinks of the brain as "the most fascinating of all research objects." But how did it all begin? Being very versatile, she was not fixed on this subject to begin with.

The scientist, who is the second child in a family of lawyers, grew up in Bologna. In school she studied the classics: Greek, Latin, philosophy. She played the piano and the violin in her youth. "I would have loved to become a violinist," says Cappello, "but I wasn't

Photos: Axel Griesch (left); Silvia Cappello / MPI of Psychiatry (right)

good enough." Instead she played the violin in a punk rock band with old friends from school, until she graduated from university. Sports already played an important role for her, when she was still in school.

TRAVEL BRINGS CLARITY FOR DECISION-MAKING

However, it was in the biology lessons in her final years of secondary school that her course was determined: "I was fascinated by the subject of genetics, and desperate to learn more about it." So instead of following in her family's track – many of whom are lawyers – she opted to study biotechnology. This was never an issue for her parents: "They always allowed me complete freedom and encouraged me to trust my instincts." Her way was also smoothed by her brother, who is three years older than her: "He is a biophysicist and lives in France."

During her third year at university, the young woman came in touch with her future research object for the first time: "We looked at neurons under the microscope, and I fell in love with them right away. They look so different from all the other cells, it is simply fascinating!" Once more she followed her instincts, and wrote her degree thesis about neurotrophins and about the impact these endogenous signaling substances have on neural activity.

After this, she had to decide: should she write a doctoral thesis? And if so, which topic should it be about? "Whenever I need to make an important decision, I go on a trip," says Silvia Cappello. "And I go on my own." She flew to Ireland and spent three months backpacking across the island. During this trip she made up her mind: after her return she started working on a doctoral thesis at the University of Bologna. However, she was not particularly excited here. Perhaps she should transfer to Germany? So she packed her bags once again and went to Australia for three months. Upon her return she knew for sure: she would go to Magdalena Götz, the leader of the laboratory for stem cell research at the Helmholtz center in Munich.

"This was the most important decision of my life," Silvia Cappello says without hesitation. "Magdalena is one of the most inspiring scientists I know." Her decision also proved to be very fortunate when it comes to her personal life: in Götz's working group, she met her future husband. She also met one of her best friends, who she goes climbing with once or twice a week to this day, a doctoral student in the laboratory next door.

After conferral of their doctorates, the couple decided to go to New York together, to Columbia University. "For us this was not only about science, we also wanted it to be an important experience in our lives." Working as a postdoc with Richard Vallee at Columbia University, she went on to perform research about the genetic foundation of lissencephaly, a rare malformation of the human brain. The brain surface of affected individuals is smooth rather than convoluted, and this is caused by a disruption of neural migration.

She had found her ideal area of research. The young scientist loved her work and the atmosphere at the Institute: "Working next door to Nobel Prize winners is pretty special. And New York is really exciting, too!" She visited the Museum of Modern Art every week, as she enjoys contemporary art, especially Kandinsky. The city also had much to offer when it came to sports: the researcher regularly participated in charity runs that are very popular in the U.S.: "I love running for a good cause!"

However, she and her partner did not want to live in New York permanently: "We wanted a family and I could not imagine raising children there. I think the city is too big and too hectic for that." Munich seemed to be better suited for this purpose: "The mountains, the Isar, the way of life – it is a big city, but a very relaxed one."

And last but not least: it is close to Italy. She would be able to spend weekends and vacations with her family and her mother from Bologna at her apartment in the Italian Brenta mountains – climbing, hiking, skiing or snowboarding, depending on the time of year.

FAMILY, RESEARCH, SPORTS – ORGANIZATION IS KEY

Cappello gave Magdalena Götz a call and was offered a position at her former place of work. Just before their first son was born, the couple returned to Germany. Four years later, Silvia Cappello received a Max Planck scholarship and became the leader of an independent Research Group at the Max Planck Institute of Psychiatry. Nowadays she is a mother of two sons, aged five and nine.

Reconciling the demands of family-life, research and sports is mostly "a matter of organization" for Silvia Cappello. This is what she also tells her female students, to show them that

Discussing the situation: Silvia Cappello discusses the latest experiments and next steps with her doctoral students Isabel Buchsbaum and Fabrizia Pipicelli.

they do not have to choose between a family or a career in research: "You can do both!" She finds it unfortunate that there are still so few role models in the scientific community.

Her family life was chaotic to begin with, but she and her husband are now handling the situation very well – "not least thanks to our Google calendar that we use to coordinate our appointments." Another great help is their Italian nanny: "She picks the little one up from kindergarten and looks after him until one of us comes home. This means that I am able to calmly finish my work, without having to rush."

Unwinding after a long day at work is not an issue for the Max Planck researcher: "The kids make me think of other things right away." She is also able to relax while cooking. Dishes from her home country are her favorites: "Food is very important to me. I guess I am a typical Italian in that respect!" Science is never discussed during dinner: "When my husband and I used to work at the same Institute, we had the arrangement that talk about work was only permitted on our way home, and not afterwards. Today we can manage without this kind of rule." Her husband works for a pharmaceutical company these days.

ALWAYS COMPETING AGAINST HERSELF

Nevertheless, spending a cozy night on the sofa is not an option for Silvia Cappello: three nights a week she goes for a ten or fifteen kilometer run, as soon as the kids are in bed. "I do my best thinking while I run!" Being in excellent shape, she regularly takes part in half-marathons. She even used to train for a marathon, but had to give up shortly before the run, due to a knee injury. In competitions, she does not strive to do better than others: "I only compete against myself. It annoys me, if I do worse than the time before!"

She does not believe in competitive thinking in science, either. During our conversation she offers a lot of praise for her colleagues, and some of her cooperation partners are among her personal friends. The atmosphere in her team is easy-going and friendly too: "It is my first working group and everyone is excellent. I am very happy!" ◂

GLOSSARY

Neural stem cells: They give rise to different types of neural and glial cells. They exist in large numbers in the embryonic brain, but are rare in the adult brain.

Neural tube: Embryonic structure during early pregnancy that develops into the central nervous system, the spinal cord and the brain.

Heterotopia [from Greek hetero = different, topos = place] refers to tissue or organs that are located in unusual places. In neurology this term means that the gray matter that consists mostly of neural cell bodies is positioned in the wrong location.

Photo: Axel Griesch